INTRODUCTION

The Regional Cancer Program Formulary handbook contains all of the regimens approved for unrestricted use for cancer patients. The regimens should be used as evidence-based treatment guidelines. Individual treatment may vary at the discretion of the physician.

Authorized pharmacy staff use the Regional Cancer Program Formulary Software (RECAP-FS) to maintain the formulary on behalf of the Systemic Therapy Program Committee (STPC) and the Formulary and Therapeutics Committee (FTC).

The 2005 RECAP Formulary is produced as a portable and convenient handbook reference for clinical staff and other users. This handbook will only be printed once. Users are encouraged to use the Regional Cancer Program Formulary Software to print new regimen information and update their formulary binders as necessary. Please contact Pharmacy Services to request access to the RECAP Formulary Software.

The Committees and I would like to thank my formulary project team members for their contributions: Michelle Goulbourne (Project Manager), Sharon Meeke (JCC Pharmacist) and Jolanta Jeziorowska (Henderson Pharmacist).

We would also like to thank the oncologists, pharmacists, and disease site teams who contributed to the development and review of the regimen contents.

Sincerely,

Sandra Kagoma
Manager, Pharmaceutical Services
Juravinski Cancer Centre and Henderson Hospital Sites

Disclaimer: The information presented in the 2005 Regional Cancer Program Formulary was compiled by Pharmacy Services and the disease site teams from published references. The reviewers have made every effort to ensure that the regimen information and dosage presented are accurate at the time of publishing. Because of ongoing research and new clinical evidence the FTC ask that this book be used only as an institutional guideline before the administration and final prescribing of any chemotherapy regimen.
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DOXORUBICIN-CYCLOPHOSPHAMIDE (AC) Chemotherapy
Treatment of Breast Cancer: Adjuvant, Neoadjuvant & Advanced Disease

CYCLOPHOSPHAMIDE 600mg/m² IV Day 1 Round to nearest 10mg
- Mix in 250mL bag Normal Saline. Infuse over 10-20 minutes.

DOXORUBICIN 60mg/m² IV Day 1 Round to nearest 1mg
- Slow push through sidearm of free flowing IV. Give 2 to 4mg (1-2mL) per minute.

REPEAT EVERY 21 DAYS for a Usual Total of 4 Cycles

TESTS:
Baseline Tests WBC HB PLT ANC Cr Urea T.Bili ALT AlkPhosphatase
Day 1 WBC HB PLT ANC AST
Test Notes - Baseline: LVEF if clinically indicated.

ANTIEMETIC PRE-CHEMO REGIMEN:
Level C Day 1 - Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
- Dexamethasone 20mg PO/IV

ANTIEMETIC TAKE-HOME REGIMEN:
Level B/C Day 1 - Ondansetron 8mg PO BID for 2-3 days, or
Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3
days
- Dexamethasone 8mg PO BID for 2-3 days
- Prochlorperazine 10mg PO q4-6h prn

PATIENT VISITS and APPOINTMENT TYPE:
- Day 1 1.5hrs Type C

ANCILLARY:
- Oral hydration is strongly encouraged.
- Poorly hydrated patients may need more IV hydration.
- Inadequate total hydration may result in dose-related hemorrhagic cystitis.
- Device recommended if IV access becomes problematic.

TOXICITIES:
Hematologic
1. If ANC < 1.5 x 10⁹/L, or if PLT < 100 x 10⁹/L, HOLD chemotherapy for 1 week.

Renal Failure
1. If CrCL < 0.2mL/sec, OMIT Cyclophosphamide dose.

Hepatic Dysfunction
1. If T.Bili = 26-51umol/L, or AST = 60-180 IU/L, give 75% Doxorubicin dose.
2. If T.Bili = 52-85umol/L, or AST > 180 IU/L, give 50% Doxorubicin dose.
3. If T.Bili > 85umol/L, OMIT Doxorubicin.

SUGGESTED ACTION

CLINICAL MONITORING:
- Urinalysis (RBCs) routine for high intravenous doses; periodic for low IV dose and in
response to patient complaint.
- Baseline renal function tests (if failure suspected) and liver function tests (especially if poor Performance Status).
- Clinical exam for symptoms of CHF.
- Periodic cardiac tests for all patients with cardiac risk factors and patients at or above the threshold dose levels
(Doxorubicin 450mg/m²).

REFERENCES:
- Fisher B, Brown AM, Dimitrov NV, et al. Two months of doxorubicin/cyclophosphamide with and without interval
reinduction therapy compared with six months of Cyclophosphamide, Methotrexate and 5-Fluorouracil in node-
positive breast cancer patients with tamoxifen nonresponsive tumors: results from the NSABP B-15. J. Clin Oncol
1990 Sep;8(9):1483-96.
- Paik S, Bryant J, Tan-Chiu E, et al. HER2 and Choice of Adjuvant Chemotherapy for Invasive Breast Cancer:

Breast
**DOXORUBICIN-CYCLOPHOSPHAMIDE followed by DOCETAXEL**

*Neoadjuvant Treatment of Non-Metastatic Breast Cancer*

**Order Group 1**

**CYCLOPHOSPHAMIDE**
- 600mg/m²
- IV Day 1
- Round to nearest 10mg
- Mix in 250mL bag Normal Saline. Infuse over 10-20 minutes.

**DOXORUBICIN**
- 60mg/m²
- IV Day 1
- Round to nearest 1mg
- Slow push through sidearm of free flowing IV. Give 2 to 4mg (1-2mL) per minute.

**REPEAT EVERY 21 DAYS for a total of 4 cycles**

**Order Group 2**

To start 21 days after last administration of Doxorubicin-Cyclophosphamide (AC)

**DOCETAXEL**
- 100mg/m²
- IV Day 1
- Round to nearest 3mg
- Mix in 250mL bag 5% Dextrose or Normal Saline to a maximum concentration of 0.3-0.9mg/mL.
- Use non-PVC equipment without a filter. Infuse through main IV line.
- Elasto-gel™ gloves should be placed on both hands and treatment should begin 15 minutes before the infusion starts and conclude 15 minutes after the infusion is done.
- Gloves should be changed after 45 minutes to sustain the cold temperature.

First and Second Dose:
- Infuse at a slower rate and then increase incrementally.
- Infuse at 30mL/hr for 5 minutes, then at 60mL/hr for 5 minutes, then at 125mL/hr for 5 minutes, then finally at 250mL/hr until infusion complete.

**DEXAMETHASONE**
- 8mg PO Day 0
- 4mg tablet
- Q12H for 3 days starting one day before chemotherapy.

**DIPHENHYDRAMINE**
- 50mg IV Day 1
- Admix in 50-100mL minibag 5% Dextrose or Normal Saline.
- Give over 10-15 minutes.
- Wait 30 minutes before Docetaxel dose started.
- 50mg PO may be given instead.

**TESTS:**
- Baseline Tests: WBC HB PLT ANC Cr Urea T.Bili AST ALT AlkPhosphatase
- Docetaxel Day 1: WBC HB PLT ANC
- AC Day 1: WBC HB PLT ANC
- Test Notes: Repeat lytes, urea, Cr, LFTs every 3 cycles or prn.
- Baseline: LVEF if clinically indicated.

**ANTIEMETIC PRE-CHEMO REGIMEN:**

**Level C**
- Day 1 AC
  - Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
  - Dexamethasone 20mg PO/IV

**Level B**
- Day 1 DOCE
  - Dexamethasone 8mg PO/IV (If not taken at home prior to treatment).
  - May add Prochlorperazine 10mg PO/IV pm.

**ANTIEMETIC TAKE-HOME REGIMEN:**

**Level B/C**
- Day 1 AC
  - Ondansetron 8mg PO BID for 2-3 days, or Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days
  - Dexamethasone 8mg PO BID for 2-3 days
  - Prochlorperazine 10mg PO q4-6hr pm
  - Prochlorperazine 10mg PO q4-6hr pm

**Level A**
- Day 1 DOCE
  - Prochlorperazine 10mg PO q4-6hr pm

**PATIENT VISITS and APPOINTMENT TYPE:**
- Day 1 AC 1.5hrs Type C
- Day 1 DOCE (first 2 doses) 2hrs Type D
- Day 1 DOCE (subsequent) 2hrs Type C

**ANCILLARY:**
- Oral hydration is strongly encouraged.
- Poorly hydrated patients may need more IV hydration.
- Inadequate total hydration may result in dose-related hemorrhagic cystitis.
- Device recommended if IV access becomes problematic.

**TOXICITIES:**

**Hematologic**
- AC Regimen:
  1. If ANC < 1.5 x 10^9/L, or if PLT < 100 x 10^9/L, HOLD chemotherapy for 1 week.
- Docetaxel Regimen:
  1. If ANC < 1.5 x 10^9/L, or if PLT < 100 x 10^9/L, HOLD Docetaxel dose for 1 week.
DOXORUBICIN-CYCLOPHOSPHAMIDE followed by DOCETAXEL

Renal Failure
AC Regimen:
1. If CrCl < 0.2 mL/sec, OMIT Cyclophosphamide dose.

Hepatic Dysfunction
AC Regimen:
1. If T.Bili = 26-51 μmol/L or AST = 60-180 IU/L, give 75% Doxorubicin dose.
2. If T.Bili = 52-85 μmol/L, or AST > 180 IU/L, give 50% Doxorubicin dose.
3. If T.Bili > 85 μmol/L, OMIT Doxorubicin.

Docetaxel Regimen:
1. Decrease Docetaxel dose if LFTs > 1.5 x normal.
2. If AST or ALT > 53 IU/L, or if Alk Phos > 180 IU/L, REDUCE dose by 50%.

CLINICAL MONITORING:

Doxo-Cyclo:
- Urinalysis (RBCs) routine for high intravenous doses; periodic for low IV dose and in response to patient complaint.
- Baseline renal function tests (if failure suspected) and liver function tests (especially if poor Performance Status).
- Clinical exam for symptoms of CHF.
- Periodic cardiac tests for all patients with cardiac risk factors and patients at or above the threshold dose levels (Doxorubicin 450 mg/m²).

Doxorubicin:
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.
- Watch for symptoms of fever and infection.
- Skin assessment at each visit, including nails.

Skin Toxicity
4. Desquamation, ulceration, or necrosis

Fluid Retention
0. None 1. Mild peripheral edema 2. Pleural effusion, outpatient management
3. Pleural effusion, inpatient management 4. Intubation required

Nail Changes
1. Discoloration; ridging (koilonychias); pitting 2. Partial or complete loss of nail(s); pain in nailbed(s)

INTERFERING WITH ADL
RATED AT EACH CLINIC VISIT

HYPERSENSITIVITY:

Docetaxel Hypersensitivity Procedures:
- If hypersensitivity reaction during administration:
  1. Discontinue Docetaxel immediately if there are signs or symptoms of moderate or severe hypersensitivity. (Mild symptoms may resolve with a decrease in the rate of infusion).
  2. Rapid IV administration of Diphenhydramine 50-100mg and Hydrocortisone 100mg.
  3. Re-initiate infusion after 30 minutes, or when signs of reaction are resolved. Resume infusion at a slower rate, then increase incrementally to the initial planned rate, eg. infuse at 30 mL/hr (an 8-hour rate) for 5 minutes, then at 60 mL/hr (a 4-hour rate) for 5 minutes, then at 125 mL/hr (a 2-hour rate) for 5 minutes, then finally, resume at 250 mL/hr (1-hour infusion rate).
  4. Depending on the intensity of the reaction, additional oral or IV pre-medication with an antihistamine should also be given for the next cycle of treatment and the rate of infusion should be decreased initially and then increased back to the recommended 1-hour infusion.

INTERNAL CODE:

OPIS CODES:
- AC/DOCE ORDER GROUP 1
- AC/DOCE ORDER GROUP 2

REFERENCES:

- CCO Practice Guideline 1-20: The Role of Taxanes in Neoadjuvant Chemotherapy for Women with Non-metastatic Breast Cancer
DOXORUBICIN-CYCLOPHOSPHAMIDE followed by PACLITAXEL

Adjuvant & Neoadjuvant Treatment of Breast Cancer

Order Group 1

Cyclophosphamide

**600mg/m²** IV Day 1
- Mix in **250mL** bag Normal Saline. Infuse over 10-20 minutes.

Doxorubicin

**60mg/m²** IV Day 1
- Slow push through sidearm of free flowing IV. Give 2 to 4mg (1-2mL) per minute.

**REPEAT EVERY 21 DAYS for a total of 4 cycles**

Order Group 2

To start 21 days after last administration of Doxorubicin-Cyclophosphamide (AC)

Paclitaxel

**175mg/m²** IV Day 1
- Mix in **500mL** bag Normal Saline (dilution concentration 0.3-1.2mg/mL).
- Use non-PVC equipment, including 0.22 micron in-line filter.
- Infuse over **3 hours**.

**REPEAT EVERY 21 DAYS for a total of 4 cycles**

Dexamethasone

**20mg** PO Day 1
- Taken 12 and 6 hours before Paclitaxel administration.
- ALTERNATE DOSE 8mg PO BID for 3 days, starting 24 hours before Paclitaxel.
- If not taken at home, give 20mg Dexamethasone IV/PO 30 minutes before Paclitaxel.

Diphenhydramine

**50mg** IV Day 1
- Admix in **50-100mL** minibag 5% Dextrose or Normal Saline.
- Give over **10-15 minutes**.
- Administer 30 minutes before Paclitaxel.
- If not taken at home, give 20mg Dexamethasone IV/PO 30 minutes before Paclitaxel.

Ranitidine

**50mg** IV Day 1
- Admix in **50-100mL** minibag 5% Dextrose or Normal Saline.
- Give over **10-15 minutes**.
- Administer 30 minutes before Paclitaxel.
- 150mg PO may be given instead.

**TESTS:**

Baseline Tests

- WBC  HB  PLT  ANC  Cr  Urea  T.Bili  AST  ALT  GGT  AlkPhosphatase

AC Day 1

- WBC  HB  PLT  ANC

Paclitaxel Day 1

- WBC  HB  PLT  ANC

Test Notes - Baseline Test: LVEF if clinically indicated.
- Routine LFTs every 3 months prn.
- - Baseline Test: LVEF if clinically indicated.
- - Routine LFTs every 3 months prn.

**ANTIEMETIC PRE-CHEMO REGIMEN:**

**Level C**

- Day 1 AC
  - Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
  - Dexamethasone 20mg PO/IV

**Level A**

- Day 1 PACLI
  - See premedications

**ANTIEMETIC TAKE-HOME REGIMEN:**

**Level B/C**

- Day 1 AC
  - Ondansetron 8mg PO BID for 2-3 days, or Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days
  - Dexamethasone 8mg PO BID for 2-3 days
  - Prochlorperazine 10mg PO q4-6h pm

**Level A**

- Day 1 PACLI
  - Ondansetron 8mg PO BID for 2-3 days, or Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days
  - Dexamethasone 8mg PO BID for 2-3 days
  - Prochlorperazine 10mg PO q4-6h pm

**PATIENT VISITS and APPOINTMENT TYPE:**

- Day 1 AC  1.5hrs  Type C
- Day 1 PACLI  5hrs  Type D

**ANCILLARY:**

- Take a baseline blood pressure measurement, if prior hypotension.
- Observe patient for the first 5 minutes of the Paclitaxel infusion, then periodically for the remainder of the infusion.
- Device recommended if IV access becomes problematic.

**TOXICITIES:**

**Hematologic**

**AC Regimen:**

1. If ANC < 1.5 x 10⁹/L, or if PLT < 100 x 10⁹/L, **HOLD** chemotherapy for 1 week.

**Paclitaxel Regimen:**

1. If ANC < 1.5 x 10⁹/L, or if PLT < 100 x 10⁹/L, **HOLD** Paclitaxel dose for 1 week.

**Renal Failure**

**AC Regimen:**

1. If CrCL < 0.2mL/sec, **OMIT** Cyclophosphamide dose.
DOXORUBICIN-CYCLOPHOSPHAMIDE followed by 
PACLITAXEL

Hepatic Dysfunction
AC Regimen:
1. If T.Bili = 26-51umol/L or AST= 60-180 IU/L, give 75% Doxorubicin dose.
2. If T.Bili = 52-85umol/L, or AST > 180 IU/L, give 50% Doxorubicin dose.
3. If T.Bili > 85umol/L, OMIT Doxorubicin.

Paclitaxel Regimen:
1. If AST > 70IU/L or T.Bili < 25umol/L, give MAXIMUM Paclitaxel dose of 135mg/m2.
2. If T.Bili = 25-50umol/L, give MAXIMUM Paclitaxel dose of 75mg/m2.
3. If T.Bili > 50umol/L, give MAXIMUM Paclitaxel dose of 50mg/m2.

SUGGESTED ACTION

CLINICAL MONITORING:
- Urinalysis (RBCs): routine for high intravenous doses; periodic for low IV dose and in response to patient complaint.
- Baseline renal function tests (if failure suspected) and liver function tests (especially if poor Performance Status).
- Clinical exam for symptoms of CHF.
- Periodic cardiac tests for all patients with cardiac risk factors or patients at or above the threshold dose levels (Doxorubicin 450mg/m2).
- Watch for symptoms of fever and infection.
- Blood pressure and pulse rate monitoring during Paclitaxel administration and for the following hour.

Sensory:
1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function
2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL
3. Sensory alteration or paresthesia interfering with ADL
4. Disabling
5. Death

Flu-like Syndrome:
1. Symptoms present but not interfering with function
2. Moderate or causing difficulty performing some ADL
3. Severe symptoms interfering with ADL
4. Disabling
5. Death

Allergic Reaction:
1. Transient flushing or rash; drug fever < 38 degrees C
2. Rash; flushing; urticaria; dyspnea; drug fever > 38 degrees C
3. Symptomatic bronchospasm, with or without urticaria; parenteral medication(s) indicated; allergy-related edema/angioedema; hypotension
4. Anaphylaxis
5. Death

RATED AT EACH CLINIC VISIT

HYPERSENSITIVITY:
Paclitaxel Procedures
Retreatment for Paclitaxel Hypersensitivity Reaction:
If Paclitaxel hypersensitivity reaction occurs during administration:
1. Discontinue Paclitaxel immediately if there are signs or symptoms of hypersensitivity.
2. Rapid IV administration of Diphenhydramine 50-100mg direct IV push over 1 minute and Hydrocortisone 100mg in 100ml Normal Saline over 5-10 minutes.
3. Reinitiate Paclitaxel infusion after 30 minutes, or when signs of reaction are resolved. Resume Paclitaxel infusion at 25% of previous rate for at least 5 minutes, 50% for at least 5 minutes, 75% for at least 5 minutes. If no further symptoms develop, continue at original rate until infusion complete.
4. If reaction recurs, STOP Paclitaxel for this dose and treat patient symptoms.

Desensitization for Paclitaxel Hypersensitivity Reactions:
If Paclitaxel hypersensitivity recurs during previous administration despite retreatment plan:
1. Dexamethasone 20mg PO 36 hours and 12 hours before chemotherapy, and 20mg PO morning of chemotherapy.
2. Diphenhydramine 50-100mg per IV push over 1 minute and Hydrocortisone 100mg in 100ml Normal Saline over 5-10 minutes.
3. Paclitaxel infusion: 2mg in 100mL Normal Saline over 30min; if no reaction, 10mg in 100mL Normal Saline over 30min; if no reaction, remainder of dose in 500mL Normal Saline over 3 hours.
4. If reaction occurs, discontinue infusion; Diphenhydramine 50-100mg direct IV push over 1 minute and Hydrocortisone 100mg in 100ml Normal Saline over 5-10 minutes.
5. Restart Paclitaxel infusion after 30 minutes.

INTERNAL CODE:

OPIS CODES:
- AC/T ORDER GROUP 1
- AC/T ORDER GROUP 2

REFERENCES:
http://www.bccancer.bc.ca/HPI/DrugDatabase/DrugIndexPro/Paclitaxel.htm

Date revised: 07/02/2008
DOXORUBICIN-CYCLOPHOSPHAMIDE followed by PACLITAXEL; DOSE DENSE Treatment

Adjuvant & Neoadjuvant Treatment of Breast Cancer

Order Group 1

**CYCLOPHOSPHAMIDE**
- **600mg/m²** IV Day 1
- **Round to nearest 10mg**
  - Mix in **250mL bag Normal Saline**. Infuse over 10-20 minutes.

**DOXORUBICIN**
- **60mg/m²** IV Day 1
- **Round to nearest 1mg**
  - **Slow push through sidearm of free flowing IV**. Give 2 to 4mg (1-2mL) per minute.

Order Group 2

To start 14 days after last administration of Doxorubicin-Cyclophosphamide (AC)

**PACLITAXEL**
- **175mg/m²** IV Day 1
- **Round to nearest 3mg**
  - Mix in **500mL bag Normal Saline** (dilution concentration 0.3-1.2mg/mL).
  - Use non-PVC equipment, including 0.22 micron in-line filter.
  - Infuse over **3 hours**.

**DEXAMETHASONE**
- **20mg** PO Day 1
- **4mg tablet**
  - Taken 12 and 6 hours before Paclitaxel administration.
  - ALTERNATE DOSE 8mg PO BID for 3 days, starting 24 hours before Paclitaxel.
  - If not taken at home, give 20mg Dexamethasone IV/PO 30 minutes before Paclitaxel.

**DIPHENHYDRAMINE**
- **50mg IV** Day 1
  - Admix in **50-100mL minibag 5% Dextrose or Normal Saline**.
  - Give over **10-15 minutes**, (may be admixed with Ranitidine).
  - Administer 30 minutes before Paclitaxel.
  - 50mg PO may be given instead.

**RANITIDINE**
- **50mg IV** Day 1
  - Admix in **50-100mL minibag 5% Dextrose or Normal Saline**.
  - Give over **10-15 minutes**, (may be admixed with Diphenhydramine).
  - Administer 30 minutes before Paclitaxel.
  - 150mg PO may be given instead.

**FILGRASTIM**
- **5mcg/kg SC Days 3-10**
  - Starting dose is 5mcg/kg/day.
  - Doses may be increased in increments of 5mcg/kg/day for each chemotherapy cycle, according to duration and severity of ANC nadir.
  - May give Acetaminophen 325mg, 1-2 tablets for temporary bone pain at initiation.
  - Outpatient prescription (Keep refrigerated).
  - Vial sizes available: 300mcg and 480mcg.
  - Trade name Neupogen™

**PEGFILGRASTIM**
- **6mg SC Day 2 or 3**
  - May be given instead of Neupogen™
  - To be given 24-48 hours post chemotherapy as a single dose
  - Outpatient prescription (Keep refrigerated)
  - Trade name Neulasta™

**REPEAT EVERY 14 DAYS for a total of 4 cycles**

**TESTS:**

<table>
<thead>
<tr>
<th>Baseline Tests</th>
<th>AC Day 1</th>
<th>Paclitaxel Day 1</th>
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<tbody>
<tr>
<td>WBC HB PLT ANC</td>
<td>Urea T.Bili AST ALT GGT AlkPhosphatase</td>
<td>WBC HB PLT ANC</td>
</tr>
</tbody>
</table>

**ANTIEMETIC PRE-CHEMO REGIMEN:**

**Level C**
- Day 1 AC
  - Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
  - Dexamethasone 20mg PO/IV

**Level A**
- Day 1 PACLI
  - See premedications

**ANTIEMETIC TAKE-HOME REGIMEN:**

**Level B/C**
- Day 1 AC
  - Ondansetron 8mg PO BID for 2-3 days, or
  - Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days
  - Dexamethasone 8mg PO BID for 2-3 days
  - Prochlorperazine 10mg PO q4-6h pm

**Level A**
- Day 1 PACLI
  - Prochlorperazine 10mg PO q4-6h pm

**PATIENT VISITS and APPOINTMENT TYPE:**

- **Day 1 AC** 1.5hrs Type C
- **Day 1 PACLI** 5hrs Type D
DOXORUBICIN-CYCLOPHOSPHAMIDE followed by PACLITAXEL; DOSE DENSE Treatment

ANCILLARY:
- Take a baseline blood pressure measurement, if prior hypotension.
- Observe patient for the first 5 minutes of the Paclitaxel infusion, then periodically for the remainder of the infusion.
- Device recommended if IV access becomes problematic.

TOXICITIES:
Hematologic
AC Regimen:
1. If ANC < 1.5 x 10^9/L, or if PLT < 100 x 10^9/L, HOLD chemotherapy for 1 week.
Paclitaxel Regimen:
1. If ANC < 1.5 x 10^9/L, or if PLT < 100 x 10^9/L, HOLD Paclitaxel dose for 1 week.

Renal Failure
AC Regimen:
1. If CrCL < 0.2mL/sec, OMIT Cyclophosphamide dose.

Hepatic Dysfunction
AC Regimen:
1. If T.Bili = 26-51umol/L or AST = 60-180 IU/L, give 75% Doxorubicin dose.
2. If T.Bili = 52-85umol/L, or AST > 180 IU/L, give 50% Doxorubicin dose.
3. If T.Bili > 85umol/L, OMIT Doxorubicin.
Paclitaxel Regimen:
1. If AST > 70IU/L or T.Bili < 25umol/L, give MAXIMUM Paclitaxel dose of 135mg/m².
2. If T.Bili = 25-50umol/L, give MAXIMUM Paclitaxel dose of 75mg/m².
3. If T.Bili > 50umol/L, give MAXIMUM Paclitaxel dose of 50mg/m².

SUGGESTED ACTION
CLINICAL MONITORING:
- Urinalysis (RBCs): routine for high intravenous doses; periodic for low IV dose and in response to patient complaint.
- Baseline renal function tests (if failure suspected) and liver function tests (especially if poor Performance Status).
- Clinical exam for symptoms of CHF.
- Periodic cardiac tests for all patients with cardiac risk factors or patients at or above the threshold dose levels (Doxorubicin 450mg/m²).
- Watch for symptoms of fever and infection.
- Blood pressure and pulse rate monitoring during Paclitaxel administration and for the following hour.

Sensory:
1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function
2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL
3. Sensory alteration or paresthesia interfering with ADL
4. Disabling
5. Death

Flu-like Syndrome:
1. Symptoms present but not interfering with function
2. Moderate or causing difficulty performing some ADL
3. Severe symptoms interfering with ADL
4. Disabling
5. Death

Allergic Reaction:
1. Transient flushing or rash; drug fever < 38 degrees C
2. Rash; flushing; urticaria; dyspnea; drug fever ≥ 38 degrees C
3. Symptomatic bronchospasm, with or without urticaria; parenteral medication(s) indicated; allergy-related edema/angioedema; hypotension
4. Anaphylaxis
5. Death

RATED AT EACH CLINIC VISIT

HYPERSENSITIVITY:
Paclitaxel Procedures
Retreatment for Paclitaxel Hypersensitivity Reaction:
If Paclitaxel hypersensitivity reaction occurs during administration:
1. Discontinue Paclitaxel immediately if there are signs or symptoms of hypersensitivity.
2. Rapid IV administration of Diphenhydramine 50-100mg direct IV push over 1 minute and Hydrocortisone 100mg in 100ml Normal Saline over 5-10 minutes.
3. Reinitiate Paclitaxel infusion after 30 minutes, or when signs of reaction are resolved. Resume Paclitaxel infusion at 25% of previous rate for at least 5 minutes, 50% for at least 5 minutes, 75% for at least 5 minutes. If no further symptoms develop, continue at original rate until infusion complete.
4. If reaction recurs, STOP Paclitaxel for this dose and treat patient symptoms.

Desensitization for Paclitaxel Hypersensitivity Reactions:
If Paclitaxel hypersensitivity recurs during previous administration despite retreatment plan:
1. Dexamethasone 20mg PO 36 hours and 12 hours before chemotherapy, and 20mg PO morning of chemotherapy.
2. Dexamethasone 20mg IV. Diphenhydramine 50mg IV & Ranitidine 50mg IV about 30min before infusion.
3. Paclitaxel Infusion: 2mg in 100mL Normal Saline over 30min; if no reaction, 10mg in 100mL Normal Saline over 30min; if no reaction, remainder of dose in 500mL Normal Saline over 3 hours.
4. If reaction occurs, discontinue infusion; Diphenhydramine 50-100mg direct IV push over 1 minute and Hydrocortisone 100mg in 100ml Normal Saline over 5-10 minutes.
5. Restart Paclitaxel infusion after 30 minutes.

INTERNAL CODE:
- AC/T DD GROUP 1
- AC/T DD GROUP 2
DOXORUBICIN-CYCLOPHOSPHAMIDE followed by PACLITAXEL; DOSE DENSE Treatment

REFERENCES:
  http://www.bccancer.bc.ca/HPI/DrugDatabase/DrugIndexPro/Paclitaxel.htm

Date revised: 07/02/2008
CAPECITABINE Therapy
Advanced Breast Cancer

CAPECITABINE
2500mg/m²/day PO Days 1-14 150mg & 500mg tablets
- Divided into BID dosing for 14 days (1250mg/m² twice daily).
- Outpatient prescription available in 150mg and 500mg tablets.
- Trade name is Xeloda™

- REPEAT EVERY 21 DAYS

TESTS:
Baseline Tests WBC HB PLT ANC Cr T.Bili AST ALT AlkPhosphatase
Day 1 WBC HB PLT ANC
Test Notes - Repeat prn.

ANTIEMETIC PRE-CHEMO REGIMEN:
Level B Days 1-14 - Dexamethasone 8mg PO/IV
- May add or substitute Prochlorperazine 10mg PO/IV prn

ANTIEMETIC TAKE-HOME REGIMEN:
Level A Days 1-14 - Prochlorperazine 10mg PO q4-6h prn

ANCILLARY:
- Take tablets WITH FOOD (within 30 minutes of a meal).
- Prophylaxis to Prevent Hand-Foot Skin Reaction: Take Pyridoxine (Vitamin B6) PO 100mg BID or 50mg TID continuously. Apply Lac-Hydrin™ Lotion to hands and feet once or twice daily.

TOXICITIES:
Gastrointestinal
1. If any Toxicity Score = Grade 2, HOLD Capecitabine until score = 0 or 1, resume at 100% of dose (if second occurrence, resume at 75% dose, third occurrence at 50%, if fourth occurrence STOP Capecitabine).
2. If any Toxicity Score = Grade 3, HOLD Capecitabine until score = 0 or 1, resume at 75% dose or 1000mg/m² BID (if second occurrence, resume at 50%, if third occurrence STOP Capecitabine).
3. If any Toxicity Score = Grade 4, STOP Capecitabine.

Renal Failure
1. If CrCl = 0.5-0.8mL/sec, REDUCE Capecitabine to 75% dose.
2. If CrCl < 0.5mL/sec, OMIT Capecitabine.

SUGGESTED ACTION
CLINICAL MONITORING:
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.
- Skin assessment, especially extremities.
- Routine assessment of diarrhea, at each clinic visit and telephone reinforcement.

Diarrhea:
1. Increase of < 4 stools per day over baseline; mild increase in ostomy output compared to baseline
2. Increase of 4 - 6 stools per day over baseline; IV fluids indicated < 24hrs; moderate increase in ostomy output compared to baseline; not interfering with ADL
3. Increase of >=7 stools per day over baseline; hospitalization; severe increase in ostomy output compared to baseline; interfering with ADL
4. Life-threatening consequences (e.g., hemodynamic collapse)
5. Death

Hand-Foot Skin Reaction:
1. Minimal skin changes or dermatitis (e.g., erythema) without pain
2. Skin changes (e.g., peeling, blisters, bleeding, edema) or pain, not interfering with function
3. Ulcerative dermatitis or skin changes with pain interfering with function

RATED AT EACH CLINIC VISIT

INTERNAL CODE:
- OPIS CODE:
- CAPEC-BR
- CAPEC-BR LOW

REFERENCES:

Date revised: 08/02/2009

CCO Eligibility Form Required [] Non-Formulary Form Required []
CAPECITABINE-DOCETAXEL Chemotherapy

Treatment of Anthracycline Resistant Metastatic Breast Cancer (for young patients with good performance status)

CAPECITABINE

- 1875mg/m² PO Days 1-14
- 150mg & 500mg tablets
- Divided into BID dosing for 14 days.
- Outpatient prescription available in 150mg and 500mg tablets.
- Trade name is Xeloda™

DOCETAXEL

- 75mg/m² IV Day 1
- Round to nearest 3mg
- Mix in 250mL bag 5% Dextrose or Normal Saline to a maximum concentration of 0.3-0.9mg/mL.
- Use non-PVC equipment without a filter. Infuse through main IV line.
- Elasto-gel™ gloves should be placed on both hands and treatment should begin 15minutes before the infusion starts and conclude 15 minutes after the infusion is done.
- Gloves should be changed after 45 minutes to sustain the cold temperature.

First and Second Dose:
- Infuse at a slower rate and then increase incrementally.
- Infuse at 30mL/hr for 5 minutes, then at 60mL/hr for 5 minutes, then at 125mL/hr for 5 minutes, then finally at 250mL/hr until infusion complete.

Subsequent doses:
- Infuse over 1 hour.

Dexamethasone

- 8mg PO Day 0
- 4mg tablet
- Q12H for 3 days starting one day before chemotherapy.

Diphenhydramine

- 50mg IV Day 1
- Mix in 50-100mL minibag 5% Dextrose or Normal Saline.
- Give over 10-15 minutes.
- Wait 30 minutes before Docetaxel dose started.
- 50mg PO may be given instead.

TESTS:

- Repeat lytes, urea, Cr, LFTs every 3 cycles or prn.

ANTIEMETIC PRE-CHEMO REGIMEN:

- Level B
  - Day 1 - Dexamethasone 8mg PO/IV (If not taken at home prior to treatment).
  - May add Prochlorperazine 10mg PO/IV pm.

ANTIEMETIC TAKE-HOME REGIMEN:

- Level A
  - Days 1-14 - Prochlorperazine 10mg PO q4-6h prn

PATIENT VISITS and APPOINTMENT TYPE:

- Day 1 DOCE (first 2 doses) 2hrs Type D
- Day 1 DOCE (subsequent) 2hrs Type C

ANCILLARY:

- Port recommended.
- Take tablets WITH FOOD (within 30 minutes of a meal).
- Prophylaxis to Prevent Hand-Foot Skin Reaction: Take Pyridoxine (Vitamin B6) PO 100mg BID or 50mg TID continuously. Apply Lac-Hydrin™ Lotion to hands and feet once or twice daily.

TOXICITIES:

Hematologic

1. If ANC < 1.5 x 10⁹/L, or if PLT < 100 x 10⁹/L, HOLD chemotherapy for 1 week.

Renal Failure

1. If CrCl = 0.5-0.8mL/sec, REDUCE Capecitabine to 75% dose.
2. If CrCl < 0.5mL/sec, OMIT Capecitabine.

Hepatic Dysfunction

1. Decrease Docetaxel dose if LFTs > 1.5 x ULN.
2. If AST or ALT > 53 IU/L, or if Alk Phos > 180 IU/L, REDUCE DOCETAXEL dose by 50%.
3. Use of Capecitabine in severe hepatic dysfunction has not been studied.

Gastrointestinal

1. If any Toxicity Score = Grade 2, HOLD Capecitabine until score = 0 or 1, resume at 100% of dose (if second occurrence, resume at 75% dose, third occurrence at 50%, if fourth occurrence STOP Capecitabine).
2. If any Toxicity Score = Grade 3, HOLD Capecitabine until score = 0 or 1, resume at 75% dose or 1000mg/m² BID (if second occurrence, resume at 50%, if third occurrence STOP Capecitabine).
3. If any Toxicity Score = Grade 4, STOP Capecitabine.

SUGGESTED ACTION
CAPECITABINE-DOCETAXEL Chemotherapy

CLINICAL MONITORING:
- Caution is advised in patients with lung toxicities (lung metastases, effusions).
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.
- Skin assessment, especially extremities.
- Routine assessment of diarrhea, at each clinic visit and telephone reinforcement.
- Watch for symptoms of fever and infection.
- Skin assessment at each visit, including nails.

Skin Toxicity
4. Desquamation, ulceration, or necrosis

Fluid Retention
0. None 1. Mild peripheral edema 2. Pleural effusion, outpatient management
3. Pleural effusion, inpatient management 4. Intubation required

Diarrhea:
1. Increase of <4 stools per day over baseline; mild increase in ostomy output compared to baseline
2. Increase of 4-6 stools per day over baseline; IV fluids indicated <24 hrs; moderate increase in ostomy output compared to baseline; not interfering with ADL
3. Increase of >=7 stools per day over baseline; incontinence; IV fluids >=24 hrs; hospitalization; severe increase in ostomy output compared to baseline; interfering with ADL
4. Life-threatening consequences (e.g., hemodynamic collapse)
5. Death

Hand-foot skin reaction:
1. Minimal skin changes or dermatitis (e.g., erythema) without pain
2. Skin changes (e.g., peeling, blisters, bleeding, edema) or pain, not interfering with function
3. Ulcerative dermatitis or skin changes with pain interfering with function

Nail Changes:
1. Discoloration; ridging (koilonychia); pitting
2. Partial or complete loss of nail(s); pain in nailbed(s)
3. Interfering with ADL

HALF-DOSE AT EACH CLINIC VISIT

HYPERSENSITIVITY:
Docetaxel Hypersensitivity Procedures:
- If hypersensitivity reaction during administration:
1. Discontinue Docetaxel immediately if there are signs or symptoms of moderate or severe hypersensitivity. (Mild symptoms may resolve with a decrease in the rate of infusion).
2. Rapid IV administration of Diphenhydramine 50-100mg and Hydrocortisone 100mg.
3. Re-initiate infusion after 30 minutes, or when signs of reaction are resolved. Resume infusion at a slower rate, then increase incrementally to the initial planned rate, eg. infuse at 30mL/hr (an 8-hour rate) for 5 minutes, then at 60mL/hr (a 4-hour rate) for 5 minutes, then at 125mL/hr (a 2-hour rate) for 5 minutes, then finally, resume at 250mL/hr (1-hour infusion rate).
4. Depending on the intensity of the reaction, additional oral or IV pre-medication with an antihistamine should also be given for the next cycle of treatment and the rate of infusion should be decreased initially and then increased back to the recommended 1-hour infusion.

REFERENCES:
- CCO Practice Guideline 1-3: The Role of the Taxanes in the Management of Metastatic Breast Cancer.
**CYCLOPHOSPHAMIDE (PO)-DOXORUBICIN-FLUOROURACIL (CAF) Chemotherapy**

**Adjuvant or Advanced Breast Cancer Treatment**

**CYCLOPHOSPHAMIDE** 100mg/m² PO Days 1-14 25mg tablet
- QAM x 14 days.
- Outpatient prescription available in 25mg and 50mg tablets.
- Trade name is Procytox™

**DOXORUBICIN** 30mg/m² IV Days 1 & 8 Round to nearest 1mg
- Slow push through sidearm of free flowing IV.
- Give 2 to 4mg (1-2mL) per minute.

**5-FLUOROURACIL** 500mg/m² IV Days 1 & 8 Round to nearest 25mg
- Slow push through sidearm of free flowing IV.
- Patients are recommended to suck on ice chips about 5 minutes before treatment begins until 30 minutes after treatment is completed to reduce the incidence and severity of stomatitis.

**REPEAT EVERY 28 DAYS**

**TESTS:**
- **Baseline Tests**
  - WBC
  - HB
  - PLT
  - ANC
  - Cr
  - Urea
  - T.Bili
  - AST
  - ALT
  - AlkPhosphatase

- **Days 1 & 8**
  - WBC
  - HB
  - PLT
  - ANC

- **Test Notes**
  - Repeat T.Bili & LFTs prn.
  - LVEF if clinically indicated.

**ANTIEMETIC PRE-CHEMO REGIMEN:**
- **Level C**
  - Days 1 & 8
    - Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
    - Dexamethasone 20mg PO/IV

**ANTIEMETIC TAKE-HOME REGIMEN:**
- **Level B/C**
  - Days 1 & 8
    - Ondansetron 8mg PO BID for 2-3 days, or
      Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days
    - Dexamethasone 8mg PO BID for 2-3 days
    - Prochlorperazine 10mg PO q4-6h prn

**PATIENT VISITS and APPOINTMENT TYPE:**
- **Days 1 & 8**
  - 45min Type B

**ANCILLARY:**
- Device recommended if IV access becomes problematic or for advanced disease.

**TOXICITIES:**

**Hematologic**
1. If ANC < 1.5 x 10⁹/L, or if PLT < 100 x 10⁹/L, HOLD chemotherapy for 1 week.

**Renal Failure**
1. If CrCl < 0.2mL/sec, OMIT all drugs.

**Hepatic Dysfunction**
1. If T.Bili = 26-51umol/L, or AST = 60-180 IU/L, give 75% of Doxorubicin dose.
2. If T.Bili = 52-85umol/L, or AST > 180 IU/L, give 50% of Doxorubicin dose.
3. If T.Bili > 85umol/L, OMIT all drugs.

**SUGGESTED ACTION**

**CLINICAL MONITORING:**
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.
- Urinalysis (RBCs)- ONLY in response to patient complaint.
- Baseline liver function tests.
- Clinical exam for symptoms of CHF.
- Periodic cardiac tests for all patients with cardiac risk factors and patients at or above the threshold dose levels (Doxorubicin 450mg/m²).
- Oral hydration is strongly encouraged; poorly hydrated patients may need more IV hydration.

**REFERENCES:**
**CYCLOPHOSPHAMIDE PO- EPIRUBICIN- FLUOROURACIL Chemotherapy**

*Adjuvant & Neoadjuvant Treatment for Breast Cancer*

<table>
<thead>
<tr>
<th>Medication</th>
<th>Route</th>
<th>Days</th>
<th>Frequency</th>
<th>Comments</th>
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</table>
| CYCLOPHOSPHAMIDE    | PO    | 1-14   | 25mg tablet | - QAM for 14 days.  
- Outpatient prescription available in 25mg and 50mg tablets.  
- Trade name is ProcytexistM |
| EPIRUBICIN          | IV    | 1 & 8  | Round to nearest 1mg | - Slow push through sidearm of free flowing IV at a rate of 10mg/5ml per minute.  
- Inject by direct IV push over 1-3 minutes, followed by a Normal Saline flush.  
- Patients are recommended to suck on ice chips about 5 minutes before treatment begins until 30 minutes after treatment is completed to reduce the incidence and severity of stomatitis.  
- REPEAT EVERY 28 DAYS (for a usual total of 6 cycles) |
| 5-FLUOROURACIL      | IV    | 1 & 8  | Round to nearest 25mg | - Inject by direct IV push over 1-3 minutes, followed by a Normal Saline flush.  
- Patients are recommended to suck on ice chips about 5 minutes before treatment begins until 30 minutes after treatment is completed to reduce the incidence and severity of stomatitis.  
- REPEAT EVERY 28 DAYS (for a usual total of 6 cycles) |

**ANTIMICROBIAL PROPHYLAXIS:**
- CO-TRIMOXAZOLE 2 tablets PO BID or CIPROFLOXACIN 500mg PO BID

**TESTS:**
- Baseline Tests: WBC HB PLT ANC Cr Urea T.Bili AST ALT AlkPhosphatase LVEF
- Days 1 & 8: WBC HB PLT ANC
- Test Notes: - Repeat lytes, urea, Cr, LFTs after 3 cycles or prn.  
- LVEF if clinically indicated.

**ANTIEMETIC PRE-CHEMO REGIMEN:**
- Level C: Days 1 & 8 - Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV  
- Dexamethasone 20mg PO/IV

**ANTIEMETIC TAKE-HOME REGIMEN:**
- Level B/C: Days 1 & 8 - Ondansetron 8mg PO BID for 2-3 days, or  
- Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days  
- Dexamethasone 8mg PO BID for 2-3 days  
- Prochlorperazine 10mg PO q4-6h pm

**PATIENT VISITS and APPOINTMENT TYPE:**
- Days 1 & 8: 45min Type B

**ANCILLARY:**
- Device recommended if IV access becomes problematic.

**TOXICITIES:**

### Hematologic
1. If ANC< 1.5 x 10⁹/L, or if PLT< 100 x 10⁹/L, HOLD chemotherapy for 1 week.

### Renal Failure
1. If CrCl < 0.2mL/sec, OMIT all drugs.

### Hepatic Dysfunction
1. If T.Bili = 26-51umol/L or AST= 60-180 IU/L, give 75% Epirubicin dose.  
2. If T.Bili = 52-85umol/L or AST> 180 IU/L, give 50% Epirubicin dose.  
3. If T.Bili > 85umol/L, OMIT all drugs.

**SUGGESTED ACTION**

**CLINICAL MONITORING:**

- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.  
- Urinalysis (RBCs)- ONLY in response to patient complaint.  
- Clinical exam for symptoms of CHP.  
- Periodic cardiac tests for all patients with cardiac risk factors.  
- Serious, irreversible cardiomyopathy with delayed congestive heart failure may be encountered as the cumulative dose approaches 1000mg/m². Cardiac monitoring is advised when cumulative dose exceeds 650mg/m² of Epirubicin.

**INTERNAL CODE:**
- OPIS CODES:  
  - CEF CYCLO PO, CIPRO  
  - CEF CYCLO PO, SEPTRA

**REFERENCES:**

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Date revised: 07/02/2008
CISPLATIN-ETOPOSIDE Chemotherapy

**Advanced Breast Cancer**

**CISPLATIN**
- 25mg/m²
- IV
- Days 1-3
- Round to nearest 1mg
- Admix in 250mL bag **Normal Saline**; Infuse over 30-60 minutes.
- May also admix 10G Mannitol (50mL of 20% solution or 100mL of 10% solution) with Cisplatin.
- Dose ≤ 200mg, mix in **500mL Normal Saline**; Infuse over 30-60 minutes.
- Dose > 200mg, mix in **1000mL Normal Saline**; Infuse over 120 minutes.
- Use Non-PVC equipment and filter.
- Adjust rate if blood pressure drops.
- Give Etoposide AFTER Cisplatin.
- May also admix 10G Mannitol (50mL of 20% solution or 100mL of 10% solution) with Cisplatin.

**ETOPOSIDE**
- 100mg/m²
- IV
- Days 1-3
- Round to nearest 10mg
- Dose ≤ 200mg, mix in **500mL Normal Saline**; Infuse over 30-60 minutes.
- Dose > 200mg, mix in **1000mL Normal Saline**; Infuse over 120 minutes.
- Use Non-PVC equipment and filter.
- Adjust rate if blood pressure drops.
- Give Etoposide AFTER Cisplatin.

**HYDRATION:**
- Pre: Infuse 500mL Normal Saline IV over 1 hour.

**TESTS:**
- Baseline Tests: WBC HB PLT ANC Ca K Na Chloride Mg Glucose Cr Urea T.Bili Albumin AST ALT GGT AlkPhosphatase
- Day 1: WBC HB PLT ANC K Na Chloride Mg Cr Urea

**ANTIEMETIC PRE-CHEMO REGIMEN:**
- Level C: Days 1-3 - Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
  - Dexamethasone 20mg PO/IV

**ANTIEMETIC TAKE-HOME REGIMEN:**
- Level B/C: Day 3 - Ondansetron 8mg PO BID for 2-3 days, or
  - Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days
  - Dexamethasone 8mg PO BID for 2-3 days
  - Prochlorperazine 10mg PO q4-6h prn

**ANCILLARY:**
- Adjust Etoposide rate of infusion if blood pressure drops.
- Port recommended.

**TOXICITIES:**

**Hematologic**
1. If ANC < 1.5 x 10⁹/L, or PLT < 100 x 10⁹/L, HOLD dose.

**Renal Failure**
1. If CrCl = 0.5-1.0mL/sec, or SrCr = 136-185umol/L, REDUCE Cisplatin to 50% dose and Etoposide to 75% dose.
2. If CrCl < 0.5mL/sec, or SrCr > 185umol/L, OMIT Cisplatin dose.
3. If CrCl < 0.2mL/sec, REDUCE Etoposide to 50% dose.

**Hepatic Dysfunction**
1. If T.Bili = 26-51umol/L, or AST = 60-180 IU/L, REDUCE Etoposide to 50% dose.
2. If T.Bili = 52-85umol/L, REDUCE Etoposide to 25% dose.
3. If T.Bili > 85umol/L, or AST > 180 IU/L, OMIT Etoposide.

**SUGGESTED ACTION**

**CLINICAL MONITORING:**
- Baseline & periodic liver function tests (esp. if poor Performance Status).
- Sensory: 1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function  2. Sensory alteration or paresthesia (including tingling), interfering with function but not interfering with ADL  3. Sensory alteration or paresthesia interfering with ADL  4. Disabling  5. Death

**FORMULAE:**
- CrCl - Cockcroft & Gault (mL/sec): Male: \[\frac{(140 \text{- age(yrs)}) \times \text{TBW(Kg)}}{[50 \times \text{SCR(umol/L)}]}\]
- CrCl - Cockcroft & Gault (mL/sec): Female: \[\frac{(140 \text{- age(yrs)}) \times \text{TBW(Kg)}}{[50 \times \text{SCR(umol/L)}] 	imes 0.85}\]

**INTERNAL CODE:**
- OPIS CODE: CISP-ETOP BR

**REFERENCES:**

_CCO Eligibility Form Required_ [ ] _Non-Formulary Form Required_ [ ]  _Date revised:_ 05/02/2008
CLODRONATE THERAPY
Advanced Breast Cancer

CLODRONATE 1600mg PO Daily 400mg tablet

- To reduce GI distress, Clodronate may be started at 400mg daily and titrated upwards to 800mg BID.
- Administer concurrently with first-line/salvage chemotherapy.
- If corrected serum calcium < 2.10mmol/L, HOLD dose for 1 week or until serum calcium levels within normal range.
- Outpatient prescription available in 400mg capsules.
- Trade name is Bonefos™ and Clasteon™

CONTINUOUS TREATMENT

TESTS:
Baseline Tests Ca Cr Albumin
Every 3 months Ca Cr Albumin

ANCILLARY:
- If oral Clodronate cannot be tolerated, IV Pamidronate may be substituted.

FORMULAE:
Corrected Serum Calcium (mmol/L) = Measured Serum Calcium + [(40 - serum albumin) x 0.02]

INTERNAL CODE:
OPIS CODE: CLOD*PO BR

REFERENCES:

Date revised: 07/02/2008
CYCLOPHOSPHAMIDE IV-METHOTREXATE-FLUOROURACIL (CMF*IV) Chemotherapy

**Breast Cancer - Adjuvant or Advanced Treatment**

**CYCLOPHOSPHAMIDE** 600mg/m² IV Day 1 Round to nearest 10mg
- Mix in 250mL bag Normal Saline, Infuse over 10-20 minutes.

**METHOTREXATE** 40mg/m² IV Day 1 Round to nearest 5mg
- Inject by direct IV push, followed by a Normal Saline flush (if no IV line has been set up).
- May give by slow push through sidearm of free flowing IV (D5W, Normal Saline).
- Rate of administration < 10mg per minute.
- Doses > 100mg, mix in 50-100mL Normal Saline and infuse over 30-60 minutes.

**5-FLUOROURACIL** 600mg/m² IV Day 1 Round to nearest 25mg
- Inject by direct IV push over 1-3 minutes, followed by a Normal Saline flush.
- Patients are recommended to suck on ice chips about 5 minutes before treatment begins until 30 minutes after treatment is completed to reduce the incidence and severity of stomatitis.

**REPEAT EVERY 21 DAYS**

**TESTS:**
Baseline Tests: WBC HB PLT ANC Cr Urea T.Bili AST ALT AlkPhosphatase
- Day 1: WBC HB PLT ANC

**ANTIEMETIC PRE-CHEMO REGIMEN:**
Level C Day 1 - Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
- Dexamethasone 20mg PO/IV

**ANTIEMETIC TAKE-HOME REGIMEN:**
Level A Day 1 - Prochlorperazine 10mg PO q4-6h prn

**PATIENT VISITS and APPOINTMENT TYPE:**
- Day 1: 60min Type B

**ANCILLARY:**
- Device recommended if IV access becomes problematic or for advanced disease.

**TOXICITIES:**
- Hematologic
  1. If ANC < 1.5 x 10⁹/L, or if PLT< 100 x 10⁹/L, HOLD chemotherapy for 1 week.

- Renal Failure
  1. If CrCl = 0.2 - 0.8mL/sec, or SrCr = 100-180umol/L, give 50% Methotrexate dose.
  2. If CrCl < 0.2mL/sec, or SrCr >180umol/L, OMIT Methotrexate and Cyclophosphamide.

- Hepatic Dysfunction
  1. If T.Bili = 50-85umol/L, or AST > 180 IU/L, give 50% Methotrexate dose.
  2. If T.Bili > 85umol/L, OMIT 5-Fluorouracil and Methotrexate.

- CLINICAL MONITORING:
  - Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.
  - Urinalysis (RBCs)- ONLY in response to patient complaint.
  - Oral hydration strongly encouraged; poorly hydrated patients may need more IV hydration.

**REFERENCES:**
CYCLOPHOSPHAMIDE (PO)-METHOTREXATE-FLUOROURACIL (CMF*PO) Chemotherapy

Cyclophosphamide
- 100mg/m² PO Days 1-14
- Trade name is Procyctox™

Methotrexate
- 40mg/m² IV Days 1 & 8
- Inject by direct IV push, followed by a Normal Saline flush (if no IV line has been set up).
- Rate of administration < 10mg per minute.
- Doses > 100mg, mix in 50-100mL Normal Saline and infuse over 30-60 minutes.

5-Fluorouracil
- 600mg/m² IV Days 1 & 8
- Inject by direct IV push over 1-3 minutes, followed by a Normal Saline flush.
- Patients are recommended to suck on ice chips about 5 minutes before treatment begins until 30 minutes after treatment is completed to reduce the incidence and severity of stomatitis.

Repeat every 28 days for a usual total of 6 cycles

Tests:
Baseline Tests: WBC HB PLT ANC Cr Urea T.Bili AST ALT AlkPhosphatase
- Days 1 & 8: WBC HB PLT ANC
- Test Notes: Repeat lytes, urea, Cr, LFTs every 3 months or prn.

Antiemetic Pre-Chemo Regimen:
Level B
- Day 1: Dexamethasone 8mg PO/IV
- May add or substitute Prochlorperazine 10mg PO/IV prn

Antiemetic Take-Home Regimen:
Level A
- Day 1: Prochlorperazine 10mg PO q4-6h prn

Patient Visits and Appointment Type:
- Days 1 & 6: 15min Type A

Ancillary:
- Device recommended if IV access becomes problematic or for advanced disease.

Toxicities:
Hematologic
1. If ANC < 1.5 x 10⁹/L, or if PLT < 100 x 10⁹/L, Hold chemotherapy dose for 1 week.

Renal Failure
1. If CrCl = 0.2 - 0.8mL/sec, or SrCr = 100-180umol/L, give 50% Methotrexate dose.
2. If CrCL < 0.2mL/sec, or SrCr >180umol/L, OMIT Methotrexate and Cyclophosphamide.

Hepatic Dysfunction
1. If T.Bili = 50-85umol/L or AST > 180 IU/L, give 50% Methotrexate dose.
2. If T.Bili > 85umol/L, OMIT 5-Fluorouracil and Methotrexate.

Suggested Action:
Clinical Monitoring:
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.
- Urinalysis (RBCs) ONLY in response to patient complaint.
- Oral hydration strongly encouraged; poorly hydrated patients may need more IV hydration.

References:

Breast
CYCLOPHOSPHAMIDE LOW DOSE

Metastatic Breast Cancer

CYCLOPHOSPHAMIDE 25-50mg PO Daily 25mg tablet
- 25mg qAM x 14 days. If counts adequate, continue at 50mg qAM continuously.
- Outpatient prescription available in 25mg and 50mg tablets.
- Trade name is Procyctox™

CONTINUOUS

TESTS:
Baseline Tests: WBC HB PLT ANC Cr Urea T.Bili AST ALT AlkPhosphatase
Monthly Tests: WBC HB PLT ANC
Test Notes: Repeat tests pm.

ANTIEMETIC PRE-CHEMO REGIMEN:
Level A Daily - Prochlorperazine 10mg PO pm

ANTIEMETIC TAKE-HOME REGIMEN:
Level A Daily - Prochlorperazine 10mg PO q4-6h pm

TOXICITIES:
Hematologic
1. If ANC < 1.5 x 10^9/L, or if PLT < 100 x 10^9/L, HOLD Cyclophosphamide dose.

INTERNAL CODE:
OPIS CODE: CYCLO*PO BR

Date revised: 03/07/2005

Breast
# DOCETAXEL Weekly Chemotherapy

## Advanced Breast Cancer

**DOCETAXEL** 33mg/m² IV Day 1 Round to nearest 3mg

- Mix in 100mL bag 5% Dextrose or Normal Saline to a maximum concentration at or below 0.9mg/mL.
- Range: (0.3 to 0.9mg/mL); Use non-PVC equipment without a filter.
- Infuse through main IV line.
- Elasto-gel™ gloves should be placed on both hands and treatment should begin 15 minutes before the infusion starts and conclude 15 minutes after the infusion is done.
- Gloves should be changed after 45 minutes to sustain the cold temperature.

### First and Second Dose:
- Infuse at a slower rate and then increase incrementally.
- Infuse at 30mL/hr for 5 minutes, then at 60mL/hr for 5 minutes, then at 125mL/hr for 5 minutes, then finally at 200mL/hr until infusion complete.

### Subsequent doses:
- Infuse over 30 minutes.

**REPEAT EVERY 7 DAYS (Option: 3 weeks on, 1 week off)**

**DEXAMETHASONE** 8mg PO Day 0 4mg tablet

- May give 8mg po q12h for 3 doses, starting the night before chemotherapy.

**DIPHENHYDRAMINE** 25-50mg IV Day 1

- PRN - If previous hypersensitivity reaction.
- May be mixed in 50-100mL minibag 5% Dextrose or Normal Saline. Give over 10-15 minutes.
- Wait 30 minutes before Docetaxel dose started.

## Tests:

<table>
<thead>
<tr>
<th>Baseline Tests</th>
<th>WBC HB PLT ANC Cr Urea T.Bili AST ALT AlkPhosphatase</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Day 1</strong></td>
<td>WBC HB PLT ANC</td>
</tr>
</tbody>
</table>

**Test Notes:** Repeat lytes, urea, Cr, LFTs every 3 cycles or prn.

## Antiemetic Pre-Chemo Regimen:

**Level B**
- Day 1 - Dexamethasone 8mg IV/PO (If dexamethasone not taken at home as pre-medication).
- May add Prochlorperazine 10mg PO/IV prn

## Antiemetic Take-Home Regimen:

**Level A**
- Day 1 - Prochlorperazine 10mg PO q4-6h prn

## Patient Visits and Appointment Type:

- **Day 1 DOCE (first 2 doses)** 60min Type C
- **Day 1 DOCE (subsequent)** 60min Type B

## Ancillary:
- Port recommended.

## Toxicities:

### Hematologic
1. If ANC < 1.5 x 10⁹/L, or if PLT < 100 x 10⁹/L, HOLD Docetaxel dose for 1 week.

### Hepatic Dysfunction
1. Decrease Docetaxel dose if LFTs > 1.5 x normal.
2. If AST or ALT > 53 IU/L, or if Alk Phos > 180 IU/L, REDUCE dose by 50%.

### Clinical Monitoring:
- Caution is advised in patients with lung toxicities (lung metastases, effusions).
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.
- Watch for symptoms of fever and infection.
- Skin assessment at each visit, including nails.

### Skin Toxicity
4. Desquamation, ulceration, or necrosis

### Fluid Retention
0. None 1. Mild peripheral edema 2. Pleural effusion, out-patient management
3. Pleural effusion, in-patient management 4. Intubation required

### Nail Changes
0. None 1. Discoloration; ridging (koilonychias); pitting 2. Partial or complete loss of nail(s); pain in nailbed(s) 3. Interfering with ADL

**Rated at each clinic visit**
**HYPERSENSITIVITY:**

Docetaxel Hypersensitivity Procedures:

1. Discontinue Docetaxel immediately if there are signs or symptoms of moderate or severe hypersensitivity. (Mild symptoms may resolve with a decrease in the rate of infusion).
2. Rapid IV administration of Diphenhydramine 50-100mg and Hydrocortisone 100mg.
3. Re-initiate infusion after 30 minutes, or when signs of reaction are resolved. Resume infusion at a slower rate, then increase incrementally to the initial planned rate, eg. infuse at 30mL/hr (a 3.3-hour rate) for 5 minutes, then at 60mL/hr (a 1.6-hour rate) for 5 minutes, then at 125mL/hr (a 0.8-hour rate) for 5 minutes, then finally, resume at 200mL/hr (0.5-hour infusion rate).
4. Depending on the intensity of the reaction, additional oral or IV pre-medication with an antihistamine should also be given for the next cycle of treatment and the rate of infusion should be decreased initially and then increased back to the recommended 1-hour infusion.

**REFERENCES:**

- CCO Practice Guideline 1-3: The Role of the Taxanes in the Management of Metastatic Breast Cancer.
**DOCETAXEL Chemotherapy**

**Advanced Breast Cancer**

**DOCETAXEL**

100mg/m² IV Day 1 Round to nearest 3mg

- Mix in 250mL bag 5% Dextrose or Normal Saline to a maximum concentration of 0.3-0.9mg/mL.
- Use non-PVC equipment without a filter; Infuse through main IV line.
- Elasto-gel™ gloves should be placed on both hands and treatment should begin 15 minutes before the infusion starts and conclude 15 minutes after the infusion is done.
- Gloves should be changed after 45 minutes to sustain the cold temperature.

**First and Second Dose:**

- Infuse at a slower rate and then increase incrementally.
- Infuse at 30mL/hr for 5 minutes, then at 60mL/hr for 5 minutes, then at 125mL/hr for 5 minutes, then finally at 250mL/hr until infusion complete.

**Subsequent doses:**

- Infuse over 1 hour.

**REPEAT EVERY 21 DAYS**

**DEXAMETHASONE**

8mg PO Day 0 4mg tablet

- Q12H for 3 days starting one day before chemotherapy.

**DIPHENHYDRAMINE**

50mg IV Day 1

- Admix in 50-100mL minibag 5% Dextrose or Normal Saline.
- Give over 10-15 minutes.
- Wait 30 minutes before Docetaxel dose started.
- 50mg PO may be given instead.

**TESTS:**

Baseline Tests: WBC HB PLT ANC Cr Urea T.Bili ALT AlkPhosphatase

Day 1 WBC HB PLT ANC

Test Notes: - Repeat lytes, urea, Cr, LFTs every 3 cycles or prn.

**ANTIEMETIC PRE-CHEMO REGIMEN:**

**Level B**

Day 1 - Dexamethasone 8mg PO/IV (If not taken at home prior to treatment).
- May add Prochlorperazine 10mg PO/IV pm.

**ANTIEMETIC TAKE-HOME REGIMEN:**

**Level A**

Day 1 - Prochlorperazine 10mg PO q4-6h pm

**PATIENT VISITS and APPOINTMENT TYPE:**

- Day 1 DOCE (first 2 doses) 2hrs Type D
- Day 1 DOCE (subsequent) 2hrs Type C

**ANCILLARY:**

- Port recommended.

**TOXICITIES:**

**Hematologic**

1. If ANC < 1.5 x 10⁹/L, or if PLT < 100 x 10⁹/L, HOLD Docetaxel dose for 1 week.

**Hepatic Dysfunction**

1. Decrease Docetaxel dose if LFTs > 1.5 x normal.
2. If AST or ALT > 53 IU/L, or if Alk Phos > 180 IU/L, REDUCE dose by 50%.

**SUGGESTED ACTION**

**CLINICAL MONITORING:**

- Caution is advised in patients with lung toxicities (lung metastases, effusions).
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.
- Watch for symptoms of fever and infection.
- Skin assessment at each visit, including nails.

**Skin Toxicity**


4. Desquamation, ulceration, or necrosis

**Fluid Retention**

0. None 1. Mild peripheral edema 2. Pleural effusion, outpatient management

3. Pleural effusion, inpatient management 4. Intubation required

**Nail Changes**

1. Discoloration; ridging (koilonychias); pitting 2. Partial or complete loss of nail(s); pain in nailbed(s) 3. Interfering with ADL

**Rated at each Clinic Visit**

Breast
DOCETAXEL Chemotherapy

HYPERSENSITIVITY:
Docetaxel Hypersensitivity Procedures:
1. If hypersensitivity reaction during administration:
   - Discontinue Docetaxel immediately if there are signs or symptoms of moderate or severe hypersensitivity. (Mild symptoms may resolve with a decrease in the rate of infusion).
2. Rapid IV administration of Diphenhydramine 50-100mg and Hydrocortisone 100mg.
3. Re-initiate infusion after 30 minutes, or when signs of reaction are resolved. Resume infusion at a slower rate, then increase incrementally to the initial planned rate, eg. infuse at 30mL/hr (an 8-hour rate) for 5 minutes, then at 60mL/hr (a 4-hour rate) for 5 minutes, then at 125mL/hr (a 2-hour rate) for 5 minutes, then finally, resume at 250mL/hr (1-hour infusion rate).
4. Depending on the intensity of the reaction, additional oral or IV pre-medication with an antihistamine should also be given for the next cycle of treatment and the rate of infusion should be decreased initially and then increased back to the recommended 1-hour infusion.

INTERNAL CODE:
OPIS CODE: DOCETAX-BR

REFERENCES:
- CCO Practice Guideline 1-3: The Role of the Taxanes in the Management of Metastatic Breast Cancer.

Date revised: 07/02/2008
DOCETAXEL-TRASTUZUMAB Chemotherapy (7 Day docetaxel and 21 Day trastuzumab regimen)

Treatment of Advanced Breast Cancer in Women whose Tumours Overexpress the HER2 Protein, and Who Have Been Previously Treated with Anthracycline containing Chemotherapy

TRASTUZUMAB

8mg/Kg, then IV Day 1 Round to nearest 1mg
6mg/Kg
- Mix in 250mL Normal saline. DO NOT MIX in 5% Dextrose.

21 DAY TRASTUZUMAB REGIMEN:

LOADING DOSE: (8mg/Kg) Day 1 Only
- Infuse over 90 minutes, then observe for 60 minutes.
MAINTENANCE DOSE: (6mg/Kg)
- Infuse over 30 minutes, then observe for 30 minutes.
- If no reaction after 3 doses, no observation period required.
- If reaction on maintenance dose, drug should be infused over 60 minutes, then observe for 30 minutes.
- If no reaction after 3 doses at 60 minutes, may change infusion time to 30 minutes and follow as above.
- If reaction at 60 minutes, dose should be infused over 90 minutes and observe for 60 minutes.
DO NOT ADMINISTER AS IV PUSH OR BOLUS

REPEAT EVERY 21 DAYS (at 6mg/Kg)

DOCETAXEL

33mg/m² IV Day 1 Round to nearest 3mg
- Mix in 100mL bag 5% Dextrose or Normal saline to a maximum concentration at or below 0.9mg/mL.
- Range: (0.3 to 0.9mg/mL); Use non-PVC equipment without a filter.
- Infuse through main IV line.
- Elasto-gel™ gloves should be placed on both hands and treatment should begin 15 minutes before the infusion starts and conclude 15 minutes after the infusion is done.
- Gloves should be changed after 45 minutes to sustain the cold temperature.
First and Second Dose:
- Infuse at a slower rate and then increase incrementally.
- Infuse at 30mL/hr for 5 minutes, then at 60mL/hr for 5 minutes, then at 125mL/hr for 5 minutes, then finally at 100mL/hr until infusion complete.
Subsequent doses:
- Infuse over 30 minutes

REPEAT EVERY 7 DAYS

PREMeds

ACETAMINOPHEN
650mg PO Day 1 325mg tablet
- Prn before Trastuzumab.

DEXAMETHASONE
8mg PO Day 1 4mg tablet
- May give 8mg po q12h for 3 doses, starting the night before chemotherapy.

DIPHENHYDRAMINE
50mg IV Day 1
- PRN, if previous hypersensitivity reaction.
- May be mixed in 50-100mL minibag 5% Dextrose or Normal saline; Give over 10-15 minutes.
- Wait 30 minutes before Docetaxel dose started.

TESTS:

Baseline Tests: WBC HB PLT ANC Urea T.Bili AST ALT AlkPhosphatase LVEF
Day 1 WBC HB PLT ANC
Test Notes: - Repeat lytes, urea, Cr, LFTs every 3 cycles or prn.
- LVEF every 6 months or prn.

ANTIEMETIC PRE-CHEMO REGIMEN:
Level B Day 1
- Dexamethasone 8mg IV/PO (If dexamethasone not taken as pre-medication).
- May add Prochlorperazine 10mg PO/IV pm
- Note: antipyretics, antihistamines, corticosteroids may be ordered to prevent infusion-related reactions to Trastuzumab.

ANTIEMETIC TAKE-HOME REGIMEN:
Level A Day 1
- Prochlorperazine 10mg po q4-6h pm

PATIENT VISITS and APPOINTMENT TYPE:
- OR Docetaxel Trastuzumab 21 Day (Loading dose only) 3.5hrs Type C
- Docetaxel 7 Day (first 2 doses) 1hr Type C
- Docetaxel 7 Day & Trastuzumab 21 Day (Maint) 1.5hrs Type C
- Docetaxel 7 Day & Trastuzumab 21 Day (Maint) after 3 doses 1hr Type C

Breast
DOCETAXEL-TRASTUZUMAB Chemotherapy (7 Day docetaxel and 21 Day trastuzumab regimen)

ANCILLARY:
- Port recommended.

TOXICITIES:

Hematologic
1. If ANC < 1.5 x 10^9/L, or if PLT < 100 x 10^9/L, HOLD Docetaxel dose for 1 week.

Hepatic Dysfunction
1. Decrease Docetaxel dose if LFTs > 1.5 x normal.
2. If AST or ALT > 53 IU/L, or if Alk Phos > 180 IU/L, REDUCE Docetaxel by 50%.

SUGGESTED ACTION

CLINICAL MONITORING:

Trastuzumab:
- Close observation for infusion-related symptoms: fever, chills, pain (including pain in tumour), asthenia, and other flu like symptoms.
- Periodic cardiac tests for all patients with cardiac risk factors or suspected cardiac toxicity.

LV Systolic Dysfunction
1. Asymptomatic, resting ejection fraction (EF) < 60 - 50%; shortening fraction (SF) < 30 - 24%
2. Asymptomatic, resting EF < 50 - 40%; SF < 24 - 15%
3. Symptomatic CHF responsive to intervention; EF < 40 - 20%; SF < 15%
4. Refractory CHF or poorly controlled; EF < 20%; intervention such as ventricular assist device, ventricular reduction surgery, or heart transplant indicated
5. Death

Docetaxel:
- Caution is advised in patients with lung toxicities (lung metastases, effusions)
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.
- Watch for symptoms of fever and infection.
- Skin assessment at each visit, including nails.

Skin Toxicity
4. Desquamation, ulceration, or necrosis

Fluid Retention
0. None 1. Mild peripheral edema 2. Pleural effusion, outpatient management
3. Pleural effusion, inpatient management 4. Intubation required

Nail Changes
1. Discoloration; ridging (koilonychias); pitting 2. Partial or complete loss of nail(s); pain in nailbed(s) 3. Interfering with ADL

RATED AT EACH CLINIC VISIT

HYPERSENSITIVITY:

Docetaxel Hypersensitivity Procedures:
- If hypersensitivity reaction during administration:
  1. Discontinue Docetaxel immediately if there are signs or symptoms of moderate or severe hypersensitivity. (Mild symptoms may resolve with a decrease in the rate of infusion).
  2. Rapid IV administration of Diphenhydramine 50-100mg and Hydrocortisone 100mg.
  3. Re-initiate infusion after 30 minutes, or when signs of reaction are resolved. Resume infusion at a slower rate, then increase incrementally to the initial planned rate, eg. infuse at 30mL/hr (an 8-hour rate) for 5 minutes, then at 60mL/hr (a 4-hour rate) for 5 minutes, then at 125mL/hr (a 2-hour rate) for 5 minutes, then finally, resume at 250mL/hr (1-hour infusion rate).
  4. Depending on the intensity of the reaction, additional oral or IV pre-medication with an antihistamine should also be given for the next cycle of treatment and the rate of infusion should be decreased initially and then increased back to the recommended 1-hour infusion.

INTERNAL CODE:

OPIS CODES:
- DOCE-TRAS 7D/21D LOAD
- DOCE-TRAS 7D/21D MAINT

REFERENCES:
- CCO Practice Guideline 1-3: The Role of the Taxanes in the Management of Metastatic Breast Cancer.
- CCO Practice Guideline 1-15: ES Use of Trastuzumab (Herceptin) in Metastatic Breast Cancer.

Date revised: 07/02/2008
TRASTUZUMAB 8mg/Kg, then 6mg/Kg
- Mix in 250mL Normal Saline. DO NOT MIX in 5% Dextrose.
LOADING DOSE: (8mg/Kg) Day 1 Only
- Infuse over 90 minutes, then observe for 60 minutes.
MAINTENANCE DOSE: (6mg/Kg)
- Infuse over 30 minutes, then observe for 30 minutes.
- If no reaction after 3 doses, no observation period required.
- If reaction on maintenance dose, drug should be infused over 60 minutes, then observe for 30 minutes.
- If no reaction after 3 doses at 60 minutes, may change infusion time to 30 minutes and follow as above.
- If reaction at 60 minutes, dose should be infused over 90 minutes then observe for 60 minutes.
DO NOT ADMINISTER AS IV PUSH OR BOLUS

DOCETAXEL 100mg/m²
- Mix in 250mL bag 5% Dextrose or Normal Saline to a maximum concentration of 0.3-0.9mg/mL.
- Use non-PVC equipment without a filter; Infuse through main IV line.
- Elasto-gel™ gloves should be placed on both hands and treatment should begin 15 minutes before the infusion starts and conclude 15 minutes after the infusion is done.
- Gloves should be changed after 45 minutes to sustain the cold temperature.
First and Second Dose:
- Infuse at a slower rate and then increase incrementally.
- Infuse at 30mL/hr for 5 minutes, then at 60mL/hr for 5 minutes, then at 125mL/hr for 5 minutes, then finally at 250mL/hr until infusion complete.
Subsequent doses:
- Infuse over 1 hour.

REPEAT EVERY 21 DAYS

ACETAMINOPHEN 650mg PO Day 1 325mg tablet
- Prn before Trastuzumab.

DEXAMETHASONE 8mg PO Day 1 4mg tablet
- Q12H for 3 days starting one day before chemotherapy.

DIPHENHYDRAMINE 50mg IV Day 1
- Admix in 50-100mL minibag 5% Dextrose or Normal Saline.
- Give over 10-15 minutes.
- Wait 30 minutes before Docetaxel dose started.
- 50mg PO may be given instead.

TESTS:
Baseline Tests
WBC HB PLT ANC Cr Urea T.Bili AST ALT AlkPhosphatase LVEF
Day 1
WBC HB PLT ANC
Test Notes
- Repeat lytes, urea, Cr, LFTs every 3 cycles or prn.
- LVEF every 6 months or prn.

ANTIEMETIC PRE-CHEMO REGIMEN:
Level B Day 1
- Dexamethasone 8mg PO/IV (If not taken at home prior to treatment).
- May add Prochlorperazine 10mg PO/IV pm
- Note: antipyretics, antihistamines, corticosteroids may be ordered to prevent infusion-related reactions to Trastuzumab.

ANTIEMETIC TAKE-HOME REGIMEN:
Level A Day 1
- Prochlorperazine 10mg po q4-6h pm

PATIENT VISITS and APPOINTMENT TYPE:
⇒ Docetaxel 21 Day & Trastuzumab 21 Day
  Loading Dose 4hrs Type D
⇒ Docetaxel 21 Day & Trastuzumab 21 Day Maint.
  Dose 2.5hrs Type C
⇒ Docetaxel 21 Day & Trastuzumab 21 Day Maint.
  Dose (after 3 doses) 2hrs Type C

ANCILLARY:
- Port recommended.

TOXICITIES:
Hematologic
1. If ANC < 1.5 x 10⁹/L, or if PLT < 100 x 10⁹/L, HOLD Docetaxel dose for 1 week.
DOCETAXEL-TRASTUZUMAB Chemotherapy (21 Day Trastuzumab & Docetaxel)

**Hepatic Dysfunction**
1. Decrease Docetaxel dose if LFTs > 1.5 x normal.
2. If AST or ALT > 53 IU/L, or if Alk Phos > 180 IU/L, REDUCE Docetaxel by 50%.

**SUGGESTED ACTION**

**CLINICAL MONITORING:**
- Close observation for infusion-related symptoms: fever, chills, pain (including pain in tumour), asthenia, and other flu-like symptoms.
- Periodic cardiac tests for all patients with cardiac risk factors or suspected cardiac toxicity.

**LV Systolic Dysfunction:**
1. Asymptomatic, resting ejection fraction (EF) < 60 - 50%; shortening fraction (SF) < 30 - 24%
2. Asymptomatic, resting EF < 50 - 40%; SF < 24 - 15%
3. Symptomatic CHF responsive to intervention; EF < 40 - 20% SF < 15%
4. Refractory CHF or poorly controlled; EF < 20%; intervention such as ventricular assist device, ventricular reduction surgery, or heart transplant indicated
5. Death

**Docetaxel**
- Caution is advised in patients with lung toxicities (lung metastases, effusions).
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.
- Watch for symptoms of fever and infection.
- Skin assessment at each visit, including nails.

**Skin Toxicity**
0. None
1. Hyperpigmentation
2. Atrophy
3. Subcutaneous fibrosis
4. Desquamation, ulceration, or necrosis

**Fluid Retention**
0. None
1. Mild peripheral edema
2. Pleural effusion, outpatient management
3. Pleural effusion, inpatient management
4. Intubation required

**Nail Changes**
1. Discoloration; ridging (koilonychias); pitting
2. Partial or complete loss of nail(s); pain in nailbed(s)
3. Interfering with ADL

**HYPERSENSITIVITY:**

**Docetaxel Hypersensitivity Procedures:**
- If hypersensitivity reaction during administration:
  1. Discontinue Docetaxel immediately if there are signs or symptoms of moderate or severe hypersensitivity. (Mild symptoms may resolve with a decrease in the rate of infusion).
  2. Rapid IV administration of Diphenhydramine 50-100mg and Hydrocortisone 100mg.
  3. Re-initiate infusion after 30 minutes, or when signs of reaction are resolved. Resume infusion at a slower rate, then increase incrementally to the initial planned rate, eg. infuse at 30mL/hr (an 8-hour rate) for 5 minutes, then at 60mL/hr (a 4-hour rate) for 5 minutes, then at 125mL/hr (a 2-hour rate) for 5 minutes, then finally, resume at 250mL/hr (1-hour infusion rate).
  4. Depending on the intensity of the reaction, additional oral or IV pre-medications with an antihistamine should also be given for the next cycle of treatment and the rate of infusion should be decreased initially and then increased back to the recommended 1-hour infusion.

**INTERNAL CODE:**

**OPIS CODES:**
- DOCE-TRAS 21D/21D LOAD
- DOCE-TRAS 21D/21D MAINT

**REFERENCES:**

**Date revised:** 07/02/2008
DOXORUBICIN Low Dose Chemotherapy

Advanced Breast Cancer

DOXORUBICIN 30mg IV Day 1 Round to nearest 1mg
- Slow push through sidearm of free flowing IV
- Give 2 to 4mg (1-2mL) per minute.

REPEAT EVERY 7 DAYS

TESTS:
Baseline Tests  WBC HB PLT ANC Cr Urea T.Bili AST ALT AlkPhosphatase
Day 1  WBC HB PLT ANC
Test Notes - Repeat lys, urea, Cr, LFTs every 3 months or prn.

ANTIEMETIC PRE-CHEMO REGIMEN:
Level B  Day 1  - Dexamethasone 8mg PO/IV
- May add or substitute Prochlorperazine 10mg PO/IV prn

ANTIEMETIC TAKE-HOME REGIMEN:
Level A  Day 1  - Prochlorperazine 10mg PO q4-6h prn

PATIENT VISITS and APPOINTMENT TYPE:
Day 1:  30min Type B

ANCILLARY:
- Port recommended.

TOXICITIES:
Hematologic
1. If ANC < 1.5 x 10^9/L, or if PLT < 100 x 10^9/L, HOLD Doxorubicin dose for 1 week.

Renal Failure
1. If SrCr > 265umol/L, REDUCE Doxorubicin dose to 50%.

Hepatic Dysfunction
1. If T.Bili = 26-51umol/L, or AST = 60-180 IU/L, REDUCE Doxorubicin to 25% dose.
2. If T.Bili = 52-85umol/L, or AST > 180 IU/L, REDUCE Doxorubicin to 50% dose.
3. If T.Bili > 85umol/L, OMIT Doxorubicin.

SUGGESTED ACTION
CLINICAL MONITORING:
- Clinical exam for symptoms of CHF.
- Periodic cardiac tests for all patients with cardiac risk factors at or above the threshold dose levels.

LV Systolic Dysfunction:
1. Asymptomatic, resting ejection fraction (EF) < 60 - 50%; shortening fraction (SF) < 30 - 24%
2. Asymptomatic, resting EF < 50 - 40%; SF < 24 - 15%
3. Symptomatic CHF responsive to intervention; EF < 40 - 20%; SF < 15%
4. Refractory CHF or poorly controlled; EF < 20%; intervention such as ventricular assist device, ventricular reduction surgery, or heart transplant indicated
5. Death
RATED AT EACH CLINIC VISIT
- For Cardiac Toxicity Ratings: First rating at the cumulative dose threshold of 450mg/m^2, and repeat ratings at each cumulative dose increment of 100mg/m^2 above threshold. (Cumulative dose sooner for high risk patients, eg. pre-existing cardiac disease, prior chest irradiation).
- Note: Threshold Cumulative dose reduced proportionately if other anthracycline or anthracenedione drugs have been given; cardiotoxicity is additive.

REFERENCES:

Date revised: 07/02/2008

CCO Eligibility Form Required  Non-Formulary Form Required
LIPOSOMAL DOXORUBICIN Chemotherapy

First or Second Line Treatment of Metastatic Breast Cancer in Patients who have Cardiac Risk Factors

DOXORUBICIN LIPOSOMAL

- If dose < 90mg, mix in 250mL Dextrose 5% or If dose > 90mg, mix in 500mL Dextrose 5%.
- Test dose: 20mg admix into 100mL D5W and infuse over 1 hour.
- If no reaction occurs, admix the remaining dose into a 250mL D5W and infuse at 150mL/hr for 10 minutes then 200mL/hr for 10 minutes then if tolerated full rate.
- For the subsequent infusions:
  - Infuse 250mL over 1 hour.
  - REPEAT EVERY 28 DAYS

TESTS:
Baseline Tests: WBC HB PLT ANC Cr Urea T.Bili AST ALT GGT AlkPhosphatase
Day 1: WBC HB PLT ANC

ANTIEMETIC PRE-CHEMO REGIMEN:
- Level B Day 1:
  - Dexamethasone 8mg PO/IV
  - May add or substitute Prochlorperazine 10mg PO/IV pm

ANTIEMETIC TAKE-HOME REGIMEN:
- Level A Day 1:
  - Prochlorperazine 10mg PO q4-6h pm

PATIENT VISITS and APPOINTMENT TYPE:
- Day 1 1.5hrs Type B

ANCILLARY:
- Port recommended.

TOXICITIES:
Hematologic
1. If ANC < 1.5 x 10^9/L, or if PLT < 100 x 10^9/L, HOLD dose for 1 week.

Renal Failure
1. If SrCr > 265umol/L, REDUCE dose to 50%.

Hepatic Dysfunction
1. If T.Bili = 26-51umol/L, or AST = 60-180 IU/L, GIVE 75% dose.
2. If T.Bili = 52-85umol/L, or AST > 180 IU/L, GIVE 50% dose.
3. If T.Bili > 85umol/L, OMIT dose.

CLINICAL MONITORING:
- Observation for infusion reaction (back pain, flushing, chest tightness) during and for 30 minutes after first injection.
- Emergency treatment must be available, eg. antihistamine injection.

HYPERSENSITIVITY:
Management of Hypersensitivity Reactions During Doxorubicin Liposomal (CAELYX™) Infusion:
- Mild (mild flushing, rash, pruritis)
  - Complete infusion. Supervise at bedside. No treatment required.
- Moderate (moderate rash, flushing, mild dyspnea, chest discomfort, mild hypotension, back pain)
  - Stop infusion. Give IV Diphenhydramine 25-50mg and IV Dexamethasone 10mg.
  - After recovery of symptoms, resume infusion at a rate of 50% of the initial rate of infusion.
- Severe (one or more of respiratory distress requiring treatment, generalized urticaria, angioedema, hypotension requiring therapy)
  - Stop infusion.
  - Give IV antihistamine and steroid as above. Add Epinephrine or bronchodilators if indicated.

INTERNAL CODE:
OPIS CODE: DOXORUBICIN LIPO BR

REFERENCES:

Date revised: 05/02/2008
CYCLOPHOSPHAMIDE (IV)-DOXORUBICIN-FLUOROURACIL (FAC) Chemotherapy

Advanced Breast Cancer

5-FLUOROURACIL  500mg/m² IV Days 1 & 8  Round to nearest 25mg
- Inject by direct IV push over 1-3 minutes, followed by a Normal Saline flush.
- Patients are recommended to suck on ice chips about 5 minutes before treatment begins until 30 minutes after treatment is completed to reduce the incidence and severity of stomatitis.

DOXORUBICIN  50mg/m² IV Day 1  Round to nearest 1mg
- Slow push through sidearm of free flowing IV. Give 2 to 4mg (1-2mL) per minute.

CYCLOPHOSPHAMIDE  500mg/m² IV Day 1  Round to nearest 10mg
- Mix in 250mL bag Normal Saline. Infuse over 10-20 minutes.

REPEAT EVERY 21 DAYS

TESTS:
Baseline Tests  WBC HB PLT ANC Cr Urea T.Bili AST ALT AlkPhosphatase
Days 1 & 8  WBC HB PLT ANC
Test Notes - Repeat lytes, urea, Cr, LFTs every 3 cycles or prn.

ANTIEMETIC PRE-CHEMO REGIMEN:
Level C
- Day 1 - Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
  - Dexamethasone 20mg PO/IV
  - Prochlorperazine 10mg PO/IV pm

Level A
- Day 8 - Dexamethasone 20mg PO/IV

ANTIEMETIC TAKE-HOME REGIMEN:
Level B/C
- Day 1 - Ondansetron 8mg PO BID for 2-3 days. or
  - Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days
  - Dexamethasone 8mg PO BID for 2-3 days
  - Prochlorperazine 10mg PO q4-6h pm
  - Prochlorperazine 10mg PO q4-6h pm

Level A
- Day 8 - Prochlorperazine 10mg PO q4-6h pm

PATIENT VISITS and APPOINTMENT TYPE:
- Day 1  1.5hrs Type C
- Day 8  15min Type A

ANCILLARY:
- Oral hydration strongly encouraged; poorly hydrated patients may need more IV hydration.
  - Port recommended.

TOXICITIES:
Hematologic
1. If ANC < 1.5 x 10⁹/L, or if PLT < 100 x 10⁹/L, HOLD chemotherapy for 1 week.
Renal Failure
1. If CrCL < 0.2mL/sec, OMIT all drugs.
Hepatic Dysfunction
1. If T.Bili = 26-51umol/L, or AST = 60-180 IU/L, GIVE 75% Doxorubicin dose.
2. If T.Bili = 52-85umol/L, or AST > 180 IU/L, GIVE 50% Doxorubicin dose.
3. If T.Bili > 85umol/L, OMIT all drugs.

SUGGESTED ACTION
CLINICAL MONITORING:
- Clinical exam for symptoms of CHF.
- Periodic cardiac tests for all patients with cardiac risk factors at or above the threshold dose levels.
LV Systolic Dysfunction:
1. Asymptomatic, resting ejection fraction (EF) < 60 - 50%; shortening fraction (SF) < 30 - 24%
2. Asymptomatic, resting EF < 50 - 40%; SF < 24 - 15%
3. Symptomatic CHF responsive to intervention; EF < 40 - 20%; SF < 15%
4. Refractory CHF or poorly controlled; EF < 20%; intervention such as ventricular assist device, ventricular reduction surgery, or heart transplant indicated
5. Death
RATED AT EACH CLINIC VISIT
- For Cardiac Toxicity Ratings: First rating at the cumulative dose threshold of 450mg/m², and repeat ratings at each cumulative dose increment of 100mg/m² above threshold. (Cumulative dose sooner for high risk patients, eg. pre-existing cardiac disease, prior chest irradiation).
- Note: Threshold Cumulative dose reduced proportionately if other anthracycline or anthrancenedione drugs have been given; cardiotoxicity is additive.
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.
- Urinalysis (RBCs) - ONLY in response to patient complaint.
CYCLOPHOSPHAMIDE (IV)-DOXORUBICIN-FLUOROURACIL (FAC) Chemotherapy

REFERENCES:
- Nabholz JA, Paterson A, Dirix J et al. A phase III randomized trial comparing docetaxel (T), doxorubicin (A) and cyclophosphamide (C) (TAC) to FAC as first line chemotherapy (CT) for patients with metastatic breast cancer (MBC). Proceedings ASCO 2001: Abstract #83.

CCO Eligibility Form Required  [ ]  Non-Formulary Form Required  [ ]  Date revised: 07/02/2008
CYCLOPHOSPHAMIDE (IV)-DOXORUBICIN-FLUOROURACIL (FAC) Chemotherapy -weekly

**Advanced Breast Cancer**

**5-FLUOROURACIL**
- **325mg/m² IV Day 1**
- Round to nearest 25mg
- **Inject by direct IV push over 1-3 minutes**, followed by a Normal Saline flush.
- Patients are recommended to suck on ice chips about 5 minutes before treatment begins until 30 minutes after treatment is completed to reduce the incidence and severity of stomatitis.

**DOXORUBICIN**
- **15mg/m² IV Day 1**
- Round to nearest 1mg
- **Slow push through sidearm of free flowing IV**

**CYCLOPHOSPHAMIDE**
- **125mg/m² IV Day 1**
- Round to nearest 10mg
- **Mix in 250mL bag Normal Saline. Infuse over 10-20 minutes.**

**REPEAT EVERY 7 DAYS**

**TESTS:**
- **Baseline Tests**
  - WBC  HB  PLT  ANC  Cr  Urea  T.Bili  AST  ALT  AlkPhosphatase
  - **Day 1**
  - WBC  HB  PLT  ANC
- **Test Notes**
  - Repeat lytes, urea, Cr, LFTs every 3 months or prn.
  - Baseline Tests: LVEF if clinically indicated.
  - LVEF every 6 months prn.

**ANTIEMETIC PRE-CHEMO REGIMEN:**
- **Level B**
  - **Day 1**
  - Prochlorperazine 10mg PO/IV
  - May add Dexamethasone 2-4mg PO/IV and Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV

**ANTIEMETIC TAKE-HOME REGIMEN:**
- **Level B/C**
  - **Day 1**
  - Prochlorperazine 10mg PO q4-6h prn
  - May add:
    - Ondansetron 8 mg PO BID for 2-3 days, or Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days prn
    - Dexamethasone 8 mg PO BID for 2-3 days prn

**PATIENT VISITS and APPOINTMENT TYPE:**
- **Day 1 45min Type B**

**ANCILLARY:**
- Oral hydration strongly encouraged; poorly hydrated patients may need more IV hydration.
- Inadequate total hydration may result in dose-related hemorrhagic cystitis.
- Port recommended.

**TOXICITIES:**

**Hematologic**
1. If ANC < 1.5 x 10⁹/L, or if PLT < 100 x 10⁹/L, **HOLD chemotherapy for 1 week.**

**Renal Failure**
1. If CrCL < 0.2mL/sec, **OMIT all drugs.**

**Hepatic Dysfunction**
1. If T.Bili = 26-51umol/L, or AST = 60-180 IU/L, **GIVE 75% Doxorubicin dose.**
2. If T.Bili = 52-85umol/L, or AST > 180 IU/L, **GIVE 50% Doxorubicin dose.**
3. If T.Bili > 85umol/L, **OMIT all drugs.**

**SUGGESTED ACTION**

**CLINICAL MONITORING:**
- Clinical exam for symptoms of CHF.
- Periodic cardiac tests for all patients with cardiac risk factors at or above the threshold dose levels.

**LV Systolic Dysfunction:**
1. Asymptomatic, resting ejection fraction (EF) < 60 - 50%; shortening fraction (SF) < 30 - 24%
2. Asymptomatic, resting EF < 50 - 40%; SF < 24 - 15%
3. Symptomatic CHF responsive to intervention; EF < 40 - 20%; SF < 15%
4. Refractory CHF or poorly controlled; EF < 20%; intervention such as ventricular assist device, ventricular reduction surgery, or heart transplant indicated
5. Death

**For Cardiac Toxicity Ratings:** First rating at the cumulative dose threshold of 450mg/m², and repeat ratings at each cumulative dose increment of 100mg/m² above threshold. (Cumulative dose sooner for high risk patients, eg. pre-existing cardiac disease, prior chest irradiation).
- Note: Threshold Cumulative dose reduced proportionately if other anthracycline or anthrancenedione drugs have been given; cardiotoxicity is additive.
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.
- Urinalysis (RBCs) - **ONLY in response to patient complaint.**

**REFERENCES:**

**Date revised:** 07/02/2008

- CCO Eligibility Form Required
- Non-Formulary Form Required

Breast
FLUOROURACIL-EPIRUBICIN-CYCLOPHOSPHAMIDE followed by DOCETAXEL Chemotherapy

Adjuvant for Node-positive and High Risk Node-negative Breast Cancer (for young patients with good performance status)

5-FLUOROURACIL 500mg/m² IV Day 1 Round to nearest 25mg
- Inject by direct IV push over 1-3 minutes, followed by a Normal Saline flush.
- Patients are recommended to suck on ice chips about 5 minutes before treatment begins until 30 minutes after treatment is completed to reduce the incidence and severity of stomatitis.

EPIRUBICIN 100mg/m² IV Day 1 Round to nearest 1mg
- Slow push through sidearm of free flowing IV at a rate of 10mg/5ml per minute.

CYCLOPHOSPHAMIDE 500mg/m² IV Day 1 Round to nearest 10mg
- Mix in 250mL bag Normal Saline, Infuse over 10-20 minutes.

REPEAT EVERY 21 DAYS for total of 3 cycles

Order Group 2
To start 21 days after last administration of Fluorouracil, Epirubicin and Cyclophosphamide (FEC)

DOCETAXEL 100mg/m² IV Day 1 Round to nearest 3mg
- Mix in 250mL bag 5% Dextrose or Normal Saline to a maximum concentration of 0.3-0.9mg/mL.
- Use non-PVC equipment without a filter; Infuse through main IV line.
- Elasto-gel™ gloves should be placed on both hands and treatment should begin 15 minutes after the infusion starts and conclude 15 minutes after the infusion is done.
- Gloves should be changed after 45 minutes to sustain the cold temperature.

First and Second Dose:
- Infuse at a slower rate and then increase incrementally.
- Infuse at 30mL/hr for 5 minutes, then at 60mL/hr for 5 minutes, then at 125mL/hr for 5 minutes, then finally at 250mL/hr until infusion complete.

Subsequent doses:
- Infuse over 1 hour.

REPEAT EVERY 21 DAYS for total of 3 cycles

DEXAMETHASONE 8mg PO Day 0 4mg tablet
- Q12H for 3 days starting one day before chemotherapy.

DIPHENHYDRAMINE 50mg IV Day 1
- Admix in 50-100mL minibag 5% Dextrose or Normal Saline.
- Give over 10-15 minutes.
- Wait 30 minutes before Docetaxel dose started.
- 50mg PO may be given instead.

TESTS:
Baseline Tests WBC HB PLT ANC Cr Urea T.Bili AST ALT AlkPhosphatase LVEF
FEC Day 1 WBC HB PLT ANC
DOCE Day 1 WBC HB PLT ANC
Test Notes - Repeat lytes, urea, Cr, LFTs after 3 cycles or prn.
- LVEF if clinically indicated.

ANTIEMETIC PRE-CHEMO REGIMEN:
Level C Day 1 FEC
- Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
- Dexamethasone 20mg PO/IV
- May add Prochlorperazine 10mg PO/IV prn.

Level A Day 1 DOCE
- Ondansetron 8mg PO BID for 3-4 days, or
- Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days
- Dexamethasone 8mg PO BID for 2-3 days
- Prochlorperazine 10mg PO q4-6h pm
- Prochlorperazine 10mg PO q4-6h pm

ANTIEMETIC TAKE-HOME REGIMEN:
Level B/C Day 1 FEC
- Ondansetron 8mg PO BID for 3-4 days, or
- Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days
- Dexamethasone 8mg PO BID for 2-3 days
- Prochlorperazine 10mg PO q4-6h pm
- Prochlorperazine 10mg PO q4-6h pm

PATIENT VISITS and APPOINTMENT TYPE:
- Day 1 FEC 1.25hr Type C
- Day 1 DOCE (first 2 doses) 2hrs Type D
- Day 1 DOCE (subsequent) 2hrs Type C

ANCILLARY:
- Oral hydration is strongly encouraged.
- Poorly hydrated patients may need more IV hydration.
- Inadequate total hydration may result in dose-related hemorrhagic cystitis.
- Device recommended if IV access becomes problematic.
TOXICITIES:

Hematologic
FEC Regimen:
1. If ANC < 1.5 x 10^9/L, or if PLT < 100 x 10^9/L, HOLD chemotherapy for 1 week.

Docetaxel Regimen:
1. If ANC < 1.5 x 10^9/L, or if PLT < 100 x 10^9/L, HOLD Docetaxel dose for 1 week.

Renal Failure
FEC Regimen:
1. If CrCl < 0.2mL/sec, OMIT Cyclophosphamide dose.

Liver Dysfunction
FEC Regimen:
1. If T.Bili = 26-51umol/L or AST= 60-180 IU/L, give 75% Epirubicin dose.
2. If T.Bili = 52-85umol/L, or AST > 180 IU/L, give 50% Epirubicin dose.
3. If T.Bili > 85umol/L, OMIT Epirubicin.

Docetaxel Regimen:
1. If AST or ALT > 42 IU/L, and if Alk Phos > 300 IU/L, reduce Docetaxel dose to 75mg/m².
2. If AST or ALT > 84 IU/L, Alk Phos > 720 IU/L and T.Bili > 18umol/L, discontinue Docetaxel.

SUGGESTED ACTION

CLINICAL MONITORING:
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.
- Urinalysis (RBCs) routine for high intravenous doses; periodic for low IV dose and in response to patient complaint.
- Baseline renal function tests (if failure suspected) and liver function tests (especially if poor Performance Status).
- Clinical exam for symptoms of CHF.
- Serious, irreversible cardiomyopathy with delayed congestive heart failure may be encountered as the cumulative dose approaches 1000mg/m². Cardiac monitoring is advised when cumulative dose exceeds 650mg/m² of Epirubicin.

Docetaxel:
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.
- Watch for symptoms of fever and infection.
- Skin assessment at each visit, including nails.

Hand-foot Skin Reaction:
1. Minimal skin changes or dermatitis (e.g., erythema) without pain  2. Skin changes (e.g., peeling, blisters, bleeding, edema) or pain, not interfering with function  3. Ulcerative dermatitis or skin changes with pain interfering with function

Fluid Retention
0. None  1. Mild peripheral edema  2. Pleural effusion, outpatient management  3. Pleural effusion, inpatient management  4. Intubation required

Nail Changes
1. Discoloration; ridging (koilonychias); pitting  2. Partial or complete loss of nail(s); pain in nailbed(s)  3. Interfering with ADL

RATED AT EACH CLINIC VISIT

HYPERSENSITIVITY:

Docetaxel Hypersensitivity Procedures:
- If hypersensitivity reaction during administration:
  1. Discontinue Docetaxel immediately if there are signs or symptoms of moderate or severe hypersensitivity. (Mild symptoms may resolve with a decrease in the rate of infusion).
  2. Rapid IV administration of Diphenhydramine 50-100mg and Hydrocortisone 100mg.
  3. Re-initiate infusion after 30 minutes, or when signs of reaction are resolved. Resume infusion at a slower rate, then increase incrementally to the initial planned rate, eg. infuse at 30mL/hr (an 8-hour rate) for 5 minutes, then at 60mL/hr (a 4-hour rate) for 5 minutes, then at 125mL/hr (a 2-hour rate) for 5 minutes, then finally, resume at 250mL/hr (1-hour infusion rate).
  4. Depending on the intensity of the reaction, additional oral or IV pre-medication with an antihistamine should also be given for the next cycle of treatment and the rate of infusion should be decreased initially and then increased back to the recommended 1-hour infusion.

INTERNAL CODE:

OPIS CODES:
- FEC-DOCE ORDER GROUP 1
- FEC-DOCE ORDER GROUP 2

REFERENCES:
- CCO Practice Guideline 1-7: Adjuvant Taxane Therapy for Early-stage Invasive Breast Cancer

CCO Eligibility Form Required ☑ Non-Formulary Form Required ☐ Date revised: 07/02/2008
# HORMONAL Therapy - Breast

**For Adjuvant and Advanced Breast Carcinoma**

<table>
<thead>
<tr>
<th>Medicine</th>
<th>Dosage</th>
<th>Route</th>
<th>Day</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ANASTROZOLE</strong></td>
<td>1mg</td>
<td>PO</td>
<td>Day 1</td>
</tr>
<tr>
<td>- 1mg once daily.</td>
<td></td>
<td></td>
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<tr>
<td>- Continue until Disease Progression.</td>
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<tr>
<td>- Outpatient prescription.</td>
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<tr>
<td>- Trade name = Arimidex™</td>
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<tr>
<td><strong>EXEMESTANE</strong></td>
<td>25mg</td>
<td>PO</td>
<td>Day 1</td>
</tr>
<tr>
<td>- 25mg once daily.</td>
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<td></td>
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</tr>
<tr>
<td>- Hormonal treatment of: adjuvant treatment after 2-3 years of Tamoxifen &amp; treatment of advanced breast cancer in women with natural or artificially induced post-menopausal status whose disease has progressed following anti-estrogen therapy.</td>
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<tr>
<td>- Outpatient prescription.</td>
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<tr>
<td>- Trade name = Aromasin™</td>
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<tr>
<td><strong>LETRIZOLE</strong></td>
<td>2.5mg</td>
<td>PO</td>
<td>Day 1</td>
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<tr>
<td>- 2.5mg once daily.</td>
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<tr>
<td>- Adjuvant treatment post 5 years of Tamoxifen.</td>
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<tr>
<td>- First line hormonal treatment of advanced breast cancer in postmenopausal women.</td>
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<tr>
<td>- Hormonal treatment of advanced breast cancer in postmenopausal women who have disease progression following anti-estrogen therapy.</td>
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<tr>
<td>- Outpatient prescription.</td>
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<tr>
<td>- Trade name = Femara™</td>
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<tr>
<td><strong>MEGESTROL</strong></td>
<td>160mg</td>
<td>PO</td>
<td>Day 1</td>
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<tr>
<td>- 160mg once daily.</td>
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<tr>
<td>- Advanced breast cancer.</td>
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<tr>
<td>- Outpatient prescription.</td>
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<tr>
<td>- Trade name = Megace™</td>
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<tr>
<td><strong>TAMOXIFEN</strong></td>
<td>20mg</td>
<td>PO</td>
<td>Day 1</td>
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<tr>
<td>- 20mg once daily.</td>
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<tr>
<td>- Breast cancer (hormone receptor positive tumors).</td>
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<tr>
<td>- Continuous Treatment for 5 Years.</td>
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<td>- Outpatient prescription.</td>
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<tr>
<td>- Trade name = Nolvadex™</td>
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<tr>
<td><strong>FULVESTRANT</strong></td>
<td>250mg</td>
<td>IM</td>
<td>Day 1</td>
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<tr>
<td>- 250mg into the buttock every month</td>
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<tr>
<td>- For locally advanced or metastatic breast cancer in postmenopausal women, who have disease progression following prior endocrine therapy</td>
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<tr>
<td>- Outpatient prescription (needs to be refrigerated).</td>
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<tr>
<td>- Trade name = Faslodex™</td>
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<tr>
<td><strong>GOSERELIN</strong></td>
<td>3.6mg</td>
<td>SC</td>
<td>Day 1</td>
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<tr>
<td>- 3.6mg into the upper abdomen every 28 days</td>
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<tr>
<td>- For advanced breast cancer in pre and perimenopausal women whose tumours contain estrogen and/or progesterone receptors OR for adjuvant therapy of early breast cancer in women who are unsuitable for or refuse chemotherapy</td>
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<tr>
<td>- Outpatient prescription.</td>
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<tr>
<td>- Trade name = Zoladex™</td>
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</table>

**Test Notes**

- Laboratory tests prn.

- Patients are seen every 3 months and LFTs are done at that time to gauge progression of disease.
**CLINICAL MONITORING:**

**Precautions:**
- Exemestane:
  - A possible decrease of exemestane plasma levels by known inducers of CYP3A4 cannot be excluded. Avoid grapefruit juice.

- Letrozole:
  - Letrozole is a strong inhibitor of CYP2A6 and a moderate inhibitor of CYP2C19. Thus, caution is advised with concomitant administration of drugs, whose metabolism is mainly dependent on these isoenzymes.

- Megestrol:
  - Contraindicated in select patients with a history of significant thromboembolic disease.

- Tamoxifen:
  - Contraindicated in select patients with a history of significant thromboembolic disease.

**Drug interactions:**
- Do not give concurrently with aminogluthethimide since combination decreases tamoxifen concentration.
- Monitor prothrombin time when patient is on oral anticoagulant therapy.
- Caution with administration of cytotoxic chemotherapy due to increased incidence of thromboembolic events.

- Fulvestrant:
  - Use with caution in patients with bleeding disorders or on anticoagulants.

- Goserelin:
  - Do not use in females with undiagnosed abnormal vaginal bleeding.

**INTERNAL CODE:**

**OPIS CODES:**
- ANASTRO
- EXEMESTANE
- LETRO
- MEGES
- TAMOX
- FULVEST
- GOSER
**REFERENCES:**

**Anastrozole:**

**Exemestane:**

**Letrozole:**

**Letrozole:**

**Tamoxifen:**
- CCO Practice Guideline (in Progress) 1-18: The Role of Aromatase Inhibitors as Adjuvant Therapy for Women with Hormone Receptor-positive Breast Cancer. (Draft Practice Guideline).

**Fulvestrant:**
- Fulvestrant: Drug Information. In: UpToDate, Rose, BD (ed), UpToDate, Waltham, MA, 2008.

**Goserelin:**
- Goserelin: Drug Information. In: UpToDate, Rose, BD (ed), UpToDate, Waltham, MA, 2008.
MITOMYCIN C Chemotherapy

Advanced Breast Cancer

MITOMYCIN 6mg/m² IV Day 1 Round to nearest 0.5mg

- Slow push through sidearm of free flowing IV; Give 1.5mg (3mL) per minute.

REPEAT EVERY 14 DAYS

TESTS:
Baseline Tests WBC HB PLT ANC Cr Urea T.Bili AST ALT AlkPhosphatase
Day 1 WBC HB PLT ANC

ANTIEMETIC PRE-CHEMO REGIMEN:
Level B Day 1 - Dexamethasone 8mg PO/IV
- May add or substitute Prochlorperazine 10mg PO/IV prn

ANTIEMETIC TAKE-HOME REGIMEN:
Level A Day 1 - Prochlorperazine 10mg PO q4-6h prn

PATIENT VISITS and APPOINTMENT TYPE:
➔ Day 1: 30min Type B

ANCILLARY:
- Port recommended.

TOXICITIES:
Hematologic
1. If ANC < 1.5 x 10⁹/L, or if PLT < 100 x 10⁹/L, HOLD Mitomycin dose for 1-2 weeks (or until PLT ≥ 120-150 x 10⁹/L).

Renal Failure
1. If CrCL < 0.2mL/sec, give 75% Mitomycin dose.

Hepatic Dysfunction
1. If T.Bili = 50-85umol/L, or AST > 180 IU/L, give 75% Mitomycin dose.

SUGGESTED ACTION

CLINICAL MONITORING:
- Blood pressure at each visit.
- Clinical pulmonary exam, including auscultation, pulmonary toxicity ratings (Cough, SOB).
- Baseline & periodic renal function tests (if failure suspected).

Cough
1. Symptomatic, non-narcotic medication only indicated 2. Symptomatic and narcotic medication indicated 3. Symptomatic and significantly interfering with sleep or ADL

Dyspnea
1. Dyspnea on exertion, but can walk 1 flight of stairs without stopping 2. Dyspnea on exertion but unable to walk 1 flight of stairs or 1 city block (0.1km) without stopping 3. Dyspnea with ADL 4. Dyspnea at rest; intubation/ventilator indicated 5. Death

RATED AT EACH CLINIC VISIT

REFERENCES:

CCO Eligibility Form Required [ ] Non-Formulary Form Required [ ] Date revised: 07/02/2008
NANOPARTICLE ALBUMIN BOUND (nab)-PACLITAXEL (ABRAXANE) Chemotherapy

For metastatic breast cancer patients with previous taxane infusion reactions or severe toxicity

NAB-PACLITAXEL

260mg/m² IV Day 1

- Add into a sterile, empty PVC IV bag, and infuse over 30 minutes.
- Use of an in-line filter is NOT recommended.
- Do not substitute nab-Paclitaxel (Abraxane)™ for or with other Paclitaxel formulations.

REPEAT EVERY 21 DAYS for a usual total of 6 cycles

TESTS:

Baseline Tests: WBC HB PLT ANC Cr Urea T.Bili AST ALT AlkPhosphatase

Day 1: WBC HB PLT ANC

Test Notes: Repeat lytes, urea, Cr, LFTs every 3 cycles or prn.

- Nab-Paclitaxel has not been used in patients with hepatic or renal dysfunction. In the randomized control trial, patients were excluded for baseline serum bilirubin >1.5mg/dL or baseline serum creatinine >2mg/dL.

ANTIEMETIC TAKE-HOME REGIMEN:

Level A

Day 1: Prochlorperazine 10mg PO q4-6h prn

PATIENT VISITS and APPOINTMENT TYPE:

Day 1: 30 min Type B

ANCILLARY:

- Take a baseline blood pressure measurement, if prior hypotension.
- Port recommended.

TOXICITIES:

Hematologic

1. If ANC < 1.5 x 10⁹/L, or if PLT < 100 x 10⁹/L, HOLD nab-Paclitaxel dose for 1 week.
2. If Grade 4 neutropenia ≥ 7 days, REDUCE nab-Paclitaxel dose to 220mg/m².
3. If recur, dose reduce to 180mg/m² for subsequent cycles.

Neurologic

1. If Grade 3 or 4 sensory neuropathy, HOLD nab-Paclitaxel until resolved to Grade 1 or 2, followed by a dose reduction to 220mg/m².
2. If recur, HOLD nab-Paclitaxel until resolved to Grade 2 followed by a dose reduction to 180mg/m² or discontinue further therapy.

SUGGESTED ACTION

CLINICAL MONITORING:

Sensory:

1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function
2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL
3. Sensory alteration or paresthesia interfering with ADL
4. Disabling
5. Death

Flu-like syndrome:

1. Symptoms present but not interfering with function
2. Moderate or causing difficulty performing some ADL
3. Severe symptoms interfering with ADL
4. Disabling
5. Death

Allergic Reaction:

1. Transient flushing or rash; drug fever < 38°C
2. Rash; flushing; urticaria; dyspnea; drug fever ≥ 38°C
3. Symptomatic bronchospasm, with or without urticaria; parenteral medication(s) indicated; allergy-related edema/angioedema; hypotension
4. Anaphylaxis
5. Death

RATED AT EACH CLINIC VISIT

INTERNAL CODE:

OPIS CODE: NAB-PACLI (Q3WKS)

REFERENCES:

- Abraxane™ current product monograph, Abraxis Bioscience Inc.
NANOPARTICLE ALBUMIN BOUND (nab)-PACLITAXEL  
(ABRAXANE) Chemotherapy-weekly

For metastatic breast cancer patients with previous taxane infusion reactions or severe toxicity

NAB-PACLITAXEL  
100mg/m²  IV  Day 1  Round to nearest 2.5mg

- Add into a sterile, empty PVC IV bag, and infuse over 30 minutes.
- Use of an in-line filter is NOT recommended.
- Do not substitute nab-Paclitaxel (Abraxane™) for or with other Paclitaxel formulations.

REPEAT EVERY 7 DAYS for a usual total of 6 cycles

TESTS:
Baseline Tests  WBC  HB  PLT  ANC  Cr  Urea  T.Bili  AST  ALT  AlkPhosphatase

Day 1  WBC  HB  PLT  ANC

Test Notes - Repeat lytes, urea, Cr, LFTs every 3 cycles or prn.
- Nab-Paclitaxel has not been used in patients with hepatic or renal dysfunction. In the randomized control trial, patients were excluded for baseline serum bilirubin >1.5mg/dL or baseline serum creatinine >2mg/dL.

ANTIEMETIC TAKE-HOME REGIMEN:
Level A  Day 1  Prochlorperazine 10mg PO q4-6h prn

PATIENT VISITS and APPOINTMENT TYPE:
⇒ Day 1  30 min  Type B

ANCILLARY:
- Take a baseline blood pressure measurement, if prior hypotension.
- Port recommended.

TOXICITIES:
Hematologic
1. If ANC < 1.5 x 10⁹/L, or if PLT < 100 x 10⁹/L, HOLD nab-Paclitaxel dose for 1 week.

SUGGESTED ACTION

CLINICAL MONITORING:
Sensory:
1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function 2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL 3. Sensory alteration or paresthesia interfering with ADL 4. Disabling 5. Death

Flu-like syndrome:

Allergic Reaction:
1. Transient flushing or rash; drug fever < 38°C 2. Rash; flushing; urticaria; dyspnea; drug fever > 38°C 3. Symptomatic bronchospasm, with or without urticaria; parenteral medication(s) indicated; allergy-related edema/angioedema; hypotension 4. Anaphylaxis 5. Death

RATED AT EACH CLINIC VISIT

INTERNAL CODE:
OPIS CODE: NAB-PACL (weekly)

REFERENCES:
- Abraxane™ current product monograph, Abraxis Bioscience Inc.

Date revised: 07/02/2008
## PACLITAXEL Chemotherapy

### Advanced Breast Cancer

**PACLITAXEL**

175mg/m² IV Day 1

- Mix in 500mL bag **Normal Saline** (dilution concentration 0.3-1.2mg/mL).
- Use non-PVC equipment, including 0.22 micron in-line filter.
- Infuse over 3 hours.

**REPEAT EVERY 21 DAYS**

**DEXAMETHASONE**

20mg PO Day 1 4mg tablet

- 12 and 6 hours before Paclitaxel administration (if not taken at home, give 20mg Dexamethasone IV/PO 30 minutes before Paclitaxel).
- **ALTERNATE DOSE:** 8mg PO Bid for 3 days, starting 24 hours before Paclitaxel.

**DIPHENHYDRAMINE**

50mg IV Day 1

- Admix in **50-100mL**, minibag 5% Dextrose or **Normal Saline**.
- Give over **10-15 minutes**, (may be admixed with Ranitidine).
- Administer 30 minutes before Paclitaxel.
- 50mg PO may be given instead.

**RANITIDINE**

50mg IV Day 1

- Admix in **50-100mL**, minibag 5% Dextrose or **Normal Saline**.
- Give over **10-15 minutes**, (may be admixed with Diphenhydramine).
- Administer 30 minutes before Paclitaxel.
- 150mg PO may be given instead.

### TESTS:

<table>
<thead>
<tr>
<th>Baseline Tests</th>
<th>WBC HB PLT ANC Cr Urea T.Bili AST ALT AlkPhosphatase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1</td>
<td>WBC HB PLT ANC</td>
</tr>
</tbody>
</table>

**Test Notes:** Repeat lytes, urea, Cr, LFTs every 3 cycles or prn.

### ANTIEMETIC PRE-CHEMO REGIMEN:

**Level B**  
Day 1 - Dexamethasone - see regimen information regarding pre-medications.
- May add Prochlorperazine 10mg PO/IV pm

### ANTIEMETIC TAKE-HOME REGIMEN:

**Level A**  
Day 1 - Prochlorperazine 10mg PO q4-6h pm

### PATIENT VISITS and APPOINTMENT TYPE:

- Day 1 5hrs Type E

### ANCILLARY:

- Take a baseline blood pressure measurement, if prior hypotension.
- Observe patient for the first 5 minutes of the Paclitaxel infusion, then periodically for the remainder of the infusion.
- Port recommended.

### TOXICITIES:

**Hematologic**

1. If ANC < 1.5 x 10⁹/L, or if PLT < 100 x 10⁹/L, **HOLD** Paclitaxel dose for 1 week.

**Hepatic Dysfunction**

1. If AST > 70 IU/L or Bili < 25 umol/L, give MAXIMUM Paclitaxel dose of **135mg/m²**.
2. If T.Bili = 25-50 umol/L, give MAXIMUM Paclitaxel dose of **75mg/m²**.
3. If T.Bili > 50 umol/L, give MAXIMUM Paclitaxel dose of **50mg/m²**.

**SUGGESTED ACTION**

**CLINICAL MONITORING:**

- Watch for symptoms of fever and infection.
- Blood pressure and pulse rate monitoring during drug administration and for the following hour.

**Sensory:**

1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function  
2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL  
3. Sensory alteration or paresthesia interfering with ADL  
4. Disabling  
5. Death

**Flu-like Syndrome:**

1. Symptoms present but not interfering with function  
2. Moderate or causing difficulty performing some ADL  
3. Severe symptoms interfering with ADL  
4. Disabling  
5. Death

**Allergic Reaction:**

1. Transient flushing or rash; drug fever < 38 degrees C  
2. Rash; flushing; urticaria; dyspnea; drug fever ≥ 38 degrees C  
3. Symptomatic bronchospasm, with or without urticaria; parenteral medication(s) indicated; allergy-related edema/angioedema; hypotension  
4. Anaphylaxis  
5. Death

**RATED AT EACH CLINIC VISIT**
PACLITAXEL Chemotherapy

HYPERSENSITIVITY:

PACLITAXEL Procedures

Retreatment for Paclitaxel Hypersensitivity Reaction:

1. Discontinue Paclitaxel immediately if there are signs or symptoms of hypersensitivity.
2. Rapid IV administration of Diphenhydramine 50-100mg direct IV push over 1 minute and Hydrocortisone 100mg in 100ml Normal Saline over 5-10 minutes.
3. Reinitiate Paclitaxel infusion after 30 minutes, or when signs of reaction are resolved. Resume Paclitaxel infusion at 25% of previous rate for at least 5 minutes, 50% for at least 5 minutes, 75% for at least 5 minutes. If no further symptoms develop, continue at original rate until infusion complete.
4. If reaction recurs, STOP Paclitaxel for this dose and treat patient symptoms.

Desensitization for Paclitaxel Hypersensitivity Reactions:

If Paclitaxel hypersensitivity recurs during previous administration despite retreatment plan:

1. Dexamethasone 20mg PO 36 hours and 12 hours before chemotherapy, and 20mg PO morning of chemotherapy.
2. Dexamethasone 20mg IV, Diphenhydramine 50mg IV & Ranitidine 50mg IV about 30min before infusion.
3. Paclitaxel Infusion: 2mg in 100mL Normal Saline over 30min; if no reaction, 10mg in 100mL Normal Saline over 30min; if no reaction, remainder of dose in 500mL Normal Saline over 3 hours.
4. If reaction occurs, discontinue infusion; Diphenhydramine 50-100mg direct IV push over 1 minute and Hydrocortisone 100mg in 100ml Normal Saline over 5-10 minutes.
5. Restart Paclitaxel infusion after 30 minutes.

REFERENCES:

- CCO Practice Guideline 1-3: The Role of the Taxanes in the Management of Metastatic Breast Cancer.
  http://www.bccancer.bc.ca/HP/DrugDatabase/DrugIndexPro/Paclitaxel.htm

Date revised: 07/15/2008
**PACLITAXEL Chemotherapy (weekly)**

**Advanced Breast Cancer**

**PACLITAXEL**

58mg/m²  IV  Day 1  Round to nearest 3mg

- Mix in 250mL bag Normal Saline (dilution concentration 0.3-1.2mg/mL).
- Use non-PVC equipment, including 0.22 micron in-line filter.
- Infuse over 1 hour.

**DEXAMETHASONE**

8mg  PO  Day 1  4mg tablet

- 12 and 6 hours before Paclitaxel (if not taken at home, give 8mg IV/PO 30 minutes before Paclitaxel).

**DIPHENHYDRAMINE**

50mg  IV  Day 1

- Admix in 50-100mL minibag 5% Dextrose or Normal Saline.
- Give over 10-15 minutes. (may be admixed with Ranitidine).
- Administer 30 minutes before Paclitaxel.
- 50mg PO may be given instead.

**RANITIDINE**

50mg  IV  Day 1

- Admix in 50-100mL minibag 5% Dextrose or Normal Saline.
- Give over 10-15 minutes. (may be admixed with Diphenhydramine).
- Administer 30 minutes before Paclitaxel.
- 150mg PO may be given instead.

**TESTS:**

Baseline Tests

<table>
<thead>
<tr>
<th>WBC</th>
<th>HB</th>
<th>PLT</th>
<th>ANC</th>
<th>Cr</th>
<th>Urea</th>
<th>T.Bili</th>
<th>AST</th>
<th>ALT</th>
<th>AlkPhosphatase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1</td>
<td>WBC</td>
<td>HB</td>
<td>PLT</td>
<td>ANC</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Test Notes**

- Repeat lytes, urea, Cr, LFTs every 3 months or prn.

**ANTIEMETIC PRE-CHEMO REGIMEN:**

Level A

Day 1 - Prochlorperazine 10mg PO/IV pm

**ANTIEMETIC TAKE-HOME REGIMEN:**

Level A

Day 1 - Prochlorperazine 10mg PO q4-6h pm

**PATIENT VISITS and APPOINTMENT TYPE:**

Day 1  90min  Type D

**ANCILLARY:**

- Take a baseline blood pressure measurement, if prior hypotension.
- Observe patient for the first 5 minutes of the Paclitaxel infusion, then periodically for the remainder of the infusion.
- Port recommended.

**TOXICITIES:**

**Hematologic**

1. If ANC < 1.5 x 10⁹/L, or if PLT < 100 x 10⁹/L, HOLD Paclitaxel dose for 1 week.

**Hepatic Dysfunction**

1. If AST > 70 IU/L, or T.Bili < 25umol/L, give MAXIMUM dose of 45mg/m².
2. If T.Bili = 25-50umol/L, give MAXIMUM dose of 25mg/m².
3. If T.Bili > 50umol/L, give MAXIMUM dose of 16mg/m².

**SUGGESTED ACTION**

**CLINICAL MONITORING:**

- Watch for symptoms of fever and infection.
- Blood pressure and pulse rate monitoring during drug administration and for the following hour.

**Sensory:**

1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function
2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL
3. Sensory alteration or paresthesia interfering with ADL
4. Disabling
5. Death

**Flu-like Syndrome:**

1. Symptoms present but not interfering with function
2. Moderate or causing difficulty performing some ADL
3. Severe symptoms interfering with ADL
4. Disabling
5. Death

**Allergic Reaction:**

1. Transient flushing or rash; drug fever < 38 degrees C
2. Rash; flushing; urticaria; dyspnea; drug fever ≥ 38 degrees C
3. Symptomatic bronchospasm, with or without urticaria; parenteral medication(s) indicated; allergy-related edema/angioedema; hypotension
4. Anaphylaxis
5. Death

RATED AT EACH CLINIC VISIT
PACLITAXEL Chemotherapy (weekly)

HYPERSENSITIVITY:

Paclitaxel Procedures

Retreatment for Paclitaxel Hypersensitivity Reaction:

If Paclitaxel hypersensitivity reaction occurs during administration:
1. Discontinue Paclitaxel immediately if there are signs or symptoms of hypersensitivity.
2. Rapid IV administration of Diphenhydramine 50-100mg direct IV push over 1 minute and Hydrocortisone 100mg in 100ml Normal Saline over 5-10 minutes.
3. Reinitiate Paclitaxel infusion after 30 minutes, or when signs of reaction are resolved. Resume Paclitaxel infusion at 25% of previous rate for at least 5 minutes, 50% for at least 5 minutes, 75% for at least 5 minutes. If no further symptoms develop, continue at original rate until infusion complete.
4. If reaction recurs, STOP Paclitaxel for this dose and treat patient symptoms.

Desensitization for Paclitaxel Hypersensitivity Reactions:
If Paclitaxel hypersensitivity recurs during previous administration despite retreatment plan:
1. Dexamethasone 20mg PO 36 hours and 12 hours before chemotherapy, and 20mg PO morning of chemotherapy.
2. Dexamethasone 20mg IV, Diphenhydramine 50mg IV & Ranitidine 50mg IV about 30min before infusion.
3. Paclitaxel Infusion: 2mg in 100mL Normal Saline over 30min; if no reaction, 10mg in 100mL Normal Saline over 30min; if no reaction, remainder of dose in 500mL Normal Saline over 3 hours.
4. If reaction occurs, discontinue infusion; Diphenhydramine 50-100mg direct IV push over 1 minute and Hydrocortisone 100mg in 100ml Normal Saline over 5-10 minutes.
5. Restart Paclitaxel infusion after 30 minutes.

INTERNAL CODE:
OPIS CODE: PACLI WEEKLY 58MG/M2

REFERENCES:
- CCO Practice Guideline 1-3: The Role of the Taxanes in the Management of Metastatic Breast Cancer.
  http://www.bccancer.bc.ca/HPI/DrugDatabase/DrugIndexPro/Paclitaxel.htm

CCO Eligibility Form Required ✔ Non-Formulary Form Required □ Date revised: 07/18/2008
**PAMIDRONATE Therapy**

*Treatment of Bone Metastases or Bony Pain Associated With Advanced Breast Cancer*

**PAMIDRONATE**

90mg  IV  Day 1

**FOR ALL DOSES:**
- Admix 90mg into **250mL Normal Saline** ambulatory pump (Intermate LV100) and infuse over **2.5 hours** at home.
- All **first dose** patients are required to remain in the chemotherapy suite for 30 minutes after the start of the Pamidronate pump, in case of any potential reactions.
- Presently the Centre Pharmacy dispenses the premixed Pamidronate Intermates prepared by Baxter.

**REPEAT EVERY 28 DAYS**

**TESTS:**
- **Baseline Tests**
  - Ca Cr Urea Albumin
- **Test Notes**
  - Repeat lytes, Ca & albumin every 3 months or prn.
  - Check creatinine regularly.

**PATIENT VISITS and APPOINTMENT TYPE:**
- First dose 30min  Type A
- Subsequent doses 15min  Type A

**CLINICAL MONITORING:**
- Creatinine should be monitored regularly.
- Consider a reduced initial dose or an infusion time of at least 4 hours in patients with pre-existing renal impairment (CrCl<30ml/min).
- Use is not recommended for the treatment of bone metastases in patients with severe renal impairment.
- In patients who develop renal deterioration during bisphosphonate therapy (>44umol/L in patients with normal baseline or >88umol/L in patients with abnormal baseline), consider holding dose. Resumption of therapy (at the same dose) may be considered when serum creatinine returns to within 10% of baseline.
- Monitor calcium.
- If corrected serum calcium < 2.10mmol/L, HOLD Pamidronate for 1 week, or until Serum Calcium levels are in normal range.

**Hypocalcemia**

0. Serum calcium > 2.10mmol/L
1. Serum calcium = 2.10-1.93mmol/L
2. Serum calcium = 1.92-1.74mmol/L
3. Serum calcium = 1.73-1.51mmol/L
4. Serum calcium <1.50mmol/L

- Rated on assessment of anti-hypercalcemia response and at periodic visits, or in response to patient complaint.

**FORMULAE:**

- **Corrected Serum Calcium (mmol/L)**
  - Male: \[\text{Measured Serum Calcium} + [(40 - 
  \text{serum albumin}) \times 0.02]\]
  - Female: \[\text{[140-age(yrs)] \times TBW(Kg)} / [50 \times \text{SCr(umol/L)}]\]

**INTERNAL CODE:**
- OPIS CODES:
  - PAMID 30MG
  - PAMID 60MG
  - PAMID 90MG

**REFERENCES:**

**Date revised:** 10/10/2006
**PACLITAXEL-TRASTUZUMAB Chemotherapy (7 Day Paclitaxel)**

*Treatment of Advanced Breast Cancer in Women whose Tumours Overexpress the HER2 Protein, and Who Have Been Previously Treated with Anthracyline containing Chemotherapy*

### TRASTUZUMAB
8mg/Kg, then 6mg/Kg  
- Mix in **250mL** bag **Normal Saline**, DO NOT MIX in 5% Dextrose.  
- **Loading dose** = 8mg/Kg  
  - Infuse over **90 minutes**, then observe for 60 minutes.  
- **Maintenance dose** = 6mg/Kg  
  - Infuse over **30 minutes**, then observe for 30 minutes.  
- If no reaction after 3 doses, no observation period required.  
- If reaction on maintenance dose, drug should be infused over **60 minutes**, then observe for 30 minutes.  
- If no reaction after 3 doses at 60 minutes, may change infusion time to **30 minutes** and follow as above.  
- If reaction at 60 minutes, dose should be infused over **90 minutes**, then observe for 60 minutes.  

**REPEAT EVERY 21 DAYS (6mg/Kg)**

### PACLITAXEL
58mg/m²  
- Mix in **250mL** bag **Normal Saline** (dilution concentration 0.3-1.2mg/mL).  
- Use non-PVC equipment, including 0.22 micron in-line filter.  
- Infuse over **1 hour**.

**REPEAT EVERY 7 DAYS**

### PREMEDI
**ACETAMINOPHEN** 650mg PO Day 0  
- Prn before Trastuzumab.

**DEXAMETHASONE** 8mg PO Day 0  
- 12 and 6 hours before Paclitaxel (if not taken at home, give 8mg IV/PO 30 minutes before Paclitaxel).

**DIPHENHYDRAMINE** 50mg IV Day 1  
- Admix in **50-100mL** minibag 5% Dextrose or **Normal Saline**, (may be admixed with Ranitidine).  
- Give over **10-15 minutes**, (may be admixed with Diphenhydramine).  
- Administer 30 minutes before Paclitaxel.  
- 50mg PO may be given instead.

**RANITIDINE** 50mg IV Day 1  
- Admix in **50-100mL** minibag 5% Dextrose or **Normal Saline**, (may be admixed with Diphenhydramine).  
- Give over **10-15 minutes**, (may be admixed with Ranitidine).  
- Administer 30 minutes before Paclitaxel.  
- 150mg PO may be given instead.

### TESTS:

<table>
<thead>
<tr>
<th>Baseline Tests</th>
<th>WBC HB PLT ANC Cr Urea T.Bili AST ALT AlkPhosphatase LVEF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1</td>
<td>WBC HB PLT ANC</td>
</tr>
<tr>
<td>Test Notes</td>
<td>- Repeat lytes, urea, Cr, LFTs every 3 cycles or prn.</td>
</tr>
<tr>
<td></td>
<td>- LVEF every 6 months or prn.</td>
</tr>
</tbody>
</table>

### ANTIEMETIC PRE-CHEMO REGIMEN:

<table>
<thead>
<tr>
<th>No Level</th>
<th>Day 0</th>
<th>- Note: antipyretics, antihistamines, corticosteroids may be ordered to prevent infusion-related reactions.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1</td>
<td></td>
<td>- See pre-medications in Regimen information.</td>
</tr>
</tbody>
</table>

### ANTIEMETIC TAKE-HOME REGIMEN:

<table>
<thead>
<tr>
<th>Level A</th>
<th>Day 1</th>
<th>- Prochlorperazine 10mg po q4-6h pm</th>
</tr>
</thead>
</table>

### PATIENT VISITS and APPOINTMENT TYPE:

- **Trast 21 day (Loading dose only)** 3hrs **Type C**  
- **Pacli 7 day without Tras** 1.5hrs **Type D**  
- **Pacli 7 Day & Trast 21 Day(Maint)** 2.5hrs **Type D**  
- **Pacli 7 Day & Trast 21 Day(Maint)** 2hrs **Type D**  

### ANCILLARY:
- Take a baseline blood pressure measurement, if prior hypotension.  
- After first cycle, may administer Trastuzumab and Paclitaxel on same day.  
- Port recommended.

### TOXICITIES:

<table>
<thead>
<tr>
<th>Hematologic</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. If ANC &lt; 1.5 x 10⁹/L, or if PLT &lt; 100 x 10⁹/L, HOLD Paclitaxel dose for 1 week.</td>
</tr>
</tbody>
</table>

*Breast*
**Hepatic Dysfunction**
1. If AST > 70 IU/L, or T.Bili < 25umol/L, give MAXIMUM Paclitaxel dose of 135mg/m².
2. If T.Bili = 25-50umol/L, give MAXIMUM Paclitaxel dose of 75mg/m².
3. If T.Bili > 50umol/L, give MAXIMUM Paclitaxel dose of 50mg/m².

**SUGGESTED ACTION**

**CLINICAL MONITORING:**
- Trastuzumab:
  - Close observation for infusion-related symptoms: fever, chills, pain (including pain in tumour), asthenia, and other flu like symptoms.
  - Periodic cardiac tests for all patients with cardiac risk factors or suspected cardiac toxicity.
- LV Systolic Dysfunction:
  1. Asymptomatic, resting ejection fraction (EF) < 60 - 50%; shortening fraction (SF) < 30 - 24%
  2. Asymptomatic, resting EF < 50 - 40%; SF < 24 - 15%
  3. Symptomatic CHF responsive to intervention; EF < 40 - 20% SF < 15%
  4. Refractory CHF or poorly controlled; EF < 20%; intervention such as ventricular assist device, ventricular reduction surgery, or heart transplant indicated
- Paclitaxel:
  - Watch for symptoms of fever and infection.
  - Blood pressure and pulse rate monitoring during drug administration and for the following hour.
- Sensory:
  1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function
  2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL
  3. Sensory alteration or paresthesia interfering with ADL
  4. Disabling
  5. Death
- Flu-like Syndrome:
  1. Symptoms present but not interfering with function
  2. Moderate or causing difficulty performing some ADL
  3. Severe symptoms interfering with ADL
  4. Death

**HYPERSENSITIVITY:**

- **Paclitaxel Procedures**
  - **Retreatment for Paclitaxel Hypersensitivity Reaction:**
    1. Discontinue Paclitaxel immediately if there are signs or symptoms of hypersensitivity.
    2. Rapid IV administration of Diphenhydramine 50-100mg direct IV push over 1 minute and Hydrocortisone 100mg in 100ml Normal Saline over 5-10 minutes.
    3. Reinitiate Paclitaxel infusion after 30 minutes, or when signs of reaction are resolved. Resume Paclitaxel infusion at 25% of previous rate for at least 5 minutes, 50% for at least 5 minutes, 75% for at least 5 minutes. If no further symptoms develop, continue at original rate until infusion complete.
    4. If reaction recurs, STOP Paclitaxel for this dose and treat patient symptoms.
  - **Desensitization for Paclitaxel Hypersensitivity Reactions:**
    1. Dexamethasone 20mg PO 36 hours and 12 hours before chemotherapy, and 20mg PO morning of chemotherapy.
    2. Dexamethasone 20mg IV, Diphenhydramine 50mg IV & Ranitidine 50mg IV about 30min before infusion.
    3. Paclitaxel Infusion: 2mg in 100mL Normal Saline over 30min; if no reaction, 10mg in 100mL Normal Saline over 30min; if no reaction, remainder of dose in 500mL Normal Saline over 3 hours.
    4. If reaction occurs, discontinue infusion; Diphenhydramine 50-100mg direct IV push over 1 minute and Hydrocortisone 100mg in 100ml Normal Saline over 5-10 minutes.
    5. Restart Paclitaxel infusion after 30 minutes.

**INTERNAL CODE:**
- OPIS CODES:
  - PAC-TRAS 7D/21D LOAD
  - PAC-TRAS 7D/21D MAINT

**REFERENCES:**
- CCO Practice Guideline 1-3: The Role of the Taxanes in the Management of Metastatic Breast Cancer.
- CCO Practice Guideline 1-15: ES Use of Trastuzumab (Herceptin) in Metastatic Breast Cancer.
http://www.bccancer.bc.ca/HPI/DrugDatabase/DrugIndexPro/Paclitaxel.htm

**Date revised:** 07/02/2008
PACLITAXEL-TRASTUZUMAB Chemotherapy (21 Day Paclitaxel)

Treatment of Advanced Breast Cancer in Women whose Tumours Overexpress the HER2 Protein, and Who Have Been Previously Treated with Anthracycline containing Chemotherapy

**TRASTUZUMAB**

**8mg/Kg, then IV Day 0**
- Mix in **250mL Normal Saline**, DO NOT MIX in 5% Dextrose.
- **Loading dose**= (8mg/Kg) Day 0 Only
  - Infuse over **90 minutes**, then observe for 60 minutes.
- **Maintenance dose**= (6mg/Kg)
  - Mix into **250mL Normal Saline**, DO NOT MIX in 5% Dextrose.
  - Infuse over **30 minutes**, then observe for 30 minutes.
  - If no reaction after 3 doses, no observation period required.
  - If reaction on maintenance dose, drug should be infused over **60 minutes**, then observe for 30 minutes.
  - If no reaction after 3 doses at 60 minutes, may change infusion time to **30 minutes** and follow as above.
  - If reaction at 60 minutes, dose should be infused over **90 minutes** then observe for 60 minutes.
  - **DO NOT ADMINISTER AS IV PUSH OR BOLUS.**

REPEAT EVERY 21 DAYS (6mg/Kg Tras)

**PACLITAXEL**

**175mg/m² IV Day 1**
- Mix in **500mL bag Normal Saline** (dilution concentration 0.3-1.2 mg/mL).
- Use non-PVC equipment, including 0.22 micron in-line filter.
- Infuse over **3 hours**.

REPEAT EVERY 21 DAYS

**PREMeds**

**ACETAMINOPHEN**
650mg PO Day 0 325mg tablet
- Prn pre Trastuzumab.

**DEXAMETHASONE**
20mg PO Day 1 4mg tablet
- To be administered at home 12 and 6 hours before Paclitaxel (if not taken at home, Dexamethasone **20mg IV/PO** 30 minutes before Paclitaxel).
- **OR ALTERNATE DOSE:**
  - 8mg PO BID for 3 days, starting 24 hours before Paclitaxel.

**DIPHENHYDRAMINE**
50mg IV Day 1
- Adminix in **50-100mL** minbag 5% Dextrose or **Normal Saline**.
- Give over **10-15 minutes**, (may be admixed with Ramitidine).
- Administer 30 minutes before Paclitaxel.
- 50mg PO may be given instead.

**RANITIDINE**
50mg IV Day 1
- Adminix in **50-100mL** minbag 5% Dextrose or **Normal Saline**.
- Give over **10-15 minutes**, (may be admixed with Diphenhydramine).
- Administer 30 minutes before Paclitaxel.
- 150mg PO may be given instead.

**TESTS:**

- **Baseline Tests**
  - WBC HB PLT ANC Cr Urea T.Bili AST ALT AlkPhosphatase LVEF
- **Day 1**
  - WBC HB PLT ANC
- **Test Notes**
  - Repeat lytes, urea, Cr, LFTs every 3 cycles or prn.
  - LVEF every 6 months or prn.

**ANTIEMETIC PRE-CHEMO REGIMEN:**

No Level Day 0
- Note: antipyretics, antihistamines, corticosteroids may be ordered to prevent infusion-related reactions.
- See pre-medications in Regimen information.

**ANTIEMETIC TAKE-HOME REGIMEN:**

**Level A** Day 1
- Prochlorperazine 10mg po q4-6h prn

**PATIENT VISITS and APPOINTMENT TYPE:**

- **Trast 21day (Loading dose only)** 3hrs Type C
- **Pacl 21 Day & Tras 21 Day** (Maint) 4.5hrs Type D
- **Pacl 21 Day & Tras 21 Day** (Maint) after 3 doses 4hrs Type D

**ANCILLARY:**

- Take a baseline blood pressure measurement, if prior hypotension.
- After first cycle, may administer Trastuzumab and Paclitaxel on same day.
- Port recommended.
TOXICITIES:

Hematologic
1. If ANC < 1.5 x 10⁹/L, or if PLT < 100 x 10⁹/L, HOLD Paclitaxel dose for 1 week.

Hepatic Dysfunction
1. If AST > 70 IU/L, or T.Bili < 25µmol/L, give MAXIMUM Paclitaxel dose of 135mg/m².
2. If T.Bili = 25-50µmol/L, give MAXIMUM Paclitaxel dose of 75mg/m².
3. If T.Bili > 50µmol/L, give MAXIMUM Paclitaxel dose of 50mg/m².

SUGGESTED ACTION

CLINICAL MONITORING:

Trastuzumab:
- Close observation for infusion-related symptoms: fever, chills, pain (including pain in tumour), asthenia, and other flu-like symptoms.
- Periodic cardiac tests for all patients with cardiac risk factors or suspected cardiac toxicity.

LV Systolic Dysfunction:
1. Asymptomatic, resting ejection fraction (EF) < 60 - 50%; shortening fraction (SF) < 30 - 24%
2. Asymptomatic, resting EF < 50 - 40%; SF < 24 - 15%
3. Symptomatic CHF responsive to intervention; EF < 40 - 20% SF < 15%
4. Refractory CHF or poorly controlled; EF < 20%; intervention such as ventricular assist device, ventricular reduction surgery, or heart transplant indicated
5. Death

Paclitaxel:
- Watch for symptoms of fever and infection.
- Blood pressure and pulse rate monitoring during drug administration and for the following hour.

Sensory:
1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function
2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL
3. Sensory alteration or paresthesia interfering with ADL
4. Severe symptoms interfering with ADL
5. Death

Flu-like Syndrome:
1. Symptoms present but not interfering with function
2. Moderate or causing difficulty performing some ADL
3. Severe symptoms interfering with ADL
4. Disabling
5. Death

Allergic Reaction:
1. Transient flushing or rash; drug fever < 38 degrees C
2. Rash; flushing; urticaria; dyspnea; drug fever > 38 degrees C
3. Symptomatic bronchospasm, with or without urticaria; parenteral medication(s) indicated; allergy-related edema/angioedema; hypotension
4. Anaphylaxis
5. Death

RATED AT EACH CLINIC VISIT

HYPERSENSITIVITY:

Paclitaxel Procedures

Retreatment for Paclitaxel Hypersensitivity Reaction:
If Paclitaxel hypersensitivity reaction occurs during administration:
1. Discontinue Paclitaxel immediately if there are signs or symptoms of hypersensitivity.
2. Rapid IV administration of Diphenhydramine 50-100mg direct IV push over 1 minute and Hydrocortisone 100mg in 100ml Normal Saline over 5-10 minutes.
3. Reinitiate Paclitaxel infusion after 30 minutes, or when signs of reaction are resolved. Resume Paclitaxel infusion at 25% of previous rate for at least 5 minutes, 50% for at least 5 minutes, 75% for at least 5 minutes. If no further symptoms develop, continue at original rate until infusion complete.
4. If reaction recurs, STOP Paclitaxel for this dose and treat patient symptoms.

Desensitization for Paclitaxel Hypersensitivity Reactions:
If Paclitaxel hypersensitivity recurs during previous administration despite retreatment plan:
1. Dexamethasone 20mg PO 36 hours and 12 hours before chemotherapy, and 20mg PO morning of chemotherapy.
2. Diphenhydramine 50mg IV & Ranitidine 50mg IV about 30min before infusion.
3. Paclitaxel Infusion: 2mg in 100mL Normal Saline over 30min; if no reaction, 10mg in 100mL Normal Saline over 30min; if no reaction, remainder of dose in 500mL Normal Saline over 3 hours.
4. If reaction occurs, discontinue infusion; Diphenhydramine 50-100mg direct IV push over 1 minute and Hydrocortisone 100mg in 100ml Normal Saline over 5-10 minutes.
5. Restart Paclitaxel infusion after 30 minutes.

INTERNAL CODE:

OPIS CODES:
- PAC-TRAS 21D/21D LOAD
- PAC-TRAS 21D/21D MAINT

REFERENCES:
- CCO Practice Guideline 1-3: The Role of the Taxanes in the Management of Metastatic Breast Cancer.
- CCO Practice Guideline 1-15: ES Use of Trastuzumab (Herceptin) in Metastatic Breast Cancer.
http://www.bccancer.bc.ca/HPI/DrugDatabase/DrugIndexPro/Paclitaxel.htm

Date revised: 07/02/2008
**DOCETAXEL** and **CYCLOPHOSPHAMIDE**

Adjuvant treatment of Breast Cancer in Women with Contraindication(s) to an Anthracycline-Containing Regimen.

**CYCLOPHOSPHAMIDE**  600mg/m²  IV  Day 1  Round to nearest 10mg
- Mix in 250mL bag **Normal Saline**, Infuse over 10-20 minutes.

**DOCETAXEL**  75mg/m²  IV  Day 1  Round to nearest 3mg
- Mix in 250mL bag 5% Dextrose or **Normal Saline** to a maximum concentration of 0.3-0.9mg/mL.
- Use non-PVC equipment without a filter; Infuse through main IV line.
- Elasto-gel™ gloves should be placed on both hands and treatment should begin 15 minutes before the infusion starts and conclude 15 minutes after the infusion is done.
- Gloves should be changed after 45 minutes to sustain the cold temperature.

First and Second Dose:
- Infuse at a slower rate and then increase incrementally.
- Infuse at 30mL/hr for 5 minutes, then at 60mL/hr for 5 minutes, then at 125mL/hr for 5 minutes, then finally at 250mL/hr until infusion complete.

Subsequent doses:
- Infuse over 1 hour.

**REPEAT EVERY 21 DAYS for a total of 4 cycles**

**DEXAMETHASONE**  8mg  PO  Day 0  4mg tablet
- Q12H for 3 days starting one day before chemotherapy.

**DIPHENHYDRAMINE**  50mg  IV  Day 1
- Admix in 50-100mL minibag 5% Dextrose or **Normal Saline**.
- Give over 10-15 minutes.
- Administer 30 minutes before Docetaxel dose started.
- 50mg PO may be given instead.

**TESTS:**

<table>
<thead>
<tr>
<th>Baseline Tests</th>
<th>WBC  HB  PLT  ANC  Cr  Urea  T.Bili  AST  ALT  AlkPhosphatase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1</td>
<td>WBC  HB  PLT  ANC</td>
</tr>
</tbody>
</table>

**ANTIEMETIC PRE-CHEMO REGIMEN:**

**Level C**  Day 1
- Ondansetron  8mg PO/IV or Granisetron 1mg PO/IV
- Dexamethasone 20mg PO/IV (if not taken at home prior to chemotherapy)

**ANTIEMETIC TAKE-HOME REGIMEN:**

**Level B/C**  Day 1
- Ondansetron  8mg PO BID for 2-3 days, or
  - Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days
- Dexamethasone 8mg PO BID for 2-3 days
- Prochlorperazine 10mg PO q4-6h pm

**PATIENT VISITS and APPOINTMENT TYPE:**

| ➔ Day 1 (first 2 doses)  | 3hrs  | Type D |
| ➔ Day 1 (subsequent)    | 2hrs  | Type C |

**ANCILLARY:**
- Oral hydration is strongly encouraged.
- Poorly hydrated patients may need more IV hydration.
- Inadequate total hydration may result in dose-related hemorrhagic cystitis.
- Device recommended if IV access becomes problematic.

**TOXICITIES:**

**Hematologic**
1. If ANC < 1.5 x 10⁹/L, or if PLT < 100 x 10⁹/L, HOLD chemotherapy for 1 week.

**Renal Failure**
Cyclophosphamide:
1. If CrCl < 0.2mL/sec, OMIT Cyclophosphamide dose.

**Hepatic Dysfunction**
Docetaxel:
1. Decrease Docetaxel dose if LFTs > 1.5 x normal.
2. If AST or ALT > 53 IU/L, or if Alk Phos > 180 IU/L, REDUCE dose by 50%.

**SUGGESTED ACTION**
DOCETAXEL and CYCLOPHOSPHAMIDE

CLINICAL MONITORING:

Cyclophosphamide:
- Urinalysis (RBCs) routine for high intravenous doses; periodic for low IV dose and in response to patient complaint.
- Baseline renal function tests (if failure suspected) and liver function tests (especially if poor Performance Status).

Docetaxel:
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.
- Watch for symptoms of fever and infection.
- Skin assessment at each visit, including nails.

Skin Toxicity
4. Desquamation, ulceration, or necrosis

Fluid Retention
0. None 1. Mild peripheral edema 2. Pleural effusion, outpatient management
3. Pleural effusion, inpatient management 4. Intubation required

Nail Changes
1. Discoloration; ridging (koilonychia); pitting 2. Partial or complete loss of nail(s); pain in nailbed(s) 3. Interfering with ADL

RATED AT EACH CLINIC VISIT

HYPERSENSITIVITY:

Docetaxel Hypersensitivity Procedures:
- If hypersensitivity reaction during administration:
  1. Discontinue Docetaxel immediately if there are signs or symptoms of moderate or severe hypersensitivity. (Mild symptoms may resolve with a decrease in the rate of infusion).
  2. Rapid IV administration of Diphenhydramine 50-100mg and Hydrocortisone 100mg.
  3. Re-initiate infusion after 30 minutes, or when signs of reaction are resolved. Resume infusion at a slower rate, then increase incrementally to the initial planned rate, eg. infuse at 30mL/hr (an 8-hour rate) for 5 minutes, then at 60mL/hr (a 4-hour rate) for 5 minutes, then at 125mL/hr (a 2-hour rate) for 5 minutes, then finally, resume at 250mL/hr (1-hour infusion rate).
  4. Depending on the intensity of the reaction, additional oral or IV pre-medication with an antihistamine should also be given for the next cycle of treatment and the rate of infusion should be decreased initially and then increased back to the recommended 1-hour infusion.

INTERNAL CODE:

OPIS CODES:
- TC

REFERENCES:

Date revised: 07/02/2008
## TRASTUZUMAB-DOCETAXEL-CARBOPLATIN Chemotherapy

Adjuvant treatment of Breast Cancer in Women whose Tumours Overexpress the HER2 Protein with contraindication(s) to an anthracycline-containing regimen.

### TRASTUZUMAB

- **8mg/Kg**, then **IV Day 1**
- **LOADING DOSE**: (8mg/Kg) Day 1 Only
- **MAINTENANCE DOSE**: (6mg/Kg)
- **Mix in 250mL Normal Saline**, DO NOT MIX in 5% Dextrose.
- **Infuse over 90 minutes**, then observe for 60 minutes.
- **If no reaction after 3 doses**, no observation period required.
- **If reaction on maintenance dose**, drug should be infused over 60 minutes, then observed for 30 minutes.
- **If no reaction after 3 doses at 60 minutes**, may change infusion time to 30 minutes and follow as above.

### DOCETAXEL

- **75mg/m²**, then **IV Day 1**
- **LOADING DOSE**: (8mg/m²) Day 1 Only
- **MAINTENANCE DOSE**: (6mg/m²)
- **Mix in 250mL bag 5% Dextrose or Normal Saline** to a maximum concentration of 0.3-0.9mg/mL.
- **Use non-PVC equipment without a filter; Infuse through main IV line.**
- **Elasto-gel™ gloves should be placed on both hands and treatment should begin 15 minutes before the infusion starts and conclude 15 minutes after the infusion is done.**
- **Gloves should be changed after 45 minutes to sustain the cold temperature.**

### CARBOPLATIN

- **AUC 6**, then **IV Day 1**
- **LOADING DOSE**: (8mg/m²) Day 1 Only
- **MAINTENANCE DOSE**: (6mg/m²)
- **Mix in 250mL bag 5% Dextrose**.
- **Infuse over 30 to 60 minutes**.

### PREMEDS

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dose or Dosage</th>
<th>Administration</th>
<th>Day(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ACETAMINOPHEN</strong></td>
<td>650mg PO</td>
<td>Day 1</td>
<td>325mg tablet</td>
</tr>
<tr>
<td><strong>DEXAMETHASONE</strong></td>
<td>8mg PO</td>
<td>Day 1</td>
<td>4mg tablet</td>
</tr>
<tr>
<td><strong>DIPHENHYDRAMINE</strong></td>
<td>50mg IV</td>
<td>Day 1</td>
<td></td>
</tr>
</tbody>
</table>

### TESTS:

Baseline Tests: WBC HB PLT ANC Cr Urea T.Bili AST ALT AlkPhosphatase LVEF

Day 1: WBC HB PLT ANC Cr Urea

Test Notes: - Repeat lytes, LFTs every 3 cycles or prn.
- LVEF at baseline and every 3 months.

### ANTIEMETIC PRE-CHEMO REGIMEN:

**Level C**

**Day 1**

- Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
- Dexamethasone 20mg PO/IV (if not taken at home prior to chemotherapy)
- Note: antipyretics, antihistamines, corticosteroids may be ordered to prevent infusion-related reactions to Trastuzumab.

### ANTIEMETIC TAKE-HOME REGIMEN:

**Level B/C**

**Day 1**

- Ondansetron 8mg PO BID for 2-3 days, or
- Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days
- Dexamethasone 8mg PO BID for 2-3 days
- Prochlorperazine 10mg PO q4-6h prn

### PATIENT VISITS and APPOINTMENT TYPE:

- **Day 1 Loading Dose** 5hrs Type D
- **Day 1 Maintenance Dose** 4hrs Type D
ANCILLARY:
- Device recommended if IV access becomes problematic.

TOXICITIES:

Hematologic
1. If ANC < 1.5 x 10^9/L, or if PLT < 100 x 10^9/L, HOLD Docetaxel and Carboplatin dose for 1 week.

Hepatic Dysfunction
1. Decrease Docetaxel dose if LFTs > 1.5 x normal.
2. If AST or ALT > 53 IU/L, or if Alk Phos > 180 IU/L, REDUCE Docetaxel by 50%.

Renal Failure
1. ADJUST Carboplatin dose if estimated CrCl changes > 10%.

SUGGESTED ACTION

CLINICAL MONITORING:

Trastuzumab:
- Close observation for infusion-related symptoms: fever, chills, pain (including pain in tumour), asthenia, and other flu like symptoms.
- Periodic cardiac tests for all patients with cardiac risk factors or suspected cardiac toxicity.

LV Systolic Dysfunction:
1. Asymptomatic, resting ejection fraction (EF) < 60 - 50%; shortening fraction (SF) < 30 - 24%
2. Asymptomatic, resting EF < 50 - 40%; SF < 24 - 15%
3. Symptomatic CHF responsive to intervention; EF < 40 - 20%
4. Refractory CHF or poorly controlled; EF < 20%; intervention such as ventricular assist device, ventricular reduction surgery, or heart transplant indicated

Docetaxel
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.
- Watch for symptoms of fever and infection.
- Skin assessment at each visit, including nails.

Skin Toxicity
0. None
1. Hyperpigmentation
2. Atrophy
3. Subcutaneous fibrosis
4. Desquamation, ulceration, or necrosis

Nail Changes
1. Discoloration; ridging (koilonychias); pitting
2. Partial or complete loss of nail(s); pain in nailbed(s)

Interfering with ADL
0. None
1. Mild peripheral edema
2. Pleural effusion, outpatient management
3. Pleural effusion, inpatient management
4. Intubation required

FORMULAE:

CrCl - Cockcroft & Gault (mL/sec)
Male: [140-age(yrs)] x TBW(Kg) / [50 x SCr(umol/L)]
Female: [140-age(yrs)] x TBW(Kg) / [50 x SCr(umol/L)] x 0.85

ml/min = 60 x CrCl mL/sec

Dose (in mg) = target AUC x (GFR + 25) GFR in ml/min

INTERNAL CODE:
OPIS CODES:
- TDCARB 21D LOAD
- TDCARB 21D MAINT

REFERENCES:

Date revised: 05/02/2008
**TRASTUZUMAB 21 Day Therapy**

*Treatment of HER2/neu positive patients with node positive or node negative (tumour >1cm) primary breast cancer who are or have received adjuvant or neoadjuvant chemotherapy or treatment of advanced breast cancer in women whose tumours overexpress the HER2 protein and who have been previously treated with chemotherapy.*

**TRASTUZUMAB**

**8mg/kg IV LOADING DOSE Day 1**

Round to nearest 1mg **ONLY**

**21 DAY DOSING:**
- **Loading dose = 8mg/Kg**
- Mix in **250mL Normal Saline**, DO NOT MIX in 5% Dextrose.
- Infuse over **90 minutes**, then observe for 60 minutes.
- DO NOT ADMINISTER AS IV PUSH OR BOLUS.

**LOADING DOSE - ADMINISTER ON DAY 1 ONLY**

**TRASTUZUMAB**

**6mg/kg IV MAINTENANCE DOSE**

Round to nearest 1mg **ONLY**

**21 DAY DOSING:**
- **Maintenance dose = 6mg/Kg**.
- Mix into **250mL Normal Saline**, DO NOT MIX in 5% Dextrose.
- Infuse over **30 minutes**, then observe for 30 minutes.
- If no reaction after 3 doses, no observation period required.
- If reaction on maintenance dose, drug should be infused over **60 minutes**, then observed for 30 minutes.
- If no reaction after 3 doses at 60 minutes, may change infusion time to 30 minutes and follow as above.
- If reaction at 60 minutes, dose should be infused over **90 minutes** then observed for 60 minutes.
- DO NOT ADMINISTER AS IV PUSH OR BOLUS.

**REPEAT EVERY 21 DAYS (6mg/kg) (for 1 year or until disease recurrence for early breast cancer)**

**ACETAMINOPHEN**

- **650mg PO Day 1**
- **325mg tablet Prn pre Trastuzumab**.

**TESTS:**

- **Baseline Tests**
  - WBC HB PLT ANC Urea T.Bili Cr AST ALT AlkPhosphatase LVEF
- **Test Notes**
  - LVEF every 3 months or pm for early breast cancer patients.
  - LVEF every 6 months or pm for advanced breast cancer patients.

**ANTIEMETIC PRE-CHEMO REGIMEN:**

**Level A**

**Day 1**
- Prochlorperazine 10mg PO/IV pm
- Note: antipyretics, antihistamines, corticosteroids may be ordered to prevent infusion-related reactions.

**ANTIEMETIC TAKE-HOME REGIMEN:**

**Level A**

**Day 1**
- Prochlorperazine 10mg PO q4-6h pm

**PATIENT VISITS and APPOINTMENT TYPE:**

- **21 D LOADING DOSE Day 1**
  - **3hrs** Type C
  - **ONLY**

- **21 D MAINTENANCE DOSE Day 1**
  - **1hr** Type C

- **21 D MAINTENANCE DOSE Day 1 after 3 doses**
  - **45min** Type C

**ANCILLARY:**

- Port recommended.

**CLINICAL MONITORING:**

- Close observation for infusion-related symptoms: fever, chills, pain (including pain in tumour), asthenia, and other flu-like symptoms.
- Periodic cardiac tests for all patients with cardiac risk factors or suspected cardiac toxicity.
- LV Systolic Dysfunction:
  1. Asymptomatic, resting ejection fraction (EF) < 60 - 50%; shortening fraction (SF) < 30 - 24%
  2. Asymptomatic, resting EF < 50 - 40%; SF < 24 - 15%
  3. Symptomatic CHF responsive to intervention; EF < 40 - 20% SF < 15%
  4. Refractory CHF or poorly controlled; EF < 20%; intervention such as ventricular assist device, ventricular reduction surgery, or heart transplant indicated
  5. Death

**RATED AT EACH CLINIC VISIT**

**INTERNAL CODE:**

- OPIS CODES:
  - TRAS 21D LOAD
  - TRAS 21D MAINT
TRASTUZUMAB 21 Day Therapy

REFERENCES:
- CCO Practice Guideline 1-15: ES Use of Trastuzumab (Herceptin) in Metastatic Breast Cancer.

Date revised: 07/02/2008
**VINORELBINE Chemotherapy**

*Advanced Breast Cancer*

**VINORELBINE** 25-30mg/m² IV Days 1, 8 & 15 Round to nearest 1mg

- Add to **50mL Normal Saline** minibag.
- Infuse over **6-10 minutes** into the sidearm of a free-flowing IV line.
- Flush IV line with at least 100mL Normal Saline or 5% Dextrose.
- Hydrocortisone 100mg IV may be given if patient experiences pain on administration.
- Acute pain syndrome at the tumour site can be managed with nonsteroidal anti-inflammatory drugs or corticosteroids.

**ALTERNATE DOSING:**
- Days 1 & 8 repeated every 21 days (for advanced breast cancer patients).

**REPEAT EVERY 28 DAYS** (weekly administration for 3 out of 4 weeks)

**TESTS:**

<table>
<thead>
<tr>
<th>Baseline Tests</th>
<th>WBC</th>
<th>HB</th>
<th>PLT</th>
<th>ANC</th>
<th>Cr</th>
<th>Urea</th>
<th>T.Bili</th>
<th>AST</th>
<th>ALT</th>
<th>AlkPhosphatase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Days 1, 8 &amp; 15</td>
<td>WBC</td>
<td>HB</td>
<td>PLT</td>
<td>ANC</td>
<td>Cr</td>
<td>Urea</td>
<td>T.Bili</td>
<td>AST</td>
<td>ALT</td>
<td>AlkPhosphatase</td>
</tr>
</tbody>
</table>

**ANTIEMETIC PRE-CHEMO REGIMEN:**

- Level A Days 1, 8 & 15 - Prochlorperazine 10mg PO pm.

**ANTIEMETIC TAKE-HOME REGIMEN:**

- Level A Days 1, 8 & 15 - Prochlorperazine 10mg PO q4-6h pm

**PATIENT VISITS and APPOINTMENT TYPE:**

- Days 1, 8 & 15 30min Type A

**ANCILLARY:**
- Port recommended.

**TOXICITIES:**

**Hematologic**
1. If ANC < 1.5 x 10⁹/L, or if PLT < 100 x 10⁹/L, **HOLD** Vinorelbine dose.

**CLINICAL MONITORING:**

- Watch for symptoms of fever and infection.

**Sensory:**
1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function
2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL
3. Sensory alteration or paresthesia interfering with ADL
4. Disabling
5. Death

**Constipation**
1. Occasional or intermittent symptoms; occasional use of stool softeners, laxatives, dietary modification, or enema
2. Persistent symptoms with regular use of laxatives or enemas indicated
3. Symptoms interfering with ADL; obstipation with manual evacuation indicated
4. Life-threatening consequences (e.g., obstruction, toxic megacolon)
5. Death

RATED AT EACH CLINIC VISIT

**REFERENCES:**


Date revised: 07/18/2008
VINORELBINE-TRASTUZUMAB 21 Day Chemotherapy

Treatment of women with HER2/neu overexpressing metastatic breast cancer whose disease has progressed with anthracycline or taxane therapy in the adjuvant or metastatic setting.

**VINORELBINE**

- Add to 50mL Normal Saline minibag.
- Infuse over 6-10 minutes into the sidearm of a free-flowing IV line.
- Flush IV line with at least 100mL Normal Saline or 5% Dextrose.
- Hydrocortisone 100mg IV may be given if patient experiences pain on administration.
- Acute pain syndrome at the tumour site can be managed with nonsteroidal anti-inflammatory drugs or corticosteroids.

**ALTERNATE DOSING:**
- Days 1 & 8 repeated every 21 days (for advanced breast cancer patients).

<table>
<thead>
<tr>
<th>TRASTUZUMAB</th>
<th>8mg/Kg</th>
<th>IV</th>
<th>LOADING DOSE Day 1</th>
<th>Round to nearest 1mg ONLY</th>
</tr>
</thead>
</table>

21 DAY DOISING:
- Loading dose = 8mg/Kg
  - Mix in 250mL Normal Saline, DO NOT MIX in 5% Dextrose.
  - Infuse over 90 minutes, then observe for 60 minutes.
  - DO NOT ADMINISTER AS IV PUSH OR BOLUS.

<table>
<thead>
<tr>
<th>TRASTUZUMAB</th>
<th>6mg/Kg</th>
<th>IV</th>
<th>MAINTENANCE DOSE</th>
<th>Round to nearest 1mg</th>
</tr>
</thead>
</table>

21 DAY DOISING:
- Maintenance dose = 6mg/Kg.
  - Mix into 250mL Normal Saline, DO NOT MIX in 5% Dextrose.
  - Infuse over 30 minutes, then observe for 30 minutes.
  - If no reaction after 3 doses, no observation period required.
  - If no reaction after 3 doses at 60 minutes, may change infusion time to 30 minutes and follow as above.
  - If reaction at 60 minutes, dose should be infused over 90 minutes then observe for 60 minutes.
  - DO NOT ADMINISTER AS IV PUSH OR BOLUS.

<table>
<thead>
<tr>
<th>ACETAMINOPHEN</th>
<th>650mg</th>
<th>PO</th>
<th>Day 1</th>
<th>325mg tablet</th>
</tr>
</thead>
</table>
- Prn before Trastuzumab.

**TESTS:**
Baseline Tests: WBC HB PLT ANC Cr Urea T.Bili AST ALT AlkPhosphatase LVEF
Vinorelbine Days 1, 8 & 15: WBC HB PLT ANC

**ANTIEMETIC PRE-CHEMO REGIMEN:**
Level A: Days 1, 8 & 15 - Prochlorperazine 10mg PO pm.

**ANTIEMETIC TAKE-HOME REGIMEN:**
Level A: Days 1, 8 & 15 - Prochlorperazine 10mg po q4-6h prn

**PATIENT VISITS AND APPOINTMENT TYPE:**
- Vinorelbine & Tras 21 Day Loading 3hrs Type D
- Vinorelbine without Tras 30min Type A
- Vinorelbine & Tras 21 Day (Maint) 1.5hrs Type C
- Vinorelbine & Tras 21 Day (Maint) after 3 doses 1hr Type C

**ANCILLARY:**
- Port recommended.

**TOXICITIES:**
- Hematologic
  1. If ANC < 1.5 x 10^9/L, or if PLT < 100 x 10^9/L, HOLD Vinorelbine dose.

SUGGESTED ACTION
CLINICAL MONITORING:

Trastuzumab:
- Close observation for infusion-related symptoms: fever, chills, pain (including pain in tumour), asthenia, and other flu like symptoms.
- Periodic cardiac tests for all patients with cardiac risk factors or suspected cardiac toxicity.

LV Systolic Dysfunction:
1. Asymptomatic, resting ejection fraction (EF) < 60 - 50%; shortening fraction (SF) < 30 - 24%
2. Asymptomatic, resting EF < 50 - 40%; SF < 24 - 15%
3. Symptomatic CHF responsive to intervention; EF < 40 - 20% SF < 15%
4. Refractory CHF or poorly controlled; EF < 20%; intervention such as ventricular assist device, ventricular reduction surgery, or heart transplant indicated
5. Death

Vinorelbine:
- Watch for symptoms of fever and infection.

Sensory:
1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function
2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL
3. Sensory alteration or paresthesia interfering with ADL
4. Disabling
5. Death

Constipation:
1. Occasional or intermittent symptoms; occasional use of stool softeners, laxatives, dietary modification, or enema
2. Persistent symptoms with regular use of laxatives or enemas indicated
3. Symptoms interfering with ADL; obstipation with manual evacuation indicated
4. Life-threatening consequences (e.g., obstruction, toxic megacolon)
5. Death

RATED AT EACH CLINIC VISIT

INTERNAL CODE:
- VINOR-TRAS 21D LOAD
- VINOR-TRAS 21D MAINT

REFERENCES:

Date revised: 07/02/2008
LOMUSTINE Chemotherapy
Glioma - Adjuvant or Palliative Treatment

LOMUSTINE 130mg/m² PO Day 1 Round to nearest 10mg
- Single dose of Lomustine should be given on an empty stomach at bedtime to prevent nausea and vomiting.
- If compromised marrow function, decrease dose to 100mg/m².
- 10mg, 40mg and 100mg capsules available.
- Trade name = CeeNU™

REPEAT EVERY 6-8 WEEKS

TESTS:
Baseline Tests WBC HB PLT ANC Glucose Cr Urea T.Bili ALT AlkPhosphatase
Day 1 WBC HB PLT ANC Glucose Cr Urea T.Bili ALT AlkPhosphatase
Weekly WBC HB PLT ANC

ANTIEMETIC PRE-CHEMO REGIMEN:
Level C
- Ondansetron 8mg PO or Granisetron 2mg PO daily before each oral chemotherapy dose and/or Dexamethasone 8mg PO daily before each dose.

ANTIEMETIC TAKE-HOME REGIMEN:
Level C Day 1
- Ondansetron 8mg PO BID for 1 day, or Granisetron 1mg PO Q12H or 2mg PO QO for 1 day after chemotherapy dose.
- Dexamethasone 8mg PO BID for 2-3 days after chemotherapy dose.
- Prochlorperazine 10mg PO q4-6h pm

TOXICITIES:
Hematologic
1. If ANC  < 1.4 x 10⁹/L, or if PLT < 100 x 10⁹/L, HOLD Lomustine.
Dosage adjustment from nadir counts:
1. If ANC 2.0-2.99 x 10⁹/L, or if PLT 50-74.99 x 10⁹/L, GIVE 75% of prior dose.
2. If ANC < 2.0 x 10⁹/L, or if PLT 25-49.99 x 10⁹/L, GIVE 50% of prior dose.
3. If ANC < 2.0 x 10⁹/L, or if PLT < 25 x 10⁹/L, GIVE 25% of prior dose.
Renal Failure
1. If CrCl = 0.2-0.8mL/sec, GIVE 75% of previous dose.
1. If CrCl < 0.2mL/sec, GIVE 25-50% of previous dose.
Pulmonary
- Pulmonary toxicity (infiltrates and/or fibrosis) has occurred after 6 months (or longer) of treatment with a cumulative dose greater than 1,100 mg/m². One report of toxicity occurred at a cumulative dose of 600mg.

CLINICAL MONITORING:
- Clinical pulmonary exam, including auscultation, pulmonary toxicity ratings (Cough, Dyspnea).
- Watch for symptoms of fever and infection.
- Baseline & periodic renal function tests (if failure suspected).
Cough
1. Symptomatic, non-narcotic medication only indicated
2. Symptomatic and narcotic medication indicated
3. Symptomatic and significantly interfering with sleep or ADL
Dyspnea
1. Dyspnea on exertion, but can walk 1 flight of stairs without stopping
2. Dyspnea on exertion but unable to walk 1 flight of stairs or 1 city block (0.1km) without stopping
3. Dyspnea with ADL
4. Dyspnea at rest; intubation/ventilator indicated
5. Death
RATED AT EACH CLINIC VISIT

REFERENCES:

CCO Eligibility Form Required ☐ Non-Formulary Form Required ☐ Date revised: 09/03/2008
# Temozolomide Chemotherapy

## Glioblastoma Multiforme or Anaplastic Astrocytoma - Palliative Treatment after Recurrence or Progression from Standard Therapy

### Temozolomide

<table>
<thead>
<tr>
<th>Dosage</th>
<th>Route</th>
<th>Days</th>
<th>Capsules</th>
</tr>
</thead>
<tbody>
<tr>
<td>150mg/m²</td>
<td>PO</td>
<td>1-5</td>
<td>5, 20, 100 &amp; 250mg</td>
</tr>
</tbody>
</table>

- Oral administration Days 1 to 5.
- May increase to 200mg/m² if no myelosuppression at Day 22 nadir.
- Outpatient prescription available as 5mg, 20mg, 100mg & 250mg capsules.
- Trade name = Temodal™

### Repeats

Repeat every 28 days.

### Tests

Baseline Tests: WBC, HB, PLT, ANC, Glucose, Cr, Urea, T.Bili, Albumin, ALT, AlkPhosphatase

Day 21: WBC, HB, PLT, ANC

### Antiemetic Take-Home Regimen:

**Level C**
- Days 1-5: Ondansetron 8mg PO or Granisetron 2mg PO daily before each oral chemotherapy dose and/or Dexamethasone 8mg PO daily before each dose.
- Ondansetron 8mg PO BID or Granisetron 2mg PO daily for 1 day after chemotherapy.
- Prochlorperazine 10mg po q4-6h pm.

**Level B/C**
- Day 6: Ondansetron 8mg PO or Granisetron 2mg PO daily for 1 day after chemotherapy.

### Toxicities:

**Hematologic**
1. If ANC < 1.5 x 10⁹/L, or if PLT < 125 x 10⁹/L on Day 1, **HOLD** dose for 5-7 days.
2. If ANC < 0.5 x 10⁹/L, or if PLT < 75 x 10⁹/L at Day 22, **HOLD** dose for 1 week and continue at 150mg/m² or lower dose.

**Renal Failure**
- If CrCl < 1.0mL/sec, **REDUCE** dose by 25-50%.

### Suggested Action

### Internal Code:

**OPIS Code:** TEMOZOL CN

### References:


### Dates

- **Date Revised:** 09/03/2008
TEMOZOLMIDE Concomitant & Adjuvant Chemotherapy

Glioblastoma Multiforme Concomitant With Radiotherapy

Order Group 1

TEMOZOLMIDE 75mg/m² PO Days 1-42 5, 20,100 & 250mg capsules
- Daily oral administration for 42 days concurrent with radiotherapy.
- Temozolamide to be taken 30 minutes before radiation on radiation days; to be taken at bedtime on non-radiation days.
- Outpatient prescription available as 5mg, 20mg, 100mg & 250mg capsules.
- Trade name = Temodal™

Order Group 1 RADIATION CONCURRENT Daily

Phase I:
Technique: 3 Field Conformal/ IMRT 2 phases
Modality: 6MV/18MV
Dose Specification: Isocentre 100%
Total Dose: 4600 cGy
Fraction Dose: 200 cGy (23 fractions)
Pattern: Daily

Phase II:
Technique: 3 Field Conformal/ IMRT 2 phases
Modality: 6MV/18MV
Dose Specification: Isocentre 100%
Total Dose: 1400 cGy
Fraction Dose: 200 cGy
Pattern: Daily

REPEAT EVERY 28 DAYS for a Total of 6 Cycles

TESTS:
Baseline Tests WBC HB PLT ANC Glucose Cr Urea T.Bili Albumin ALT AlkPhosphatase
Concurrent with WBC HB PLT ANC Radiation Weekly
Post Radiation Day 1 WBC HB PLT ANC

ANTIEMETIC PRE-CHEMO REGIMEN:
Level C Days 1-42 Concurrent
- Prochlorperazine 10mg PO and/or Ondansetron 8mg PO 30 minutes before each oral chemotherapy dose

Level C Days 1-5 post radiation
- Ondansetron 8mg PO or Granisetron 2mg PO daily before each oral chemotherapy dose and/or Dexamethasone 8mg PO daily before each dose.

ANTIEMETIC TAKE-HOME REGIMEN:
Level C Days 1-42 Concurrent
- Prochlorperazine 10mg PO q4-6h pm.

Level C Day 6 post radiation
- Ondansetron 8mg PO BID or Granisetron 2mg PO daily for 1 day after chemotherapy.
- Prochlorperazine 10mg PO q4-6h pm.

ANCILLARY:
- Handle with gloves.

TOXICITIES:
Hematologic
1. If ANC < 1.5 x 10⁹/L, or if PLT < 100 x 10⁹/L on Day 1, HOLD dose for 5-7 days.

Renal Failure
1. If CrCl < 1.0 mL/sec, REDUCE dose by 25-50%.

SUGGESTED ACTION
Central Nervous System

TEMOZOLOMIDE Concomitant & Adjuvant Chemotherapy

CLINICAL MONITORING:

Fever
1. 38.0 - 39.0°C (100.4 - 102.2°F)  
2. >39.0 - 40.0°C (102.3 - 104.0°F)  
3. >40.0°C (>104.0°F) for < 24 hrs  
4. > 40.0°C (>104.0°F) for >24 hrs  
5. Death

Nausea
1. Loss of appetite without alteration in eating habits  
2. Oral intake decreased without significant weight loss, dehydration or malnutrition; IV fluids indicated < 24 hrs  
3. Inadequate oral caloric or fluid intake; IV fluids, tube feedings, or TPN indicated ≥24 hrs  
4. Life-threatening consequences  
5. Death

Vomiting
1. 1 episode in 24 hrs  
2. 2-5 episodes in 24 hrs; IV fluids indicated < 24 hrs  
3. >6 episodes in 24 hrs; IV fluids, or TPN indicated ≥24 hrs  
4. Life-threatening consequences  
5. Death

RATED AT EACH CLINIC VISIT

INTERNAL CODE:
OPIS CODE: TEMOZOL-75 CN

REFERENCES:

Date revised: 02/10/2009
**Central Nervous System**

**VINCERISTINE-chemoradiotherapy CISPLATIN-CYCLOPHOSPHAMIDE-VINCERISTINE Chemotherapy**
Combined Modality; Medulloblastoma

**Order Group 1**

**VINCERISTINE**
1.5mg/m² IV Day 1 Round to nearest 0.1mg
- Mix in 50mL bag **Normal Saline**; Infuse over 10 minutes.
- Maximum dose is 2mg.

**RADIATION** IV Day 1
Technique: craniospinal
Modality: 6 MV photons
Dose Specification: 100% isodose
Total Dose: 36 Gy craniospinal and 19.8 Gy boost to posterior fossa
Fraction Dose: 1.8 Gy per fraction
Pattern: daily RT

REPEAT EVERY 7 DAYS during radiotherapy for a total of 6 doses

**Order Group 2: Maintenance Chemotherapy**

**CISPLATIN**
75mg/m² IV Day 1 Round to nearest 1mg
- Mix in 500mL bag **Normal Saline**; Infuse over 60 minutes.

**CYCLOPHOSPHAMIDE**
1000mg/m² IV Day 2 & 3 Round to nearest 10mg
- Mix in 250-500mL bag **Normal Saline**; Infuse over 20-30 minutes

**VINCERISTINE**
1.5mg/m² IV Day 1 & 8 Round to nearest 0.1mg
- Mix in 50mL bag **Normal Saline**; Infuse over 10 minutes.
- Maximum dose is 2mg.

REPEAT EVERY 28 DAYS for 6 cycles

**HYDRATION:**

Pre - Infuse 1000mL **Normal Saline** with 20mEq **Potassium Chloride** IV over 2 hours before Cisplatin.

Concurrent - Give 250mL of 20% Mannitol solution (50G) IV; Infuse through sidearm concurrent with Cisplatin.

Post - Infuse 1000mL **Normal Saline** with 10mEq **Potassium Chloride** & 2G **Magnesium Sulfate** IV over 2 hours after Cisplatin.

**TESTS:**
Baseline Tests: WBC HB PLT ANC Ca K Na Chloride Mg Glucose Cr Urea T.Bili Albumin AST ALT GGT AlkPhosphatase

Day 1 (order group 1) WBC HB PLT ANC
Day 1 (order group 2) WBC HB PLT ANC K Na Chloride Mg Cr Urea
Day 8 (order group 2) WBC HB PLT ANC

Test Notes: - Additional Baseline tests: LDH & CO₂
- Baseline & routine renal function tests, especially if there are other concurrent nephrotoxic drugs.

**ANTIEMETIC PRE-CHEMO REGIMEN:**

**Level A** Day 1 (group 1) - Prochlorperazine 10mg PO pm

**Level C** Day 1 (group 2) - Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
- Dexamethasone 20mg PO/IV
- May add Aprepitant 125mg PO before chemo (reduce PO Dexamethasone by 50%)

**ANTIEMETIC TAKE-HOME REGIMEN:**

**Level A** Day 1 (group 1) - Prochlorperazine 10mg PO q4-6h pm

**Level C** Day 1 (group 2) - Ondansetron 8mg PO BID for 2-3 days, or Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days.
- Dexamethasone 8mg PO BID for 2-3 days;
- May add Aprepitant 80mg PO on Days 2&3 (reduce PO Dexamethasone by 50%) - Prochlorperazine 10mg PO q4-6h pm

**PATIENT VISITS and APPOINTMENT TYPE:**

- Day 1 15min Type A
- Day 1 6hrs Type D
- Day 2&3 1hr Type B

**ANCILLARY:**
- Oral hydration is strongly encouraged; poorly hydrated patients may need more IV hydration (to prevent renal toxicity).

**TOXICITIES:**

Hematologic
1. If ANC < 1.5 x 10⁹/L, or if PLT < 100 x 10⁹/L, HOLD chemotherapy for 1 week.
Central Nervous System

VINCRISTINE-chemoradiotherapy CISPLATIN-CYCLOPHOSPHAMIDE-VINCRISTINE Chemotherapy

Renal Failure
1. If CrCl = 0.5-1.0 mL/sec, or SrCr = 136-185 umol/L, REDUCE Cisplatin to 50% dose.
2. If CrCl < 0.5 mL/sec, or SrCr > 185 umol/L, OMIT Cisplatin dose.

Hepatic Dysfunction
1. If T.Bili = 26-51 umol/L, or AST = 60-180 IU/L, REDUCE Vincristine to 50% dose.
2. If T.Bili = 52-85 umol/L, or AST > 180 IU/L, REDUCE Vincristine to 25% dose, and Cyclophosphamide to 75% dose.
3. If T.Bili > 85 umol/L, OMIT all drugs.

Neurologic
1. If Neurotoxicity > Grade 2, HOLD Vincristine dose for 1 week or until resolved.
2. If severe paresthesia or foot drop, REDUCE Vincristine to 50% dose.

SUGGESTED ACTION

CLINICAL MONITORING:
- Baseline renal function tests (if failure suspected) and liver function tests (especially if poor Performance Status).
- Urinalysis (RBCs) periodic and in response to patient complaint.
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.

Sensory
1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function
2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interferring with ADL
3. Sensory alteration or paresthesia interfering with ADL
4. Disabling
5. Death

Hearing
1. Asymptomatic, detected on exam/testing only
2. Symptomatic, not interfering with ADL
3. Symptomatic, interfering with ADL
4. Life-threatening; disabling
5. Death

Constipation
1. Occasional or intermittent symptoms; occasional use of stool softeners, laxatives, dietary modification, or enema
2. Persistent symptoms with regular use of laxatives or enemas indicated
3. Symptoms interfering with ADL; obstruction with manual evacuation indicated
4. Life-threatening consequences (e.g., obstruction, toxic megacolon)
5. Death

RATED AT EACH CLINIC VISIT

FORMULAE:
CrCl - Cockcroft & Gault (mL/sec)  Male: [140-age(ys)] x TBW(Kg) / [50 x SCr(umol/L)]
CrCl - Cockcroft & Gault (mL/sec)  Female: [140-age(ys)] x TBW(Kg) / [50 x SCr(umol/L)] x 0.85
Creatinine Cl  (mL/min)  mL/min = 60 x CrCl mL/sec

INTERNAL CODE:
OPIS CODE: VINCR-CCV

CCO Eligibility Form Required  Non-Formulary Form Required  Date revised: 11/25/2008

Central Nervous System
CAPECITABINE 2500mg/m²/day PO Days 1-14 150mg & 500mg tablets
- **Divided into BID dosing** for 14 days (1250mg/m² twice daily).
- For elderly, poor performance status or extensively pretreated patients, start at 1000mg/m² BID.
- Outpatient prescription available in 150mg and 500mg tablets.
- Trade name is Xeloda™

**TESTS:**
Baseline Tests: WBC HB PLT ANC K Na Cr Urea AST ALT AlkPhosphatase
Day 1: WBC HB PLT ANC
Test Notes: Weekly INR for patients on Warfarin until stable, then Day 1 only.

**ANTIEMETIC TAKE-HOME REGIMEN:**
Level A Days 1-14 - Prochlorperazine 10mg PO q4-6h prn

**ANCILLARY:**
- Take tablets WITH FOOD (within 30 minutes of a meal).
**TOXICITIES:**
**Gastrointestinal**
1. If any Toxicity Score = Grade 2, HOLD Capecitabine until score = 0 or 1, resume at 100% of dose (if second occurrence, resume at 75% dose, third occurrence at 50%, if fourth occurrence STOP Capecitabine).
2. If any Toxicity Score = Grade 3, HOLD Capecitabine until score = 0 or 1, resume at 75% dose or 1000mg/m² BID (if second occurrence, resume at 50%, if third occurrence STOP Capecitabine).
3. If any Toxicity Score = Grade 4, STOP Capecitabine.

**CLINICAL MONITORING:**
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.
- Skin assessment, especially extremities.
- Routine assessment of diarrhea.
**Diarrhea**
1. Increase of < 4 stools per day over baseline; mild increase in ostomy output compared to baseline
2. Increase of 4 - 6 stools per day over baseline; IV fluids indicated < 24hrs; moderate increase in ostomy output compared to baseline; not interfering with ADL 3. Increase of ≥ 7 stools per day over baseline; incontinence; IV fluids ≥ 24 hrs; hospitalization; severe increase in ostomy output compared to baseline; interfering with ADL 4. Life-threatening consequences (e.g., hemodynamic collapse) 5. Death

**Hand-foot Skin Reaction**
1. Minimal skin changes or dermatitis (e.g., erythema) without pain 2. Skin changes (e.g., peeling, blisters, bleeding, edema) or pain, not interfering with function 3. Ulcerative dermatitis or skin changes with pain interfering with function

RATED AT EACH CLINIC VISIT

**REFERENCES:**

Date revised: 10/27/2008
**CAPECITABINE-IRINOTECAN Chemotherapy**  
*Metastatic Colorectal Carcinoma*

### CAPECITABINE

<table>
<thead>
<tr>
<th>Dosage</th>
<th>Route</th>
<th>Duration</th>
<th>Tablets</th>
</tr>
</thead>
<tbody>
<tr>
<td>2000mg/m²/day</td>
<td>PO</td>
<td>Days 1-14</td>
<td>150mg &amp; 500mg tablets</td>
</tr>
</tbody>
</table>

- Divided into 1000mg/m² BID for 14 days.
- Start evening of day 1 and continue BID until morning of day 15.
- If renal impairment or age > 65, DECREASE Capecitabine dose to 750mg/m² BID.
- Outpatient prescription available in 150mg and 500mg tablets.
- Trade name is Xeloda™

### IRINOTECAN

<table>
<thead>
<tr>
<th>Dosage</th>
<th>Route</th>
<th>Duration</th>
<th>Preparation</th>
</tr>
</thead>
<tbody>
<tr>
<td>100mg/m²</td>
<td>IV</td>
<td>Days 1 &amp; 8</td>
<td>Round to nearest 1mg</td>
</tr>
</tbody>
</table>

- Admix in 250mL bag 5% Dextrose or Normal Saline over 30-90 minutes.
- If renal impairment or age > 65, DECREASE Irinotecan dose to 80mg/m².

### ATROPINE

<table>
<thead>
<tr>
<th>Dosage</th>
<th>Route</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.25-1mg</td>
<td>SC</td>
<td>Days 1 &amp; 8</td>
</tr>
</tbody>
</table>

- May be given pre-chemo to prevent cholinergic adverse effects or within 1 hour post-chemo for acute-onset diarrhea.
- Check BP and HR every 30 minutes x2 and until patient stable.

### LOPERAMIDE

<table>
<thead>
<tr>
<th>Dosage</th>
<th>Route</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>2mg</td>
<td>PO</td>
<td>Days 1, 8 &amp; prn</td>
</tr>
</tbody>
</table>

- 4mg PO at the onset of diarrhea, then 2mg q2h PO until patient is diarrhea free for 12 hours.
- May give 4mg q4h during night time.

### TESTS:

- Baseline Tests: WBC HB PLT ANC Cr Urea T.Bili ALT AlkPhosphatase
- Day 1: WBC HB PLT ANC Cr Urea T.Bili ALT AlkPhosphatase
- Day 8: WBC HB PLT ANC

- Weekly INR for patients on Warfarin until stable, then Day 1 only.

### ANTIEMETIC PRE-CHEMO REGIMEN:

**Level C**

- Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
- Dexamethasone 12mg PO/IV
- AVOID Prochlorperazine on the day(s) Irinotecan is administered.

### ANTIEMETIC TAKE-HOME REGIMEN:

**Level A**

- Prochlorperazine 10mg PO q4-6h pm starting Day 2 of treatment
- AVOID Prochlorperazine on the day(s) Irinotecan is administered.

### PATIENT VISITS and APPOINTMENT TYPE:

- Days 1 & 8 60min Type B

### ANCILLARY:

- Take Capecitabine tablets WITH FOOD (within 30 minutes of a meal).
- Treatment or Prophylaxis to Prevent Hand-Foot Skin Reaction: Take Pyridoxine (Vitamin B6) PO 100mg BiD or 50mg TID continuously. Apply Lac-Hydrin™ Lotion to hands and feet once or twice daily.

### TOXICITIES:

**Hematologic**

1. If ANC < 1.5 x10⁹/L, HOLD Capecitabine & Irinotecan for 1 week (or until ANC ≥ 1.5 x10⁹/L), then restart chemotherapy (no reduction).
2. If ANC < 1.0 x10⁹/L, HOLD Capecitabine & Irinotecan for 1 week (or until ANC ≥ 1.5 x10⁹/L), then restart chemotherapy reduced by 25%.
3. If ANC < 0.5 x10⁹/L, HOLD Capecitabine & Irinotecan for 1 week (or until ANC ≥ 1.5 x10⁹/L), then restart chemotherapy reduced by 50%.

**Gastrointestinal**

1. If Diarrhea = grade 2, HOLD Capecitabine & Irinotecan until score 0 or 1, restart at 100%.
2. If Diarrhea = grade 3, HOLD Capecitabine & Irinotecan until grade 0-1, then restart treatment reduced by 25%.
3. If Diarrhea = grade 4, HOLD Capecitabine & Irinotecan until grade 0-1, then restart treatment reduced by 50% or Discontinue Treatment.

**Hepatic Dysfunction**

1. Irinotecan has not been studied in patients with T.Bili > 35umol/L, transaminase > 3 x ULN if no liver metastases, or transaminase > 5 x ULN with liver metastases.

**SUGGESTED ACTION**
CAPECITABINE-IRINOTECAN Chemotherapy

CLINICAL MONITORING:
- Routine assessment of diarrhea, at each clinic visit.
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.
- Skin assessment, especially for hand-foot syndrome.

Diarrhea
1. Increase of < 4 stools per day over baseline; mild increase in ostomy output compared to baseline
2. Increase of 4 - 6 stools per day over baseline; IV fluids indicated < 24hrs; moderate increase in ostomy output compared to baseline; not interfering with ADL
3. Increase of ≥7 stools per day over baseline; incontinence; IV fluids > 24 hrs; hospitalization; severe increase in ostomy output compared to baseline; interfering with ADL
4. Life-threatening consequences (e.g., hemodynamic collapse)
5. Death

Hand-foot Skin Reaction
1. Minimal skin changes or dermatitis (e.g., erythema) without pain
2. Skin changes (e.g., peeling, blisters, bleeding, edema) or pain, not interfering with function
3. Ulcerative dermatitis or skin changes with pain interfering with function

RATED AT EACH CLINIC VISIT

CCO Eligibility Form Required ✔️ Non-Formulary Form Required ☐ Date revised: 10/27/2008
Gastrointestinal

CISPLATIN-ETOPOSIDE Chemotherapy
Advanced Gastric Carcinoma

CISPLATIN
25mg/m² IV Days 1-3 Round to nearest 1mg
- Admix in 250mL bag Normal Saline.
- Infuse over 30-60 minutes.
- May also admix 10G Mannitol (50mL of 20% solution or 100mL of 10% solution) with Cisplatin.

ETOPOSIDE
100mg/m² IV Days 1-3 Round to nearest 10mg
- Dose ≤ 200mg, mix in 500mL Normal Saline; Infuse over 30-60 minutes.
- Dose > 200mg, mix in 1000mL Normal Saline; Infuse over 120 minutes.
- Use Non-PVC equipment and filter.
- Adjust rate if blood pressure drops.
- Give Etoposide BEFORE Cisplatin, to hydrate patient.
REPEAT EVERY 21 DAYS

TESTS:
Baseline Tests WBC HB PLT ANC K Na T.Bili Albumin AST ALT GGT AlkPhosphatase
Day 1 K Na Cr
Test Notes - Baseline & routine renal function tests, especially if there are other concurrent nephrotoxic drugs.

ANTIEMETIC PRE-CHEMO REGIMEN:
Level C Days 1-3 - Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
- Dexamethasone 20mg PO/IV

ANTIEMETIC TAKE-HOME REGIMEN:
Level B/C Days 1-3 - Ondansetron 8mg PO BID for 2-3 days, or
Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days
- Dexamethasone 8mg PO BID for 2-3 days
- Prochlorperazine 10mg PO q4-6h prn

PATIENT VISITS and APPOINTMENT TYPE:
→ Days 1-3 2hrs Type C

ANCILLARY:
- Oral hydration strongly encouraged; poorly hydrated patients may need more IV hydration (to prevent renal toxicity).
- Adjust rate of Etoposide infusion if blood pressure drops.

TOXICITIES:
Hematologic
1. If ANC < 1.5 x 10⁹/L, or if PLT < 100 x 10⁹/L, HOLD dose for 1 week.
Renal Failure
1. If CrCl = 0.5-1.0mL/sec, or SrCr = 136-185umol/L, REDUCE to 50% dose.
2. If CrCl < 0.5mL/sec, or SrCr > 185umol/L, OMIT dose.
Hepatic Dysfunction
1. If T.Bili = 26-51umol/L, or AST = 60-180 IU/L, REDUCE to 50% dose.
2. If T.Bili = 52-85umol/L, REDUCE to 25% dose.
3. If T.Bili > 85umol/L, or AST > 180 IU/L, OMIT dose.
SUGGESTED ACTION

CLINICAL MONITORING:
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.
Sensory
1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function 2.
Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL 3. Sensory alteration or paresthesia interfering with ADL 4. Disabling 5. Death
Hearing
1. Asymptomatic, detected on exam/testing only 2. Symptomatic, not interfering with ADL
3. Symptomatic, interfering with ADL 4. Life-threatening; disabling 5. Death
RATED AT EACH CLINIC VISIT

FORMULAE:
CrCl - Cockcroft & Gault (ml/sec)
Male: [(140-age(yrs)] x TBW(Kg)) / [50 x SrCr(umol/L)]
Female: [(140-age(yrs)] x TBW(Kg)) / [50 x SrCr(umol/L)] x 0.85

CCO Eligibility Form Required Non-Formulary Form Required Date revised: 10/27/2008
CISPLATIN Weekly-FLUOROURACIL Continuous Infusion Chemotherapy
Squamous Cell Carcinoma of Esophagus or Anus

CISPLATIN
25mg/m² IV Day 1 each week Round to nearest 1mg
- Mix in 250mL bag Normal Saline, Infuse over 30-60 minutes.
- May also admix 100G Mannitol (50mL of 20% solution or 100mL of 10% solution) with Cisplatin.

5-FLUOROURACIL
225mg/m²/day IV Days 1-7 Round to nearest 25mg
- Continuous 7 day infusion via Infusor LV1.5 (1.5mL/hr) pump.
- Infusion through central venous access device (PICC) is recommended.
- Protect from light.

CONTINUOUS TREATMENT FOR 5-26 WEEKS (as tolerated)

HYDRATION:

Pre
- Infuse 500mL bag Normal Saline IV over 1 hour before Cisplatin.

TESTS:
Baseline Tests
WBC HB PLT ANC Ca K Na Chloride Glucose Cr Urea 24Hr CrCl T.Bili
Albumin ALT GGT AlkPhosphatase

Day 1 (weekly)
WBC HB PLT ANC K Na Chloride Mg Cr Urea

ANTIEMETIC PRE-CHEMO REGIMEN:
Level C
Day 1
- Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
- Dexamethasone 20mg PO/IV

ANTIEMETIC TAKE-HOME REGIMEN:
Level B/C
Day 1
- Ondansetron 8mg PO BID for 2-3 days, or
- Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days
- Dexamethasone 8mg PO BID for 2-3 days
- Prochlorperazine 10mg PO q4-6h prn

PATIENT VISITS and APPOINTMENT TYPE:

Day 1 2hrs Type C

ANCILLARY:
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.

TOXICITIES:
Hematologic
1. If ANC < 1.5 x 10⁹/L or if PLT < 100 x 10⁹/L, HOLD for 1 week.

Renal Failure
1. If SrCr > 110umol/L, HOLD Cisplatin dose for 1 week.

Hepatic Dysfunction
1. If T.Bili > 85umol/L, (marked hepatic dysfunction), OMIT dose.

Gastrointestinal
1. If mucositis or diarrhea > Grade 3 in previous course, REDUCE to 2/3 dose 5-FU.
SUGGESTED ACTION

CLINICAL MONITORING:
Sensory
1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function
2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL
3. Sensory alteration or paresthesia interfering with ADL
4. Disabling
5. Death

Hearing
1. Asymptomatic, detected on exam/testing only
2. Symptomatic, not interfering with ADL
3. Symptomatic, interfering with ADL
4. Life-threatening; disabling
5. Death

Diarrhea
1. Increase of < 4 stools per day over baseline; mild increase in ostomy output compared to baseline
2. Increase of 4 - 6 stools per day over baseline; IV fluids indicated < 24hrs; moderate increase in ostomy output compared to baseline; not interfering with ADL
3. Increase of > 7 stools per day over baseline; incontinence; IV fluids > 24hrs; hospitalization; severe increase in ostomy output compared to baseline; interfering with ADL
4. Life-threatening consequences (e.g., hemodynamic collapse)
5. Death

Mucositis
1. Erythema of the mucosa
2. Patchy ulcerations or pseudomembranes
3. Confluent ulcerations or pseudomembranes; bleeding with minor trauma
4. Tissue necrosis; significant spontaneous bleeding; life-threatening consequences
5. Death
RATED AT EACH CLINIC VISIT

FORMULAE:
CrCl - Cockcroft & Gault

\[ \text{CrCl (mL/sec)} = \left( \frac{140 - \text{age (yrs)}}{\text{TBW (Kg)}} \right) \times 72 \times \frac{\text{Scr (umol/L)}}{88.4} \]

\[ \text{CrCl (mL/sec)} = \left( \frac{140 - \text{age (yrs)}}{\text{TBW (Kg)}} \right) \times 72 \times \frac{\text{Scr (umol/L)}}{88.4} \times 0.85 \]

INTERNAL CODE:
OPIS CODE: CISP-FUC IV GI

CCO Eligibility Form Required [ ] Non-Formulary Form Required [ ] Date revised: 10/27/2008

Gastrointestinal
DOXORUBICIN Chemotherapy

Advanced Gastrointestinal or Endocrine Cancer

**DOXORUBICIN**

15-20mg/m² IV Day 1 Round to nearest 1mg

- Slow push through sidearm of free flowing IV. Give 2 to 4mg (1-2mL) per minute.

**TESTS:**

<table>
<thead>
<tr>
<th>Baseline Tests</th>
<th>WBC  HB  PLT  ANC  K  Na  Cr  T.Bili  Albumin  ALT  AlkPhosphatase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1</td>
<td>WBC  HB  PLT  ANC</td>
</tr>
</tbody>
</table>

**ANTIEMETIC PRE-CHEMO REGIMEN:**

**Level C** Day 1
- Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
- Dexamethasone 20mg PO/IV

**ANTIEMETIC TAKE-HOME REGIMEN:**

**Level B/C** Day 1
- Ondansetron 8mg PO BID for 2-3 days, or Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days
- Dexamethasone 8mg PO BID for 2-3 days
- Prochlorperazine 10mg PO q4-6h pm

**PATIENT VISITS and APPOINTMENT TYPE:**

- Day 1 60min Type C

**TOXICITIES:**

**Hematologic**
1. If ANC < 1.5 x 10⁹/L, or if PLT < 100 x 10⁹/L, **HOLD** dose for 1 week.

**Renal Failure**
1. If SrCr > 265umol/L, **REDUCE** dose to 50%

**Hepatic Dysfunction**
1. If T.Bili = 26-51umol/L or AST = 60-180 IU/L, **GIVE** 75% dose.
2. If T.Bili = 52-85umol/L or AST > 180 IU/L, **GIVE** 50% dose.
3. If T.Bili > 85umol/L, **OMIT** dose.

**SUGGESTED ACTION**

**CLINICAL MONITORING:**
- Clinical exam for symptoms of CHF.
- Periodic cardiac tests for all patients with cardiac risk factors and patients at or above the threshold dose levels.

**LV Systolic Dysfunction:**
1. Asymptomatic, resting ejection fraction (EF) < 60 - 50%; shortening fraction (SF) < 30 - 24%
2. Asymptomatic, resting EF < 50 - 40%; SF < 24 - 15%
3. Symptomatic CHF responsive to intervention; EF < 40 - 20%; SF < 15%
4. Refractory CHF or poorly controlled; EF < 20%; intervention such as ventricular assist device, ventricular reduction surgery, or heart transplant indicated
5. Death

**For Cardiac Toxicity Ratings:** First rating at the cumulative dose threshold of 450mg/m², and repeat ratings at each cumulative dose increment of 100mg/m² above threshold. (Cumulative dose sooner for high risk patients, eg. pre-existing cardiac disease, prior chest irradiation).

**Note:** Threshold Cumulative dose reduced proportionately if other anthracycline or anthracenedione drugs have been given; cardiotoxicity is additive.

**INTERNAL CODE:**

OPIS CODE: DOXO-LO GI

CCO Eligibility Form Required [ ]
Non-Formulary Form Required [ ]

**Date revised:** 10/27/2008
**EPIRUBICIN-CARBOPLATIN-FLUOROURACIL**

**Chemotherapy**

*Advanced Gastric Carcinoma - Palliative Intent*

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Day</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>EPIRUBICIN</td>
<td>50mg/m²</td>
<td>IV</td>
<td>Day 1</td>
<td>Round to nearest 1mg</td>
</tr>
<tr>
<td>- Slow push through sidearm of free flowing IV at a rate of 10mg/5ml per minute.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CARBOPLATIN</td>
<td>AUC = 5</td>
<td>IV</td>
<td>Day 1</td>
<td>Round to nearest 5mg</td>
</tr>
<tr>
<td>- Mix in 250mL bag 5% Dextrose.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Infuse over 30-60 minutes.</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5-FLUOROURACIL</td>
<td>200mg/m²/day</td>
<td>IV</td>
<td>Days 1, 8 &amp; 15</td>
<td>Round to nearest 25mg</td>
</tr>
<tr>
<td>- Continuous 21 day infusion using ambulatory infusion pump (Infusor LV1.5) at 1.5mL/hr.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Exchange pump every 7 days (Days 1, 8 &amp; 15).</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Infusion through central venous access device (PICC) is recommended.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**REPEAT EVERY 21 DAYS**

**TESTS:**

<table>
<thead>
<tr>
<th>Baseline Tests</th>
<th>Days 8 &amp; 15 Tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC HB PLT ANC Ca K Na Chloride Mg Glucose Cr Urea 24Hr CrCl T.Bili Albumin ALT GGT AlkPhosphatase LVEF</td>
<td>WBC HB PLT ANC Ca K Na Chloride Cr Urea</td>
</tr>
</tbody>
</table>

**ANTIEMETIC PRE-CHEMO REGIMEN:**

**Level C**

- Day 1 - Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
- Dexamethasone 20mg PO/IV

**ANTIEMETIC TAKE-HOME REGIMEN:**

**Level B/C**

- Day 1 - Ondansetron 8mg PO BID for 2-3 days, or Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days
- Dexamethasone 8mg PO BID for 2-3 days
- Prochlorperazine 10mg PO q4-6h pm
- Prochlorperazine 10mg PO q4-6h pm

**Level A**

- Days 8 & 15 - Prochlorperazine 10mg PO q4-6h prn

**PATIENT VISITS and APPOINTMENT TYPE:**

- Day 1  2hrs  Type C
- Days 8 & 15  10min (Pump exchange)  Type A

**TOXICITIES:**

**Hematologic**

1. If ANC < 1.5 x 10⁹/L, or if PLT = 75-100 x 10⁹/L, HOLD chemotherapy for 1 week.

**Renal Failure**

1. Adjust Carboplatin dose if estimated CrCl changes > 10%.

2. If SrCr > 265umol/L, REDUCE Epirubicin dose to 50%.

**Hepatic Dysfunction**

1. If T.Bili = 26-51umol/L, or AST = 60-180 IU/L, GIVE 75% Epirubicin dose.

2. If T.Bili = 52-85umol/L, or AST > 180 IU/L, GIVE 50% Epirubicin dose.

3. If T.Bili > 85umol/L, OMIT Epirubicin & 5-FU doses.

**Gastrointestinal**

1. If Mucositis or Diarrhea > Grade 3 in previous course, REDUCE to 2/3 dose of 5-FU.

SUGGESTED ACTION
CLINICAL MONITORING:
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.
- Skin assessment, especially extremities.
- Hearing and neurologic toxicity ratings (sensory) each visit.
- Clinical exam for symptoms of CHP.
- Periodic cardiac tests for all patients with cardiac risk factors and patients at or above the threshold dose levels.
- Serious, irreversible cardiomyopathy with delayed congestive heart failure may be encountered as the cumulative dose of Epirubicin approaches 1000mg/m². Cardiac monitoring is advised when cumulative dose exceeds 650mg/m².

Sensory
1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function
2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL
3. Sensory alteration or paresthesia interfering with ADL
4. Disabling
5. Death

Hearing
1. Asymptomatic, detected on exam/testing only
2. Symptomatic, not interfering with ADL
3. Symptomatic, interfering with ADL
4. Life-threatening; disabling
5. Death

Diarrhea
1. Increase of < 4 stools per day over baseline; mild increase in ostomy output compared to baseline
2. Increase of 4 - 6 stools per day over baseline; IV fluids indicated < 24hrs; moderate increase in ostomy output compared to baseline; not interfering with ADL
3. Increase of >7 stools per day over baseline; incontinence; IV fluids >24hrs; hospitalization; severe increase in ostomy output compared to baseline; interfering with ADL
4. Life-threatening consequences (e.g., hemodynamic collapse)
5. Death

Mucositis
1. Erythema of the mucosa
2. Patchy ulcerations or pseudomembranes
3. Confluent ulcerations or pseudomembranes; bleeding with minor trauma
4. Tissue necrosis; significant spontaneous bleeding; life-threatening consequences
5. Death

RATED AT EACH CLINIC VISIT

FORMULAE:

CrCl - Cockcroft & Gault (mL/sec)

Male: \[
\frac{[140-\text{age(yrs)}] \times \text{TBW(Kg)}}{[50 \times \text{SCr(umol/L)}]}
\]

Female: \[
\frac{[140-\text{age(yrs)}] \times \text{TBW(Kg)}}{[50 \times \text{SCr(umol/L)}] \times 0.85}
\]

Creatinine Cl (mL/min)

Dose (in mg) = target AUC x (GFR + 25)

GFR in mL/min

CCO Eligibility Form Required
Non-Formulary Form Required

Date revised: 10/27/2008
**GI - ECF**

**Gastrointestinal**

### EPIRUBICIN-CISPLATIN-FLUOROURACIL Chemotherapy

*Advanced Gastric Carcinoma - Palliative Intent*

<table>
<thead>
<tr>
<th>Medication</th>
<th>50mg/m²/IV</th>
<th>Day 1</th>
<th>Round to nearest 1mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>EPIRUBICIN</td>
<td>50mg/m²/IV</td>
<td>Day 1</td>
<td>Round to nearest 1mg</td>
</tr>
<tr>
<td>- Slow push through sidearm of free flowing IV at a rate of 10mg/5ml per minute.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CISPLATIN</td>
<td>60mg/m²/IV</td>
<td>Day 1</td>
<td>Round to nearest 1mg</td>
</tr>
<tr>
<td>- Mix in 500mL bag Normal Saline.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Infuse over 60 minutes. (Maximum dose = 150mg).</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5-FLUOROURACIL</td>
<td>200mg/m²/day</td>
<td>Days 1, 8 &amp; 15</td>
<td>Round to nearest 25mg</td>
</tr>
<tr>
<td>- Continuous 21 day infusion using ambulatory infusion pump at 1.5mL/hr (Infusor LV1.5).</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Exchange pump every 7 days (Days 1,8 &amp; 15).</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Infusion through central venous access device (PICC) is recommended.</td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

**REPEAT EVERY 21 DAYS**

#### HYDRATION:

- **Pre:**
  - Infuse 1000mL Normal Saline with 20mEq Potassium Chloride IV over 2 hours before Cisplatin.

- **Concurrent:**
  - May give 250mL of 20% Mannitol solution (50G) IV; Infuse through side arm concurrent with Cisplatin (if diuresis is required).

- **Post:**
  - Infuse 500mL Normal Saline with 10mEq Potassium Chloride; (2G Magnesium Sulfate may be added) over 1 hour after Cisplatin.
  - Increase fluids if poor intake.

#### TESTS:

- **Baseline Tests**
  - WBC HB PLT ANC Ca K Na Chloride Mg Glucose Cr Urea 24Hr CrCl T.Bili Albumin ALT AlkPhosphatase LVEF

- **Days 8 & 15**
  - WBC HB PLT ANC Ca Na Chloride Cr Urea

- **Day 1**
  - WBC HB PLT ANC Ca Na Chloride Cr Urea Cr T.Bili

- **Test Notes:**
  - Calcium may be checked every couple of cycles.

#### ANTIEMETIC PRE-CHEMO REGIMEN:

**Level C**

- Day 1 - Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
- Dexamethasone 20mg PO/IV

**Level B/C**

- Day 1 - Ondansetron 8mg PO BID for 2-3 days, or Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days
- Dexamethasone 8mg PO BID for 2-3 days
- Prochlorperazene 10mg PO q4-6h prn
- Prochlorperazene 10mg PO q4-6h prn

**Level A**

- Days 8 & 15 - Prochlorperazene 10mg PO q4-6h prn

#### PATIENT VISITS and APPOINTMENT TYPE:

- **Day 1**
  - 4-5hrs Type D
- **Days 8 & 15 (Pump Exchange)**
  - 10min Type A

#### TOXICITIES:

**Hematologic**

1. If ANC < 1.5 x 10⁹/L, or if PLT = 75-100 x 10⁹/L, HOLD chemotherapy for 1 week.

**Renal Failure**

1. If renal function has not returned to normal (CrCl >1.0mL/sec or SrCr >136umol/L) by day 1 of cycle, **DISCONTINUE** CISPLATIN.

2. If SrCr > 265umol/L, REDUCE Epirubicin dose to 50%.

**Hepatic Dysfunction**

1. If T.Bili = 26-51umol/L, or AST = 60-180 IU/L, GIVE 75% Epirubicin dose.

2. If T.Bili > 52-85umol/L, or AST > 180 IU/L, GIVE 50% Epirubicin dose.

3. If T.Bili > 85umol/L, **OMIT** Epirubicin and 5-FU doses.

**Gastrointestinal**

1. If Mucositis or Diarrhea ≥ Grade 3 in previous course, REDUCE to 2/3 dose of 5-FU.

**SUGGESTED ACTION**
CLINICAL MONITORING:
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.
- Skin assessment, especially extremities.
- Hearing and neurologic toxicity ratings (sensory) each visit.
- Clinical exam for symptoms of CHF.
- Periodic cardiac tests for all patients with cardiac risk factors and patients at or above the threshold dose levels.
- Serious, irreversible cardiomyopathy with delayed congestive heart failure may be encountered as the cumulative dose approaches 1000mg/m². Cardiac monitoring is advised when cumulative dose exceeds 650mg/m².

Sensory
1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function
2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL
3. Sensory alteration or paresthesia interfering with ADL
4. Disabling
5. Death

Hearing
1. Asymptomatic, detected on exam/testing only
2. Symptomatic, not interfering with ADL
3. Symptomatic, interfering with ADL
4. Life-threatening; disabling
5. Death

Diarrhea
1. Increase of < 4 stools per day over baseline; mild increase in ostomy output compared to baseline
2. Increase of 4 - 6 stools per day over baseline; IV fluids indicated < 24hrs; moderate increase in ostomy output compared to baseline; not interfering with ADL
3. Increase of ≥7 stools per day over baseline; incontinence; IV fluids >24 hrs; hospitalization; severe increase in ostomy output compared to baseline; interfering with ADL
4. Life-threatening consequences (e.g., hemodynamic collapse)
5. Death

Mucositis
1. Erythema of the mucosa
2. Patchy ulcerations or pseudomembranes
3. Confluent ulcerations or pseudomembranes; bleeding with minor trauma
4. Tissue necrosis; significant spontaneous bleeding; life-threatening consequences
5. Death

RATED AT EACH CLINIC VISIT

FORMULAE:

CrCl - Cockcroft & Gault (mL/sec)
Male: \[
\frac{140 - \text{age (yrs)}}{\text{TBW (Kg)}} \times \frac{\text{TBW (Kg)}}{[50 \times \text{SCr (umol/L)}]}
\]

CrCl - Cockcroft & Gault (mL/sec)
Female: \[
\frac{140 - \text{age (yrs)}}{\text{TBW (Kg)}} \times \frac{\text{TBW (Kg)}}{[50 \times \text{SCr (umol/L)}] \times 0.85}
\]

Date revised: 10/27/2008
EPIRUBICIN-CISPLATIN-CAPECITABINE Chemotherapy
Advanced Esophagogastric Carcinoma - Palliative Intent

**EPIRUBICIN**
50mg/m² IV Day 1 Round to nearest 1mg
- Slow push through sidearm of free flowing IV at a rate of 10mg/5ml per minute.

**CISPLATIN**
60mg/m² IV Day 1 Round to nearest 1mg
- Mix in 500mL bag Normal Saline.
- Infuse over 60 minutes.
  (Maximum dose = 150mg)

**CAPECITABINE**
1250mg/m²/day PO Day 1 150mg & 500mg tablets
- Divided into BID dosing for 21 days (625mg/m² twice daily).
- Outpatient prescription available in 150mg and 500mg tablets.
- Trade name is Xeloda™

**HYDRATION:**
Pre:
- Infuse 1000mL Normal Saline with 20mEq Potassium Chloride IV over 2 hours before Cisplatin.
Concurrent:
- May give 250mL of 20% Mannitol solution (50G) IV; Infuse through side arm concurrent with Cisplatin (if diuresis is required).
Post:
- Infuse 500mL Normal Saline with 10mEq Potassium Chloride; (2G Magnesium Sulfate may be added) over 1 hour after Cisplatin.
- Increase fluids if poor intake.

**TESTS:**
Baseline Tests: WBC HB PLT ANC Ca K Na Chloride Mg Glucose Cr Urea 24Hr CrCl T.Bili Albumin ALT AlkPhosphatase LVEF

**ANTIEMETIC PRE-CHEMO REGIMEN:**
Level C Day 1
- Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
- Dexamethasone 20mg PO/IV

**ANTIEMETIC TAKE-HOME REGIMEN:**
Level B/C Day 1
- Ondansetron 8mg PO BID for 2-3 days, or Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days
- Dexamethasone 8mg PO BID for 2-3 days
- Prochlorperazine 10mg PO q4-6h prn

**PATIENT VISITS and APPOINTMENT TYPE:**
Day 1 4-5hrs Type D

**TOXICITIES:**

**Hematologic**
1. If ANC < 1.5 x 10⁹/L, or if PLT <100 x 10⁹/L, HOLD chemotherapy for 1 week.

**Renal Failure**
1. If renal function has not returned to normal (CrCl >1.0mL/sec or SrCr >136umol/L) by day 1 of cycle, DISCONTINUE CISPLATIN.
2. If SrCr > 265umol/L, REDUCE Epirubicin dose to 50%.

**Hepatic Dysfunction**
1. If T.Bili = 26-51umol/L, or AST = 60-180 IU/L, GIVE 75% Epirubicin dose.
2. If T.Bili = 52-85umol/L, or AST > 180 IU/L, GIVE 50% Epirubicin dose.
3. If T.Bili > 85umol/L, OMIT Epirubicin and 5-FU doses.

**Gastrointestinal**
1. If any Toxicity Score = Grade 2, HOLD Capecitabine until = 0 or 1, resume at 100% of dose (if second occurrence, resume at 75% dose, third occurrence at 50%, if fourth occurrence STOP Capecitabine).
2. If any Toxicity Score = Grade 3, HOLD Capecitabine until score = 0 r 1, resume at 75% dose (if second occurrence, resume at 50%, if third occurrence STOP Capecitabine).

**SUGGESTED ACTION**
CLINICAL MONITORING:
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.
- Skin assessment, especially extremities.
- Routine assessment of Diarrhea.
- Hearing and neurologic toxicity ratings (sensory) each visit.
- Clinical exam for symptoms of CHF.
- Periodic cardiac tests for all patients with cardiac risk factors and patients at or above the threshold dose levels.
- Serious, irreversible cardiomyopathy with delayed congestive heart failure may be encountered as the cumulative dose approaches 1000mg/m². Cardiac monitoring is advised when cumulative dose exceeds 650mg/m².

Sensory
1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function 2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL 3. Sensory alteration or paresthesia interfering with ADL 4. Disabling 5. Death

Hearing
1. Asymptomatic, detected on exam/testing only 2. Symptomatic, not interfering with ADL 3. Symptomatic, interfering with ADL 4. Life-threatening; disabling 5. Death

Diarrhea
1. Increase of < 4 stools per day over baseline; mild increase in ostomy output compared to baseline
2. Increase of 4 - 6 stools per day over baseline; IV fluids indicated < 24hrs; moderate increase in ostomy output compared to baseline; not interfering with ADL 3. Increase of ≥ 7 stools per day over baseline; incontinence; IV fluids >24 hrs; hospitalization; severe increase in ostomy output compared to baseline; interfering with ADL 4. Life-threatening consequences (e.g., hemodynamic collapse) 5. Death

Hand-foot Skin Reaction
1. Minimal skin changes or dermatitis (e.g. erythema) without pain 2. Skin changes (e.g. peeling, blisters, bleeding, edema) or pain, not interfering with function 3. Ulcerative dermatitis or skin changes with pain interfering with function

RATED AT EACH CLINIC VISIT

FORMULAE:
CrCl - Cockcroft & Gault (mL/sec) Male: \[\frac{[140 - \text{age(yrs)}] \times \text{TBW(Kg)}}{[50 \times \text{Scr(umol/L)}]}\]
CrCl - Cockcroft & Gault (mL/sec) Female: \[\frac{[140 - \text{age(yrs)}] \times \text{TBW(Kg)}}{[50 \times \text{Scr(umol/L)}] \times 0.85}\]

CCO Eligibility Form Required □ Non-Formulary Form Required □ Date revised: 11/14/2008
GI - Gastrointestinal

**EPIRUBICIN-OXALIPLATIN-FLUOROURACIL Chemotherapy**

*Advanced Esophagogastric Carcinoma - Palliative Intent*

**EPIRUBICIN**

- **50mg/m² IV Day 1**
  - Round to nearest 1mg
  - Slow push through sidearm of free flowing IV at a rate of 10mg/5ml per minute.

**OXALIPLATIN**

- **130mg/m² IV Day 1**
  - Round to nearest 2.5mg
  - Mix in 500mL bag 5% Dextrose; Infuse over 120 minutes.
  - DO NOT MIX IN SALINE.

**5-FLUOROURACIL**

- **200mg/m²/day IV Days 1, 8 & 15**
  - Continuous 21 day infusion using ambulatory infusion pump at 1.5mL/hr (Infusor LV1.5).
  - Exchange pump every 7 days (Days 1,8 & 15).
  - Infusion through central venous access device (PICC) is recommended.
  - Repeat every 21 days to a maximum of 8 cycles

**HYDRATION:**

- Pre
  - Infuse 250mL 5% Dextrose in Water with 1g/10mL Calcium gluconate 10% and 1g/2mL Magesium sulfate 50% IV over 15 minutes before Chemotherapy.

- Post
  - Infuse 250mL 5% Dextrose in Water with 1g/10mL Calcium gluconate 10% and 1g/2mL Magesium sulfate 50% IV over 15 minutes post Chemotherapy.

**TESTS:**

- Baseline Tests: WBC HB PLT ANC Ca K Na Chloride Mg Glucose Cr Urea 24Hr CrCl T.Bili Albumin ALT AlkPhosphatase LVEF
- Days 8 & 15: WBC HB PLT ANC K Na Chloride Cr Urea
- Day 1: WBC HB PLT ANC K Na Chloride Cr Urea T.Bili

**Test Notes**: Calcium may be checked every couple of cycles.

**ANTIEMETIC PRE-CHEMO REGIMEN:**

- **Level C**
  - Day 1: Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
  - Dexamethasone 20mg PO/IV

**ANTIEMETIC TAKE-HOME REGIMEN:**

- **Level B/C**
  - Day 1: Ondansetron 8mg PO BID for 2-3 days, or Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days
  - Dexamethasone 8mg PO BID for 2-3 days
  - Prochlorperazine 10mg PO q4-6h prn
  - Prochlorperazine 10mg PO q4-6h prn

- **Level A**
  - Days 8 & 15

**PATIENT VISITS and APPOINTMENT TYPE:**

- Day 1 4hrs Type D
- Days 8 & 15 (Pump Exchange) 10min Type A

**TOXICITIES:**

**Hematologic**

1. If ANC < 1.5 x 10⁹/L, or if PLT < 100 x 10⁹/L, HOLD chemotherapy for 1 week.

**Neurologic**

1. If paresthesia/dysethesias are of short duration that resolve and do not interfere with function, maintain dose.
2. If paresthesias/dysethesias interfere with function, but not activities of daily living (ADL), and are parewent at start of next cycle, decrease Oxaliplatin by 15mg/m².
3. If paresthesias/dysethesias (with pain or with functional impairment) interfere with daily living and are present at the start of next cycle, discontinue Oxaliplatin.
4. If pharyngo-laryngeal dysethesias, increase duration of Oxaliplatin infusion to 6 hours.

**Hepatic Dysfunction**

1. If T.Bili = 26-51umol/L, or AST = 60-180 IU/L, GIVE 75% Epirubicin dose.
2. If T.Bili = 52-85umol/L, or AST > 180 IU/L, GIVE 50% Epirubicin dose.
3. If T.Bili > 85umol/L, OMIT Epirubicin and 5-FU doses.

**Gastrointestinal**

1. If Mucositis or Diarrhea > Grade 3 in previous course, REDUCE to 2/3 dose of 5-FU.

**SUGGESTED ACTION**
EPIRUBICIN-OXALIPLATIN-FLUOROURACIL Chemotherapy

CLINICAL MONITORING:
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.
- Skin assessment, especially extremities.
- Neurologic toxicity ratings (sensory) each visit.
- Clinical exam for symptoms of CHF.
- Periodic cardiac tests for all patients with cardiac risk factors and patients at or above the threshold dose levels.
- Serious, irreversible cardiomyopathy with delayed congestive heart failure may be encountered as the cumulative dose approaches 1000mg/m². Cardiac monitoring is advised when cumulative dose exceeds 650mg/m².

Sensory
1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function
2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL
3. Sensory alteration or paresthesia interfering with ADL
4. Disabling
5. Death

Diarrhea
1. Increase of < 4 stools per day over baseline; mild increase in ostomy output compared to baseline
2. Increase of 4 - 6 stools per day over baseline; IV fluids indicated < 24hrs; moderate increase in ostomy output compared to baseline; not interfering with ADL
3. Increase of >7 stools per day over baseline; incontinence; IV fluids >24 hrs; hospitalization; severe increase in ostomy output compared to baseline; interfering with ADL
4. Life-threatening consequences (e.g., hemodynamic collapse)
5. Death

Mucositis
1. Erythema of the mucosa
2. Patchy ulcerations or pseudomembranes
3. Confluent ulcerations or pseudomembranes; bleeding with minor trauma
4. Tissue necrosis; significant spontaneous bleeding; life-threatening consequences
5. Death

RATED AT EACH CLINIC VISIT

FORMULAE:
- \( \text{CrCl - Cockcroft & Gault} \ (\text{mL/sec}) = \frac{140 - \text{age(yrs)}}{\text{TBW(Kg)}} \times \frac{\text{SCr(umol/L)}}{50} \)
- \( \text{CrCl - Cockcroft & Gault} \ (\text{mL/sec}) \ 0.85 \) for females

CCO Eligibility Form Required: □ Non-Formulary Form Required: ✓ Date revised: 11/14/2008
Gastrointestinal

EPIRUBICIN-OXALIPLATIN-CAPECITABINE Chemotherapy
Advanced Esophagogastric Carcinoma - Palliative Intent

**EPIRUBICIN**
- **50mg/m²** IV Day 1
  - **Slow push through sidearm of free flowing IV** at a rate of 10mg/5ml per minute.

**OXALIPLATIN**
- **130mg/m²** IV Day 1
  - Mix in 500mL bag 5% Dextrose; Infuse over 120 minutes.
  - DO NOT MIX IN SALINE.

**CAPECITABINE**
- **1250mg/m²/day** IV Days 1
  - Divided into BID dosing for 21 days (625mg/m² twice daily).
  - Outpatient prescription available in 150mg and 500mg tablets.
  - Trade name is Xeloda™

**REPEAT EVERY 21 DAYS TO A MAXIMUM OF 8 CYCLES**

**HYDRATION:**

**Pre**
  - Infuse 250mL 5% Dextrose in Water with 1g/10mL Calcium gluconate 10% and 1g/2mL Magesium sulfate 50% IV over 15 minutes before Chemotherapy.

**Post**
  - Infuse 250mL 5% Dextrose in Water with 1g/10mL Calcium gluconate 10% and 1g/2mL Magesium sulfate 50% IV over 15 minutes post Chemotherapy.

**TESTS:**

**Baseline Tests**
- WBC HB PLT ANC Ca K Na Chloride Mg Glucose Cr Urea 24Hr CrCl T.Bili
- Albumin ALT AlkPhosphatase LVEF

**Day 1**
- WBC HB PLT ANC K Na Chloride Cr Urea T.Bili

**Test Notes**
- Calcium may be checked every couple of cycles.

**ANTIEMETIC PRE-CHEMO REGIMEN:**

**Level C**
- Day 1
  - Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
  - Dexamethasone 20mg PO/IV

**ANTIEMETIC TAKE-HOME REGIMEN:**

**Level B/C**
- Day 1
  - Ondansetron 8mg PO BID for 2-3 days, or
  - Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days
  - Dexamethasone 8mg PO BID for 2-3 days
  - Prochlorperazine 10mg PO q-4-6h prn

**PATIENT VISITS and APPOINTMENT TYPE:**
- Day 1 4hrs Type D

**TOXICITIES:**

**Hematologic**
1. If ANC < 1.5 x 10⁹/L, or if PLT < 100 x 10⁹/L, HOLD chemotherapy for 1 week.

**Neurologic**
1. If paresthesia/dysesthesias are of short duration that resolve and do not interfere with function, maintain dose.
2. If paresthesias/dysesthesias interfere with function, but not activities of daily living (ADL), and are parawent at start of next cycle, decrease Oxaliplatin by 15mg/m².
3. If paresthesias/dysesthesias (with pain or with functional impairment) interfere with daily living and are present at the start of next cycle, discontinue Oxaliplatin.
4. If pharyngo-laryngeal dysesthesias, increase duration of Oxaliplatin infusion to 6 hours.

**Hepatic Dysfunction**
1. If T.Bili = 26-51umol/L, or AST = 60-180 IU/L, GIVE 75% Epirubicin dose.
2. If T.Bili = 52-85umol/L, or AST > 180 IU/L, GIVE 50% Epirubicin dose.
3. If T.Bili > 85umol/L, OMIT Epirubicin and 5-FU doses.

**Gastrointestinal**
1. If any Toxicity Score = Grade 2, HOLD Capecitabine until = 0 or 1, resume at 100% of dose (if second occurrence, resume at 75% dose, third occurrence at 50%, if fourth occurrence STOP Capecitabine).
2. If any Toxicity Score = Grade 3, HOLD Capecitabine until score = 0 r 1, resume at 75% dose (if second occurrence, resume at 50%, if third occurrence STOP Capecitabine).

**SUGGESTED ACTION**
Gastrointestinal

EPIRUBICIN-OXALIPLATIN-CAPECITABINE Chemotherapy

**CLINICAL MONITORING:**
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.
- Skin assessment, especially extremities.
- Neurologic toxicity ratings (sensory) each visit.
- Clinical exam for symptoms of CHF.
- Periodic cardiac tests for all patients with cardiac risk factors and patients at or above the threshold dose levels.
- Serious, irreversible cardiomyopathy with delayed congestive heart failure may be encountered as the cumulative dose approaches 1000mg/m². Cardiac monitoring is advised when cumulative dose exceeds 650mg/m².

**Sensory**
1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function.
2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL.
3. Sensory alteration or paresthesia interfering with ADL.
4. Disabling.
5. Death.

**Diarrhea**
1. Increase of < 4 stools per day over baseline; mild increase in ostomy output compared to baseline.
2. Increase of 4 - 6 stools per day over baseline; IV fluids indicated < 24hrs; moderate increase in ostomy output compared to baseline; not interfering with ADL.
3. Increase of >7 stools per day over baseline; incontinence; IV fluids >24 hrs; hospitalization; severe increase in ostomy output compared to baseline; interfering with ADL.
4. Life-threatening consequences (e.g., hemodynamic collapse).
5. Death.

**Mucositis**
1. Erythema of the mucosa.
2. Patchy ulcerations or pseudomembranes.
3. Confluent ulcerations or pseudomembranes; bleeding with minor trauma.
4. Tissue necrosis; significant spontaneous bleeding; life-threatening consequences.
5. Death.

**Hand-foot Skin Reaction**
1. Minimal skin changes or dermatitis (e.g., erythema) without pain.
2. Skin changes (e.g., peeling, blisters, bleeding, edema) or pain, not interfering with function.
3. Ulcerative dermatitis or skin changes with pain interfering with function.

**RATED AT EACH CLINIC VISIT**

**FORMULAE:**

\[
\text{CrCl} - \text{Cockcroft & Gault (mL/sec)} \quad \text{Male:} \quad \frac{[140-\text{age(yrs)}] \times \text{TBW(Kg)}}{[50 \times \text{SCr(umol/L)}]}
\]

\[
\text{CrCl} - \text{Cockcroft & Gault (mL/sec)} \quad \text{Female:} \quad \frac{[140-\text{age(yrs)}] \times \text{TBW(Kg)}}{[50 \times \text{SCr(umol/L)}] \times 0.85}
\]

**Date revised:** 11/14/2008
Low Dose 5-FLUOROURACIL (375, 400 or 425)-
LEUCOVORIN

Advanced Colorectal/Gastric Carcinoma: Adjuvant Rectal Carcinoma

5-FLUOROURACIL

- 375, 400 or 425mg/m²
- IV Days 1-5
- Round to nearest 25mg
- Inject by direct IV push over 1-3 minutes, followed by a Normal Saline flush.
- Patients are recommended to suck on ice chips about 5 minutes before treatment begins until 30 minutes after treatment is completed to reduce the incidence and severity of stomatitis.
- Administer immediately following Leucovorin.

LEUCOVORIN

- 20mg/m²
- IV Days 1-5
- Round to nearest 1mg
- Inject by direct IV push, followed by a Normal Saline flush (if no IV line has been set up).
- May give by slow push through sidearm of free flowing IV (D5W, Normal Saline).
- Do not exceed 160mg/min.
- REPEAT EVERY 28 DAYS (Adjuvant- For a Total of 6 Months)
- During concurrent radiotherapy administration: Give 5-FU & Leucovorin on Days 1 to 4 only

TESTS:

Baseline Tests
- WBC
- HB
- PLT
- ANC
- Ca
- K
- Na
- Chloride
- Glucose
- Cr
- Urea
- T.Bili
- Albumin
- ALT
- GGT
- AlkPhosphatase

Day 1
- WBC
- HB
- PLT
- ANC

ANTIEMETIC PRE-CHEMO REGIMEN:

Level A
- Day 1
- Prochlorperazine 10mg PO/IV pm

ANTIEMETIC TAKE-HOME REGIMEN:

Level A
- Days 1-5
- Prochlorperazine 10mg PO q4-6h prn

PATIENT VISITS and APPOINTMENT TYPE:

- Days 1-5
- 10min
- Type A

ANCILLARY:
- Sucking ice chips during 5-Fluorouracil treatment is recommended to reduce mucositis following chemotherapy.

TOXICITIES:

Hematologic
1. If ANC < 1.5 x 10^9/L, or if PLT < 100 x 10^9/L, REDUCE to 75% dose.
2. If ANC < 1.0 x 10^9/L, or if PLT < 75 x 10^9/L, HOLD dose for 1 week.

Hepatic Dysfunction
1. If T.Bili > 85umol/L (marked hepatic dysfunction), OMIT dose.

Gastrointestinal
1. If Mucositis or diarrhea > Grade 3 in previous course, REDUCE to 2/3 dose.

SUGGESTED ACTION

CLINICAL MONITORING:
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.

Diarrhea
1. Increase of < 4 stools per day over baseline; mild increase in ostomy output compared to baseline
2. Increase of 4 - 6 stools per day over baseline; IV fluids indicated < 24hrs; moderate increase in ostomy output compared to baseline; not interfering with ADL. 3. Increase of >7 stools per day over baseline; incontinence; IV fluids >24 hrs; hospitalization; severe increase in ostomy output compared to baseline; interfering with ADL. 4. Life-threatening consequences (e.g., hemodynamic collapse) 5. Death

Mucositis
1. Erythema of the mucosa
2. Patchy ulcerations or pseudomembranes
3. Confluent ulcerations or pseudomembranes; bleeding with minor trauma
4. Tissue necrosis; significant spontaneous bleeding; life-threatening consequences
5. Death

RATED AT EACH CLINIC VISIT

INTERNAL CODE:

OPIS CODES:
- FL-375
- FL-400
- FL-425

REFERENCES:

Date revised: 10/27/2008
**Oxaliplatin-Leucovorin-Fluorouracil**

**Bolus Chemotherapy**

### Gastrointestinal

#### Oxaliplatin

85mg/m² IV Day 1, 15 & 29 Round to nearest 2.5mg
- Mix in 500mL bag 5% Dextrose; Infuse over 120 minutes BEFORE Leucovorin.
- DO NOT MIX IN SALINE.

#### Leucovorin

500mg/m² IV Day 1, 8, 15, 22, 29 & 36
- Mix in 250ml D5W.
- Infuse over 120 minutes AFTER Oxaliplatin on Days 1, 15 & 29, but before 5-fluorouracil.
(Oxaliplatin and leucovorin were not given concurrently in the trial)

#### 5-Fluorouracil

400mg/m² IV Day 1, 8, 15, 22, 29 & 36
- Inject by direct IV push over 1-3 minutes, given 1 hour after leucovorin infusion has begun.

**Tests:**

Baseline Tests
- WBC HB PLT ANC Cr Urea T.Bili ALT AlkPhosphatase

Day 1
- WBC HB PLT ANC Cr T.Bili ALT AlkPhosphatase

**Antiemetic Pre-Chemo Regimen:**

**Level C**

- Day 1, 15 & 29
  - Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
  - Dexamethasone 20mg PO/IV

**Level B**

- Day 8, 22 & 36
  - Prochlorperazine 10mg PO

**Antiemetic Take-Home Regimen:**

**Level B/C**

- Day 1, 15 & 29
  - Ondansetron 8mg PO BID for 2-3 days, or
  - Granisetron 1mg PO 12 hours post chemotherapy, then
  - 2mg PO OD for 2-3 days
  - Dexamethasone 8mg PO BID for 2-3 days
  - Prochlorperazine 10mg PO q4-6h prn

**Patient Visits and Appointment Type:**

- Day 1, 15 & 29 4.5hrs Type D
- Day 8, 22 & 36 2.5 hours Type C

**Ancillary:**

- NO CRYOTHERAPY.

Option:

- Give Calcium gluconate 1g/10mL and Magnesium sulfate 50% 1g/2mL admix into 250mL Dextrose 5% in water infuse over 15 minutes before and after chemotherapy.

**Toxicities:**

### Hematologic

1. If ANC < 1.5 x 10⁹/L, or if PLT < 100 x 10⁹/L, HOLD 1 week, then check weekly and treat as follows:
   - If ANC 1.0-1.49 x 10⁹/L, or if PLT 50-100 x 10⁹/L, MAINTAIN dose level.
   - If ANC 0.5-0.99 x 10⁹/L, or if PLT 10-49.9 x 10⁹/L, DECREASE: Oxaliplatin by 10mg/m², Leucovorin remains the same, 5-FU bolus by 80mg/m².
   - If AGC < 0.5 x 10⁹/L or if PLT < 10 x 10⁹/L, DECREASE: Oxaliplatin by 35mg/m², Leucovorin remains the same, 5-FU bolus by 160mg/m².

### Gastrointestinal

1. If Grade > 2 diarrhea within 24 hours of start of cycle, HOLD and check weekly then treat as follows:
   - If Diarrhea = grade 1 or 2, MAINTAIN dose level.
   - If Diarrhea = grade 3, DECREASE 5-FU bolus by 80mg/m².

### Hepatic Dysfunction

1. If T.Bili > 85umol/L (marked hepatic dysfunction), OMIT dose.

### Neurologic

1. If paresthesias/dysesthesias are of short duration that resolve and do not interfere with function, maintain dose.
2. If paresthesias/dysesthesias interfere with function, but not activities of daily living, and are present at start of next cycle, decrease Oxaliplatin to 75mg/m².
3. If paresthesias/dysesthesias (with pain or with functional impairment) interfere with daily living and are present at the start of next cycle, discontinue Oxaliplatin.
4. If pharyngo-laryngeal dysesthesias, increase duration of Oxaliplatin infusion to 6 hours.
GI - FLOX-ADJ

**OXALIPLATIN-LEUCOVORIN-FLUOROURACIL**

**BOLUS Chemotherapy**

**CLINICAL MONITORING:**
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.
- Skin assessment, especially extremities.

**Sensory**
1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function
2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL
3. Sensory alteration or paresthesia interfering with ADL
4. Disabling
5. Death

**Diarrhea**
1. Increase of < 4 stools per day over baseline; mild increase in ostomy output compared to baseline
2. Increase of 4 - 6 stools per day over baseline; IV fluids indicated < 24hrs; moderate increase in ostomy output compared to baseline; not interfering with ADL
3. Increase of ≥7 stools per day over baseline; incontinence; IV fluids ≥24 hrs; hospitalization; severe increase in ostomy output compared to baseline; interfering with ADL
4. Life-threatening consequences (e.g., hemodynamic collapse)
5. Death

**CrCl - Cockcroft & Gault (mL/sec)**
Female: \[\frac{140 - \text{age(yrs)}}{72} \times \text{TBW(Kg)}} \div \left[50 \times \text{Scr(umol/L)} \right] \times 0.85\]

**INTERNAL CODE:**
- FLOX-ADJ

**REFERENCES:**
- CCO Practice Guidelines: Adjuvant Systemic Chemotherapy for Stage II and III Colon Cancer Following Complete Resection.

**Date last revised:** 11/14/2008
**GI-FLW**

**Gastrointestinal Weekly Low Dose 5-FLUOROURACIL (375, 400 or 425) - LEUCOVORIN**

**Advanced Colorectal/Gastric Carcinoma**

**5-FLUOROURACIL**

375, 400 or 425mg/m² IV Day 1 Round to nearest 25mg

- **Inject by direct IV push over 1-3 minutes**, followed by a Normal Saline flush.
- Patients are recommended to suck on ice chips about 5 minutes before treatment begins until 30 minutes after treatment is completed to reduce the incidence and severity of stomatitis.
- Administer immediately following Leucovorin.

**LEUCOVORIN**

20mg/m² IV Day 1 Round to nearest 1mg

- **Inject by direct IV push**, followed by a Normal Saline flush (if no IV line has been set up).
- May give by slow push through sidearm of free flowing IV (D5W, Normal Saline).
- Do not exceed 160mg/min.

**REPEAT EVERY 7 DAYS**

**TESTS:**

<table>
<thead>
<tr>
<th>Baseline Tests</th>
<th>WBC HB PLT ANC Ca K Na Chloride Glucose Cr Urea T.Bili Albumin ALT GGT AlkPhosphatase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1</td>
<td>WBC HB PLT ANC</td>
</tr>
</tbody>
</table>

**ANTIEMETIC PRE-CHEMO REGIMEN:**

**Level A**

Day 1 - Prochlorperazine 10mg PO/IV pm

**ANTIEMETIC TAKE-HOME REGIMEN:**

**Level A**

Day 1 - Prochlorperazine 10mg PO q4-6h pm

**PATIENT VISITS and APPOINTMENT TYPE:**

Day 1 10min Type A

**ANCILLARY:**

- Sucking ice chips during 5-Fluorouracil treatment is recommended to reduce mucositis following chemotherapy.

**TOXICITIES:**

**Hematologic**

1. If ANC < 1.5 x 10⁹/L, or if PLT < 100 x 10⁹/L, REDUCE to 75% dose.
2. If ANC < 1.0 x 10⁹/L, or if PLT < 75 x 10⁹/L, HOLD dose for 1 week.

**Hepatic Dysfunction**

1. If T.Bili > 85umol/L (marked hepatic dysfunction), OMIT dose.

**Gastrointestinal**

1. If Mucositis or diarrhea > Grade 3 in previous course, REDUCE to 2/3 dose.

**SUGGESTED ACTION**

**CLINICAL MONITORING:**

- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.

**Diarrhea**

1. Increase of < 4 stools per day over baseline; mild increase in ostomy output compared to baseline
2. Increase of 4 - 6 stools per day over baseline; IV fluids indicated < 24hrs; moderate increase in ostomy output compared to baseline; not interfering with ADL 3. Increase of >7 stools per day over baseline; incontinence; IV fluids >24 hrs; hospitalization; severe increase in ostomy output compared to baseline; interfering with ADL 4. Life-threatening consequences (e.g., hemodynamic collapse) 5. Death

**Mucositis**

1. Erythema of the mucosa  2. Patchy ulcerations or pseudomembranes  3. Confluent ulcerations or pseudomembranes; bleeding with minor trauma  4. Tissue necrosis; significant spontaneous bleeding; life-threatening consequences  5. Death

**RATED AT EACH CLINIC VISIT**

**INTERNAL CODE:**

<table>
<thead>
<tr>
<th>OPIS CODES</th>
<th>- FLW-375</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>- FLW-400</td>
</tr>
<tr>
<td></td>
<td>- FLW-425</td>
</tr>
</tbody>
</table>

**Date revised:** 10/27/2008

**CCO Eligibility Form Required**

**Non-Formulary Form Required**
Gastrointestinal Weekly High Dose 5-FLUOROURACIL-LEUCOVORIN
Advanced Colorectal/Gastric Carcinoma:Adjuvant Rectal Carcinoma

5-FLUOROURACIL
370mg/m² IV Day 1
- Inject by direct IV push over 1-3 minutes, followed by a Normal Saline flush.
- Patients are recommended to suck on ice chips about 5 minutes before treatment begins until 30 minutes after treatment is completed to reduce the incidence and severity of stomatitis.
- Administer immediately following Leucovorin.

LEUCOVORIN
200mg/m² IV Day 1
- Mix in 50mL minibag (doses >100mg) or 100mL (doses>500mg) of Normal Saline or 5% Dextrose.
- Infuse over 15-30 minutes.
- Do not exceed 160mg/min.

REPEAT EVERY 7 DAYS

TESTS:
Baseline Tests: WBC HB PLT ANC K Na Cr Urea T.Bili Albumin ALT GGT AlkPhosphatase
Day 1 WBC HB PLT ANC

ANTIEMETIC PRE-CHEMO REGIMEN:
Level A Day 1
- Prochlorperazine 10mg PO/IV pm

ANTIEMETIC TAKE-HOME REGIMEN:
Level A Day 1
- Prochlorperazine 10mg PO q4-6h pm

PATIENT VISITS and APPOINTMENT TYPE:
Day 1: 45min Type B

ANCILLARY:
- Sucking ice chips during 5-Fluorouracil treatment is recommended to reduce mucositis following chemotherapy.
- The injection must not exceed 160mg/min of leucovorin (due to calcium content).

TOXICITIES:
Hematologic
1. If ANC < 1.5 x 10⁹/L, or if PLT < 100 x 10⁹/L, REDUCE to 75% dose.
2. If ANC < 1.0 x 10⁹/L, or if PLT < 75 x 10⁹/L, HOLD dose for 1 week.

Hepatic Dysfunction
1. If T.Bili > 85umol/L (marked hepatic dysfunction), OMIT dose.

Gastrointestinal
1. If Mucositis or diarrhea > Grade 3 in previous course, REDUCE to 2/3 dose.

SUGGESTED ACTION
CLINICAL MONITORING:
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.

Diarrhea
1. Increase of < 4 stools per day over baseline; mild increase in ostomy output compared to baseline
2. Increase of 4 - 6 stools per day over baseline; IV fluids indicated < 24hrs; moderate increase in ostomy output compared to baseline; not interfering with ADL
3. Increase of >7 stools per day over baseline; incontinence; IV fluids >24 hrs; hospitalization; severe increase in ostomy output compared to baseline; interfering with ADL
4. Life-threatening consequences (e.g., hemodynamic collapse)
5. Death

Mucositis
1. Erythema of the mucosa
2. Patchy ulcerations or pseudomembranes
3. Confluent ulcerations or pseudomembranes; bleeding with minor trauma
4. Tissue necrosis; significant spontaneous bleeding; life-threatening consequences
5. Death

RATED AT EACH CLINIC VISIT

CCO Eligibility Form Required  [ ] Non-Formulary Form Required  [ ] Date revised: 10/27/2008
**Gastrointestinal**

**IRINOTECAN** - LEUCOVORIN- FLUOROURACIL BOLUS-INFUSION Chemotherapy

Metastatic Colorectal Carcinoma

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
<th>Route</th>
<th>Day</th>
<th>Duration</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>IRINOTECAN</strong></td>
<td>180mg/m²</td>
<td>IV</td>
<td>1</td>
<td>Round</td>
<td>To nearest 1mg</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>for 90 min</td>
<td>concurrently with Leucovorin.</td>
</tr>
<tr>
<td>-</td>
<td>Mix in 500mL bag 5% Dextrose or Normal Saline; Infuse over 90 minutes concurrently with Leucovorin.</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>ATROPINE</strong></td>
<td>0.25-1mg</td>
<td>SC</td>
<td>Day 1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>-</td>
<td>May be given pre-chemo to prevent cholinergic adverse effects or within 1 hour post-chemo for acute-onset diarrhea.</td>
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</tr>
<tr>
<td>-</td>
<td>Check BP and HR every 30 minutes x2 and until patient stable.</td>
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</tr>
<tr>
<td><strong>LOPERAMIDE</strong></td>
<td>2mg PO 2mg tablet</td>
<td>Day 1 &amp; pm</td>
<td></td>
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</tr>
<tr>
<td>-</td>
<td>4mg PO at the onset of diarrhea, then 2mg q2h PO until patient is diarrhea-free for 12 hours.</td>
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<tr>
<td>-</td>
<td>May give 4mg q4h during night time.</td>
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</tr>
<tr>
<td><strong>LEUCOVORIN</strong></td>
<td>400mg/m² Round to nearest 1mg</td>
<td>IV</td>
<td>Day 1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>-</td>
<td>Mix in 250mL D5W.</td>
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<tr>
<td>-</td>
<td>Infuse over 90 minutes concurrently with Irinotecan.</td>
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<td></td>
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</tr>
<tr>
<td><strong>5-FLUOROURACIL</strong></td>
<td>400mg/m² Round to nearest 25mg</td>
<td>IV</td>
<td>Day 1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>-</td>
<td>Inject by direct IV push over 1-3 minutes, followed by a Normal Saline flush.</td>
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<tr>
<td>-</td>
<td>Patients are recommended to suck on ice chips about 5 minutes before treatment begins until 30 minutes after treatment is completed to reduce the incidence and severity of stomatitis.</td>
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</tr>
<tr>
<td>-</td>
<td>Infuse after Irinotecan &amp; Leucovorin.</td>
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</tr>
<tr>
<td><strong>5-FLUOROURACIL</strong></td>
<td>1200mg/m² Round to nearest 25mg</td>
<td>IV</td>
<td>Days 1-2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>-</td>
<td>Continuous IV infusion for 46 hours via Infusor LV5 (5mL/hr) pump.</td>
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<tr>
<td>-</td>
<td>Infusional 5-FU doses may be escalated to 3000mg/m² at Cycle 3 if the patient has experienced less than or equal to Grade 2 toxicity.</td>
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<tr>
<td>-</td>
<td>Infusion through central venous access device (PICC) is recommended.</td>
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</tbody>
</table>

**REPEAT EVERY 14 DAYS**: Reassess after 12 cycles.

**TESTS:**

Baseline Tests: WBC HB PLT ANC Cr Urea T.Bili ALT GGT AlkPhosphatase

Day 1: WBC HB PLT ANC K Na Cr Urea T.Bili ALT

**ANTIEMETIC PRE-CHEMO REGIMEN:**

<table>
<thead>
<tr>
<th>Level</th>
<th>Day</th>
<th>Drug</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>C</td>
<td>Day 1</td>
<td>Ondansetron</td>
<td>8mg PO/IV or Granisetron 1mg PO/IV</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Dexamethasone</td>
<td>20mg PO/IV</td>
</tr>
<tr>
<td></td>
<td></td>
<td>AVOID Prochlorperazine on the day(s) Irinotecan is administered.</td>
<td></td>
</tr>
</tbody>
</table>

**ANTIEMETIC TAKE-HOME REGIMEN:**

<table>
<thead>
<tr>
<th>Level</th>
<th>Day 1</th>
<th>Drug</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>B/C</td>
<td></td>
<td>Ondansetron</td>
<td>8mg PO BID for 2-3 days, or Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Dexamethasone</td>
<td>8mg PO BID for 2-3 days</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Prochlorperazine</td>
<td>10mg PO q4-6h pm</td>
</tr>
<tr>
<td></td>
<td></td>
<td>AVOID Prochlorperazine on the day(s) Irinotecan is administered.</td>
<td></td>
</tr>
</tbody>
</table>

**PATIENT VISITS and APPOINTMENT TYPE:**

- Day 1 3hrs Type D
- Day 3 (Pump disconnect) 10min Type A

**ANCILLARY:**

- Sucking ice chips during 5-Fluorouracil treatment is recommended to reduce mucositis following chemotherapy.
- The injection must not exceed 160mg/min of leucovorin (due to calcium content).

**TOXICITIES:**

**Hematologic**

1. If ANC < 1.5 x 10⁹/L, or if PLT < 75 x 10⁹/L, **HOLD** 1 week, then check weekly and treat as follows:
2. If ANC 1.0-1.49 x 10⁹/L, or if PLT 50-74.9 x 10⁹/L, **MAINTAIN** dose level.
3. If ANC 0.5-0.99 x 10⁹/L, or if PLT 10-49.9 x 10⁹/L, **DECREASE**: Irinotecan by 30mg/m², Leucovorin remains the same, 5-FU bolus by 80mg/m², 5-FU infusion by 400mg/m².
4. If AGC < 0.5 x 10⁹/L, or if PLT < 10 x 10⁹/L, **DECREASE**: Irinotecan by 60mg/m², Leucovorin remains the same, 5-FU bolus by 160mg/m² and 5-FU infusion by 800mg/m².

**Gastrointestinal**

1. If Grade > 2 diarrhea within 24 hours of start of cycle, **HOLD** and check weekly then treat as follows:
2. If Diarrhea = grade 1 or 2, **MAINTAIN** dose level.
3. If Diarrhea = grade 3, **DECREASE** doses the same as Hematologic Toxicity # 3.
4. If Diarrhea = grade 4, **DECREASE** doses the same as Hematologic Toxicity # 4.
5. If Diarrhea > grade 2 after 2 weeks of treatment, **DISCONTINUE** therapy.
**Hepatic Dysfunction**

1. Irinotecan has not been studied in patients with T.Bili > 35umol/L, transaminase > 3 x ULN if no liver metastases, or transaminase > 5 x ULN with liver metastases.
2. If T.Bili > 85umol/L (marked hepatic dysfunction), OMIT 5-Fluorouracil.

**SUGGESTED ACTION**

**CLINICAL MONITORING:**

**Diarrhea**

1. Increase of < 4 stools per day over baseline; mild increase in ostomy output compared to baseline
2. Increase of 4 - 6 stools per day over baseline; IV fluids indicated < 24hrs; moderate increase in ostomy output compared to baseline; not interfering with ADL
3. Increase of >7 stools per day over baseline; incontinence; IV fluids >24 hrs; hospitalization; severe increase in ostomy output compared to baseline; interfering with ADL
4. Life-threatening consequences (e.g., hemodynamic collapse)
5. Death

**Mucositis**

1. Erythema of the mucosa
2. Patchy ulcerations or pseudomembranes
3. Confluent ulcerations or pseudomembranes; bleeding with minor trauma
4. Tissue necrosis; significant spontaneous bleeding; life-threatening consequences
5. Death

**REFERENCES:**


**Date revised:** 11/14/2008
IRINOTECAN- LEUCOVORIN- FLUOROURACIL BOLUS-INFUSION- BEVACIZUMAB Chemotherapy

*Used in combination with intravenous 5-Fluorouracil-based chemotherapy, indicated for first-line treatment of patients with metastatic carcinoma of the colon or rectum.*

**IRINOTECAN**
- 180mg/m² IV Day 1
- Mix in 500mL bag of 5% Dextrose or Normal Saline; Infuse over 90 minutes concurrently with Leucovorin.

**ATROPINE**
- 0.25-1mg SC Day 1
- May be given pre-chemo to prevent cholinergic adverse effects or within 1 hour post-chemo for acute-onset diarrhea.
- Check BP and HR every 30 minutes x2 and until patient stable.

**LOPERAMIDE**
- 2mg PO Day 1 & pm
- 4mg PO at the onset of diarrhea, then 2mg q2h PO until patient is diarrhea-free for 12 hours.
- May give 4mg q4h during night time. Compassionate Supply.

**LEUCOVORIN**
- 400mg/m² IV Day 1
- Mix in 250mL D5W.
- Infuse over 120 minutes concurrently with Irinotecan.

**5-FLUOROURACIL**
- 400mg/m² IV Day 1
- Inject by direct IV push over 1-3 minutes, followed by a Normal Saline flush.
- Patients are recommended to suck on ice chips about 5 minutes before treatment begins until 30 minutes after treatment is completed to reduce the incidence and severity of stomatitis.
- Infuse through central venous access device (PICC) is recommended.

**BEVACIZUMAB**
- 5mg/kg IV Day 1
- Admix to a total volume of 100mL Normal Saline (DO NOT MIX IN DEXTROSE).
- DO NOT ADMINISTER AS IV PUSH OR BOLUS.
- Infuse first dose over 30 minutes, if no reaction infuse subsequent doses over 10 minutes.
- Initial dose should be administered following chemotherapy, all subsequent doses can be given before or after chemotherapy.
- Blood pressure pre and post dose for first 3 cycles then pre only for subsequent cycles.

**TESTS:**
Baseline Tests: WBC HB PLT ANC Cr Urea T.Bili ALT GGT AlkPhosphatase
Day 1: WBC HB PLT ANC K Na Cr Urea T.Bili ALT

**ANTIEMETIC PRE-CHEMO REGIMEN:**
Level C: Day 1
- Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
- Dexamethasone 20mg PO/IV
- AVOID Prochlorperazine on the day(s) Irinotecan is administered.

**ANTIEMETIC TAKE-HOME REGIMEN:**
Level B/C: Day 1
- Ondansetron 8mg PO BID for 2-3 days, or Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days
- Dexamethasone 8mg PO BID for 2-3 days
- Prochlorperazine 10mg PO q4-6h pm
- AVOID Prochlorperazine on the day(s) Irinotecan is administered.

**PATIENT VISITS and APPOINTMENT TYPE:**
- Day 1 First dose: 4.5hrs Type E
- Day 1 Second dose: 4hrs Type E
- Day 1 Subsequent doses: 3.5hrs Type E
- Day 3 Pump disconnect: 10min Type A

**ANCILLARY:**
- Sucking ice chips during 5-Fluorouracil treatment is recommended to reduce mucositis following chemotherapy.
- The injection must not exceed 160mg/min of leucovorin (due to calcium content).
IRINOTECAN- LEUCOVORIN- FLUOROURACIL BOLUS-INFUSION- BEVACIZUMAB Chemotherapy

TOXICITIES:

Hematologic
1. If ANC < 1.5 x 10^9/L, or if PLT < 75 x 10^9/L, HOLD 1 week, then check weekly and treat as follows:
2. If ANC 1.0-1.49 x 10^9/L, or if PLT 50-74.9 x 10^9/L, MAINTAIN dose level.
3. If ANC 0.5-0.99 x 10^9/L, or if PLT 10-49.9 x 10^9/L, DECREASE: Irinotecan by 30mg/m², Leucovorin remains the same, 5-FU bolus by 80mg/m², 5-FU infusion by 400mg/m².
4. If AGC < 0.5 x 10^9/L, or if PLT < 10 x 10^9/L, DECREASE: Irinotecan by 60mg/m², Leucovorin remains the same, 5-FU bolus by 160mg/m² and 5-FU infusion by 800mg/m².

Gastrointestinal
1. If Grade > 2 diarrhea within 24 hours of start of cycle, HOLD and check weekly then treat as follows:
2. If Diarrhea = grade 1 or 2, MAINTAIN dose level.
3. If Diarrhea = grade 3, DECREASE doses the same as Hematologic Toxicity # 3.
4. If Diarrhea = grade 4, DECREASE doses the same as Hematologic Toxicity # 4.
5. If Diarrhea > grade 2 after 2 weeks of treatment, DISCONTINUE therapy.

Hepatic Dysfunction
1. Irinotecan has not been studied in patients with T.Bili > 35umol/L, transaminase > 3 x ULN if no liver metastases, or transaminase > 5 x ULN with liver metastases.
2. If T.Bili > 85umol/L (marked hepatic dysfunction), OMIT 5-Fluorouracil.

SUGGESTED ACTION

CLINICAL MONITORING:

Diarrhea
1. Increase of < 4 stools per day over baseline; mild increase in ostomy output compared to baseline
2. Increase of 4 - 6 stools per day over baseline; IV fluids indicated < 24hrs; moderate increase in ostomy output compared to baseline; not interfering with ADL 3. Increase of ≥7 stools per day over baseline; incontinence; IV fluids ≥24 hrs; hospitalization; severe increase in ostomy output compared to baseline; interfering with ADL 4. Life-threatening consequences (e.g., hemodynamic collapse) 5. Death

Mucositis
1. Erythema of the mucosa 2. Patchy ulcerations or pseudomembranes 3. Confluent ulcerations or pseudomembranes; bleeding with minor trauma 4. Tissue necrosis; significant spontaneous bleeding; life-threatening consequences 5. Death

RATED AT EACH CLINIC VISIT

Bevacizumab:
- Therapy with Bevacizumab should not be initiated for at least 28 days following major surgery.
- Administration can result in development of GI perforation and wound dehiscence.
- Discontinue Bevacizumab in patients with serious hemorrhage or recent hemoptysis.
- In patients with severe hypertension that is not controlled with medical management, Bevacizumab should be temporarily held. It should be permanently discontinued in cases of hypertensive crisis.
- Discontinue treatment in patients with nephrotic syndrome.

REFERENCES:

Date revised: 11/14/2008
GI FOLFIRI-CETUX

Gastrointestinal

IRINOTECAN- LEUCOVORIN- FLUOROURACIL BOLUS-INFUSION- CETUXIMAB Chemotherapy

Treatment of EGFR Expressing, Metastatic Colorectal Carcinoma in Patients who are Refractory to Irinotecan-based Chemotherapy

DIPHENHYDRAMINE 50mg IV Day 1
- Admix in 50-100mL minibag 5% Dextrose or Normal Saline.
- Give over 10-15 minutes 30 minutes before Cetuximab dose started.

CETUXIMAB 400mg/m² IV LOADING DOSE Round to nearest 1mg
- Add into an empty IV bag and infuse undiluted over 2 hours with 0.2 micron in-line filter. (Maximum infusion rate is 5mL/min).
- Give first before starting FOLFIRI. For the first dose, observe patients for 1 hour for infusion reactions after completion of the infusion.
- NON-FORMULARY FORM REQUIRED

LOADING DOSE - ADMINISTER ON DAY 1 ONLY

CETUXIMAB 250mg/m² IV MAINTENANCE Round to nearest 1mg
- Add into an empty IV bag and infuse undiluted over 1 hour with 0.2 micron in-line filter. (Maximum infusion rate is 5mL/min).
- Give first before starting FOLFIRI. For the first and second doses, observe patients for 1 hour for infusion reactions after completion of the infusion. All subsequent doses the observation period will be 30 minutes.

ATROPINE 0.25-1mg SC Day 1
- May be given pre-chemo to prevent cholinergic adverse effects or within 1 hour post-chemo for acute-onset diarrhea.
- Check BP and HR every 30 minutes x2 and until patient stable.

LOPERAMIDE 2mg PO Day 1 & prn 2mg tablet
- 4mg PO at the onset of diarrhea, then 2mg q2h PO until patient is diarrhea-free for 12 hours.
- May give 4mg q4h during night time. Compassionate Supply.

LEUCOVORIN 400mg/m² IV Day 1 Round to nearest 1mg
- Mix in 250mL D5W.
- Infuse over 120 minutes concurrently with Irinotecan.

5-FLUOROURACIL 180mg/m² IV Day 1 Round to nearest 1mg
- Mix in 500mL bag 5% Dextrose or Normal Saline; Infuse over 90 minutes concurrently with Leucovorin.

5-FLUOROURACIL 1200mg/m²/day IV Day 1-2 Round to nearest 25mg
- Continuous IV infusion for 46 hours via Infusor LV5 (5mL/hr) pump.
- Infusional 5-FU doses may be escalated to 3000mg/m² at Cycle 3 if the patient has experienced less than or equal to Grade 2 toxicity.
- Infusion through central venous access device (PICC) is recommended.

TESTS:
Baseline Tests WBC HB PLT ANC Cr Urea T.Bili ALT GGT AlkPhosphatase
Day 1 FOLFIRI WBC HB PLT ANC K Na Cr Urea T.Bili ALT
Test Notes Cetuximab - for use in patients with wild type K-RAS tumours

ANTIEMETIC PRE-CHEMO REGIMEN:
Level C Day 1 Folfiri
- Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
- Dexamethasone 20mg PO/IV
- AVOID Prochlorperazine on the day(s) Irinotecan is administered.

PATIENT VISITS and APPOINTMENT TYPE:
Day 1 FOLFIRI & Cetuximab 5.5hrs Type E

Gastrointestinal
Gastrointestinal

IRINOTECAN- LEUCOVORIN- FLUOROURACIL BOLUS-INFUSION- CETUXIMAB Chemotherapy

- Day 1 FOLFIRI & Cetuximab 4.5hrs Type E
- Day 1 Cetuximab only 2.5hrs Type C
- Day 3 (Pump disconnect) 10min Type A

ANCILLARY:
- Sucking ice chips during 5-Fluorouracil treatment is recommended to reduce mucositis following chemotherapy.
- The injection must not exceed 160mg/min of leucovorin (due to calcium content).
- Patients should limit sun exposure (sunscreen and hats) as it may exacerbate Cetuximab induced skin reactions.

TOXICITIES:

Hematologic
1. If ANC < 1.5 x 10⁹/L, or if PLT < 75 x 10⁹/L, HOLD 1 week, then check weekly and treat as follows:
2. If ANC 1.0-1.49 x 10⁹/L, or if PLT 50-74.9 x 10⁹/L, MAINTAIN dose level.
3. If ANC 0.5-0.99 x 10⁹/L, or if PLT 10-49.9 x 10⁹/L, DECREASE: Irinotecan by 30mg/m², Leucovorin remains the same, 5-FU bolus by 80mg/m², 5-FU infusion by 400mg/m².
4. If AGC < 0.5 x 10⁹/L, or if PLT < 10 x 10⁹/L, DECREASE: Irinotecan by 60mg/m², Leucovorin remains the same, 5-FU bolus by 160mg/m² and 5-FU infusion by 800mg/m².

Gastrointestinal
1. If Grade > 2 diarrhea within 24 hours of start of cycle, HOLD and check weekly then treat as follows:
2. If Diarrhea = grade 1 or 2, MAINTAIN dose level.
3. If Diarrhea = grade 3, DECREASE doses the same as Hematologic Toxicity # 3.
4. If Diarrhea = grade 4, DECREASE doses the same as Hematologic Toxicity # 4.
5. If Diarrhea > grade 2 after 2 weeks of treatment, DISCONTINUE therapy.

Hepatic Dysfunction
1. Irinotecan has not been studied in patients with T.Bili > 35umol/L, transaminase > 3 x ULN if no liver metastases, or transaminase > 5 x ULN with liver metastases.
2. If T.Bili > 85umol/L (marked hepatic dysfunction), OMIT 5-Fluorouracil.

Cutaneous
1. If first occurrence of severe acneform rash, DELAY infusion 1-2 weeks until improvement, then continue Cetuximab at 250mg/m². If no improvement, discontinue Cetuximab.
2. If second occurrence of severe acneform rash, delay infusion 1-2 weeks until improvement, then REDUCE Cetuximab to 200mg/m². If no improvement, discontinue Cetuximab.
3. If third occurrence of severe acneform rash, delay infusion 1-2 weeks until improvement, then REDUCE Cetuximab to 150mg/m². If no improvement, discontinue Cetuximab.
4. If fourth occurrence of severe acneform rash, DISCONTINUE Cetuximab.

CLINICAL MONITORING:
- Hold Cetuximab if patient experiences acute onset or worsening of pulmonary symptoms. If Interstitial Lung Disease confirmed, discontinue Cetuximab.
- Diarrhea
  1. Increase of < 4 stools per day over baseline; mild increase in ostomy output compared to baseline
  2. Increase of 4 - 6 stools per day over baseline; IV fluids indicated < 24hrs; moderate increase in ostomy output compared to baseline; not interfering with ADL 3. Increase of ≥7 stools per day over baseline; incontinence; IV fluids >24 hrs; hospitalization; severe increase in ostomy output compared to baseline; interfering with ADL 4. Life-threatening consequences (e.g., hemodynamic collapse) 5. Death

RATED AT EACH CLINIC VISIT

HYPERSENSITIVITY:
- If the patient experiences a mild or moderate (Grade 1 or 2) infusion reaction, the infusion rate should be decreased by 50% on all subsequent Cetuximab infusions.
- If the patient experiences a severe (Grade 3 or 4) infusion reaction, discontinue Cetuximab treatment.

INTERNAL CODE:
- OPIS CODES:
  - FOLFIRI-CETUX LOAD
  - FOLFIRI-CETUX MAINT

REFERENCES:

Date revised: 11/14/2008
GI- FOLFOX-6
MODIFIED

Gastrointestinal

OXALIPLATIN-LEUCOVORIN-FLUOROURACIL BOLUS-INFUSION Chemotherapy
Adjacent Colorectal Carcinoma

OXALIPLATIN
85mg/m² IV Day 1 Round to nearest 2.5mg
- Mix in 500mL bag 5% Dextrose; Infuse over 120 minutes concurrently with Leucovorin before 5-Fluorouracil.
- DO NOT MIX IN SALINE.

LEUCOVORIN
400mg/m² IV Day 1 Round to nearest 1mg
- Mix in 250mL D5W
- Infuse over 120 minutes concurrently with Oxaliplatin.

5-FLUOROURACIL
400mg/m² IV Day 1 Round to nearest 25mg
- Inject by direct IV push over 1-3 minutes, followed by a Normal Saline flush, after Oxaliplatin & Leucovorin.

5-FLUOROURACIL
1200mg/m²/day IV Days 1-2 Round to nearest 25mg
- 2400mg/m² in total as Continuous IV infusion for 46 hours via Infusor LV5 (5mL/hr) pump.
- Infusion through central venous access device (PICC) is recommended.

REPEAT EVERY 14 DAYS

TESTS:
Baseline Tests WBC HB PLT ANC Cr Urea T.Bili ALT AlkPhosphatase
Day 1 WBC HB PLT ANC Cr T.Bili ALT AlkPhosphatase

ANTIEMETIC PRE-CHEMO REGIMEN:
Level C Day 1 - Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
- Dexamethasone 20mg PO/IV

ANTIEMETIC TAKE-HOME REGIMEN:
Level B/C Day 1 - Ondansetron 8mg PO BID for 2-3 days, or
- Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days
- Dexamethasone 8mg PO BID for 2-3 days
- Prochlorperazine 10mg PO q4-6h prn

PATIENT VISITS and APPOINTMENT TYPE:
⇒ Day 1 3hrs Type C
⇒ Day 3 (Pump disconnect) 10min Type A

ANCILLARY:
- NO CRYOTHERAPY.
- Give Calcium gluconate 1g/10mL and Magnesium sulfate 50% 1g/2mL admix into 250mL Dextrose 5% in water
infuse over 15 minutes before and after chemotherapy.

TOXICITIES:
Hematologic
1. If ANC < 1.5 x 10⁹/L, or if PLT< 75 x 10⁹/L, HOLD 1 week, then check weekly and treat as follows:
2. If ANC 1.0-1.49 x 10⁹/L, or if PLT 50-74.9 x 10⁹/L, MAINTAIN dose level.
3. If ANC 0.5-0.99 x 10⁹/L, or if PLT 10-49.9 x 10⁹/L, DECREASE: Oxaliplatin by 15mg/m², Leucovorin remains the
same, 5-FU bolus by 80mg/m², 5-FU infusion by 400mg/m².
4. If AGC < 0.5 x 10⁹/L or if PLT < 10 x 10⁹/L, DECREASE: Oxaliplatin by 35mg/m², Leucovorin remains the same,
5-FU bolus by 160mg/m², 5-FU infusion by 800mg/m².

Gastrointestinal
1. If Grade > 2 diarrhea within 24 hours of start of cycle, HOLD and check weekly then treat as follows:
2. If Diarrhea = grade 1 or 2, MAINTAIN dose level.
3. If Diarrhea = grade 3, DECREASE 5-FU bolus by 80mg/m², 5-FU infusion by 400mg/m².

Hepatic Dysfunction
1. If T.Bili > 65umol/L (marked hepatic dysfunction), OMIT dose.

Neurologic
1. If paresthesias/dysesthesias are of short duration that resolve and do not interfere with function, maintain dose.
2. If paresthesias/dysesthesias interfere with function, but not activities of daily living, and are present at start of next cycle, decrease Oxaliplatin to 75mg/m².
3. If paresthesias/dysesthesias (with pain or with functional impairment) interfere with daily living and are present at the start of next cycle, discontinue Oxaliplatin.
4. If pharyngo-laryngeal dysesthesias, increase duration of Oxaliplatin infusion to 6 hours.

SUGGESTED ACTION
CLINICAL MONITORING:
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.
- Skin assessment, especially extremities.
- Sensory
  1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function 2.
  2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL 3. Sensory alteration or paresthesia interfering with ADL 4. Disabling 5. Death

Diarthery
1. Increase of < 4 stools per day over baseline; mild increase in ostomy output compared to baseline
2. Increase of 4 - 6 stools per day over baseline; IV fluids indicated < 24hrs; moderate increase in ostomy output compared to baseline; not interfering with ADL 3. Increase of >7 stools per day over baseline; incontinence; IV fluids >24 hrs; hospitalization; severe increase in ostomy output compared to baseline; interfering with ADL 4. Life-threatening consequences (e.g., hemodynamic collapse) 5. Death

RATED AT EACH CLINIC VISIT

FORMULAE:
CrCl - Cockcroft & Gault (mL/sec)  
Male: \[
\frac{[140\text{-age(yrs)}] \times \text{TBW(Kg)}}{[50 \times \text{SCr(umol/L)}]} 
\]
CrCl - Cockcroft & Gault (mL/sec)  
Female: \[
\frac{[140\text{-age(yrs)}] \times \text{TBW(Kg)}}{[50 \times \text{SCr(umol/L)}] \times 0.85} 
\]

INTERNAL CODE:
OPIS CODES:
- FOLFOX 6 MODIFIED-85

REFERENCES:
- BCCA Cancer Agency. BCCA Protocol Summary for Palliative Combination Chemotherapy for Metastatic Colorectal Cancer Using Oxaliplatin, 5-Fluorouracil and Folinic Acid (Leucovorin).
OXALIPLATIN-LEUCOVORIN-FLUOROURACIL BOLUS-INFUSION Chemotherapy

**Adjuvant Colorectal Carcinoma**

**OXALIPLATIN**
85mg/m² IV Day 1 Round to nearest 2.5mg
- Mix in 500mL bag 5% Dextrose; Infuse over 120 minutes concurrently with Leucovorin before 5-Fluorouracil.
- DO NOT MIX IN SALINE.

**LEUCOVORIN**
400mg/m² IV Day 1 Round to nearest 1mg
- Mix in 250mL D5W.
- Infuse over 120 minutes concurrently with Oxaliplatin.

**5-FLUOROURACIL**
400mg/m² IV Day 1 Round to nearest 25mg
- **Inject by direct IV push over 1-3 minutes**, followed by a Normal Saline flush, after Oxaliplatin & Leucovorin.

**HYDRATION:**
- **Pre**
  - Admix 10g/10mL Calcium gluconate 10% and 1g/2mL Magnesium sulfate 50% in 250mL D5W.
  - Infuse over 15 minutes, just **BEFORE** Oxaliplatin.
- **Post**
  - Admix 10g/10mL Calcium gluconate 10% and 1g/2mL Magnesium sulfate 50% in 250mL D5W.
  - Infuse over 15 minutes, just **AFTER** Oxaliplatin.

**TESTS:**

<table>
<thead>
<tr>
<th>Baseline Tests</th>
<th>WBC HB PLT ANC Cr Urea T.Bili ALT AlkPhosphatase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1</td>
<td>WBC HB PLT ANC Cr T.Bili ALT AlkPhosphatase</td>
</tr>
</tbody>
</table>

**ANTIEMETIC PRE-CHEMO REGIMEN:**

**Level C**
- **Day 1**
  - Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
  - Dexamethasone 20mg PO/IV

**ANTIEMETIC TAKE-HOME REGIMEN:**

**Level B/C**
- **Day 1**
  - Ondansetron 8mg PO BID for 2-3 days, or
  - Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days
  - Dexamethasone 8mg PO BID for 2-3 days
  - Prochlorperazine 10mg PO q4-6h prn

**PATIENT VISITS and APPOINTMENT TYPE:**

- **Day 1** 3.5hrs Type D
- **Day 3** (Pump disconnect) 10min Type A

**ANCILLARY:**
- **NO CRYOTHERAPY.**

**TOXICITIES:**

**Hematologic**
1. If ANC < 1.5 x 10⁹/L, or if PLT < 75 x 10⁹/L, **HOLD** 1 week, then check weekly and treat as follows:
   - **Level C:**
     - If ANC 1.0-1.49 x 10⁹/L, or if PLT 50-74.9 x 10⁹/L, **MAINTAIN** dose level.
     - **Level B/C:**
       - If ANC 0.5-0.99 x 10⁹/L, or if PLT 10-49.9 x 10⁹/L, **DECREASE:** Oxaliplatin by 15mg/m², Leucovorin remains the same, 5-FU bolus by 80mg/m², 5-FU infusion by 400mg/m².
   - **Level C:**
     - If ANC 0.5-0.99 x 10⁹/L, or if PLT 10-49.9 x 10⁹/L, **DECREASE:** Oxaliplatin by 35mg/m², Leucovorin remains the same, 5-FU bolus by 160mg/m², 5-FU infusion by 800mg/m².

**Gastrointestinal**
1. If Diarrhea > 2 within 24 hours of start of cycle, **HOLD** and check weekly then treat as follows:
   - **Level B/C:**
     - If Diarrhea = grade 1 or 2, **MAINTAIN** dose level.
     - **Level C:**
       - If Diarrhea = grade 3, **DECREASE** 5-FU bolus by 80mg/m², 5-FU infusion by 400mg/m².

**Tonicity**
1. If T.Bili > 85umol/L (marked hepatic dysfunction), **OMIT** dose.
GI - FOLFOX-6 MODIFIED WITH HYDRATION

Gastrointestinal

OXALIPLATIN-LEUCOVORIN-FLUOROURACIL BOLUS-INFUSION Chemotherapy

Neurologic
1. If paresthesias/dysesthesias are of short duration that resolve and do not interfere with function, maintain dose.
2. If paresthesias/dysesthesias interfere with function, but not activities of daily living, and are present at start of next
   cycle, decrease Oxaliplatin to 75mg/m².
3. If paresthesias/dysesthesias (with pain or with functional impairment) interfere with daily living and are present at
   the start of next cycle, discontinue Oxaliplatin.
4. If pharyngo-laryngeal dysesthesias, increase duration of Oxaliplatin infusion to 6 hours.

SUGGESTED ACTION

CLINICAL MONITORING:
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.
- Skin assessment, especially extremities.

Sensory
1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function.
2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL.
3. Sensory alteration or paresthesia interfering with ADL.

Diarrhea
1. Increase of < 4 stools per day over baseline; mild increase in ostomy output compared to baseline
2. Increase of 4 - 6 stools per day over baseline; IV fluids indicated < 24hrs; moderate increase in ostomy output
   compared to baseline; not interfering with ADL.
3. Increase of >7 stools per day over baseline; incontinence; IV fluids >24 hrs; hospitalization; severe increase in
   ostomy output compared to baseline; interfering with ADL.
4. Life-threatening consequences (e.g., hemodynamic collapse)
5. Death

FORMULAE:

CrCl - Cockcroft & Gault (mL/sec)  
Male: \[140 - \text{age (yrs)} \times \text{TBW (Kg)} / (50 \times \text{SCR (umol/L)})\]
Female: \[140 - \text{age (yrs)} \times \text{TBW (Kg)} / (50 \times \text{SCR (umol/L)}) \times 0.85\]

INTERNAL CODE:
- OPIS CODES:
  - FOLFOX 6MODIFIED-85 with hydration

REFERENCES:
- Louvet C, de Gramont A. Colorectal cancer: integrating oxaliplatin. Current Treatment Options in Oncology 2003,
  4:405-411.
- Maindreault-Goebel F, Louvet C, Andre T, et al. Oxaliplatin added to the simplified bimonthly leucovorin and 5-
  Fluorouracil regimen as second-line therapy for metastatic colorectal cancer (FOLFOX6). Eur J Cancer 1999; 35:
  1338-42.
- Tournigand C, Andre T, Achille E et al. FOLFIRI Followed by FOLFOX6 or the Reverse Sequence in Advanced
- BCCA Cancer Agency. BCCA Protocol Summary for Palliative Combination Chemotherapy for Metastatic
  Colorectal Cancer Using Oxaliplatin, 5-Fluorouracil and Folinic Acid (Leucovorin).

CCO Eligibility Form Required [✓] Non-Formulary Form Required [☐] Date revised: 11/14/2008
5-FLUOROURACIL Continuous Infusion
Advanced Colorectal Carcinoma

5-FLUOROURACIL
225mg/m²/day IV Day 1 (Weekly) Round to nearest 25mg

- Continuous 7 day infusion using ambulatory infusion pump at 1.5mL/hr (Infusor LV1.5).
- Infusion through central venous access device (PICC) is recommended.
- Protect from light.

CONTINUOUS TREATMENT FOR UP TO 6 MONTHS (As tolerated)

TESTS:
Baseline Tests WBC HB PLT ANC K Na Cr Urea T.Bili ALT AlkPhosphatase
Weekly WBC HB PLT ANC

ANTIEMETIC PRE-CHEMO REGIMEN:
Level A Day 1 (weekly) - Prochlorperazine 10mg PO prn

ANTIEMETIC TAKE-HOME REGIMEN:
Level A Day 1 (weekly) - Prochlorperazine 10mg PO q4-6h prn

PATIENT VISITS and APPOINTMENT TYPE:
→ Day 1 (Weekly pump change) 10min Type A

TOXICITIES:
Hematologic
1. If ANC < 1.5 x 10⁹/L, or if PLT < 100 x 10⁹/L, HOLD dose for 1 week.

Hepatic Dysfunction
1. If T.Bili > 85umol/L (marked hepatic dysfunction), OMIT dose.

Gastrointestinal
1. If Mucositis or diarrhea ≥ Grade 3 in previous course, REDUCE to 2/3 dose.

Cutaneous
- If clinical evidence of palmar-plantar erythematosis (Hand-Foot Syndrome), HOLD dose until symptoms are resolved.

SUGGESTED ACTION

CLINICAL MONITORING:
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.
- Skin assessment, especially extremities.

Diarrhea
1. Increase of < 4 stools per day over baseline; mild increase in ostomy output compared to baseline
2. Increase of 4 - 6 stools per day over baseline; IV fluids indicated < 24hrs; moderate increase in ostomy output compared to baseline; not interfering with ADL 3. Increase of ≥7 stools per day over baseline; incontinence; IV fluids >24 hrs; hospitalization; severe increase in ostomy output compared to baseline; interfering with ADL 4. Life-threatening consequences (e.g., hemodynamic collapse) 5. Death

Mucositis
1. Erythema of the mucosa 2. Patchy ulcerations or pseudomembranes 3. Confluent ulcerations or pseudomembranes; bleeding with minor trauma 4. Tissue necrosis; significant spontaneous bleeding; life-threatening consequences 5. Death

Hand-foot Skin Reaction
1. Minimal skin changes or dermatitis (e.g., erythema) without pain 2. Skin changes (e.g., peeling, blisters, bleeding, edema) or pain, not interfering with function 3. Ulcerative dermatitis or skin changes with pain interfering with function

RATED AT EACH CLINIC VISIT

REFERENCES:

CCO Eligibility Form Required [ ] Non-Formulary Form Required [ ] Date revised: 11/14/2008

Gastrointestinal
GI-FU-CISP

Gastrointestinal

5-FUOROURACIL Infusion-CISPLATIN
Combined Modality: Carcinoma of the Esophagus or Anus

5-FUOROURACIL
1000mg/m²/day IV Days 1-4 Round to nearest 25mg
- Continuous infusion for 96 hours using Infusor LV2 infusion pump (2mL/hr).
- Infuse through central venous access device, if applicable.
- Maximum dose per day = 2G.

CISPLATIN
75mg/m² IV Day 1 Round to nearest 1mg
- Mix in 500mL bag Normal Saline.
- Infuse over 60 minutes.
- Maximum dose = 150mg.

WEEKS 1 & 5 OF RADIOTHERAPY, then REPEAT EVERY 21 DAYS

HYDRATION:
Pre:
- Infuse 1000mL Normal Saline with 20mEq Potassium Chloride IV over 2 hours.

Concurrent:
- May give 250mL of 20% Mannitol solution IV (50G).
- Infuse through sidearm concurrent with Cisplatin (if diuresis is required).

Post:
- Infuse 500mL Normal Saline with 10mEq Potassium Chloride (2G Magnesium Sulfate may also be added) IV over 1 hour.
- Increase fluids if poor oral intake.

TESTS:
Baseline Tests WBC HB PLT ANC Ca K Na Chloride Phosphate Mg Glucose Cr Urea 24Hr CrCl T.Bili Albumin ALT GGT AlkPhosphatase
Day 1 WBC HB PLT ANC K Na Chloride Mg Cr Urea
Test Notes - Baseline & routine renal function tests Especially if there are other concurrent nephrotoxic drugs.

ANTIEMETIC PRE-CHEMO REGIMEN:
Level C Day 1
- Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
- Dexamethasone 20mg PO/IV

ANTIEMETIC TAKE-HOME REGIMEN:
Level B/C Day 1
- Ondansetron 8mg PO BID for 2-3 days, or
Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days
- Dexamethasone 8mg PO BID for 2-3 days
- Prochlorperazine 10mg PO q4-6h prn

PATIENT VISITS and APPOINTMENT TYPE:
➤ Day 1 5hrs Type D
➤ Day 5 (Pump disconnect) 10min Type A

TOXICITIES:
Hematologic
1. If ANC < 1.5 x 10⁹/L, or if PLT = 75-100 x 10⁹/L, REDUCE 5-FU to 50% dose.
2. If ANC < 1.0 x 10⁹/L, or if PLT < 75 x 10⁹/L, HOLD dose for 1 week.

Renal Failure
1. If renal function has not returned to normal (CrCl > 1.0mL/sec or SrCr > 136umol/L) by day 1 of cycle, DISCONTINUE CISPLATIN.

Hepatic Dysfunction
1. If T.Bili > 65umol/L (marked hepatic dysfunction), OMIT dose.

Gastrointestinal
1. If Mucositis or diarrhea ≥ Grade 3 in previous course, REDUCE to 2/3 dose.

SUGGESTED ACTION
5-FLUOROURACIL Infusion-CISPLATIN

CLINICAL MONITORING:
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.
- Skin assessment, especially extremities.

Sensory
1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function
2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL
3. Sensory alteration or paresthesia interfering with ADL
4. Disabling
5. Death

Hearing
1. Asymptomatic, detected on exam/testing only
2. Symptomatic, not interfering with ADL
3. Symptomatic, interfering with ADL
4. Life-threatening; disabling
5. Death

Diarrhea
1. Increase of < 4 stools per day over baseline; mild increase in ostomy output compared to baseline
2. Increase of 4 - 6 stools per day over baseline; IV fluids indicated < 24 hrs; moderate increase in ostomy output compared to baseline; not interfering with ADL
3. Increase of ≥7 stools per day over baseline; incontinence; IV fluids >24 hrs; hospitalization; severe increase in ostomy output compared to baseline; interfering with ADL
4. Life-threatening consequences (e.g., hemodynamic collapse)
5. Death

Mucositis
1. Erythema of the mucosa
2. Patchy ulcerations or pseudomembranes
3. Confluent ulcerations or pseudomembranes; bleeding with minor trauma
4. Tissue necrosis; significant spontaneous bleeding; life-threatening consequences
5. Death

RATED AT EACH CLINIC VISIT

FORMULAE:
CrCl - Cockcroft & Gault (mL/sec)
Male: \[140 - \text{age(yrs)} \times \text{TBW(Kg)} / [50 \times \text{SCr(umol/L)}] \]
Female: \[140 - \text{age(yrs)} \times \text{TBW(Kg)} / [50 \times \text{SCr(umol/L)}] \times 0.85 \]

INTERNAL CODE:
OPIS CODE: FU-CISP GI

Date revised: 11/14/2008
5-FLUOROURACIL Infusion-CISPLATIN (Cisplatin divided into 3 days for treatment)

Combined Modality: Carcinoma of the Esophagus or Anus

**GI**

**5-FLUOROURACIL**
1000mg/m²/day IV Days 1-4 Round to nearest 25mg

- Continuous infusion for 96 hours using Infusor LV2 infusion pump (2mL/hr).
- Infusion through central venous access device (PICC) is recommended.
- Maximum dose per day = 2G.

**CISPLATIN**
25mg/m² IV Days 1-3 Round to nearest 1mg

- Mix in 250mL bag Normal Saline.
- Infuse over 30-60 minutes.
- Maximum dose = 150mg (3 day total).

**HYDRATION:**

**Pre:**
- Infuse 500mL Normal Saline with 10mEq Potassium Chloride IV over 1 hour before Cisplatin.

**Concurrent:**
- May give 250mL of 20% Mannitol solution (50G) IV.
- Infuse through sidearm concurrent with Cisplatin if diuresis is required.

**Post:**
- Infuse 500mL Normal Saline with 10mEq Potassium Chloride IV (2G Magnesium Sulfate may also be added) over 1 hour after Cisplatin.
- Increase fluids if poor oral intake.

**TESTS:**

**Baseline Tests**
- WBC
- HB
- PLT
- ANC
- Ca
- K
- Na
- Chloride
- Phosphate
- Mg
- Glucose
- Cr
- Urea
- 24Hr CrCl
- T.Bili
- Albumin
- ALT
- GGT
- AlkPhosphatase

**Day 1 Test Notes**
- Baseline & routine renal function tests especially if there are other concurrent nephrotoxic drugs.

**ANTIEMETIC PRE-CHEMO REGIMEN:**

**Level C**
- Days 1-3
- Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
- Dexamethasone 20mg PO/IV

**ANTIEMETIC TAKE-HOME REGIMEN:**

**Level B/C**
- Days 1-3
- Ondansetron 8mg PO BID for 2-3 days, or Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days
- Dexamethasone 8mg PO BID for 2-3 days
- Prochlorperazine 10mg PO q4-6h prn

**PATIENT VISITS and APPOINTMENT TYPE:**
- Days 1-3 3hrs Type D
- Day 5 (Pump disconnect) 10min Type A

**TOXICITIES:**

**Hematologic**
1. If ANC < 1.5 x 10⁹/L, or if PLT = 75-100 x 10⁹/L, REDUCE 5-FU to 50% dose.
2. If ANC < 1.0 x 10⁹/L, or if PLT < 75 x 10⁹/L, HOLD dose for 1 week.

**Renal Failure**
1. If renal function has not returned to normal (CrCl > 1.0mL/sec or SrCr > 136umol/L) by day 1 of cycle, DISCONTINUE CISPLATIN.

**Gastrointestinal**
1. If Mucositis or diarrhea > Grade 3 in previous course, REDUCE to 2/3 dose.

SUGGESTED ACTION
Gastrointestinal  5-FLUOROURACIL Infusion-CISPLATIN  (Cisplatin divided into 3 days for treatment)

CLINICAL MONITORING:
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.
- Skin assessment, especially extremities.
  Sensory
  1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function 2.
  Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL 3. Sensory alteration or paresthesia interfering with ADL 4. Disabling 5. Death

  Hearing
  1. Asymptomatic, detected on exam/testing only 2. Symptomatic, not interfering with ADL
  3. Symptomatic, interfering with ADL  4. Life-threatening; disabling  5. Death

Diarrhea
- Increase of < 4 stools per day over baseline; mild increase in ostomy output compared to baseline
- Increase of 4 - 6 stools per day over baseline; IV fluids indicated < 24hrs; moderate increase in ostomy output compared to baseline; not interfering with ADL 3. Increase of ≥7 stools per day over baseline; incontinence; IV fluids >24 hrs; hospitalization; severe increase in ostomy output compared to baseline; interfering with ADL 4. Life-threatening consequences (e.g., hemodynamic collapse) 5. Death

Mucositis
- Erythema of the mucosa  2. Patchy ulcerations or pseudomembranes  3. Confluent ulcerations or pseudomembranes; bleeding with minor trauma  4. Tissue necrosis; significant spontaneous bleeding; life-threatening consequences  5. Death

RATED AT EACH CLINIC VISIT

FORMULAE:

CrCl - Cockcroft & Gault  (mL/sec)
Male: \[\frac{[140\text{-age(yrs)}] \times \text{TBW(Kg)}}{[50 \times \text{SCr(umol/L)}]}\]
Female: \[\frac{[140\text{-age(yrs)}] \times \text{TBW(Kg)}}{[50 \times \text{SCr(umol/L)}] \times 0.85}\]

CCO Eligibility Form Required □  Non-Formulary Form Required □  Date revised: 11/14/2008
Combined Modality: Carcinoma of the Esophagus or Anus

**5-FLUOROURACIL**
- **1000mg/m²/day IV Days 1 & 29**
  - Round to nearest 25mg
  - Continuous infusion for **96 hours** using Infusor LV2 infusion pump (2mL/hr).
  - Infusion through central venous access device (PICC) is recommended.
  - Maximum dose per day = 2G.

**MITOMYCIN**
- **10mg/m² IV Days 1 & 29**
  - Round to nearest 0.25mg
  - Mitomycin on Day 1 only.
  - Esophagus: Mitomycin on Day 1 only.
  - Anus: Mitomycin on Days 1 & 29.
  - **Slow push through sidearm of free flowing IV**; Give 1.5mg (3mL) per minute.

**WEEKS 1 & 5 OF RADIOTHERAPY**

**TESTS:**
- **Baseline Tests:** WBC HB PLT ANC Cr Urea T.Bili ALT AlkPhosphatase
- **Day 1:** WBC HB PLT ANC

**Test Notes:** Baseline & routine renal function tests, especially if there are other concurrent nephrotoxic drugs.

**ANTIEMETIC PRE-CHEMO REGIMEN:**
- **Level B Days 1 & 29**
  - Dexamethasone 8mg PO/IV
  - May add or substitute Prochlorperazine 10mg PO/IV pm

**ANTIEMETIC TAKE-HOME REGIMEN:**
- **Level A Day 1**
  - Prochlorperazine 10mg PO q4-6h prn

**PATIENT VISITS and APPOINTMENT TYPE:**
- **Days 1 & 29** 45min **Type B**
- **Days 5 & 33 (Pump disconnect)** 10min **Type A**

**TOXICITIES:**

**Hematologic**
1. If ANC < 1.5 x 10⁹/L, or if PLT = 75-100 x 10⁹/L, REDUCE 5-FU to **50%** dose.
2. If ANC < 1.0 x 10⁹/L, or if PLT < 75 x 10⁹/L, **HOLD** dose for 1 week.

**Renal Failure**
1. If Mucositis or diarrhea > Grade 3 in previous course, REDUCE dose of Mitomycin to **75%** dose.

**Gastrointestinal**
1. If Mucositis or diarrhea > Grade 3 in previous course, REDUCE to **2/3 dose**.

**Hepatic Dysfunction**
1. If T.Bili = 50-85μmol/L, or AST > 180 IU/L, REDUCE dose of Mitomycin to **75%** dose.
2. If T.Bili above 85μmol/L, **STOP** both drugs.

**SUGGESTED ACTION**

**CLINICAL MONITORING:**
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.
- Skin assessment, especially extremities.

**Fatigue**
1. Mild fatigue over baseline 2. Moderate or causing difficulty performing some ADL 3. Severe fatigue interfering with ADL 4. Disabling

**Injection Site Reaction**
1. Pain; itching; erythema 2. Pain or swelling, with inflammation or phlebitis 3. Ulceration or necrosis that is severe; operative intervention indicated

**RATED UPON PATIENT COMPLAINT OR CLINICAL EVENT**

**Diarrhea**
1. Increase of < 4 stools per day over baseline; mild increase in ostomy output compared to baseline
2. Increase of 4 - 6 stools per day over baseline; IV fluids indicated < 24hrs; moderate increase in ostomy output compared to baseline; not interfering with ADL 3. Increase of >7 stools per day over baseline; incontinence; IV fluids >24 hrs; hospitalization; severe increase in ostomy output compared to baseline; interfering with ADL 4. Life-threatening consequences (e.g., hemodynamic collapse) 5. Death

**Mucositis**
1. Erythema of the mucosa 2. Patchy ulcerations or pseudomembranes 3. Confluent ulcerations or pseudomembranes; bleeding with minor trauma 4. Tissue necrosis; significant spontaneous bleeding; life-threatening consequences 5. Death

**RATED AT EACH CLINIC VISIT**

**Date revised:** 11/14/2008
5-FLUOROURACIL (IV-CIV-IV) Chemotherapy
Rectal Carcinoma - Curative Intent (Adjuvant to Radiotherapy)

5-FLUOROURACIL 500mg/m² IV Days 1-5 & 29-33 Round to nearest 25mg
- Inject by direct IV push over 1-3 minutes, followed by a Normal Saline flush.
- Patients are recommended to suck on ice chips about 5 minutes before treatment begins until 30 minutes after treatment is completed to reduce the incidence and severity of stomatitis.

5-FLUOROURACIL 225mg/m²/day IV Day 57 Round to nearest 25mg
- Continuous Infusion using ambulatory infusion pump (Infusor 1.5mL/hr) for 35 days concurrent with radiotherapy.
- Exchange pump every 7 days.
- Infusion through central venous access device (PICC) is recommended.
- Protect from light.

5-FLUOROURACIL 450mg/m² IV Days 127-131 & 159-163 Round to nearest 25mg
- Inject by direct IV push over 1-3 minutes, followed by a Normal Saline flush.
- Patients are recommended to suck on ice chips about 5 minutes before treatment begins until 30 minutes after treatment is completed to reduce the incidence and severity of stomatitis.

TESTS:
Baseline Tests
WBC  HB  PLT  ANC  K  Na  Cr  Urea  T.Bili  Albumin  ALT  AlkPhosphatase
Days 127 & 159
WBC  HB  PLT  ANC  K  Na  Cr  Urea  T.Bili  Albumin  ALT  AlkPhosphatase
Weekly starting Day
WBC  HB  PLT  ANC
57
Days 1 & 29
WBC  HB  PLT  ANC

ANTIEMETIC PRE-CHEMO REGIMEN:
Level B Each Treatment
Day
- Dexamethasone 8mg PO/IV
- May add/substitute Prochlorperazine 10mg PO/IV prn

ANTIEMETIC TAKE-HOME REGIMEN:
Level A Each Treatment
Day
- Prochlorperazine 10mg PO q4-6h prn

PATIENT VISITS and APPOINTMENT TYPE:
→ Days 1-5, 29-33,127-131 & 159-164 10min Type A
→ From Day 57 for 35 days (Weekly pump exchange) 10min Type A

ANCILLARY:
- Sucking ice chips during 5-Fluorouracil bolus treatment is recommended to reduce mucositis following chemotherapy.

TOXICITIES:
Hematologic
1. If ANC < 1.5 x 10⁹/L, or if PLT = 75-100 x 10⁹/L, REDUCE to 50% dose.
2. If ANC < 1.0 x 10⁹/L, or if PLT < 75 x 10⁹/L, HOLD dose for 1 week.

Hepatic Dysfunction
1. If T.Bili > 85µmol/L (marked hepatic dysfunction), OMIT dose.

Gastrointestinal
1. If Mucositis or diarrhea > Grade 3 in previous course, REDUCE to 2/3 dose.

SUGGESTED ACTION
CLINICAL MONITORING:
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.
- Skin assessment, especially extremities.

Diarrhea
1. Increase of < 4 stools per day over baseline; mild increase in ostomy output compared to baseline
2. Increase of 4 - 6 stools per day over baseline; IV fluids indicated < 24hrs; moderate increase in ostomy output compared to baseline; not interfering with ADL 3. Increase of >7 stools per day over baseline; incontinence; IV fluids >24 hrs; hospitalization; severe increase in ostomy output compared to baseline; interfering with ADL 4. Life-threatening consequences (e.g., hemodynamic collapse) 5. Death

Mucositis
1. Erythema of the mucosa
2. Patchy ulcerations or pseudomembranes
3. Confluent ulcerations or pseudomembranes; bleeding with minor trauma
4. Tissue necrosis; significant spontaneous bleeding; life-threatening consequences
5. Death

RATED AT EACH CLINIC VISIT
INTERNAL CODE:
OPIS CODES:
- FU-NEOADJ DAYS 1-33
- FU-NEOADJ DAYS 57-92
- FU-NEOADJ D 127-163

REFERENCES:
- CCO Practice Guideline 2-3: Postoperative Adjuvant Radiotherapy and/or Chemotherapy for Resected Stage II or III Rectal Cancer.

Date revised: 11/14/2008
GEMCITABINE Chemotherapy
Advanced Unresectable Pancreatic Carcinoma

GEMCITABINE 1000mg/m² IV Days 1, 8 & 15 Round to nearest 19mg
- Admix in 250mL bag 5% Dextrose or Normal Saline; Infuse over 30 minutes.
REPEAT EVERY 28 DAYS

TESTS:
Baseline Tests: WBC HB PLT ANC Ca K Na Chloride Glucose Cr Urea T.Bili Albumin AST ALT GGT AlkPhosphatase
Days 1, 8 & 15: WBC HB PLT ANC Cr Urea T.Bili
Test Notes: Baseline & periodic renal function tests (if failure suspected).

ANTIEMETIC PRE-CHEMO REGIMEN:
Level B: Days 1, 8 & 15 - Dexamethasone 8mg PO/IV
- May add or substitute Prochlorperazine 10mg PO/IV prn

ANTIEMETIC TAKE-HOME REGIMEN:
Level A: Days 1, 8 & 15 - Prochlorperazine 10mg PO q4-6h prn

PATIENT VISITS and APPOINTMENT TYPE:
Days 1, 8 & 15 45min Type A

TOXICITIES:

Hematologic
1. If ANC < 1.5 x 10⁹/L, or if PLT = 75-100 x 10⁹/L, REDUCE to 50% dose.
2. If ANC < 1.0 x 10⁹/L, or if PLT < 75 x 10⁹/L, HOLD dose for 1 week.

Gastrointestinal
1. If Mucositis or diarrhea > Grade 3 in previous course, REDUCE to 2/3 dose.

SUGGESTED ACTION

CLINICAL MONITORING:

Edema limb
1. 5 - 10% inter-limb discrepancy in volume or circumference at point of greatest visible difference; swelling or obscuration of anatomic architecture on close inspection; pitting edema 2. >10 - 30% inter-limb discrepancy in volume or circumference at point of greatest visible difference; readily apparent obscuration of anatomic architecture; obliteration of skin folds; readily apparent deviation from normal anatomic contour 3. >30% inter-limb discrepancy in volume; lymphorrhea; gross deviation from normal anatomic contour; interfering with ADL  4. Progression to malignancy (i.e., lymphangiosarcoma); amputation indicated; disabling  5. Death
RATED IF EDEMA NOTED ON ROUTINE VISITS

Diarrhea
1. Increase of < 4 stools per day over baseline; mild increase in ostomy output compared to baseline
2. Increase of 4 - 6 stools per day over baseline; IV fluids indicated < 24hrs; moderate increase in ostomy output compared to baseline; not interfering with ADL 3. Increase of > 7 stools per day over baseline; incontinence; IV fluids >24 hrs; hospitalization; severe increase in ostomy output compared to baseline; interfering with ADL 4. Life-threatening consequences (e.g., hemodynamic collapse)  5. Death
RATED AT EACH CLINIC VISIT

Mucositis
1. Erythema of the mucosa 2. Patchy ulcerations or pseudomembranes 3. Confluent ulcerations or pseudomembranes; bleeding with minor trauma 4. Tissue necrosis; significant spontaneous bleeding; life-threatening consequences  5. Death
RATED AT EACH CLINIC VISIT

INTERNAL CODE:
OPIS CODE: GEMCIT-GI

Date revised: 11/14/2008
Gastrointestinal

GEMCITABINE Chemotherapy
Adjuvant Pancreatic Carcinoma

GEMCITABINE 1000mg/m² IV Days 1, 8 & 15 Round to nearest 19mg
- Admix in 250mL bag 5% Dextrose or Normal Saline; Infuse over 30 minutes.
REPEAT EVERY 28 DAYS FOR 6 CYCLES

TESTS:
Baseline Tests  WBC HB PLT ANC Ca K Na Chloride Glucose Cr Urea T.Bili Albumin AST ALT GGT AlkPhosphatase
Days 1, 8 & 15 WBC HB PLT ANC Cr Urea T.Bili
Test Notes - Baseline & periodic renal function tests (if failure suspected).

ANTIEMETIC PRE-CHEMO REGIMEN:
Level B Days 1,8 & 15 - Dexamethasone 8mg PO/IV
- May add or substitute Prochlorperazine 10mg PO/IV prn

ANTIEMETIC TAKE-HOME REGIMEN:
Level A Days 1,8 & 15 - Prochlorperazine 10mg PO q4-6h prn

PATIENT VISITS and APPOINTMENT TYPE:
Days 1, 8 & 15 45min Type A

TOXICITIES:
Hematologic
1. If ANC < 1.5 x 10⁹/L, or if PLT = 75-100 x 10⁹/L, REDUCE to 50% dose.
2. If ANC < 1.0 x 10⁹/L, or if PLT < 75 x 10⁹/L, HOLD dose for 1 week.

Gastrointestinal
1. If Mucositis or diarrhea > Grade 3 in previous course, REDUCE to 2/3 dose.

SUGGESTED ACTION

CLINICAL MONITORING:
Edema limb
1. 5 - 10% inter-limb discrepancy in volume or circumference at point of greatest visible difference; swelling or obscuration of anatomic architecture on close inspection; pitting edema 2. >10 - 30% inter-limb discrepancy in volume or circumference at point of greatest visible difference; readily apparent obscuration of anatomic architecture; obliteration of skin folds; readily apparent deviation from normal anatomic contour 3. >30% inter-limb discrepancy in volume; lymphorrhea; gross deviation from normal anatomic contour; interfering with ADL 4. Progression to malignancy (i.e., lymphangiosarcoma); amputation indicated; disabling 5. Death

RATED IF EDEMA NOTED ON ROUTINE VISITS

Diarrhea
1. Increase of < 4 stools per day over baseline; mild increase in ostomy output compared to baseline
2. Increase of 4 - 6 stools per day over baseline; IV fluids indicated < 24hrs; moderate increase in ostomy output compared to baseline; not interfering with ADL 3. Increase of ≥7 stools per day over baseline; incontinence; IV fluids >24 hrs; hospitalization; severe increase in ostomy output compared to baseline; interfering with ADL 4. Life-threatening consequences (e.g., hemodynamic collapse) 5. Death

Mucositis
1. Erythema of the mucosa 2. Patchy ulcerations or pseudomembranes 3. Confluent ulcerations or pseudomembranes; bleeding with minor trauma 4. Tissue necrosis; significant spontaneous bleeding; life-threatening consequences 5. Death

RATED AT EACH CLINIC VISIT

INTERNAL CODE:
OPIS CODE: GI-GEMCIT-ADJUVANT

Date revised: 11/14/2008
**Gastrointestinal**

**IRINOTECAN Chemotherapy**

**Metastatic Colorectal Carcinoma**

**IRINOTECAN** 80mg/m² IV Days 1,8,15 & 22 Round to nearest 1mg
- Mix in 250mL bag 5% Dextrose or Normal Saline; Infuse over 30-90 minutes.
- BSA capped at 2m²

**ATROPINE**
0.25-1mg SC Days 1,8,15 & 22
- May be given pre-chemo to prevent cholinergic adverse effects or within 1 hour post-chemo for acute-onset diarrhea.
- Check BP and HR every 30 minutes x2 and until patient stable.

**LOPERAMIDE**
2mg PO Day 1 & prn 2mg tablet
- 4mg PO at the onset of diarrhea, then 2mg q2h PO until patient is diarrhea-free for 12 hours.
- May give 4mg q4h during night time.

**TESTS:**

- Baseline Tests
  - WBC HB PLT ANC Cr Urea T.Bili ALT AlkPhosphatase

- **Days 1,8,15 & 22**
  - WBC HB PLT ANC T.Bili

**Test Notes** - Glucose test required if diabetic patient.

**ANTIEMETIC PRE-CHEMO REGIMEN:**

**Level C**
- Days 1,8,15 & 22
- Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
- Dexamethasone 20mg PO/IV
- AVOID Prochlorperazine on the day(s) Irinotecan is administered.

**ANTIEMETIC TAKE-HOME REGIMEN:**

**Level A**
- Days 2, 9, 16 & 23
- Prochlorperazine 10mg PO q4-6h prn starting on day after Irinotecan chemotherapy
- AVOID Prochlorperazine on the day(s) Irinotecan is administered.

**PATIENT VISITS and APPOINTMENT TYPE:**

- Days 1,8,15 & 22 1hr Type C

**TOXICITIES:**

**Hematologic**
1. If ANC < 1.5 x 10⁹/L, or if PLT < 100 x 10⁹/L, HOLD dose for 1 week.
2. If ANC < 1.0 x 10⁹/L, or if PLT < 75 x 10⁹/L, HOLD dose for 1 week, then restart Irinotecan at dose reduced by 50%.

**Gastrointestinal**
1. If Diarrhea = Grade 2, REDUCE Irinotecan by 25mg/m².
2. If Diarrhea = Grade 3, HOLD Irinotecan until < grade 2, then restart at dose reduced by 25mg/m².
3. If Diarrhea = Grade 4, HOLD Irinotecan until < grade 2, then restart at dose reduced by 50mg/m².

**Hepatic Dysfunction**
1. Irinotecan has not been studied in patients with T.Bili > 35umol/L, transaminase > 3 x ULN if no liver metastases, or transaminase > 5 x ULN with liver metastases.

**CLINICAL MONITORING:**

**Diarrhea**
1. Increase of < 4 stools per day over baseline; mild increase in ostomy output compared to baseline
2. Increase of 4 - 6 stools per day over baseline; IV fluids indicated < 24hrs; moderate increase in ostomy output compared to baseline; not interfering with ADL
3. Increase of >7 stools per day over baseline; incontinence; IV fluids >24 hrs; hospitalization; severe increase in ostomy output compared to baseline; interfering with ADL 4. Life-threatening consequences (e.g., hemodynamic collapse) 5. Death

**RATED AT EACH CLINIC VISIT**

**INTERNAL CODE:**

- OPIS CODE: IRINO 80MG/M2

- CCO Eligibility Form Required ✔ Non-Formulary Form Required ☐

**Date revised:** 11/14/2008

Gastrointestinal
IRINOTECAN-CETUXIMAB Chemotherapy
Treatment of EGFR Expressing, Metastatic Colorectal Carcinoma in Patients who are Refractory to Irinotecan-based Chemotherapy

DIPHENHYDRAMINE
50mg IV Day 1
- Admix in 50-100mL minibag 5% Dextrose or Normal Saline.
- Give over 10-15 minutes 30 minutes before Cetuximab dose started.

CETUXIMAB
400mg/m² IV LOADING DOSE Round to nearest 1mg
- Add into an empty IV bag and infuse undiluted over 2 hours. (Maximum infusion rate is 5mL/min).
- Use non-PVC equipment, including 0.22 micron in-line filter.
- Give first before starting Irinotecan. For the first dose, observe patients for 1 hour for infusion reactions after completion of the infusion.
- NON-FORMULARY FORM REQUIRED

ATROPINE
0.25-1mg SC Day 1
- May be given pre-chemo to prevent cholinergic adverse effects or within 1 hour post-chemo for acute-onset diarrhea.
- Check BP and HR every 30 minutes x2 and until patient stable.

IRINOTECAN
100mg/m² IV Day 1 Round to nearest 1mg
- Mix in 250mL bag 5% Dextrose or Normal Saline; Infuse over 30 - 90 minutes.

LOPERAMIDE
2mg PO Day 1 & prn 2mg tablet
- 4mg PO at the onset of diarrhea, then 2mg q2h PO until patient is diarrhea-free for 12 hours.
- May give 4mg q4h during night time. Compassionate Supply.

REPEAT EVERY 7 DAYS Reassess after 6 cycles

TESTS:
Baseline Tests WBC HB PLT ANC Cr Urea T.Bili ALT GGT AlkPhosphatase
Day 1 FOLFIRI WBC HB PLT ANC K Na Urea T.Bili ALT
Test Notes Cetuximab - for use in patients with wild type K-RAS tumours

ANTIEMETIC PRE-CHEMO REGIMEN:
Level C Day 1
- Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
- Dexamethasone 20mg PO/IV
- AVOID Prochlorperazine on the day(s) Irinotecan is administered.

ANTIEMETIC TAKE-HOME REGIMEN:
Level A Day 1
- Prochlorperazine 10mg PO q4-6h pm starting on day after Irinotecan chemotherapy
- AVOID Prochlorperazine on the day(s) Irinotecan is administered.

PATIENT VISITS and APPOINTMENT TYPE:
➔ Day 1 Irinotecan & Cetuximab Loading Dose 3.5hrs Type D
➔ Day 1 Irinotecan & Cetuximab Maintenance 2.5hrs Type C

ANCILLARY:
- Patients should limit sun exposure (sunscreen and hats) as it may exacerbate Cetuximab induced skin reactions.

TOXICITIES:
Hematologic
1. If ANC < 1.5 x 10⁹/L, or if PLT < 100 x 10⁹/L, HOLD dose for 1 week.
2. If ANC < 1.0 x 10⁹/L, or if PLT < 75 x 10⁹/L, HOLD dose for 1 week, then restart Irinotecan at dose reduced by 50%.

Gastrointestinal
1. If Diarrhea = Grade 2, REDUCE Irinotecan by 25mg/m².
2. If Diarrhea = Grade 3, HOLD Irinotecan until < grade 2, then restart at dose reduced by 25mg/m².
3. If Diarrhea = Grade 4, HOLD Irinotecan until < grade 2, then restart at dose reduced by 50mg/m².

Hepatic Dysfunction
1. Irinotecan has not been studied in patients with T.Bili > 35umol/L, transaminase > 3 x ULN if no liver metastases, or transaminase > 5 x ULN with liver metastases.
IRINOTECAN-CETUXIMAB Chemotherapy

Cutaneous
1. If first occurrence of severe acneform rash, DELAY infusion 1-2 weeks until improvement, then continue Cetuximab at 250mg/m². If no improvement, discontinue Cetuximab.
2. If second occurrence of severe acneform rash, delay infusion 1-2 weeks until improvement, then REDUCE Cetuximab to 200mg/m². If no improvement, discontinue Cetuximab.
3. If third occurrence of severe acneform rash, delay infusion 1-2 weeks until improvement, then REDUCE Cetuximab to 150mg/m². If no improvement, discontinue Cetuximab.
4. If fourth occurrence of severe acneform rash, DISCONTINUE Cetuximab.

SUGGESTED ACTION:

CLINICAL MONITORING:
- Hold Cetuximab if patient experiences acute onset or worsening of pulmonary symptoms. If Interstitial Lung Disease confirmed, discontinue Cetuximab.

Diarrhea
1. Increase of <4 stools per day over baseline; mild increase in ostomy output compared to baseline.
2. Increase of 4-6 stools per day over baseline; IV fluids indicated <24hrs; moderate increase in ostomy output compared to baseline; not interfering with ADL
3. Increase of >=7 stools per day over baseline; incontinence; IV fluids >=24 hrs; hospitalization; severe increase in ostomy output compared to baseline; interfering with ADL
4. Life-threatening consequences (e.g., hemodynamic collapse)
5. Death

RATED AT EACH CLINIC VISIT

HYPERSENSITIVITY:
- If the patient experiences a mild or moderate (Grade 1 or 2) infusion reaction, the infusion rate should be decreased by 50% on all subsequent Cetuximab infusions.
- If the patient experiences a severe (Grade 3 or 4) infusion reaction, discontinue Cetuximab treatment.

INTERNAL CODE:
OPIS CODES:
- IRINO100-CETUX'L
- IRINO100-CETUX*M

REFERENCES:

Date revised: 11/14/2008
**GI-IRINO-LO**

**Gastrointestinal**

<table>
<thead>
<tr>
<th><strong>IRINOTECAN Chemotherapy</strong></th>
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<tr>
<td><strong>Metastatic Colorectal Carcinoma</strong></td>
</tr>
</tbody>
</table>

**IRINOTECAN** 125mg/m² IV Days 1,8,15 & 22 Round to nearest 1mg

- Mix in **250mL bag 5% Dextrose** or Normal Saline; **Infuse over 30-90 minutes**.
- BSA capped at 2m²

**REPEAT EVERY 42 DAYS** Rest period of 2 weeks between cycles

<table>
<thead>
<tr>
<th><strong>ATROPINE</strong></th>
<th>0.25-1mg</th>
<th>SC</th>
<th>Days 1,8,15 &amp; 22</th>
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</table>
- May be given pre-chemo to prevent cholinergic adverse effects or within 1 hour post-chemo for acute-onset diarrhea.
- Check BP and HR every 30 minutes x2 and until patient stable.

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<tr>
<th><strong>LOPERAMIDE</strong></th>
<th>2mg PO</th>
<th>Day 1 &amp; prn 2mg tablet</th>
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</table>
- 4mg PO at the onset of diarrhea, then 2mg q2h PO until patient is diarrhea-free for 12 hours.
- May give 4mg q4h during night time.

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<tr>
<th><strong>TESTS:</strong></th>
<th><strong>Baseline Tests</strong></th>
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<tbody>
<tr>
<td><strong>Days 1,8,15 &amp; 22</strong></td>
<td>WBC HB PLT ANC Cr Urea T.Bili ALT AlkPhosphatase</td>
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**ANTIEMETIC PRE-CHEMO REGIMEN:**

- **Level C** Days 1, 8, 15 & 22 - Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
- Dexamethasone 20mg PO/IV
- AVOID Prochlorperazine on the day(s) Irinotecan is administered.

**ANTIEMETIC TAKE-HOME REGIMEN:**

- **Level A** Day 2, 9, 16 & 23 - Prochlorperazine 10mg PO q4-6h prn starting on day after Irinotecan chemotherapy
- AVOID Prochlorperazine on the day(s) Irinotecan is administered.

**PATIENT VISITS and APPOINTMENT TYPE:**

- Days 1,8,15 & 22 1hr Type B

**TOXICITIES:**

- **Hematologic**
  1. If ANC < 1.5 x 10⁹/L, or if PLT < 100 x 10⁹/L, **HOLD** dose for 1 week.
  2. If ANC < 1.0 x 10⁹/L, or if PLT < 75 x 10⁹/L, **HOLD** dose for 1 week, then restart Irinotecan at dose reduced by 50%.

- **Gastrointestinal**
  1. If Diarrhea = Grade 2, **REDUCE** Irinotecan by 25mg/m².
  2. If Diarrhea = Grade 3, **HOLD** Irinotecan until < grade 2, then restart at dose reduced by 25mg/m².
  3. If Diarrhea = Grade 4, **HOLD** Irinotecan until < grade 2, then restart at dose reduced by 50mg/m².

- **Hepatic Dysfunction**
  1. Irinotecan has not been studied in patients with T.Bili > 35umol/L, transaminase > 3 x ULN if no liver metastases, or transaminase > 5 x ULN with liver metastases.

**SUGGESTED ACTION**

**CLINICAL MONITORING:**

**Diarrhea**

1. Increase of < 4 stools per day over baseline; mild increase in ostomy output compared to baseline.
2. Increase of 4 - 6 stools per day over baseline; IV fluids indicated < 24hrs; moderate increase in ostomy output compared to baseline; not interfering with ADL.
3. Increase of >=7 stools per day over baseline; incontinence; IV fluids >=24 hrs; hospitalization; severe increase in ostomy output compared to baseline; interfering with ADL.
4. Life-threatening consequences (e.g., hemodynamic collapse)
5. Death

RATED AT EACH CLINIC VISIT

**REFERENCES:**


**Date revised:** 11/14/2008
MITOMYCIN C Chemotherapy
Advanced Gastrointestinal Cancers

MITOMYCIN
6mg/m² IV Day 1 Round to nearest 0.5mg
- Slow push through sidearm of free flowing IV; Give 1.5mg (3mL) per minute.

REPEAT EVERY 14 DAYS

TESTS:
Baseline Tests WBC HB ANC Ca K Na Chloride Phosphate Mg Glucose Cr Urea 24Hr
CrCl T.Bili Albumin ALT GGT AlkPhosphatase
Day 1 WBC HB PLT ANC Cr T.Bili
Test Notes - Baseline & periodic renal function tests (if failure suspected).

ANTIEMETIC PRE-CHEMO REGIMEN:
Level B Day 1 - Dexamethasone 8mg PO/IV
- May add or substitute Prochlorperazine 10mg PO/IV prn

ANTIEMETIC TAKE-HOME REGIMEN:
Level A Day 1 - Prochlorperazine 10mg PO q4-6h prn

PATIENT VISITS and APPOINTMENT TYPE:
- Day 1: 30min Type B

ANCILLARY:
- Oral hydration is strongly encouraged; poorly hydrated patients may need more IV hydration.

TOXICITIES:
Hematologic
1. If ANC < 1.5 x 10⁹/L, or if PLT < 100 x 10⁹/L, HOLD dose for 1-2 weeks (or until PLT > 120-150 x 10⁹/L).
2. If PLT drop 20%, HOLD dose until platelet count stable.

Renal Failure
1. If CrCl < 0.2mL/sec, GIVE 75% dose.

Hepatic Dysfunction
1. If T.Bili = 50-85 umol/L or AST > 180 IU/L, GIVE 75% dose.

SUGGESTED ACTION
CLINICAL MONITORING:
- Clinical pulmonary exam, including auscultation, pulmonary toxicity ratings (Cough, SOB).
- Blood pressure and CBC at each visit

Dyspnea
1. Dyspnea on exertion, but can walk 1 flight of stairs without stopping 2. Dyspnea on exertion but unable to walk 1 flight of stairs or 1 city block (0.1km) without stopping 3. Dyspnea with ADL 4. Dyspnea at rest; intubation/ventilator indicated 5. Death

Cough
1. Symptomatic, non-narcotic medication only indicated 2. Symptomatic and narcotic medication indicated 3. Symptomatic and significantly interfering with sleep or ADL
RATED AT EACH CLINIC VISIT

Date revised: 11/14/2008
OCTREOTIDE Therapy
Carcinoid Syndrome, VIPomas, Glucagonomas, GRFomas- Palliative Intent

OCTREOTIDE
Dosage varies SC Continuous Treatment

- SC treatment:
  - Dosage range = 50mcg-1500mcg/day in 2 to 4 divided doses (experience with doses above 750mcg/day is limited).
  - Supplied as: 100mcg/1mL and 500mcg/1mL ampoules or 200mcg/mL 5mL vial.
  - IM treatment (Long Acting Injection):
    - Dose = 20mg or 30mg, every 4 weeks for the first 3 months, then adjusted as per symptoms.
    - Supplied as: 20mg/vial or 30mg/vial.
  - Outpatient prescription.

CONTINUOUS TREATMENT

TESTS:
Baseline Tests: WBC HB PLT ANC Cr Urea T.Bili ALT AlkPhosphatase

CLINICAL MONITORING:
- Ultrasonograph of the gall bladder, to assess the presence of gallstones (during long-term therapy).

Date revised: 11/14/2008
GI-PANITUMUMAB

PANITUMUMAB MONOTHERAPY

For patients with confirmed non-mutated (wild type) K-RAS oncogene mCRC
3rd line after failure of Fluoropyrimidine, Oxaliplatin, and Irinotecan

GI-PANITUMUMAB MONOTHERAPY

Metastatic Colorectal Cancer

For patients with confirmed non-mutated (wild type) K-RAS oncogene mCRC
3rd line after failure of Fluoropyrimidine, Oxaliplatin, and Irinotecan

PANITUMUMAB

6mg/kg/day IV Day 1 Round to the nearest 10mg

- Admix to a TOTAL of 100mL with Normal Saline to a MAXIMUM of 10mg/mL.
- Infuse over 1 hour, using a low protein binder tubing with a 0.2 or 0.22um filter.
(Doses above 1000mg should be diluted to 150mL and infuse over 90 minutes)
- Infusion line should be flushed with saline before and after Panitumumab administration.
DO NOT ADMINISTER AS AN IV PUSH OR BOLUS

REPEAT EVERY 14 DAYS, UNTIL DISEASE PROGRESSION

TESTS:

Baseline Tests: WBC HB PLT ANC Ca K Na Chloride Phosphate Mg Cr Urea T.Bili AST ALT AlkPhosphatase

Each Visit: Ca K Na Chloride Phosphate Mg

K-RAS testing of the tumour block prior to initiation of treatment.

ANTIEMETIC PRE-CHEMO REGIMEN:

No Level Day 1 No premeds required

PATIENT VISITS and APPOINTMENT TYPE:

-> Day 1 1 hour Type C

TOXICITIES:

Hypomagnesemia:
- Patients should be periodically monitored for hypomagnesemia and accompanying hypocalcemia during, and for 8 weeks after, the completion of treatment.

Pulmonary
- Acute onset or worsening of pulmonary symptoms, Panitumumab treatment should be interrupted.
If pneumonitis or lung infiltrates are confirmed, Panitumumab should be discontinued.

Cutaneous
- Most common adverse events observed were skin rash with variable presentations.

Rash:
- Usually will improve with time but early intervention with steroid cream and/or antibiotic cream (Clindamycin) is recommended.
- If severe rash, may consider oral antibiotics such as Minocycline or Doxycycline. If severe rash despite appropriate management, may require treatment interruption and/or dose modification. Once improved, re-start administration at 50% of the original dose. If toxicities do not worsen, escalate each additional dose by 25% increments of the original dose until the starting dose is reached. If toxicity does not resolve to at least grade 2 after withholding, or if toxicity worsens or becomes intolerable at 50% of the original dose, then Panitumumab should be discontinued permanently.

Dermatitis Acneiform/Rash:
- Most common on face, upper back and chest, multiple pustular, maular or papular appearing lesions, advise patients on signs of secondary infection, do not use acne medication, nor perfumes or scented creams; avoid the sun and to wear sunscreen.

Pruritus:
- Topical or oral antihistamines may help.

Skin drying and Fissures:
- Moisturize

Paronychia:
- Counsel on hand hygiene, avoid nail biting, avoid trimming or pushing back cuticles, avoid tight shoes and artificial nails.

Others:
- Erythema and exfoliative rash

Gastrointestinal
- Monitor for abdominal pain & constipation.

Diarrhea:
- Optimal use of antidiarrheal medication such as Loperamide or Diphenoxylate/Atropine. If severe, may require treatment interruption and/or dose modification.

Gastrointestinal
PANITUMUMAB MONOTHERAPY

**CLINICAL MONITORING:**
- Monitor for dehydration, pulmonary fibrosis, pulmonary embolism, erythema, rash, and skin fissures.
- It is recommended that patients wear sunscreen and a hat and limit sun exposure while receiving Panitumab as sunlight can exacerbate any skin reactions that may occur.

**Pruritus**
1. Mild or localized; 2. Intense or widespread; 3. Intense or widespread and interfering with ADL;

**Dry Skin**
1. Asymptomatic; 2. Symptomatic, not interfering with ADL; 3. Interfering with ADL

**Nail Changes**
1. Discoloration, ridging; pitting; 2. Partial or complete loss of nail(s); pain in nailbed(s); 3. Interfering with ADL

**Pneumonitis**
1. Asymptomatic, radiographic findings only; 2. Symptomatic not interfering with ADL; 3. Symptomatic, interfering with ADL; O2 indicated; 4. Life-threatening; ventilatory support indicated; 5. Death

**Diarrhea**
1. Increase of <4 stools per day over baseline; mild increase in ostomy output compared to baseline; 2. Increase of 4-6 stools per day over baseline; IV fluids indicated <24 hrs; moderate increase in ostomy output compared to baseline; not interfering with ADL; 3. Increase of >7 stools per day over baseline; incontinence; IV fluids >24 hrs; hospitalization; severe increase in ostomy output compared to baseline; interfering with ADL; 4. Life-threatening consequences (eg. hemodynamic collapse); 5. Death

**HYPERSENSITIVITY:**
- Severe infusion reactions occurred in approximately 1% of patients; identified by reports of anaphylactic reaction, bronchospasm, fever, chills, and hypotension. STOP infusion if a severe infusion reaction occurs, and treat accordingly.

**REFERENCES:**
Vectibix, Prescribing Information, Product Monograph, Amgen Oncology Canada Inc. April 2008
Scarborough General Hospital Pharmacy Flowsheet November 2008

CCO Eligibility Form Required Yes [✓] Non-Formulary Form Required No [ ] Date revised: 12/02/2008
RALTITREXED Chemotherapy
Advanced Colorectal Carcinoma- Palliative Intent

RALTITREXED 3mg/m² IV Day 1 Round to nearest 1mg
- Mix in 100mL minibag Normal Saline or 5% Dextrose; Infuse over 15 minutes.
- Trade name = Tomudex™

REPEAT EVERY 21 DAYS

TESTS:
Baseline Tests: WBC HB PLT ANC K Na Chloride Cr Urea T.Bili ALT AlkPhosphatase
Day 1: WBC HB PLT ANC Cr T.Bili

ANTIEMETIC PRE-CHEMO REGIMEN:
Level C Day 1
- Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
- Dexamethasone 20mg PO/IV

ANTIEMETIC TAKE-HOME REGIMEN:
Level B/C Day 1
- Ondansetron 8mg PO BID for 2-3 days, or Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days
- Dexamethasone 8mg PO BID for 2-3 days
- Prochlorperazine 10mg PO q4-6h prn

PATIENT VISITS and APPOINTMENT TYPE:
The Day 1 30min Type A

TOXICITIES:
Hematologic
1. If ANC < 1.5 x 10⁹/L, or if PLT = 75-100 x 10⁹/L, REDUCE to 50% dose.
2. If ANC < 1.0 x 10⁹/L, or if PLT < 75 x 10⁹/L, HOLD dose for 1 week.

Renal Failure
1. If CrCl < 65mL/min, REDUCE to 75% dose every 4 weeks.
2. If CrCl < 55mL/min, use % dose equivalent to mL/min every 4 weeks (eg. 30mL/mL=30% dose).
3. If CrCl < 25mL/min, NO treatment.

Gastrointestinal
1. If Mucositis or Diarrhea ≥ Grade 3 in previous course, REDUCE to 2/3 dose.

SUGGESTED ACTION

CLINICAL MONITORING:
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.

Diarrhea
1. Increase of < 4 stools per day over baseline; mild increase in ostomy output compared to baseline
2. Increase of 4 - 6 stools per day over baseline; IV fluids indicated < 24hrs; moderate increase in ostomy output compared to baseline; not interfering with ADL 3. Increase of >7 stools per day over baseline; incontinence; IV fluids >24 hrs; hospitalization; severe increase in ostomy output compared to baseline; interfering with ADL 4. Life-threatening consequences (e.g., hemodynamic collapse) 5. Death

Mucositis
1. Erythema of the mucosa 2. Patchy ulcerations or pseudomembranes 3. Confluent ulcerations or pseudomembranes; bleeding with minor trauma 4. Tissue necrosis; significant spontaneous bleeding; life-threatening consequences 5. Death

RATED AT EACH CLINIC VISIT

FORMULAE:
CrCl - Cockcroft & Gault (mL/sec) Male: [140-age(yrs)] x TBW(Kg) / [50 x SCr(umol/L)]
CrCl - Cockcroft & Gault (mL/sec) Female: [140-age(yrs)] x TBW(Kg) / [50 x SCr(umol/L)] x 0.85
Creatinine Cl (mL/min) mL/min = 60 x CrCl mL/sec

REFERENCES:

CCO Eligibility Form Required ✔ Non-Formulary Form Required □ Date revised: 11/14/2008
STREPTOZOCIN-5-FLUOROURACIL Chemotherapy
Metastatic Carcinoid- Palliative Intent

STREPTOZOCIN
500mg/m² IV Days 1-5 Round to nearest 10mg
- Mix in 50mL bag 5% Dextrose or Normal Saline.
- Infuse over 15-30 minutes through rapid free-flowing IV.
- Notify Pharmacy in advance. Streptozocin is not kept in stock, and will require a few days to obtain.

5-FLUOROURACIL
400-500mg/m² IV Days 1-5 Round to nearest 25mg
- Inject by direct IV push over 1-3 minutes, followed by a Normal Saline flush.
- Patients are recommended to suck on ice chips about 5 minutes before treatment begins until 30 minutes after treatment is completed to reduce the incidence and severity of stomatitis.

REPEAT EVERY 28 DAYS

TESTS:
Baseline Tests: WBC HB PLT ANC K Na Chloride Glucose Cr Urea T.Bili Albumin ALT GGT AlkPhosphatase
Day 1: WBC HB PLT ANC K Na Chloride Glucose Cr Urea T.Bili Albumin ALT GGT AlkPhosphatase

ANTIEMETIC PRE-CHEMO REGIMEN:
Level C Days 1-5 - Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
- Dexamethasone 20mg PO/IV

ANTIEMETIC TAKE-HOME REGIMEN:
Level B/C Days 1-5 - Ondansetron 8mg PO BID for 2-3 days, or Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days
- Dexamethasone 8mg PO BID for 2-3 days
- Prochlorperazine 10mg PO q4-6h prn

PATIENT VISITS and APPOINTMENT TYPE:
 Days 1-5: 45min Type B

TOXICITIES:
Hematologic
1. If ANC < 1.5 x 10⁹/L, or if PLT < 100 x 10⁹/L, HOLD dose for 1 week.
Renal Failure
1. If CrCl = 0.2-0.8mL/sec, REDUCE Streptozocin to 75% dose.
2. If CrCl < 0.2mL/sec, REDUCE Streptozocin to 50% dose.
Hepatic Dysfunction
1. If T.Bili > 85 umol/L or AST > 180 IU/L, OMIT dose.

SUGGESTED ACTION
CLINICAL MONITORING:
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.
- Urinalysis (for proteinuria).

Date revised: 11/14/2008
STREPTOZIN-DOXORUBICIN chemotherapy
Islet Cell/Neuroendocrine Carcinoma - Palliative Intent

STREPTOZOCIN
500mg/m² IV Days 1-5 Round to nearest 10mg
- Mix in 50mL bag 5% Dextrose or Normal Saline.
- Infuse over 15-30 minutes through rapid free-flowing IV.
- Notify Pharmacy in advance. Streptozocin is not kept in stock, and will require a few days to obtain.

DOXORUBICIN
50mg/m² IV Days 1 & 22 Round to nearest 1mg
- Slow push through sidearm of free flowing IV.
- Give 2 to 4mg (1-2mL) per minute.
- REPEAT EVERY 42 DAYS UNTIL DISEASE PROGRESSION

TESTS:
Baseline Tests
WBC HB PLT ANC K Na Chloride Glucose Cr Urea T.Bili Albumin ALT GGT AlkPhosphatase
Day 1
WBC HB PLT ANC K Na Chloride Glucose Cr Urea T.Bili Albumin ALT GGT AlkPhosphatase

ANTIEMETIC PRE-CHEMO REGIMEN:
Level C Days 1-5 & 22
- Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
- Dexamethasone 20mg PO/IV

ANTIEMETIC TAKE-HOME REGIMEN:
Level B/C Days 1-5 & 22
- Ondansetron 8mg PO BID for 2-3 days, or Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days
- Dexamethasone 8mg PO BID for 2-3 days
- Prochlorperazine 10mg PO q4-6h prn

PATIENT VISITS and APPOINTMENT TYPE:
- Day 1 2 h Type C
- Days 2-5 45min Type B
- Day 22 60min Type C

TOXICITIES:
Hematologic
1. If ANC < 1.5 x 10⁹/L, or if PLT < 100 x 10⁹/L, HOLD dose for 1 week.
Renal Failure
1. If CrCl = 0.2-0.8mL/sec, REDUCE Streptozocin to 75% dose.
2. If CrCl < 0.2mL/sec, REDUCE Streptozocin to 50% dose.
3. If SrCr >265umol/L, REDUCE dose to 50% of Doxorubicin.
Hepatic Dysfunction
1. If T.Bili > 85 umol/L or AST > 180 IU/L, OMIT dose of Streptozocin.
2. If T.Bili = 52-85umol/L or AST = 60-180 IU/L, GIVE 75% dose of Doxorubicin.
3. If T.Bili = 26-51umol/L or AST = 24-60 IU/L, GIVE 50% dose of Doxorubicin.
4. If T.Bili > 25umol/L, OMIT dose of Doxorubicin.

SUGGESTED ACTION
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.
- Urinalysis for proteinuria.
- Clinical assessment of glucose tolerance with periodic testing.
- Clinical exam for symptoms of CHF.
- Periodic cardiac tests for all patients with cardiac risk factors and patients at or above the threshold dose levels.
- For Cardiac Toxicity Ratings: First rating at the cumulative dose threshold of 450mg/m², & repeat ratings at each cumulative dose increment of 100mg/m² above threshold (Cumulative dose sooner for high risk patients, eg. pre-existing cardiac disease, prior chest irradiation).
- Note: Threshold Cumulative dose reduced proportionately if other anthracycline or anthracenedione drugs have been given; cardiotoxicity is additive.

LV Systolic Dysfunction
1. Asymptomatic, resting ejection fraction (EF) < 60 - 50%; shortening fraction (SF) < 30 - 24%
2. Asymptomatic, resting EF < 50 - 40%; SF < 24 - 15%
3. Symptomatic CHF responsive to intervention; EF < 40 - 20%
4. Symptomatic CHF refractory to intervention; EF < 20%
5. Death

For Cardiac Toxicity Ratings: First rating at the cumulative dose threshold of 450mg/m², and repeat ratings at each cumulative dose increment of 100mg/m² above threshold. (Cumulative dose sooner for high risk patients, eg. pre-existing cardiac disease, prior chest irradiation).

ClINICAL MONITORING:
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.
- Urinalysis for proteinuria.
- Clinical assessment of glucose tolerance with periodic testing.
- Clinical exam for symptoms of CHF.
- Periodic cardiac tests for all patients with cardiac risk factors and patients at or above the threshold dose levels.

LV Systolic Dysfunction
1. Asymptomatic, resting ejection fraction (EF) < 60 - 50%; shortening fraction (SF) < 30 - 24%
2. Asymptomatic, resting EF < 50 - 40%; SF < 24 - 15%
3. Symptomatic CHF responsive to intervention; EF < 40 - 20%
4. Symptomatic CHF refractory to intervention; EF < 20%
5. Death

FORMULAE:
CrCl - Cockcroft & Gault (mL/sec)
Male: [140-age(yrs)] x TBW(Kg) / [50 x Scr(umol/L)]
CrCl - Cockcroft & Gault (mL/sec)
Female: [140-age(yrs)] x TBW(Kg) / [50 x Scr(umol/L)] x 0.85

REFERENCES:

Date revised: 11/14/2008
CAPECITABINE-IRINOTECAN Chemotherapy
Metastatic Colorectal Carcinoma

CAPECITABINE
2000mg/m²/day PO Days 1-14 150mg & 500mg tablets
- Divided into BID dosing (1000mg/m² BID) for 14 days.
- Start evening of day 1 and continue BID until morning of day 15.
- If renal impairment or age > 65, DECREASE Capecitabine dose to 750mg/m² BID.
- Outpatient prescription available in 150mg and 500mg tablets.
- Trade name is Xeloda™

IRINOTECAN
250mg/m² IV Day 1 Round to nearest 1mg
- Admix in 500ml bag 5% Dextrose or Normal Saline over 90 minutes.
- If renal impairment or age > 65, DECREASE Irinotecan dose to 200mg/m².

ATROPINE
0.25-1mg SC Day 1
- May be given pre-chemo to prevent cholinergic adverse effects or within 1 hour post-chemo for acute-onset diarrhea.
- Check BP and HR every 30 minutes x2 and until patient stable.

LOPERAMIDE
2mg PO Day 1 & prn 2mg tablet
- 4mg PO at the onset of diarrhea, then 2mg q2h PO until patient is diarrhea free for 12 hours.
- May give 4mg q4h during night time.

TESTS:
Baseline Tests WBC HB PLT ANC Cr Urea T.Bili ALT AlkPhosphatase
Day 1 WBC HB PLT ANC Cr Urea T.Bili ALT AlkPhosphatase
Test Notes - Weekly INR for patients on Warfarin until stable, then Day 1 only.

ANTIEMETIC PRE-CHEMO REGIMEN:
Level C Day 1
- Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
- Dexamethasone 12mg PO/IV
- AVOID Prochlorperazine on the day(s) irinotecan is administered.

ANTIEMETIC TAKE-HOME REGIMEN:
Level A Day 1
- Prochlorperazine 10mg PO q4-6h pm starting Day 2 of treatment
- AVOID Prochlorperazine on the day(s) irinotecan is administered.

PATIENT VISITS and APPOINTMENT TYPE:
- Day 1 2hrs Type C

ANCILLARY:
- Take Capecitabine tablets WITH FOOD (within 30 minutes of a meal).
- Treatment or Prophylaxis to Prevent Hand-Foot Skin Reaction: Take Pyridoxine (Vitamin B6) PO 100mg BID or 50mg TID continuously. Apply Lac-Hydrin™ Lotion to hands and feet once or twice daily.

TOXICITIES:
Hematologic
1. If ANC < 1.5 x 10⁹/L, HOLD Capecitabine & Irinotecan for 1 week (or until AGC ≥ 1.5 x 10⁹/L), then restart chemotherapy (no reduction).
2. If ANC < 1.0 x 10⁹/L, HOLD Capecitabine & Irinotecan for 1 week (or until AGC ≥ 1.5 x 10⁹/L), then restart chemotherapy reduced by 25%.
3. If ANC < 0.5 x 10⁹/L, HOLD Capecitabine & Irinotecan for 1 week (or until AGC ≥ 1.5 x 10⁹/L), then restart chemotherapy reduced by 50%.

Gastrointestinal
1. If Diarrhea = grade 2, HOLD Capecitabine & Irinotecan until score 0 or 1, restart at 100%.
2. If Diarrhea = grade 3, HOLD Capecitabine & Irinotecan until grade 0 - 1, then restart treatment reduced by 25%.
3. If Diarrhea = grade 4, HOLD Capecitabine & Irinotecan until grade 0 - 1, then restart treatment reduced by 50% or Discontinue Treatment.

Hepatic Dysfunction
1. Irinotecan has not been studied in patients with T.Bili > 35μmol/L, transaminase > 3 x ULN if no liver metastases.
2. If Diarrhea = grade 2, HOLD Capecitabine & Irinotecan until score 0 or 1, restart at 100%.
3. If Diarrhea = grade 3, HOLD Capecitabine & Irinotecan until grade 0 - 1, then restart treatment reduced by 25%.
4. If Diarrhea = grade 4, HOLD Capecitabine & Irinotecan until grade 0 - 1, then restart treatment reduced by 50% or Discontinue Treatment.

SUGGESTED ACTION

CLINICAL MONITORING:
- Routine assessment of diarrhea, at each clinic visit.
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.
- Skin assessment, especially for Hand-Foot Syndrome.

Diarrhea
1. Increase of < 4 stools per day over baseline; mild increase in ostomy output compared to baseline
2. Increase of 4 - 6 stools per day over baseline; IV fluids indicated < 24hrs; moderate increase in ostomy output compared to baseline; not interfering with ADL.
3. Increase of > 7 stools per day over baseline; incontinence; IV fluids >24 hrs; hospitalization; severe increase in ostomy output compared to baseline; interfering with ADL.
4. Life-threatening consequences (e.g., hemodynamic collapse) 5. Death

Hand-foot Skin Reaction
1. Minimal skin changes or dermatitis (e.g., erythema) without pain
2. Skin changes (e.g., peeling, blisters, bleeding, edema) or pain, not interfering with function
3. Ulcerative dermatitis or skin changes with pain interfering with function

RATED AT EACH CLINIC VISIT

CCO Eligibility Form Required ☑ Non-Formulary Form Required ☐ Date revised: 11/14/2008

Gastrointestinal
CAPECITABINE-OXALIPLATIN Chemotherapy

**Metastatic Colorectal Carcinoma**

**CAPECITABINE**

- **2000mg/m²/day PO Days 1-14**
- **150mg & 500mg tablets**
- Divided into BID dosage for 14 days.
- Start evening of day 1 and continue BID until morning of day 15.
- Outpatient prescription available in 150mg and 500mg tablets.
- Trade name is Xeloda™

**OXALIPLATIN**

- **130mg/m² IV Day 1**
- Round to nearest 2.5mg
- Admix in 500mL bag 5% Dextrose over 120 minutes.
- **DO NOT MIX IN NORMAL SALINE.**
- Repeat every 21 days.

**TESTS:**

<table>
<thead>
<tr>
<th>Baseline Tests</th>
<th>WBC</th>
<th>HB</th>
<th>PLT</th>
<th>ANC</th>
<th>Cr</th>
<th>T.Bili</th>
<th>ALT</th>
<th>AlkPhosphatase</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Day 1</strong></td>
<td>WBC</td>
<td>HB</td>
<td>PLT</td>
<td>ANC</td>
<td>Cr</td>
<td>T.Bili</td>
<td>ALT</td>
<td>AlkPhosphatase</td>
</tr>
</tbody>
</table>

**Test Notes:**
- Weekly INR for patients on Warfarin until stable, then Day 1 only.

**ANTIEMETIC PRE-CHEMO REGIMEN:**

- **Level C Day 1**
  - Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
  - Dexamethasone 20mg PO/IV

**ANTIEMETIC TAKE-HOME REGIMEN:**

- **Level B/C Day 1**
  - Ondansetron 8mg PO BID for 2-3 days, or
  - Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days
  - Dexamethasone 8mg PO BID for 2-3 days
  - Prochlorperazine 10mg PO q4-6h prn

**PATIENT VISITS and APPOINTMENT TYPE:**

- Day 1 2hrs Type C

**ANCILLARY:**
- **NO CRYOTHERAPY**
- Take Capecitabine tablets WITH FOOD (within 30 minutes of a meal).
- Treatment or Prophylaxis to Prevent Hand-Foot Skin Reaction: Take Pyridoxine (Vitamin B6) PO 100mg BID or 50mg TID continuously. Apply Lac-Hydrin™ Lotion to hands and feet once or twice daily.

**TOXICITIES:**

**Hematologic**
1. If ANC < 1.5 x 10⁹/L, HOLD Capecitabine & Oxaliplatin for 1 week (or until AGC > 1.5 x 10⁹/L), then restart chemotherapy (no reduction).
2. If ANC < 1.0 x 10⁹/L, HOLD Capecitabine & Oxaliplatin for 1 week (or until AGC > 1.5 x 10⁹/L), then restart chemotherapy reduced by 25%.
3. If ANC < 0.5 x 10⁹/L, HOLD Capecitabine & Oxaliplatin for 1 week (or until AGC > 1.5 x 10⁹/L), then restart chemotherapy reduced by 50%.

**Gastrointestinal**
1. If Diarrhea = grade 2, HOLD Capecitabine & Oxaliplatin until score 0 or 1, restart at 100%.
2. If Diarrhea = grade 3, HOLD Capecitabine & Oxaliplatin until grade 0-1, then restart treatment reduced by 25%.
3. If Diarrhea = grade 4, HOLD Capecitabine & Oxaliplatin until grade 0-1, then restart treatment reduced by 50% or Discontinue Treatment.

**Neurologic**
1. If paraesthesia without functional impairment persists until next cycle, REDUCE dose of Oxaliplatin by 25%.
2. If paraesthesia with functional impairment persists until next cycle, DISCONTINUE Oxaliplatin.
3. If acute laryngopharyngeal dysaesthesia occurs during the infusion, stop infusion until symptoms resolve then slow the rate of infusion, subsequent Oxaliplatin infusion administered over 6 hours.

**SUGGESTED ACTION**
CAPECITABINE-OXALIPLATIN Chemotherapy

CLINICAL MONITORING:
- Routine assessment of diarrhea, at each clinic visit.
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.
- Skin assessment, especially for Hand-Foot Syndrome.

Diarrhea
1. Increase of < 4 stools per day over baseline; mild increase in ostomy output compared to baseline
2. Increase of 4 - 6 stools per day over baseline; IV fluids indicated < 24hrs; moderate increase in ostomy output compared to baseline; not interfering with ADL 3. Increase of >7 stools per day over baseline; incontinence; IV fluids <24 hrs; hospitalization; severe increase in ostomy output compared to baseline; interfering with ADL 4. Life-threatening consequences (e.g., hemodynamic collapse) 5. Death

Hand-foot Skin Reaction
1. Minimal skin changes or dermatitis (e.g., erythema) without pain 2. Skin changes (e.g., peeling, blisters, bleeding, edema) or pain, not interfering with function 3. Ulcerative dermatitis or skin changes with pain interfering with function

Sensory
1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function 2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL 3. Sensory alteration or paresthesia interfering with ADL 4. Disabling 5. Death

RATED AT EACH CLINIC VISIT

REFERENCES:

Date revised: 11/14/2008
CISPLATIN-ETOPOSIDE-BLEOMYCIN (PEB) Chemotherapy

Testicular Cancer

**CISPLATIN**
- 20mg/m²
- IV Days 1-5
- Round to nearest 1mg
- Mix in **500mL** bag **Normal Saline**; Infuse over **60 minutes**.

**ETOPOSIDE**
- 100mg/m²
- IV Days 1-5
- Round to nearest 10mg
- Dose ≤ 200mg, mix in **500mL** **Normal Saline**; Infuse over **30-60 minutes**.
- Dose > 200mg, mix in **1000mL** **Normal Saline**; Infuse over **1 to 2 hours**.
- Use Non-PVC equipment and filter.
- Adjust rate if blood pressure drops.
- Give Etoposide BEFORE Cisplatin, to hydrate patient.

**BLEOMYCIN**
- 30units
- IV Days 1, 8 &15
- Round to nearest unit
- Slow push through sidearm of free flowing IV over 10 minutes.
- May be given by direct IV push, followed by a Normal Saline flush.

**ACETAMINOPHEN**
- 650mg
- PO Days 1, 8 &15
- 325mg tablet
- Administer before Bleomycin dose.

**HYDRATION:**
- **Pre**
  - Infuse **1000mL Normal Saline** with **20mEq Potassium Chloride** IV over **1 hour** on Days 1-5.
- **Post**
  - Infuse **1000mL Normal Saline** IV over **1-2 hours** on Days 1-5.

**TESTS:**
- **Baseline Tests**
  - WBC HB PLT ANC K Na Chloride Mg Glucose Cr Urea AST ALT AlkPhosphatase
- **Day 1**
  - WBC HB PLT ANC Cr
- **Days 8 & 15**
  - WBC HB PLT ANC Cr
- **Test Notes**
  - Baseline & routine renal function tests, especially if there are other concurrent nephrotoxic drugs.

**ANTIEMETIC PRE-CHEMO REGIMEN:**
- **Level C**
  - Days 1-5
    - Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
    - Dexamethasone 20mg PO/IV
    - Prochlorperazine 10mg PO pm
- **Level A**
  - Days 8 & 15
    - Ondansetron 8mg PO BID for 2-3 days, or Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days
    - Dexamethasone 8mg PO BID for 2-3 days
    - Prochlorperazine10 mg PO q4-6h pm
    - Prochlorperazine 10mg PO q4-6h pm

**ANTIEMETIC TAKE-HOME REGIMEN:**
- **Level B/C**
  - Day 5
    - Ondansetron 8mg PO BID for 2-3 days, or Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days
    - Dexamethasone 8mg PO BID for 2-3 days
    - Prochlorperazine10 mg PO q4-6h pm
    - Prochlorperazine 10mg PO q4-6h pm
- **Level A**
  - Days 8 & 15

**PATIENT VISITS and APPOINTMENT TYPE:**
- **Days 1-5**
  - 5hrs Type C
- **Days 8 & 15**
  - 30min Type A

**ANCILLARY:**
- Increase fluids if poor oral intake.

**TOXICITIES:**
- **Hematologic**
  1. If ANC < 1.5 x 10⁹/L, or if PLT < 75 x 10⁹/L, **HOLD** dose for 1 week.
- **Renal Failure**
  1. If CrCl = 0.5-1.0mL/sec, or SrCr = 136-185umol/L, **REDUCE** Cisplatin to **50%** dose, and Bleomycin & Etoposide to **75%** dose.
  2. If CrCl < 0.5mL/sec, or SrCr > 185umol/L, **OMIT** Cisplatin dose.
  3. If CrCl < 0.2mL/sec, **REDUCE** Bleomycin and Etoposide to **50%** dose.
- **Hepatic Dysfunction**
  1. If T.Bili = 26-51umol/L, or AST = 60-180 IU/L, **REDUCE** Etoposide to **25%** dose.
  2. If T.Bili = 52-85umol/L, **REDUCE** Etoposide to **50%** dose.
  3. If T.Bili > 85umol/L, or AST > 180 IU/L, **OMIT** Etoposide dose.

**SUGGESTED ACTION**
Genitourinary

**CISPLATIN-ETOPOSIDE-BLEOMYCIN (PEB) Chemotherapy**

**CLINICAL MONITORING:**
- Oral examination upon patient complaint of a sore mouth.
- Clinical pulmonary exam at each visit, including auscultation, pulmonary toxicity ratings (Cough, SOB).

**Sensory**
1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function
2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL
3. Sensory alteration or paresthesia interfering with ADL
4. Disabling
5. Death

**Hearing**
1. Asymptomatic, detected on exam/testing only
2. Symptomatic, not interfering with ADL
3. Symptomatic, interfering with ADL
4. Life-threatening; disabling
5. Death

**Dyspnea**
1. Dyspnea on exertion, but can walk 1 flight of stairs without stopping
2. Dyspnea on exertion but unable to walk 1 flight of stairs or 1 city block (0.1km) without stopping
3. Dyspnea with ADL
4. Dyspnea at rest; intubation/ventilator indicated
5. Death

**Cough**
1. Symptomatic, non-narcotic medication only indicated
2. Symptomatic and narcotic medication indicated
3. Symptomatic and significantly interfering with sleep or ADL

**FORMULAE:**

<table>
<thead>
<tr>
<th>Formula</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>CrCl - Cockcroft &amp; Gault (mL/sec)</td>
<td>Male: [140-age(yrs)] x TBW(Kg) / [50 x SCr(umol/L)]</td>
</tr>
<tr>
<td>CrCl - Cockcroft &amp; Gault (mL/sec)</td>
<td>Female: [140-age(yrs)] x TBW(Kg) / [50 x SCr(umol/L)] x 0.85</td>
</tr>
<tr>
<td>Creatinine Cl (mL/min)</td>
<td>mL/min = 60 x CrCl mL/sec</td>
</tr>
</tbody>
</table>

**REFERENCES:**

Date revised: 07/17/2008
GU-CISP*RT
Genitourinary

CISPLATIN Chemotherapy
Bladder Cancer

CISPLATIN 75mg/m² IV Day 1 Round to nearest 1mg
- Mix in 500mL Normal Saline; Infuse over 60 minutes.

RADIATION
2 Phase Daily
For radical bladder cases regardless of chemo regimen.
Technique: 4 field, 2 phase
Modality: 6 MV or 18 MV
Dose Specification: Isocentre
Total Dose: 6500 cGy
Fraction Dose: 180-200 cGy per day
Pattern: Daily

REPEAT EVERY 14 DAYS for 3 cycles concurrent with pelvic radiotherapy

HYDRATION:
Pre
- Infuse 1000mL Normal Saline with 20mEq Potassium Chloride IV over 2 hours.
Concurrent
- Give 250mL of 20% Mannitol solution (50G) IV; Infuse through sidearm concurrent with Cisplatin.
Post
- Infuse 500mL Normal Saline with 10mEq Potassium Chloride & 2G Magnesium Sulfate IV over 1 hour.

TESTS:
Baseline Tests WBC HB PLT ANC Cr Urea
Day 1 WBC HB PLT ANC Cr Urea
Test Notes - Baseline and routine renal function tests, especially if there are other concurrent nephrotoxic drugs.

ANTIEMETIC PRE-CHEMO REGIMEN:
Level C Day 1
- Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
- Dexamethasone 20mg PO/IV
- May add Aprepitant 125mg PO before chemo (reduce PO Dexamethasone by 50%)

ANTIEMETIC TAKE-HOME REGIMEN:
Level B/C Day 1
- Ondansetron 8mg PO BID for 2-3 days, or Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days
- Dexamethasone 8mg PO BID for 2-3 days
- May add Aprepitant 80mg PO on Days 2&3 (reduce PO Dexamethasone by 50%)
- Prochlorperazine 10mg PO q4-6h prn

PATIENT VISITS and APPOINTMENT TYPE:
- Day 1 4-6hrs Type D

ANCILLARY:
- Oral hydration is strongly encouraged, poorly hydrated patients may need more IV hydration to prevent renal toxicity.

TOXICITIES:
Hematologic
- If ANC < 1.5 x 10⁹/L, or if PLT < 100 x 10⁹/L, HOLD dose for 1 week.
Renal Failure
1. If CrCl = 0.5-1.0mL/sec, or SrCr = 136umol/L, REDUCE Cisplatin to 50% dose.
2. If CrCl < 0.5mL/sec, or SrCr > 185umol/L, OMIT Cisplatin dose.
SUGGESTED ACTION

CLINICAL MONITORING:
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.
Hearing
1. Asymptomatic, detected on exam/testing only 2. Symptomatic, not interfering with ADL 4. Life-threatening; disabling 5. Death
Sensory
1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function 2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL 3. Sensory alteration or paresthesia interfering with ADL 4. Disabling 5. Death
RATED AT EACH CLINIC VISIT

FORMULAE:
CrCl - Cockcroft & Gault (mL/sec)
Male: [140-age(yrs)] x TBW(Kg) / [50 x SCr(umol/L)]
CrCl - Cockcroft & Gault (mL/sec)
Female: [140-age(yrs)] x TBW(Kg) / [50 x SCr(umol/L)] x 0.85
Creatinine Cl (mL/min)
mL/min = 60 x CrCl mL/sec

INTERNAL CODE:
OPIS CODE: CISP-RT

REFERENCES:

CCO Eligibility Form Required ☐ Non-Formulary Form Required ☐ Date revised: 06/03/2008
CISPLATIN Chemotherapy
Bladder Cancer

CISPLATIN
40mg/m² IV Day 1 Round to nearest 1mg
- Mix in 500mL Normal Saline; Infuse over 60 minutes.

RADIATION
2 Phase Daily
For radical bladder cases regardless of chemo regimen.
Technique: 4 field, 2 phase
Modality: 6 MV or 18 MV
Dose Specification: Isocentre
Total Dose: 6500 cGy
Fraction Dose: 180-200 cGy per day
Pattern: Daily

REPEAT EVERY 7 DAYS DURING RADIOTHERAPY For a usual total of 5 cycles

HYDRATION:
Pre
- Infuse 1000mL Normal Saline with 20mEq Potassium Chloride IV over 2 hours.

Concurrent
- May give 250mL of 20% Mannitol solution (50G) IV. Infuse through side arm concurrent with Cisplatin (if diuresis is required).

Post
- Infuse 500mL Normal Saline with 10mEq Potassium Chloride & 2G Magnesium Sulfate IV over 1 hour.

TESTS:
Baseline Tests WBC HB PLT ANC Cr Urea
Day 1 WBC HB PLT ANC Cr Urea
Test Notes - Baseline and routine renal function tests, especially if there are other concurrent nephrotoxic drugs.

ANTIEMETIC PRE-CHEMO REGIMEN:
Level C Day 1 - Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
- Dexamethasone 20mg PO/IV

ANTIEMETIC TAKE-HOME REGIMEN:
Level B/C Day 1 - Ondansetron 8mg PO BID for 2-3 days, or Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days
- Dexamethasone 8mg PO BID for 2-3 days
- Prochlorperazine 10mg PO q4-6h prn

PATIENT VISITS and APPOINTMENT TYPE:
→ Day 1 4-6hrs Type D

ANCILLARY:
- Oral hydration is strongly encouraged, poorly hydrated patients may need more IV hydration to prevent renal toxicity.

TOXICITIES:
Hematologic
- If ANC < 1.5 x 10⁹/L, or if PLT < 100 x 10⁹/L, HOLD dose for 1 week.

Renal Failure
1. If CrCl = 0.5-1.0mL/sec, or SrCr = 136umol/L, REDUCE Cisplatin to 50% dose.
2. If CrCl < 0.5mL/sec, or SrCr > 185umol/L, OMIT Cisplatin dose.

SUGGESTED ACTION

CLINICAL MONITORING:
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.

Hearing
1. Asymptomatic, detected on exam/testing only 2. Symptomatic, not interfering with ADL
3. Symptomatic, interfering with ADL 4. Life-threatening; disabling 5. Death

Sensory
1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function 2.
Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL 3. Sensory alteration or paresthesia interfering with ADL 4. Disabling 5. Death

RATED AT EACH CLINIC VISIT

FORMULAE:
CrCl - Cockcroft & Gault (mL/sec)
Male: [140-age(yrs)] x TBW(Kg) / [50 x SCr(umol/L)]
CrCl - Cockcroft & Gault (mL/sec)
Female: [140-age(yrs)] x TBW(Kg) / [50 x SCr(umol/L)] x 0.85

INTERNAL CODE:
OPIS CODE: CISP-RT(weekly)

Date revised: 07/14/2008

Genitourinary
GU-CISP-ETOP

CISPLATIN-ETOPOSIDE Chemotherapy
Small Cell (Neuroendocrine) of the Prostate; Testicular Cancer

**CISPLATIN**
- 25mg/m² IV Days 1-3 Round to nearest 1mg
  - Mix in 100-250mL bag Normal Saline; Infuse over 30-60 minutes.
  - May also admix 10G Mannitol (50mL of 20% solution or 100mL of 10% solution) with Cisplatin.

**ETOPOSIDE**
- 100mg/m² IV Days 1-3 Round to nearest 10mg
  - Dose ≤ 200mg, mix in 500mL Normal Saline; Infuse over 30-60 minutes.
  - Dose > 200mg, mix in 1000mL Normal Saline; Infuse over 1 to 2 hours.
  - Use Non-PVC equipment and filter.
  - Adjust rate if blood pressure drops.
  - Give Etoposide BEFORE Cisplatin, to hydrate patient.

**REPEAT EVERY 21 DAYS**

**TESTS:**
Baseline Tests: WBC HB PLT ANC Ca K Na Chloride Phosphate Mg Glucose Cr Urea T.Bili Albumin AST ALT GGT AlkPhosphatase
Day 1: WBC HB PLT ANC K Na Chloride Mg Glucose Cr Urea AST ALT AlkPhosphatase

**ANTIEMETIC PRE-CHEMO REGIMEN:**
Level C Days 1-3 - Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
- Dexamethasone 20mg PO/IV
- May add Aprepitant 125mg po 1 hour before chemo (reduce PO Dexamethasone by 50%)

**ANTIEMETIC TAKE-HOME REGIMEN:**
Level B/C Days 1-3 - Ondansetron 8mg PO BID for 2-3 days. or Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days
- Dexamethasone 8mg PO BID for 2-3 days
- Prochlorperazine 10mg PO q4-6h prn

**PATIENT VISITS and APPOINTMENT TYPE:**
Days 1-3 2hrs Type C

**ANCILLARY:**
- Oral hydration is strongly encouraged; poorly hydrated patients may need more IV hydration.
- Adjust rate of Etoposide infusion if blood pressure drops.

**TOXICITIES:**
**Hematologic**
1. If ANC < 1.5 x 10⁹/L, or if PLT < 100 x 10⁹/L, HOLD dose for 1 week.

**Renal Failure**
1. If CrCl = 0.5-1.0mL/sec, or SrCr = 136-185umol/L, REDUCE to 50% dose.
2. If CrCl < 0.5mL/sec, or SrCr > 185umol/L, OMIT dose.

**Hepatic Dysfunction**
1. If T.Bili = 26-51umol/L, or AST = 60-180 IU/L, REDUCE to 50% dose.
2. If T.Bili = 52-85umol/L, REDUCE to 25% dose.
3. If T.Bili > 85umol/L, or AST > 180 IU/L, OMIT dose.

**CLINICAL MONITORING:**
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.

**Sensory**
1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function
2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL
3. Sensory alteration or paresthesia interfering with ADL
4. Disabling
5. Death

**Hearing**
1. Asymptomatic, detected on exam/testing only
2. Symptomatic, not interfering with ADL
3. Symptomatic, interfering with ADL
4. Life-threatening, disabling 5. Death

**FORMULAE:**
CrCl - Cockcroft & Gault (mL/sec) Male: [140-age(yrs)] x TBW(Kg) / [50 x SCR(umol/L)]
CrCl - Cockcroft & Gault (mL/sec) Female: [140-age(yrs)] x TBW(Kg) / [50 x SCR(umol/L)] x 0.85

**REFERENCES:**

**Date revised:** 06/03/2008
CISPLATIN-GEMCITABINE Chemotherapy

Bladder Cancer

GEMCITABINE
1000mg/m² IV Days 1, 8 & 15 Round to nearest 19mg
- Mix in 100-250mL bag Normal Saline; Infuse over 30 minutes through free-flowing IV.

CISPLATIN
70mg/m² IV Day 2 Round to nearest 1mg
- Mix in 500mL Normal Saline; Infuse over 60 minutes.

REPEAT EVERY 28 DAYS

HYDRATION:

Pre
- Infuse 1000mL Normal Saline with 20mEq/L Potassium Chloride IV over 2 hours before Cisplatin.

Concurrent
- Physician may order 250mL of 20% Mannitol Potassium Chloride IV. Infuse through sidearm concurrent with Cisplatin (may give Furosemide 40mg IV/PO instead of Mannitol).

Post
- Infuse 500mL Normal Saline with 10mEq Potassium Chloride IV (2G Magnesium Sulfate may also be ordered) over 1 hour after Cisplatin.

TESTS:

Baseline Tests
WBC HB PLT ANC Mg Cr Urea

Days 1 & 2
WBC HB PLT ANC Mg Cr Urea

Test Notes
- Baseline and routine renal function tests, especially if there are other concurrent nephrotoxic drugs.
- Baseline & periodic liver function tests.

ANTIEMETIC PRE-CHEMO REGIMEN:

Level A Days 1, 8 & 15
- Prochlorperazine 10mg PO prn
- Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
- Dexamethasone 20mg PO/IV
- May add Aprepitant 125mg po 1 hour before chemo (reduce PO Dexamethasone by 50%)

Level C Day 2
- Prochlorperazine 10mg PO q4-6h prn
- Ondansetron 8mg PO BID for 2-3 days, or Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days
- Dexamethasone 8mg PO BID for 2-3 days
- May add Aprepitant 80mg PO on Days 2&3 (reduce PO Dexamethasone by 50%)
- Prochlorperazine 10mg PO q4-6h prn

ANTIEMETIC TAKE-HOME REGIMEN:

Level A Days 1, 8 & 15
- Prochlorperazine 10mg PO q4-6h prn
- Ondansetron 8mg PO BID for 2-3 days, or Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days
- Dexamethasone 8mg PO BID for 2-3 days
- May add Aprepitant 80mg PO on Days 2&3 (reduce PO Dexamethasone by 50%)
- Prochlorperazine 10mg PO q4-6h prn

Level B/C Day 2
- Prochlorperazine 10mg PO q4-6h prn
- Ondansetron 8mg PO BID for 2-3 days, or Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days
- Dexamethasone 8mg PO BID for 2-3 days
- May add Aprepitant 80mg PO on Days 2&3 (reduce PO Dexamethasone by 50%)
- Prochlorperazine 10mg PO q4-6h prn

PATIENT VISITS and APPOINTMENT TYPE:

⇒ Days 1, 8 & 15: 45min Type B
⇒ Day 2: 5hrs Type D

ANCILLARY:
- Oral hydration is strongly encouraged; poorly hydrated patients may need more IV hydration (to prevent renal toxicity).

TOXICITIES:

Hematologic
1. If ANC < 1.5 x 10⁹/L, or if PLT < 100 x 10⁹/L, HOLD dose for 1 week.

Renal Failure
1. If CrCl = 0.5-1.0mL/sec, or SrCr = 136-185umol/L, REDUCE Cisplatin to 50% dose.
2. If CrCl < 0.5mL/sec, or SrCr >185umol/L, OMIT Cisplatin dose.

Gastrointestinal
1. If Mucositis or Diarrhea > Grade 3 in previous course, REDUCE to 2/3 dose.

SUGGESTED ACTION
CISPLATIN-GEMCITABINE Chemotherapy

**CLINICAL MONITORING:**

**Hearing**
1. Asymptomatic, detected on exam/testing only
2. Symptomatic, not interfering with ADL
3. Symptomatic, interfering with ADL
4. Life-threatening; disabling
5. Death

**Sensory**
1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function
2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL
3. Sensory alteration or paresthesia interfering with ADL
4. Disabling
5. Death

**Diarrhea**
1. Increase of < 4 stools per day over baseline; mild increase in ostomy output compared to baseline
2. Increase of 4 - 6 stools per day over baseline; IV fluids indicated < 24hrs; moderate increase in ostomy output compared to baseline; not interfering with ADL
3. Increase of >=7 stools per day over baseline; incontinence; IV fluids >=24 hrs; hospitalization; severe increase in ostomy output compared to baseline; interfering with ADL
4. Life-threatening consequences (e.g., hemodynamic collapse)
5. Death

**Mucositis**
1. Erythema of the mucosa
2. Patchy ulcerations or pseudomembranes
3. Confluent ulcerations or pseudomembranes; bleeding with minor trauma
4. Tissue necrosis; significant spontaneous bleeding; life-threatening consequences
5. Death

RATED AT EACH CLINIC VISIT

**Edema limb**
1. 5 - 10% inter-limb discrepancy in volume or circumference at point of greatest visible difference; swelling or obscuration of anatomic architecture on close inspection; pitting edema
2. >10 - 30% inter-limb discrepancy in volume or circumference at point of greatest visible difference; readily apparent obscuration of anatomic architecture; obliteration of skin folds; readily apparent deviation from normal anatomic contour
3. >30% inter-limb discrepancy in volume; lymphorrhea; gross deviation from normal anatomic contour; interfering with ADL
4. Progression to malignancy (i.e., lymphangiosarcoma); amputation indicated; disabling
5. Death

RATED IF EDEMA NOTED ON ROUTINE VISITS.

**FORMULAE:**

\[ \text{CrCl - Cockcroft & Gault (mL/sec)} \]

- Male: \([140-\text{age (yrs)}] \times \text{TBW (Kg)} / [50 \times \text{SCr (umol/L)}] \]
- Female: \([140-\text{age (yrs)}] \times \text{TBW (Kg)} / [50 \times \text{SCr (umol/L)}] \times 0.85 \]

**INTERNAL CODE:**

- OPIS CODE:
  - CISP Q28D-GEM Q7D
  - CISP-GEM-GU

**REFERENCES:**

- BCCA protocol summary for palliative therapy for urothelial carcinoma using cisplatin and gemcitabin. BC Cancer Agency, Care & Research.
- CCO Practice Guideline 3-12: Use of Chemotherapy in Advanced Unresectable or Metastatic Transitional Cell Carcinoma of the Bladder or Urothelium.

**Date revised:** 06/03/2008
**DOCETAXEL Chemotherapy (weekly)**

**Hormone-Refractory Prostate Cancer**

**DOCETAXEL** 30mg/m² IV Day 1,8,15,22 and 29 Round to nearest 3mg

- Mix in **100mL** bag 5% Dextrose or **Normal Saline** to a maximum concentration at or below 0.9mg/mL.
- Range:(0.3 to 0.9mg/mL); Use non-PVC equipment without a filter.
- Infuse through main IV line.
- Elasto-gel® gloves should be placed on both hands and treatment should begin 15 minutes before the infusion starts and conclude 15 minutes after the infusion is done.
- Gloves should be changed after 45 minutes to sustain the cold temperature.
- First and Second Dose:
  - Infuse at a slower rate and then increase incrementally.
  - Infuse at **30mL/hr for 5 minutes**, then at **60mL/hr for 5 minutes**, then at **125mL/hr for 5 minutes**, then finally at **200mL/hr** until infusion complete.
  - Subsequent doses:
  - Infuse over **30 minutes**.

**REPEAT EVERY 6 WEEKS** (weekly administration for 5 out of 6 weeks)

**DEXAMETHASONE** 8mg PO Day 0 4mg tablet

- BID For 3 doses, starting the night before chemotherapy.

**DIPHENHYDRAMINE** 50mg IV Day 1

- If previous hypersensitivity reaction.
- May be mixed in **50mL** minibag **Normal Saline** (or 5% Dextrose); Give over **10-15 minutes**.

**PREDNISONE** 5mg PO Continuous 5mg tablet

- BID
- Outpatient prescription.

**TESTS:**

Baseline Tests WBC HB PLT ANC Ca K Na Chloride Glucose Urea T.Bili Albumin AST ALT GGT AlkPhosphatase

Day 1 WBC HB PLT ANC

Test Notes - LFTs to be done monthly.

**ANTIEMETIC PRE-CHEMO REGIMEN:**

**Level B**

**Day 1**

- Dexamethasone 4-8mg PO/IV (if patient has not taken PO dexamethasone at home).
- May add Prochlorperazine 10mg PO/IV if needed.

**ANTIEMETIC TAKE-HOME REGIMEN:**

**Level A**

**Day 1**

- Prochlorperazine 10mg PO q4-6h prn

**PATIENT VISITS and APPOINTMENT TYPE:**

- Day 1 (first 2 doses) 60min Type C
- Day 1 DOCE (subsequent) 60min Type B

**TOXICITIES:**

**Hematologic**

1. If ANC < 1.5 x 10⁹/L, or if PLT < 100 x 10⁹/L, HOLD dose for 1 week.

2. If AST or ALT > 53 IU/L, or if Alk Phos > 180 IU/L, REDUCE dose by 50%.

**SUGGESTED ACTION**

**CLINICAL MONITORING:**

- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.
- Watch for symptoms of fever and infection.
- Skin assessment at each visit, including nails.
- **Skin Toxicity**
  - None
  - 1. Hyperpigmentation
  - 2. Atrophy
  - 3. Subcutaneous fibrosis
  - 4. Desquamation, ulceration, or Necrosis

**Fluid Retention**

- None
- 1. Mild peripheral edema
- 2. Pleural effusion, outpatient management
- 3. Pleural effusion, inpatient management
- 4. Intubation required

**Nail Changes**

- 1. Discoloration; ridging (koilonychias); pitting
- 2. Partial or complete loss of nail(s); pain in nailbed(s)
- 3. Interfering with ADL

RATED AT EACH CLINIC VISIT
DOCETAXEL Chemotherapy (weekly)

HYPERSENSITIVITY:
Docetaxel Hypersensitivity Procedures:
1. Discontinue Docetaxel immediately if there are signs or symptoms of moderate or severe hypersensitivity. (Mild symptoms may resolve with a decrease in the rate of infusion).
2. Rapid IV administration of Diphenhydramine 50mg and Hydrocortisone 100mg.
3. Re-initiate infusion after 30 minutes, or when signs of reaction are resolved. Resume infusion at a slower rate, then increase incrementally to the initial planned rate, eg. infuse at 30mL/hr (a 3.3-hour rate) for 5 minutes, then at 60mL/hr (a 1.6-hour rate) for 5 minutes, then at 125mL/hr (a 0.8-hour rate) for 5 minutes, then finally, resume at 200mL/hr (0.5-hour infusion rate).
4. Depending on the intensity of the reaction, additional oral or IV pre-medication with an antihistamine should also be given for the next cycle of treatment and the rate of infusion should be decreased initially and then increased back to the recommended 1-hour infusion.

INTERNAL CODE:
OPIS CODE: DOCE WEEKLY-GU

REFERENCES:

Date revised: 09/27/2005
**DOCETAXEL Chemotherapy**
*Hormone-Refractory Prostate Cancer*

**DOCETAXEL** 75mg/m² IV Day 1 Round to nearest 3mg

- Mix in **250mL** bag 5% Dextrose or **Normal Saline** to a maximum concentration of 0.3 - 0.9 mg/mL.
- Use non-PVC equipment without a filter; Infuse through main IV line.
- Elasto-gel™ gloves should be placed on both hands and treatment should begin 15 minutes after the infusion starts and conclude 15 minutes after the infusion is done.
- Gloves should be changed after 45 minutes to sustain the cold temperature.

**First and Second Dose:**
- Infuse at a slower rate and then increase incrementally.
- Infuse at **30mL/hr** for 5 minutes, then at **60mL/hr** for 5 minutes, then at **125mL/hr** for 5 minutes, then finally at **250mL/hr** until infusion complete.

**Subsequent doses:**
- Infuse over 1 hour.

**DEXAMETHASONE** 8mg PO Day 0 4mg tablet
- BID for 3 days, starting evening before chemotherapy.

**DIPHENHYDRAMINE** 50mg IV Day 1
- If previous hypersensitivity reaction.
- May be mixed in **50mL** minibag (Normal Saline or 5% Dextrose); Give over 10-15 minutes.
- Wait 30 minutes before Docetaxel infusion started.

**PREDNISONE** 5mg PO Continuous 5mg tablet
- BID
- Outpatient prescription.

**TESTS:**

**Baseline Tests**
- WBC  HB  PLT  ANC  Ca  K  Na  Chloride  Mg  Glucose  Cr  Urea  T.Bili  Albumin
- AST  ALT  GGT  AlkPhosphatase

**Day 1**
- WBC  HB  PLT  ANC  K  Na  Chloride  Cr  Urea  T.Bili  Albumin  AST  ALT  GGT  AlkPhosphatase

**ANTIEMETIC PRE-CHEMO REGIMENT:**

**Level B** Day 1
- Dexamethasone 8mg PO/IV (if patient has not taken PO dexamethasone at home)
- May add or substitute Prochlorperazine 10mg PO/IV prn

**ANTIEMETIC TAKE-HOME REGIMENT:**

**Level A** Day 1
- Prochlorperazine 10mg PO q4-6h prn

**PATIENT VISITS and APPOINTMENT TYPE:**

- Day 1 DOCE (first 2 doses) 2 hrs Type D
- Day 1 DOCE (subsequent) 2hrs Type C

**TOXICITIES:**

**Hematologic**
1. If ANC < 1.5 x 10^9/L, or if PLT < 100 x 10^9/L, HOLD dose for 1 week.

**Hepatic Dysfunction**
1. DECREASE dose if LFTs > 1.5 x normal.
2. If AST or ALT > 53 IU/L, or if Alk Phos > 180 IU/L, REDUCE dose by 50%.

**SUGGESTED ACTION**

**CLINICAL MONITORING:**
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.
- Watch for symptoms of fever and infection.
- Skin assessment at each visit, including nails.

**Skin Toxicity**
0. None
1. Hyperpigmentation
2. Atrophy
3. Subcutaneous fibrosis
4. Desquamation, ulceration, or Necrosis

**Fluid Retention**
0. None
1. Mild peripheral edema
2. Pleural effusion, outpatient management
3. Pleural effusion, inpatient management
4. Intubation required

**Nail Changes**
1. Discoloration; ridging (koilonychias); pitting
2. Partial or complete loss of nail(s); pain in nailbed(s)
3. Interfering with ADL

RATED AT EACH CLINIC VISIT
HYPERSENSITIVITY:

Docetaxel Hypersensitivity Procedures:

1. Discontinue Docetaxel immediately if there are signs or symptoms of moderate or severe hypersensitivity. (Mild symptoms may resolve with a decrease in the rate of infusion.)
2. Rapid IV administration of Diphenhydramine 50mg and Hydrocortisone 100mg.
3. Re-initiate infusion after 30 minutes, or when signs of reaction are resolved. Resume infusion at a slower rate, then increase incrementally to the initial planned rate, eg. infuse at 30mL/hr (an 8-hour rate) for 5 minutes, then at 60mL/hr (a 4-hour rate) for 5 minutes, then at 125mL/hr (a 2-hour rate) for 5 minutes, then finally, resume at 250mL/hr (1-hour infusion rate).
4. Depending on the intensity of the reaction, additional oral or IV pre-medication with an antihistamine should also be given for the next cycle of treatment and the rate of infusion should be decreased initially and then increased back to the recommended 1-hour infusion.

INTERNAL CODE:
OPIS CODE: DOCETAX-GU

REFERENCES:

Date revised: 09/27/2005
GEMCITABINE Chemotherapy
Bladder Cancer

GEMCITABINE 1200mg/m² IV Days 1, 8 & 15
- Mix in 100-250mL Normal Saline; Infuse over 30 minutes through free-flowing IV. Round to nearest 19mg
- REPEAT EVERY 28 DAYS

TESTS:
- Baseline Tests: WBC HB PLT ANC Days 1, 8 & 15
- Test Notes: Baseline and periodic liver function tests

ANTIEMETIC PRE-CHEMO REGIMEN:
- Level A Days 1, 8 & 15: Prochlorperazine 10mg PO pm

ANTIEMETIC TAKE-HOME REGIMEN:
- Level A Days 1, 8 & 15: Prochlorperazine 10mg PO q4-6h pm

PATIENT VISITS and APPOINTMENT TYPE:
- Days 1, 8 & 15: 45min Type A

TOXICITIES:
Hematologic
1. If ANC < 1.5 x 10⁹/L, or if PLT < 75-100 x 10⁹/L, REDUCE to 50% dose.
2. If ANC < 1.0 x 10⁹/L, or if PLT < 75 x 10⁹/L, HOLD dose for 1 week.

Gastrointestinal
1. If Mucositis or Diarrhea ≥ Grade 3 in previous course, REDUCE to 2/3 dose.

SUGGESTED ACTION
CLINICAL MONITORING:
Edema limb
1. 5 - 10% inter-limb discrepancy in volume or circumference at point of greatest visible difference; swelling or obscuration of anatomic architecture on close inspection; pitting edema
2. >10 - 30% inter-limb discrepancy in volume or circumference at point of greatest visible difference; readily apparent obscuration of anatomic architecture; obliteration of skin folds; readily apparent deviation from normal anatomic contour
3. >30% inter-limb discrepancy in volume; lymphorrhea; gross deviation from normal anatomic contour; interfering with ADL
4. Progression to malignancy (i.e., lymphangiosarcoma); amputation indicated; disabling
5. Death
RATED IF EDEMA NOTED ON ROUTINE VISITS

Mucositis
1. Erythema of the mucosa
2. Patchy ulcerations or pseudomembranes
3. Confluent ulcerations or pseudomembranes; bleeding with minor trauma
4. Tissue necrosis; significant spontaneous bleeding; life-threatening consequences
5. Death

Diarrhea
1. Increase of < 4 stools per day over baseline; mild increase in ostomy output compared to baseline
2. Increase of 4 - 6 stools per day over baseline; IV fluids indicated < 24hrs; moderate increase in ostomy output compared to baseline; not interfering with ADL
3. Increase of ≥ 7 stools per day over baseline; incontinence; IV fluids >24 hrs; hospitalization; severe increase in ostomy output compared to baseline; interfering with ADL
4. Life-threatening consequences (e.g., hemodynamic collapse)
5. Death
RATED AT EACH CLINIC VISIT

INTERNAL CODE:
OPIS CODE: GEM Q7D

REFERENCES:

Date revised: 03/07/2005
# LHRH Agonist & Antiandrogen Therapy

Prostate Cancer (Locally Advanced- Stage C) - Neoadjuvant Curative Intent; Prostate Cancer (Metastatic- Stage D) - Palliative Intent

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<th>Dosage</th>
<th>Route</th>
<th>Schedule</th>
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<td>- 9.45mg SC every 3 months.</td>
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<td>SC</td>
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<td></td>
</tr>
<tr>
<td>Depot Injections:</td>
<td>- 3.6mg SC every 28 days.</td>
<td></td>
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<tr>
<td></td>
<td>- 10.8mg SC every 3 months.</td>
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<td></td>
<td>- Outpatient prescription.</td>
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<tr>
<td></td>
<td>- Trade Name = Zoladex™ &amp; Zoladex LA™</td>
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<tr>
<td></td>
<td>- LHRH Agonist</td>
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<tr>
<td><strong>LEUPROLIDE</strong></td>
<td>7.5-30mg</td>
<td>IM</td>
<td>Day 1</td>
<td></td>
</tr>
<tr>
<td>Depot Injections:</td>
<td>- 7.5mg IM every month.</td>
<td></td>
<td></td>
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</tr>
<tr>
<td></td>
<td>- 22.5mg IM every 3 months.</td>
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<tr>
<td></td>
<td>- 30mg IM every 4 months.</td>
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<td></td>
<td>- Outpatient prescription.</td>
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<tr>
<td></td>
<td>- Trade Name = Lupron Depot™</td>
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<td>- LHRH Agonist</td>
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<tr>
<td><strong>TRIPTORELIN</strong></td>
<td>3.75-11.25mg</td>
<td>IM</td>
<td>Day 1</td>
<td></td>
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<tr>
<td>Depot Injections:</td>
<td>- 3.75mg IM monthly</td>
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<tr>
<td></td>
<td>- 11.25mg IM every 3 months.</td>
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<td></td>
<td>- Outpatient prescription.</td>
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<tr>
<td></td>
<td>- Trade Name = Trelstar™ &amp; Trelstar LA™</td>
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<tr>
<td></td>
<td>- LHRH Agonist</td>
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</tr>
</tbody>
</table>

**Tests:**
- Baseline Tests: T.Bili, Albumin, AST, ALT, GGT, AlkPhosphatase
- LHRH Agonists Before Each Inf: WBC, HB, PLT, ANC
- Antiandrogens Every 60 Days: T.Bili, Albumin, AST, ALT, GGT, AlkPhosphatase
LHRH Agonist & Antiandrogen Therapy

Baseline LHRH Agonists

Test Notes - First baseline test is for Antiandrogen medications.
- No routine lab tests with Megestrol.
- Bicalutamide lab tests prn after baseline.

TOXICITIES:

Hepatic Dysfunction
- Bicalutamide, Flutamide, Nilutamide: If AST or ALT > 105 IU/L, STOP treatment.
- Cyproterone: Baseline & periodic liver function tests.

INTERNAL CODE:

OPIS CODES:
- BICAL
- CYPROT
- FLUTAR
- MEGES
- NILUT
- BUSER
- BUSER 3M
- GOSER
- GOSER 3M
- LEUPRO
- LEUPRO 3M
- LEUPRO 4M

REFERENCES:

Bicalutamide:

Buserelin:

Goserelin:

Flutamide:

Leuprolide:

Nilutamide:
MITOXANTRONE-PREDNISONE Chemotherapy
Hormone-Resistant Prostate Cancer

MITOXANTRONE 12mg/m² IV Day 1 Round to nearest 1mg
- Slow push through sidearm of free flowing IV. Give 4mg/2mL per minute.
- Threshold dose of Mitoxantrone = 140mg/m²

PREDNISONE 5mg PO Starting Day 1 5mg tablet
- BID
- Outpatient prescription.

REPEAT EVERY 21 DAYS until disease progression

TESTS:
Baseline Tests WBC HB PLT ANC Glucose Cr Urea T.Bili Albumin AST ALT GGT AlkPhosphatase LVEF
Day 1 WBC HB PLT ANC Glucose LVEF
Test Notes - LVEF at baseline if cardiac history.
- LVEF during treatment if cardiac symptoms and at threshold dose (>140mg/m² Mitoxantrone).

ANTIEMETIC PRE-CHEMO REGIMEN:
Level B Day 1 - Dexamethasone 8mg PO/IV
- May add or substitute Prochlorperazine 10mg PO/IV pm

ANTIEMETIC TAKE-HOME REGIMEN:
Level A Day 1 - Prochlorperazine 10mg PO q4-6h prn

PATIENT VISITS and APPOINTMENT TYPE:
→ Day 1: 30min Type B

TOXICITIES:
Hematologic
1. If ANC < 1.5 x 10⁹/L or if PLT < 100 x 10⁹/L, HOLD dose for 1 week.

Hepatic Dysfunction
1. If T.Bili > 50umol/L, or AST > 180 IU/L, REDUCE Mitoxantrone to 50% dose.

SUGGESTED ACTION

CLINICAL MONITORING:
- Clinical exam for symptoms of CHF.
- Periodic cardiac tests for all patients with cardiac risk factors and patients at or above the threshold dose levels (doses > 140mg/m²).

Left ventricular systolic dysfunction
1. Asymptomatic, resting ejection fraction (EF) <60-50%; shortening fraction (SF) <30-24% 2. Asymptomatic, resting EF<50-40%; SF<24-15% 3. Symptomatic CHF responsive to intervention; EF<40-20%;SF,15% 4. Refractory CHF or poorly controlled; EF<20%; intervention such as ventricular assist device, ventricular reduction surgery, or heart transplant indicated 5. Death

RATED AT EACH CLINIC VISIT

REFERENCES:

Date revised: 06/04/2008

CCO Eligibility Form Required ☐ Non-Formulary Form Required ☐
METHOTREXATE-VINBLASTINE-DOXORUBICIN-CISPLATIN

High Dose Chemotherapy with Filgrastim (G-CSF)

**Bladder Carcinoma-Adjuvant/Palliative Intent**

**METHOTREXATE**
- 30mg/m² IV Day 1
  - *Inject by direct IV push*, followed by a Normal Saline flush (if no IV line has been set up).
  - *May give by slow push through sidearm of free flowing IV (D5W, Normal Saline).*
  - *Rate of administration < 10mg per minute.*
  - *Doses > 100mg, mix in 50-100mL Normal Saline and infuse over 30-60 minutes.*

**VINBLASTINE**
- 3mg/m² IV Day 2
  - *Slow push through sidearm of free flowing IV; Inject over 1 minute*

**DOXORUBICIN**
- 30mg/m² IV Day 2
  - *Slow push through sidearm of free flowing IV; Give 2 to 4mg (1-2mL) per minute*

**CISPLATIN**
- 70mg/m² IV Day 2
  - *Admix in 500mL-1000mL bag Normal Saline; Infuse over 60 minutes.*

**FILGRASTIM**
- 5mcg/kg SC Days 4-10
  - *Starting dose is 5mcg/kg/day.*
  - *Doses may be increased in increments of 5mcg/kg/day for each chemotherapy cycle, according to duration and severity of ANC nadir.*
  - *May give Acetaminophen 325mg, 1-2 tablets for temporary bone pain at initiation.*
  - *Outpatient prescription (Keep refrigerated).*
  - *Vial sizes available: 300mcg and 480mcg.*
  - *Trade name Neupogen™*

**PEGFILGRASTIM**
- 6mg SC Day 4
  - *May be given instead of Neupogen™*
  - *To be given 24-48 hours post chemotherapy as a single dose*
  - *Outpatient prescription (Keep refrigerated).*
  - *Trade name Neulasta™*

**HYDRATION:**
- Pre
  - *Infuse 1000mL Normal Saline with 20mEq Potassium Chloride IV over 2 hours before Cisplatin.*
- Concurrent
  - *Give 250mL of 20% Mannitol solution (50G) IV; Infuse through sidearm concurrent with Cisplatin.*
- Post
  - *Infuse 500mL Normal Saline over 1 hour after Cisplatin.*

**TESTS:**
- Baseline Tests: WBC HB PLT ANC Ca K Na Mg Glucose Cr Urea T.Bili Albumin AST ALT GGT AlkPhosphatase
- Day 1: WBC HB PLT ANC Mg Cr Urea T.Bili AST

**ANTIEMETIC PRE-CHEMO REGIMEN:**
- **Level A**
  - Day 1: Prochlorperazine 10mg PO pm
  - *Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV*
  - *Dexamethasone 20mg PO/IV*
  - *May add Aprepitant 125mg po 1 hour before chemo (reduce PO Dexamethasone by 50%)*
- **Level C**
  - Day 2: Prochlorperazine 10mg PO q4-6h pm
  - *Ondansetron 8mg PO BID for 2-3 days, or Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days*
  - *Dexamethasone 8mg PO BID for 2-3 days*
  - *May add Aprepitant 80mg PO on Days 2-3 (reduce PO Dexamethasone by 50%)*
  - *Prochlorperazine 10mg PO q4-6h pm.*

**ANTIEMETIC TAKE-HOME REGIMEN:**
- **Level A**
  - Day 1: Prochlorperazine 10mg PO q4-6h pm
  - *Ondansetron 8mg PO BID for 2-3 days, or Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days*
  - *Dexamethasone 8mg PO BID for 2-3 days*
  - *May add Aprepitant 80mg PO on Days 2-3 (reduce PO Dexamethasone by 50%)*
  - *Prochlorperazine 10mg PO q4-6h pm.*
- **Level B/C**
  - Day 2: Prochlorperazine 10mg PO q4-6h pm
  - *Ondansetron 8mg PO BID for 2-3 days, or Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days*
  - *Dexamethasone 8mg PO BID for 2-3 days*
  - *May add Aprepitant 80mg PO on Days 2-3 (reduce PO Dexamethasone by 50%)*
  - *Prochlorperazine 10mg PO q4-6h pm.*

**PATIENT VISITS and APPOINTMENT TYPE:**
- **Day 1**
  - *10 min Type A*
- **Day 2**
  - *4-6hrs Type D*

**ANCILLARY:**
- *Oral hydration is strongly encouraged; poorly hydrated patients may need more IV hydration.*

**TOXICITIES:**

**Hematologic**
- 1. If ANC < 1.5 x 10⁹/L, HOLD dose for 1 week.
METHOTREXATE-VINBLASTINE-DOXORUBICIN-CISPLATIN
High Dose Chemotherapy with Filgrastim (G-CSF)

Hepatic Dysfunction
1. If T.Bili = 26-51umol/L, or AST = 60-180 IU/L, REDUCE Vinblastine to 50% dose and Doxorubicin to 75% dose.
2. If T.Bili = 52-85umol/L, or AST > 180 IU/L, REDUCE Vinblastine to 25% dose, Doxorubicin to 50% dose and Methotrexate to 75% dose.
3. If T.Bili > 85umol/L, OMIT Vinblastine, Doxorubicin and Methotrexate.

Renal Failure
1. If CrCl = 0.5-1.0mL/sec, or SrCr = 136-185umol/L, REDUCE Cisplatin & Methotrexate to 50% dose.
2. If CrCl < 0.5mL/sec, or SrCr > 185umol/L, OMIT Cisplatin & Methotrexate.

SUGGESTED ACTION

CLINICAL MONITORING:
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.
- Clinical exam for symptoms of CHF.
- Periodic cardiac tests for all patients with cardiac risk factors, or patients at or above the threshold dose levels (Doxorubicin > 450mg/m²).

Sensory
1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function.
2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL.
3. Sensory alteration or paresthesia interfering with ADL.
4. Life-threatening; disabling.
5. Death

Hearing
1. Asymptomatic, detected on exam/testing only.
2. Symptomatic, not interfering with ADL.
3. Symptomatic, interfering with ADL.
4. Life-threatening; disabling.
5. Death

RATED AT EACH CLINIC VISIT

FORMULAE:
CrCl - Cockcroft & Gault (mL/sec) Male: \( [140 - \text{age(yrs)}] \times \text{TBW(Kg)} / [50 \times \text{SCr(umol/L)}] \)
CrCl - Cockcroft & Gault (mL/sec) Female: \( [140 - \text{age(yrs)}] \times \text{TBW(Kg)} / [50 \times \text{SCr(umol/L)}] \times 0.85 \)

REFERENCES:
- CCO Practice Guideline 3-12: Use of Chemotherapy in Advanced Unresectable or Metastatic Transitional Cell Carcinoma of the Bladder or Urothelium.

CCO Eligibility Form Required [ ] Non-Formulary Form Required [ ] Date revised: 05/21/2008
**GU-MVDC Genitourinary**

**METHOTREXATE-VINBLASTINE-DOXORUBICIN-CISPLATIN (M/VAC) Chemotherapy**

**Bladder Carcinoma- Palliative Intent**

**METHOTREXATE**  
30mg/m² IV Days 1,15 & 22  
*Round to nearest 5mg*  
- **Slow push through sidearm of free flowing IV** at a rate of ≤ 10mg per minute.  
- **Doses > 100mg,** mix in 50-100mL Normal Saline and infuse over 30-60 minutes.

**VINBLASTINE**  
3mg/m² IV Days 2,15 & 22  
*Round to nearest 0.1mg*  
- **Slow push through sidearm of free flowing IV,** Inject over 1 minute

**DOXORUBICIN**  
30mg/m² IV Day 2  
*Round to nearest 1mg*  
- **Slow push through sidearm of free flowing IV:** Give 2 to 4mg (1-2mL) per minute

**CISPLATIN**  
70mg/m² IV Day 2  
*Round to nearest 1mg*  
- **Alternate dose:** 35mg/m² IV Days 2 and 3.  
- **Mix in 100-250mL bag Normal Saline:** Infuse over 30-60 minutes.  
- **May admix 50mL of 20% Mannitol solution(10G) (or 100mL of 10%) with Cisplatin.**

**REPEAT EVERY 28 DAYS**

**HYDRATION:**

**Pre**  
- **Infuse** 1000mL Normal Saline with 20mEq Potassium Chloride IV over 2 hours before Cisplatin.

**Post**  
- **Infuse** 1000mL Normal Saline over 2 hours after Cisplatin.

**TESTS:**

<table>
<thead>
<tr>
<th>Baseline Tests</th>
<th>WBC HB PLT ANC Ca K Na Glucose Cr Urea T.Bili Albumin AST ALT GGT AlkPhosphatase</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Days 15 &amp; 22</strong></td>
<td>WBC HB PLT ANC Cr T.Bili AST</td>
</tr>
<tr>
<td><strong>Days 1 &amp; 2</strong></td>
<td>WBC HB PLT ANC Mg Cr T.Bili</td>
</tr>
</tbody>
</table>

**ANTIEMETIC PRE-CHEMO REGIMEN:**

| **Level A** | Days 1,15 & 22  
- Prochlorperazine 10mg PO pm |
| **Level C** | Day 2  
- Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV  
- Dexamethasone 20mg PO/IV  
- May add Aprepitant 125mg po 1 hour before chemo (reduce PO Dexamethasone by 50%) |

**ANTIEMETIC TAKE-HOME REGIMEN:**

| **Level A** | Days 1,15 & 22  
- Prochlorperazine 10mg PO q4-6h pm |
| **Level BC** | Day 2  
- Ondansetron 8mg PO BID for 2-3 days, or Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days  
- Dexamethasone 8mg PO BID for 2-3 days  
- May add Aprepitant 80mg PO on Days 2-3 (reduce PO Dexamethasone by 50%)  
- Prochlorperazine 10mg PO q4-6h pm |

**PATIENT VISITS and APPOINTMENT TYPE:**

- **Days 1,15 & 22:**  
  - 30min  
  - Type B  
- **Day 2  
  & 3 if needed:**  
  - 4-6hrs  
  - Type D

**ANCILLARY:**

- Oral hydration is strongly encouraged; poorly hydrated patients may need more IV hydration.

**TOXICITIES:**

**Hematologic**

1. If ANC < 1.5 x 10⁹/L, **HOLD** dose for 1 week.

**Hepatic Dysfunction**

1. If T.Bili = 26-51umol/L, or AST = 60-180 IU/L, **REDUCE** Vinblastine to 50% dose and Doxorubicin to 75% dose.
2. If T.Bili = 52-85umol/L, or AST > 180 IU/L, **REDUCE** Vinblastine to 25% dose, Doxorubicin to 50% dose and Methotrexate to 75% dose.
3. If T.Bili > 85umol/L, **OMIT** Vinblastine, Doxorubicin and Methotrexate.

**Renal Failure**

1. If CrCl = 0.5-1.0mL/sec, or SrCr = 136-185umol/L, **REDUCE** Cisplatin & Methotrexate to 50% dose.
2. If CrCl < 0.5mL/sec, or SrCr > 185umol/L, **OMIT** Cisplatin & Methotrexate.

**SUGGESTED ACTION**
METHOTREXATE-VINBLASTINE-DOXORUBICIN-CISPLATIN (M/VAC) Chemotherapy

CLINICAL MONITORING:
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.
- Clinical exam for symptoms of CHF.
- Periodic cardiac tests for all patients with cardiac risk factors, or patients at or above the threshold dose levels (Doxorubicin > 450mg/m²).

Sensory
1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function  
2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL  
3. Sensory alteration or paresthesia interfering with ADL  
4. Disabling  
5. Death

Hearing
1. Asymptomatic, detected on exam/testing only  
2. Symptomatic, not interfering with ADL  
3. Symptomatic, interfering with ADL  
4. Life-threatening; disabling  
5. Death

RATED AT EACH CLINIC VISIT

FORMULAE:
CrCl - Cockcroft & Gault (mL/sec)  
Male: \[\frac{140 - \text{age(yrs)}}{50 \times \text{SCR(umol/L)}} \times \text{TBW(Kg)}\]  
Female: \[\frac{140 - \text{age(yrs)}}{50 \times \text{SCR(umol/L)}} \times 0.85 \times \text{TBW(Kg)}\]

REFERENCES:
- CCO Practice Guideline 3-12: Use of Chemotherapy in Advanced Unresectable or Metastatic Transitional Cell Carcinoma of the Bladder or Urothelium.

Date revised: 06/04/2008
SORAFENIB Therapy
Locally advanced/metastatic renal cell (clear cell) carcinoma in patients who failed prior cytokine therapy or are considered unsuitable for such therapy.

**SORAFENIB** 400mg PO Continuous 200mg

- Sorafenib (Nexavar™) is taken orally 400mg twice daily.
- Should be swallowed with an 8 ounce glass of water, without food.
- Do not take with a high fat meal as this may make Sorafenib less effective.
- Exceptional Access Program (Section 16) with specific criteria
- Outpatient prescription in 200mg capsules.

**CONTINUOUS TREATMENT**

<table>
<thead>
<tr>
<th>TESTS:</th>
<th>WBC</th>
<th>HB</th>
<th>PLT</th>
<th>ANC</th>
<th>Ca</th>
<th>K</th>
<th>Na</th>
<th>Chloride</th>
<th>Phosphate</th>
<th>Mg</th>
<th>Cr</th>
<th>Urea</th>
<th>T.Bili</th>
<th>Albumin</th>
<th>AST</th>
<th>ALT</th>
<th>GGT</th>
<th>AlkPhosphatase</th>
<th>Urate</th>
<th>LVEF</th>
</tr>
</thead>
</table>

**Baseline Tests**
- Regular INR for patients receiving coumadin.
- MUGA scan or ECG if clinically indicated or history of cardiac problems.
- Blood pressure monitoring every 2 weeks for first several cycles.
- Thyroid function test if patients develop symptoms suggestive of hypothyroidism.
- Sorafenib has not been studied in patients with severe hepatic or severe renal impairment.

**TOXICITIES:**

**Cutaneous**
1. If any Toxicity Score = Grade 1, continue treatment with Sorafenib and consider topical therapy for symptomatic relief.
2. If any Toxicity Score = Grade 2, if first occurrence, continue treatment with Sorafenib and consider topical therapy for symptomatic relief. If no improvement within 7 days or 2nd or 3rd occurrence, **HOLD** Sorafenib dose until toxicity resolves to Grade 0-1. When resuming treatment, **DECREASE** Sorafenib dose by one dose level (400mg daily or 400mg every other day).
3. If any Toxicity Score = Grade 3, if 1st or 2nd occurrence, **HOLD** Sorafenib treatment until toxicity resolves to Grade 0-1. When resuming treatment, **DECREASE** Sorafenib dose by one dose level (400mg daily or 400mg every other day). If 3rd occurrence, **DISCONTINUE** Sorafenib treatment.

**SUGGESTED ACTION**

**CLINICAL MONITORING:**

**Hand-Foot Skin Reaction**
1. Minimal skin changes or dermatitis (e.g., erythema) without pain. 2. Skin changes (e.g., peeling, blisters, bleeding, edema) or pain, not interfering with function. 3. Ulcerative dermatitis or skin changes with pain interfering with function.

**RATED AT EACH CLINIC VISIT**

**INTERNAL CODE:**

**OPIS CODE:** SORAF

**REFERENCES:**

**Date revised:** 05/26/2008
SUNITINAB Therapy

Metastatic Renal Cell Carcinoma with clear cell component

SUNITINIB

50mg PO Day 1

12.5mg

- Sunitinib (Sutent™) is taken orally 50mg once daily for 4 weeks followed by 2 weeks rest.
- May be given with or without food but should not be given with grapefruits or grapefruit juice.

Alternate Dosing:
- If patient shows rapid progression during the 2 week break then Sunitinib may be given as 37.5mg once daily continuously.
- Exceptional Access Program (Section 16) with specific criteria
- Outpatient prescription available as 12.5mg, 25mg, and 50mg capsules.

Tests:

Baseline Tests
WBC HB PLT ANC Ca K Na Chloride Phosphate Mg Cr Urea T.Bili Albumin AST ALT GGT AlkPhosphatase Urate LVEF

Day 1
WBC HB PLT ANC Cr Urea T.Bili ALT

Test Notes
- Blood pressure monitoring every 2 weeks for first several cycles.
- MUGA scan or echocardiogram if clinically indicated or if history of cardiac problems.
- Thyroid function test if patients develop symptoms suggestive of hypothyroidism.
- Clinical toxicity assessments (including bleeding, congestive heart failure, adrenal insufficiency and pancreatitis).
- Sunitinib has not been studied in patient with hepatic or renal impairment.

Toxicities:

Hematologic
1. If ANC < 1.0 x 10^9/L, or if PLT < 75 x 10^9/L, HOLD Sunitinib dose for 1 week.

Suggested Action

Clinical Monitoring:

Hand-Foot Skin Reaction
1. Minimal skin changes or dermatitis (e.g., erythema) without pain. 2. Skin changes (e.g., peeling, blisters, bleeding, edema) or pain, not interfering with function. 3. Ulcerative dermatitis or skin changes with pain interfering with function.

RATED AT EACH CLINIC VISIT

Internal Code:

OPIS Code: SUNIT

References:
- Sunitinib™ current product monograph, Pfizer Canada Inc.

Date revised: 05/28/2008
TEMSESIROLIMUS Chemotherapy
Metastatic Renal Cell Carcinoma

**DIPHENHYDRAMINE**
25-50mg IV Day 1
- Admix into 50-100ml Normal Saline and infuse over 10-15 minutes.
- Give 30 minutes PRIOR to Temsirolimus infusion.

**TEMSESIROLIMUS**
25mg FLAT dose IV Day 1 1mg
- Admix into 250ml Normal Saline and infuse over 30-60 minutes using non-PVC equipment with in-line filter. Use UV bag.

**Dose Modifications:**
Standard 25mg
Dose level-1 20mg
Dose level-2 15mg

For Temsirolimus related toxicities NCI CTCAE version 3 Grade 0-2 no dose adjustment needed. Grade 2 toxicities that are persistent and intolerable can result in dose delays or dose reductions to the next lowest level. For Grade 3-4 related toxicities, hold therapy until recovery to Grade 0-2. If recovery within 3 weeks, reduce dose by one dose level for subsequent treatments.

**SUGGESTED ACTION**
REPEAT EVERY 7 DAYS

**TESTS:**
**Baseline Tests**
WBC HB PLT ANC Ca K Na Chloride Phosphate Mg Glucose Cr Urea T.Bili AST AlkPhosphatase

**Day 1**
WBC HB PLT ANC

**Every 2 weeks for first 2 months**
WBC HB PLT ANC Glucose

**Monthly**
Ca K Na Chloride Phosphate Mg Glucose Cr Urea T.Bili AST

**Test Notes**
- PT/PTT: patients receiving anticoagulants should be monitored weekly for the first 4 weeks of treatment, then monthly.
- Radiographic evaluations: CT Chest/Abdomen/Pelvis done every 2 - 3 months.
- Monitor LDH, total cholesterol and triglycerides monthly at the physician’s discretion.

**PATIENT VISITS and APPOINTMENT TYPE:**
Day 1 1 hr 15 mins Type C

**TOXICITIES:**
**Hematologic**
1. If ANC < 1.0 x 10^9/L, or if PLT < 75 x 10^9/L, HOLD Temsirolimus dose for 1 week.

**SUGGESTED ACTION**

**CLINICAL MONITORING:**
**Pneumonitis**
1. Asymptomatic, radiographic findings only 2. Symptomatic, not interfering with ADL 3. Symptomatic, interfering with ADL; O2 indicated 4.Life-threatening; ventilatory support indicated 5. Death

Caution is advised for patients with significant lung dysfunction due to the risk for pneumonitis (mTOR inhibitor class effect).

**Rash**
1. Macular or papular eruption or erythema without associated symptoms 2. Macular or papular eruption or erythema with pruritus or other associated symptoms; localized desquamation or other lesions covering < 50% of body surface area (BSA) 3. Severe, generalized erythroderma or macular, papular or vesicular eruption; desquamation covering >=50% BSA 4. Generalized exfoliative, ulcerative, or bullous dermatitis 5. Death

**Hyperglycemia** (defined as fasting unless otherwise specified)
1. >ULN-160mg/dL or >ULN-8.9mmol/L 2. >160-250mg/dL or >8.9-13.9mmol/L 3. >250-500mg/dL or >13.9-27.8mmol/L 4. >500mg/dL or >27.8mmol/L or acidosis 5. Death

RATED AT EACH CLINIC VISIT

**HYPERSENSITIVITY:**
Temsirolimus Hypersensitivity Procedures:
- If hypersensitivity reaction during administration:
  1. Discontinue Temsirolimus immediately if there are signs or symptoms of hypersensitivity.
  2. Observe patient for at least 30 to 60 minutes (depending on the severity of the reaction).
  3. At the discretion of the treating physician, treatment may be resumed with the administration of a histamine H2-receptor antagonist (IV Famotidine 20mg or IV Ranitidine 50mg) approximately 30 minutes before restarting the Temsirolimus infusion.
  4. Depending on the intensity of the reaction, additional oral or IV pre-medication with an antihistamine should also be given for the next cycle of treatment and the rate of infusion may be slowed to 60 minutes if necessary.

**INTERNAL CODE:**
OPIS CODE: TEMSESIROLIMUS

**REFERENCES:**
- Torisel™ current product monograph, Wyeth Canada.

CCO Eligibility Form Required [ ] Non-Formulary Form Required [✓] Date revised: 02/27/2008
ZOLEDRONIC ACID Therapy
Genitourinary Hormone Refractory Prostate Cancer

ZOLEDRONIC ACID 3-4mg IV Day 1
- Mix in 100mL bag 5% Dextrose or Normal Saline.
- Infuse over a minimum of 15 minutes.
- Serum creatinine should be measured before each dose.

Dosing for mild to moderate renal impairment:
1. If baseline CrCl > 60mL/min, give 4mg dose.
2. If baseline CrCl 50-60mL/min, give 3.5mg dose.
3. If baseline CrCl 40-49mL/min, give 3.3mg dose.
4. If baseline CrCl 30-39mL/min, give 3mg dose.
- Do not mix with Calcium-containing infusion solutions eg. Lactated Ringer’s solution.

REPEAT EVERY 21 DAYS

TESTS:
Baseline Tests  WBC  HB  PLT  ANC  Ca  K  Na  Chloride  Cr  Urea  Albumin
Day 1  WBC  HB  PLT  ANC  Ca  K  Na  Chloride  Cr  Urea  Albumin

PATIENT VISITS and APPOINTMENT TYPE:
- Day 1: 15min Type A

TOXICITIES:
Renal Failure
- During treatment, serum creatinine should be measured before each dose and treatment should be withheld for renal deterioration.

In the clinical studies, renal deterioration was defined as follows:
- For patients with normal baseline creatinine (< 123umol/L), an increase of 44umol/L.
- For patients with abnormal baseline creatinine (> 123umol/L), an increase of 88umol/L.
- In the clinical studies, treatment was resumed at the same dose when the creatinine level returned to within 10% of the baseline value.

FORMULAE:
CrCl - Cockcroft & Gault (mL/sec)
Male: [140-age(yrs)] x TBW(Kg) / [50 x SCr(umol/L)]
CrCl - Cockcroft & Gault (mL/sec)
Female: [140-age(yrs)] x TBW(Kg) / [50 x SCr(umol/L)] x 0.85
Creatinine Cl (mL/min)
mL/min = 60 x CrCl mL/sec
Corrected Serum Calcium (mmol/L)
Measured Serum Calcium + [(40 - serum albumin) x 0.02]

INTERNAL CODE:
OPIS CODE: ZOLED ACID

REFERENCES:

CCO Eligibility Form Required  ✔  Non-Formulary Form Required  ☐ Date revised: 10/13/2005
CARBOPLATIN Chemotherapy
Ovarian or Endometrial Cancer

CARBOPLATIN
AUC 6
IV Day 1
Round to nearest 5mg

- Mix in 250mL bag 5% Dextrose.
- Infuse over 30 to 60 minutes.
(Alternate dose = 350mg/m²)

REPEAT EVERY 28 DAYS for a usual total of 6 cycles

TESTS:
Baseline Tests WBC HB PLT ANC Cr Urea 24Hr CrCl T.Bili Albumin AST ALT GGT
AlkPhosphatase
Day 1 WBC HB PLT ANC Cr Urea
Test Notes - Baseline & routine renal function tests, especially if there are other concurrent nephrotoxic drugs.

ANTIEMETIC PRE-CHEMO REGIMEN:
Level C Day 1 - Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
- Dexamethasone 8mg PO/IV

ANTIEMETIC TAKE-HOME REGIMEN:
Level B/C Day 1 - Ondansetron 8mg PO BID for 2-3 days, or Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days
- Dexamethasone 4mg PO BID for 2-3 days
- Prochlorperazine 10mg PO q4-6h prn

PATIENT VISITS and APPOINTMENT TYPE:
Day 1 1.5hrs Type B

ANCILLARY:
- Oral hydration is strongly encouraged, poorly hydrated patients may need more IV hydration.

TOXICITIES:
Hematologic
1. If ANC < 1.5 x 10⁹/L, or if PLT < 100 x 10⁹/L, HOLD dose for 1 week.

Renal Failure
1. ADJUST Carboplatin dose if estimated CrCl changes > 20%.

SUGGESTED ACTION

CLINICAL MONITORING:
Sensory
1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function. 2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL. 3. Sensory alteration or paresthesia interfering with ADL. 4. Disabling. 5. Death
RATED AT EACH CLINIC VISIT

FORMULAE:
Calvert Formula
Dose (in mg) = target AUC x (GFR + 25) GFR in mL/min
CrCl - Cockcroft & Gault (mL/sec)
Creatinine Cl (mL/min)
Female: [140-age(yrs)] x TBW(Kg) / [50 x SCr(umol/L)] x 0.85
mL/min = 60 x CrCl mL/sec

INTERNAL CODE:
- OPIS CODE:
- CARBO*6
- CARBO*5

REFERENCES:

CCO Eligibility Form Required ☐ Non-Formulary Form Required ☐ Date revised: 07/14/2008
CARBOPLATIN Chemotherapy for Patients with Hypersensitivity (Inpatient Regimen)
Ovarian or Endometrial Cancer

CARBOPLATIN

AUC 6 Day 1 Round to nearest 1mg
(Range 5-7)

- Mix total dose of Carboplatin in 5% Dextrose in concentration as below:
  Bag #1 Carboplatin (0.3mg/mL) Mix in 250mL bag 5% Dextrose - infuse over 3 hours.
  Bag #2 Carboplatin (0.6mg/mL) Mix in 250mL bag 5% Dextrose - infuse over 3 hours.
  Bag #3 Carboplatin (1mg/mL) Mix in 250mL bag 5% Dextrose - infuse over 3 hours.
- Total dose to be infused over 9 hours.

REPEAT EVERY 21 DAYS for a usual total of 6 cycles

DIPHENHYDRAMINE 50mg IV Day 1
- Infuse 30 minutes prior to Carboplatin and repeat in 6 hours.

DEXAMETHASONE 20mg IV Day 1
- Infuse Dexamethasone 20mg prior to Carboplatin.

RANITIDINE 50mg IV Day 1
- Infuse 30 minutes prior to Carboplatin.

DEXAMETHASONE 4mg IV Day 1 Q6H
- Give Dexamethasone 4mg IV or PO Q6H.
- Start 4 hours after Carboplatin infusion.

ACETAMINOPHEN 325-650mg PO Q4H pm
- Give 1-2 tablets of Acetaminophen 325mg q4h pm.

REPEAT EVERY 21 DAYS for a usual total of 6 cycles

HYDRATION:

Pre IV Normal Saline TKVO

TESTS:
Baseline Tests WBC HB PLT ANC Cr Urea 24Hr CrCl T.Bili Albumin AST ALT AlkPhosphatase
Test Notes - Baseline & routine renal function tests/if there are other concurrent nephrotoxic drugs.

ANTIEMETIC PRE-CHEMO REGIMEN:
Level C
- Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
- Prochlorperazine 10mg PO/IV Q6H pm

ANCILLARY:
- Oral hydration is strongly encouraged, poorly hydrated patients may need more IV hydration.

TOXICITIES:
Hematologic
1. If ANC < 1.5 x 10^9/L, or if PLT < 100 x 10^9/L, HOLD dose for 1 week.
Renal Failure
1. ADJUST Carboplatin dose if estimated CrCl changes > 20%.

SUGGESTED ACTION

CLINICAL MONITORING:
Sensory
1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function. 2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL. 3. Sensory alteration or paresthesia interfering with ADL. 4. Disabling. 5. Death

RATED AT EACH CLINIC VISIT

FORMULAE:
CrCl - Cockcroft & Gault (mL/sec)
Male: [140-age(yrs)] x TBW(Kg) / [50 x SCr(umol/L)]
Female: [140-age(yrs)] x TBW(Kg) / [50 x SCr(umol/L)] x 0.85
Dose (in mg) = target AUC x (GFR + 25) GFR in mL/min

Creatinine Cl (mL/min)
Calvert Formula

Date revised: 10/08/2008

Gynecological
CARBOPLATIN-GEMCITABINE Chemotherapy

Recurrent Ovarian Carcinoma

CARBOPLATIN
AUC 4-5
IV Day 1
Round to nearest 5mg
- Administer in 250mL bag 5% Dextrose; Infuse over 30-60 minutes.

GEMCITABINE
1000mg/m²
IV Days 1 & 8
Round to nearest 19mg
- Administer in 250mL bag Normal Saline or 5% Dextrose; Infuse over 30 minutes.

TESTS:
Baseline Tests
WBC HB PLT ANC Ca K Na Chloride Glucose Cr Urea 24Hr CrCl T.Bili
Albumin AST ALT GGT AlkPhosphatase
Day 8
WBC HB PLT ANC
Day 1
WBC HB PLT ANC K Na Chloride Cr Urea
Test Notes - Additional Baseline tests: LDH & CO₂

ANTIEMETIC PRE-CHEMO REGIMEN:

Level C
Day 1
- Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
- Dexamethasone 12mg PO/IV

Level B
Day 8
- Dexamethasone 8mg PO/IV
- May add or substitute Prochlorperazine 10mg PO/IV prn

ANTIEMETIC TAKE-HOME REGIMEN:

Level B/C
Day 1
- Ondansetron 8mg PO BID for 2-3 days, or
Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days
- Dexamethasone 8mg PO BID for 2-3 days
- Prochlorperazine 10mg PO q4-6h prn

Level A
Day 8
- Prochlorperazine 10mg PO q4-6h prn

PATIENT VISITS and APPOINTMENT TYPE:
- Day 1 2hrs Type C
- Days 1 & 8 45min Type B

TOXICITIES:

Hematologic
Day 1:
1. If ANC < 1.5 x 10⁹/L, or if PLT < 100 x 10⁹/L, HOLD chemotherapy.
Day 8:
1. If ANC < 1.5 x 10⁹/L, or if PLT = 75-100 x 10⁹/L, REDUCE Gemcitabine dose to 50%
2. If ANC < 1.0 x 10⁹/L, or if PLT < 75 x 10⁹/L, HOLD Gemcitabine dose for 1 week.

Renal Failure
1. Adjust Carboplatin dose if estimated CrCl changes > 20%.

SUGGESTED ACTION

CLINICAL MONITORING:
- Baseline & routine renal function tests especially if there are other concurrent nephrotoxic drugs.
Sensory
1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function 2.
Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL 3. Sensory alteration or paresthesia interfering with ADL 4. Disabling 5. Death
RATED AT EACH CLINIC VISIT
Edema limb
1. 5 - 10% inter-limb discrepancy in volume or circumference at point of greatest visible difference; swelling or obscuration of anatomic architecture on close inspection; pitting edema 2. >10 - 30% inter-limb discrepancy in volume or circumference at point of greatest visible difference; readily apparent obscuration of anatomic architecture; obliteration of skin folds; readily apparent deviation from normal anatomic contour 3. >30% inter-limb discrepancy in volume; lymphorrhea; gross deviation from normal anatomic contour; interfering with ADL 4. Progression to malignancy (i.e., lymphangiosarcoma); amputation indicated; disabling 5. Death
RATED IF EDEMA NOTED ON ROUTINE VISITS.

FORMULAE:
Calvert Formula
Dose (in mg) = target AUC x (GFR + 25)  GFR in mL/min
CrCl - Cockcroft & Gault (mL/sec)
Creatinine Cl (mL/min)

INTERNAL CODE:
OPIS CODE: CARBO-GEM (GYNE)

REFERENCES:
- Pfisterer J, Plante M, Vergote I et al, J Clin Oncol 2006; 24(29):4699-4707

Date revised: 10/22/2008
GY CEB
Gynecological

CISPLATIN-ETOPOSIDE-BLEOMYCIN (PEB) Chemotherapy
Germ Cell Tumours of Ovary

CISPLATIN 20mg/m² IV Days 1-5 Round to nearest 1mg
- Mix in 500mL bag Normal Saline; Infuse over 30-60 minutes.
- May also admix 10G Mannitol (50mL of 20% solution or 100mL of 10% solution) with Cisplatin.

ETOPOSIDE 100mg/m² IV Days 1-5 Round to nearest 10mg
- Dose ≤ 200mg, mix in 500mL Normal Saline; Infuse over 30-60 minutes.
- Dose > 200mg, mix in 1000mL Normal Saline; Infuse over 120 minutes.
- Use Non-PVC equipment and filter.
- Adjust rate if blood pressure drops.
- Give Etoposide BEFORE Cisplatin, to hydrate patient.

BLEOMYCIN 30units IV Days 1, 8 & 15
- Slow push through sidearm of free flowing IV.
- May be given by direct IV push, followed by a Normal Saline flush, if no IV line has been set.

ACETAMINOPHEN 650mg PO Days 1, 8 & 15 325mg tablet
- Administer before Bleomycin dose.

HYDRATION:
Pre
- Infuse 1000mL Normal Saline with 20mEq Potassium Chloride IV over 2 hours on Days 1-5.
Post
- Infuse 1000mL Normal Saline IV over 1-2 hours on Days 1-5.

TESTS:
Baseline Tests WBC HB PLT ANC Ca K Na Chloride 24Hr CrCl T.Bili AST ALT GGT AlkPhosphatase
Day 1 WBC HB PLT ANC Cr Urea
Days 8 & 15 WBC HB PLT ANC

Test Notes & routine renal function tests especially if there are other concurrent nephrotoxic drugs.

ANTIEMETIC PRE-CHEMO REGIMEN:
Level C Days 1-5
- Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
- Dexamethasone 20mg PO/IV

Level A Days 8 & 15
- Prochlorperazine 10mg PO prn

ANTIEMETIC TAKE-HOME REGIMEN:
Level B/C Day 5
- Ondansetron 8mg PO BID for 2-3 days, or Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days
- Dexamethasone 4mg PO BID for 2-3 days
- Prochlorperazine 10mg PO q4-6h prn
- Prochlorperazine 10mg PO q4-6h prn

Level A Days 8 & 15

PATIENT VISITS and APPOINTMENT TYPE:
迦 Days 1-5 5hrs Type D
迦 Days 8 & 15: 30min Type A

ANCILLARY:
- Increase fluids if poor oral intake.

TOXICITIES:
Hematologic
1. If ANC < 1.5 x 10⁹/L, or if PLT < 75 x 10⁹/L, HOLD dose for 1 week.

Renal Failure
1. If CrCl = 0.5-1.0mL/sec, or SrCr = 136-185umol/L, REDUCE Cisplatin to 50% dose, and Bleomycin and Etoposide to 75% dose.
2. If CrCl < 0.5ml/sec, or SrCr > 185umol/L, OMIT Cisplatin dose.
3. If CrCl < 0.2ml/sec, REDUCE Bleomycin and Etoposide to 50% dose.

Hepatic Dysfunction
1. If T.Bili = 26-51umol/L, or AST = 60-180 IU/L, REDUCE Etoposide to 25% dose.
2. If T.Bili = 52-85umol/L, REDUCE Etoposide to 50% dose.
3. If T.Bili > 85umol/L, or AST > 180 IU/L, OMIT Etoposide dose.

SUGGESTED ACTION
GY-CEB

CISPLATIN-ETOPOSIDE-BLEOMYCIN (PEB) Chemotherapy

CLINICAL MONITORING:
- Oral examination upon patient complaint of a sore mouth.
- Clinical pulmonary exam at each visit, including auscultation, pulmonary toxicity ratings (Cough, SOB).

Sensory
1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function.
2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL.
3. Sensory alteration or paresthesia interfering with ADL.
4. Disabling.
5. Death

Hearing
1. Asymptomatic, detected on exam/testing only.
2. Symptomatic, not interfering with ADL.
3. Symptomatic, interfering with ADL.
4. Life-threatening; disabling.
5. Death

Dyspnea (Shortness of Breath)
1. Dyspnea on exertion, but can walk 1 flight of stairs without stopping.
2. Dyspnea on exertion but unable to walk 1 flight of stairs or 1 city block (0.1km) without stopping.
3. Dyspnea with ADL.
4. Dyspnea at rest; intubation/ventilator indicated.
5. Death

Cough
1. Symptomatic, non-narcotic medication only indicated.
2. Symptomatic and narcotic medication indicated.
3. Symptomatic and significantly interfering with sleep or ADL.

FORMULAE:
Creatinine Cl (mL/min) = mL/min = 60 x CrCl mL/sec
CrCl - Cockcroft & Gault (mL/sec)
Female: \([140\text{-age(yrs)}] \times TBW(Kg) / [50 \times SCr(umol/L)] \times 0.85\)

REFERENCES:

CCO Eligibility Form Required [ ] Non-Formulary Form Required [ ] Date revised: 07/16/2008
GY-CISP*W

CISPLATIN Concurrent (Cervix) Chemoradiotherapy

Cervical Cancer

CISPLATIN

40mg/m² IV Day 1 Round to nearest 1mg
- Mix in 500mL bag Normal Saline; Infuse over 60 minutes.

RADIATION

2 phase Daily
External Beam
Technique: Four field conformal
Modality: 18MV photons
Dose Specification: Isocentre
Total Dose: 4500cGy
Dose Fraction: 180cGy
Pattern: Daily x 5 weeks
Brachytherapy
Technique: Intracavitary
Modality: Ir192
Dose Specification: Point A
Total Dose: 2600cGy
Dose Fraction: 650cGy
Pattern: Weekly x 4 weeks

REPEAT EVERY 7 DAYS DURING RADIOTHERAPY For a usual total of 5 cycles

HYDRATION:

Pre
- Infuse 1000mL Normal Saline with 20mEq Potassium Chloride IV over 2 hours.

Concurrent
- May give 250mL of 20% Mannitol solution (50G) IV. Infuse through side arm concurrent with Cisplatin (if diuresis is required).

Post
- Infuse 500mL Normal Saline with 10mEq Potassium Chloride IV; (2G Magnesium sulfate may also be added) over 1 hour.
- Increase fluids if poor oral intake.

TESTS:

Baseline Tests WBC HB PLT ANC Cr Urea
Day 1 WBC HB PLT ANC Cr Urea

ANTIEMETIC PRE-CHEMO REGIMEN:
Level C
- Day 1 - Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
- Dexamethasone 8mg PO/IV

ANTIEMETIC TAKE-HOME REGIMEN:
Level B/C
- Day 1 - Ondansetron 8mg PO BID for 2-3 days, or Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days.
- Dexamethasone 4mg PO BID for 2-3 days
- Prochlorperazine 10mg PO q4-6h prn

PATIENT VISITS and APPOINTMENT TYPE:
- Day 1 4-6hrs Type B

ANCILLARY:
- Oral hydration is strongly encouraged; poorly hydrated patients may need more IV hydration.

TOXICITIES:

Hematologic
1. If ANC < 1.5 x 10⁹/L, or if PLT < 100 x 10⁹/L, HOLD dose for 1 week.

Renal Failure
1. If CrCl = 0.5-1.0mL/sec, or SrCr = 136-185umol/L, REDUCE to 50% dose.
2. If CrCl < 0.5mL/sec, or SrCr > 185umol/L, OMIT dose.

Hepatic Dysfunction
1. If T.Bili = 26-51umol/L, or AST = 60-180 IU/L, REDUCE to 50% dose.
2. If T.Bili = 52-85umol/L, REDUCE to 25% dose.
3. If T.Bili > 85umol/L, or AST > 180 IU/L, OMIT dose.

SUGGESTED ACTION

CLINICAL MONITORING:
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.

SENSORY
1. Asymptomatic
2. Symptomatic, not interfering with ADL
3. Symptomatic, interfering with ADL
4. Life-threatening; disabling
5. Death

HEARING
1. Asymptomatic, detected on exam/testing only
2. Symptomatic, not interfering with ADL
3. Symptomatic, interfering with ADL
4. Life-threatening; disabling
5. Death

RATED AT EACH CLINIC VISIT

FORMULAE:

Creatinine Cl (mL/min) mL/min = 60 x CrCl mL/sec
CrCl - Cockcroft & Gault (mL/sec) Female: [140-age(yrs)] x TBW(Kg) / [50 x SrCr(umol/L)] x 0.85

REFERENCES:

Date revised: 11/12/2008
CISPLATIN-ETOPOSIDE Chemotherapy
Small Cell Neuro-Endocrine Cervical Cancer

CISPLATIN
25mg/m² IV Days 1-3 Round to nearest 1mg
- Admin in 250mL bag Normal Saline; Infuse over 30-60 minutes.
- May also admix 10G Mannitol (50mL of 20% solution or 100mL of 10% solution) with Cisplatin.

ETOPOSIDE
100mg/m² IV Days 1-3 Round to nearest 10mg
- Dose < 200mg, mix in 500mL Normal Saline; Infuse over 30-60 minutes.
- Dose > 200mg, mix in 1000mL Normal Saline; Infuse over 120 minutes.
- Use Non-PVC equipment and filter
- Give Etoposide BEFORE Cisplatin, to hydrate patient.
- Adjust Etoposide infusion rate if blood pressure drops.

TESTS:
Baseline Tests: WBC HB PLT ANC 24Hr CrCl T.Bili AST ALT GGT AlkPhosphatase
Day 1: WBC HB PLT ANC Cr Urea

ANTIEMETIC PRE-CHEMO REGIMEN:
Level C Days 1-3
- Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
- Dexamethasone 20mg PO/IV

ANTIEMETIC TAKE-HOME REGIMEN:
Level B/C Day 3
- Ondansetron 8mg PO BID for 2-3 days, or Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days
- Dexamethasone 4mg PO BID for 2-3 days
- Prochlorperazine 10mg PO q4-6h pm

PATIENT VISITS and APPOINTMENT TYPE:
- Days 1-3 2hrs Type C

ANCILLARY:
- Oral hydration is strongly encouraged; poorly hydrated patients may need more IV hydration.

TOXICITIES:
Hematologic
1. If ANC < 1.5 x 10⁹/L, or if PLT < 100 x 10⁹/L, HOLD dose for 1 week.

Renal Failure
1. If CrCl = 0.5-1.0mL/sec, or SrCr = 136-185umol/L, REDUCE to 50% dose.
2. If CrCl < 0.5mL/sec, or SrCr > 185umol/L, OMIT dose.

Hepatic Dysfunction
1. If T.Bili = 26-51umol/L, or AST = 60-180 IU/L, REDUCE to 50% dose.
2. If T.Bili = 52-85umol/L, REDUCE to 25% dose.
3. If T.Bili > 85umol/L, or AST > 180 IU/L, OMIT dose.

SUGGESTED ACTION

CLINICAL MONITORING:
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.
- Sensory
  1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function.
  2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL.
  3. Sensory alteration or paresthesia interfering with ADL.
  4. Disabling.
  5. Death
- Hearing
  1. Asymptomatic, detected on exam/testing only.
  2. Symptomatic, not interfering with ADL.
  3. Symptomatic, interfering with ADL.
  4. Life-threatening; disabling.
  5. Death
RATED AT EACH CLINIC VISIT

FORMULAE:
Creatinine Cl (mL/min) mL/min = 60 x CrCl mL/sec
CrCl - Cockcroft & Gault (mL/sec) Female: [140-age(yrs)] x TBW(Kg) / [50 x SCr(umol/L)] x 0.85

CCO Eligibility Form Required ☐ Non-Formulary Form Required ☐ Date revised: 07/16/2008
**CISPLATIN -TOPOTECAN Chemotherapy**

**Advanced/Recurrent Cervical Cancer**

**CISPLATIN**
- **50mg/m²**
- **IV** Day 1
- Round to nearest 1mg
- Mix in 500mL bag **Normal Saline**; Infuse over **60 minutes**.

**TOPOTECAN**
- **0.75mg/m²**
- **IV** Days 1-3
- Round to nearest 1mg
- Admix in 50mL bag **Normal Saline**; Infuse over **30 minutes**, followed by Cisplatin.
- Final concentration should be 20mcg-500mcg/mL.

**REPEAT EVERY 21 DAYS**

**HYDRATION:**

**Pre**
- Infuse 1000mL Normal Saline with 20mEq Potassium Chloride IV over 2 hours.

**Concurrent**
- May give 250mL of 20% Mannitol solution (50G) IV. Infuse through side arm concurrent with Cisplatin.

**Post**
- Infuse 500mL Normal Saline with 10mEq Potassium Chloride IV; (2G Magnesium sulfate may also be added) over 1 hour.
- Increase fluids if poor oral intake.

**TESTS:**

Baseline Tests: WBC HB PLT ANC Ca K Na Chloride Mg Glucose Cr Urea 24Hr CrCl T.Bili
AST ALT GGT AlkPhosphatase

Day 1: WBC HB PLT ANC Ca K Na Chloride Mg Cr Urea

**ANTIEMETIC PRE-CHEMO REGIMEN:**

**Level C**
- Day 1
  - Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
  - Dexamethasone 12mg PO/IV

**ANTIEMETIC TAKE-HOME REGIMEN:**

**Level B**
- Day 1
  - Ondansetron 8mg PO BID for 2-3 days, or Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days.
  - Dexamethasone 4mg PO BID for 2-3 days
  - Prochlorperazine 10mg PO q4-6h prn

**PATIENT VISITS and APPOINTMENT TYPE:**

- Day 1 4-6hrs Type B

**ANCILLARY:**
- Oral hydration is strongly encouraged; poorly hydrated patients may need more IV hydration.

**TOXICITIES:**

**Hematologic**
1. If ANC < 1.5 x 10⁹/L, or if PLT < 100 x 10⁹/L, HOLD dose for 1 week.

**Renal Failure**
1. If CrCl 0.67-1.0mL/sec, REDUCE to 50% dose of Topotecan.
2. If CrCl 0.33-0.67mL/sec, REDUCE to 25% dose of Topotecan.
3. If CrCl <0.33mL/sec, OMIT dose of Topotecan.
4. If CrCl >0.5-1.0mL/sec, or SrCr = 136-185umol/L, REDUCE to 50% dose of Cisplatin.
5. If CrCl <0.5mL/sec, or SrCr > 185umol/L, OMIT dose of Cisplatin.

**Hepatic Dysfunction**
1. If T.Bili = 26-51umol/L, or AST = 60-180 IU/L, REDUCE to 50% Cisplatin dose.
2. If T.Bili = 52-85umol/L, REDUCE to 25% Cisplatin dose.
3. If T.Bili > 85umol/L, or AST > 180 IU/L, OMIT Cisplatin dose

**SUGGESTED ACTION**
CISPLATIN -TOPOTECAN Chemotherapy

CLINICAL MONITORING:
- Baseline renal function tests (esp. if failure suspected).
- Pulmonary toxicity ratings at each visits (SOB).
- Watch for symptoms of fever and infection.
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.

Sensory
1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function. 2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL. 3. Sensory alteration or paresthesia interfering with ADL. 4. Disabling. 5. Death

Hearing
1. Asymptomatic, detected on exam/testing only. 2. Symptomatic, not interfering with ADL.
3. Symptomatic, interfering with ADL. 4. Life-threatening; disabling. 5. Death

Dyspnea (shortness of breath)
1. Dyspnea on exertion, but can walk 1 flight of stairs without stopping 2. Dyspnea on exertion but unable to walk 1 flight of stairs or 1 city block (0.1km) without stopping 3. Dyspnea with ADL 4. Dyspnea at rest; intubation/ventilator indicated 5. Death

Fever
1. 38.0 - 39.0°C (100.4 - 102.2°F) 2. >39.0 - 40.0°C (102.3 - 104.0°F) 3. >40.0°C (>104.0°F) for <24hrs 4. > 40.0°C (>104.0°F) for >24 hrs 5. Death

RATED AT EACH CLINIC VISIT

FORMULAE:
CrCl - Cockcroft & Gault (mL/sec) Female: [140-age(yrs)] x TBW(Kg) / [50 x SCr(umol/L)] x 0.85
Creatinine Cl (mL/min) mL/min = 60 x CrCl mL/sec

INTERNAL CODE:
OPIS CODE: CISP 50 + TOPO 0.75

REFERENCES:

Date revised: 07/16/2008
DACTINOMYCIN Chemotherapy
Gestational Trophoblast Disease - Low Risk

DACTINOMYCIN 1.25mg/m² IV Day 1 Round to nearest 0.05mg
- Slow push through sidearm of free flowing IV (5% Dextrose or Normal Saline).
- May be mixed in 50mL minibag (5% Dextrose or Normal Saline); Infuse over 10-15 minutes. Use if patient has a Central Venous Access device.
- UV protective bag required.

REPEAT EVERY 14 DAYS For a Usual Total of 1 - 2 Cycles After Normal HCG Title

TESTS:
Baseline Tests WBC HB PLT ANC Cr Urea T.Bili AST ALT GGT AlkPhosphatase
Day 1 WBC HB PLT ANC

ANTIEMETIC PRE-CHEMO REGIMEN:
Level C Day 1 - Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
- Dexamethasone 12mg PO/IV

ANTIEMETIC TAKE-HOME REGIMEN:
Level B/C Day 1 - Ondansetron 8mg PO BID for 2-3 days, or Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days
- Dexamethasone 4mg PO BID for 2-3 days
- Prochlorperazine 10mg PO q4-6h prn

PATIENT VISITS and APPOINTMENT TYPE:
⇒ Day 1 30min Type A

TOXICITIES:
Hematologic
1. If ANC < 1.5 x 10⁹/L, or if PLT < 100 x 10⁹/L, HOLD dose for 1 week.

Hepatic Dysfunction
- Consider dose reduction if LFTs elevated (eg. T.Bili or AST).

SUGGESTED ACTION

CLINICAL MONITORING:
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.

REFERENCES:
- Society of Gynecologists and Obstetricians of Canada Clinical Practice Guidelines.

CCO Eligibility Form Required ☐ Non-Formulary Form Required ☐ Date revised: 07/16/2008
DOCETAXEL-CARBOPLATIN Chemotherapy

Advanced Ovarian Cancer

**DOCETAXEL**

- 75mg/m² IV Day 1 Round to nearest 5mg
- Mix in **250mL** bag 5% Dextrose or **Normal Saline** to a maximum concentration of 0.3 - 0.9 mg/mL.
- Use non-PVC equipment without a filter; Infuse through main IV line.
- Elasto-gel™ gloves should be placed on both hands and treatment should begin 15 minutes after the infusion starts and conclude 15 minutes after the infusion is done.
- Gloves should be changed after 45 minutes to sustain the cold temperature.

**First and Second Dose:**
- Infuse at a slower rate and then increase incrementally.
- Infuse at **30mL/hr** for 5 minutes, then at **60mL/hr** for 5 minutes, then at **125mL/hr** for 5 minutes, then finally at **250mL/hr** until infusion complete.

**Subsequent doses:**
- Infuse over **1 hour**.
- **AUC = 5** IV Day 1 Round to nearest 5mg
- Mix in **250mL 5% Dextrose**.
- Infuse over 30 to **60 minutes**, after Docetaxel.

**CARBOPLATIN**

- Mix in **250mL 5% Dextrose**.
- Infuse over **30 to 60 minutes**, after Docetaxel.

**DEXAMETHASONE**

- 8mg PO Day 0 4mg tablet
- Take 8mg starting the evening before chemotherapy and the morning of chemotherapy.

**DIPHENHYDRAMINE**

- 50mg IV Day 1
- May be mixed in **50mL minbag 5% Dextrose**, **Normal Saline**; Give over **10-15 minutes**.
- Wait 30 minutes before Docetaxel started.

**Tests:**

Baseline Tests: WBC HB PLT ANC Ca K Na Chloride Mg Glucose Cr Urea T.Bili Albumin

AST ALT GGT AlkPhosphatase

Day 1 WBC HB PLT ANC Cr Urea

**Test Notes:** Additional Baseline tests: LDH & CO₂

**Antiemetic Pre-Chemo Regimen:**

Level C Day 1
- Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
- Dexamethasone 20mg PO/IV (if PO Dexamethasone not taken at home)

**Antiemetic Take-Home Regimen:**

Level B/C Day 1
- Ondansetron 8mg PO BID for 2-3 days, or Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days
- Dexamethasone 4mg PO BID for 2-3 days
- Prochlorperazine 10mg PO q4-6h prn

**Patient Visits and Appointment Type:**

- Day 1 (first 2 doses) 3hrs Type D
- Day 1 (subsequent) 3hrs Type C

**Ancillary:**

- Increase fluids if poor oral intake.

**Toxicities:**

- **Hematologic**
  1. If ANC < 1.5 x 10⁹/L, or if PLT < 100 x 10⁹/L, HOLD dose for 1 week.

- **Renal Failure**
  1. Adjust Carboplatin dose if estimated CrCl changes > 20%.

- **Hepatic Dysfunction**
  1. DECREASE Docetaxel dose if LFTs > 1.5 x normal.
  2. If AST or ALT > 53 IU/L, or if Alk Phos > 180 IU/L, REDUCE DOCETAXEL dose by 50%.

**Suggested Action**

Gynecological
CLINICAL MONITORING:
- Watch for symptoms of fever or infection.
- Blood pressure and pulse rate monitoring during drug administration and for the following hour.
- Skin assessment at each visit, including nails.

Hearing
1. Asymptomatic, detected on exam/testing only
2. Symptomatic, not interfering with ADL
3. Symptomatic, interfering with ADL
4. Life-threatening; disabling
5. Death

Sensory
1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function
2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL
3. Sensory alteration or paresthesia interfering with ADL
4. Disabling
5. Death

Allergic Reaction
1. Transient flushing or rash; drug fever < 38 degrees C
2. Rash; flushing; urticaria; dyspnea; drug fever > 38 degrees C
3. Symptomatic bronchospasm, with or without urticaria; parenteral medication(s) indicated; allergy-related edema/angioedema; hypotension
4. Anaphylaxis
5. Death

Skin Toxicity
0. None
1. Hyperpigmentation
2. Atrophy
3. Subcutaneous fibrosis
4. Desquamation, ulceration or necrosis

Fluid Retention
0. None
1. Mild peripheral edema
2. Pleural effusion, outpatient management
3. Pleural effusion, inpatient management
4. Intubation required

Nail Changes
1. Discoloration; ridging (koilonychias); pitting
2. Partial or complete loss of nail(s); pain in nailbed(s)
3. Interfering with ADL

RATED AT EACH CLINIC VISIT

Gynecological
1. Discoloration; ridging (koilonychias); pitting
2. Partial or complete loss of nail(s); pain in nailbed(s)
3. Interfering with ADL

HYPERSENSITIVITY:
Docetaxel Hypersensitivity Procedures:
- If hypersensitivity reaction during administration:
  1. Discontinue Docetaxel immediately if there are signs or symptoms of moderate or severe hypersensitivity. (Mild symptoms may resolve with a decrease in the rate of infusion.)
  2. Rapid IV administration of Diphenhydramine 50mg and Hydrocortisone 100mg.
  3. Re-initiate infusion after 30 minutes, or when signs of reaction are resolved. Resume infusion at a slower rate, then increase incrementally to the initial planned rate, eg. Infuse at 30mL/hr (an 8-hour rate) for 5 minutes, then at 60mL/hr (a 4-hour rate) for 5 minutes, then at 125mL/hr (a 2-hour rate) for 5 minutes, then finally, resume at 250mL/hr (1-hour infusion rate).
  4. Depending on the intensity of the reaction, additional oral or IV pre-medication with an antihistamine should also be given for the next cycle of treatment and the rate of infusion should be decreased initially and then increased back to the recommended 1-hour infusion.

FORMULAE:
Calvert Formula
Dose (in mg) = target AUC x (GFR + 25) GFR in mL/min
CrCl - Cockcroft & Gault (mL/sec)
Creatinine Cl (mL/min)

INTERNAL CODE:
OPIS CODE: DOCE-CARB*5

REFERENCES:
- CCO Practice Guideline4-1-2: First-line Chemotherapy for Postoperative Patients with Stage II, III or IV Epithelial Ovarian Cancer, Fallopian Tube Cancer, or Primary Peritoneal.
- Draft Evidence summary pending: 4-14 ES.

Date revised: 10/28/2008
DOXORUBICIN Chemotherapy
Gynecological Sarcoma/Leiomyosarcoma of the Uterus

DOXORUBICIN 50mg/m² IV Day 1 Round to nearest 1mg
- Slow push through sidearm of free flowing IV; Give 2 to 4mg (1-2mL) per minute.

TESTS:
Baseline Tests WBC HB PLT ANC T.Bili Albumin AST ALT GGT AlkPhosphatase
Day 1 WBC HB PLT ANC

ANTIEMETIC PRE-CHEMO REGIMEN:
Level C Day 1 - Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
- Dexamethasone 8mg PO/IV

ANTIEMETIC TAKE-HOME REGIMEN:
Level B/C Day 1 - Ondansetron 8mg PO BID for 2-3 days, or Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days
- Dexamethasone 4mg PO BID for 2-3 days
- Prochlorperazine 10mg PO q4-6h prn

PATIENT VISITS and APPOINTMENT TYPE:
⇒ Day 1 30min Type B

TOXICITIES:
Hematologic
1. If ANC < 1.5 x 10⁹/L, or if PLT < 100 x 10⁹/L, HOLD dose for 1 week.

Renal Failure
1. If SrCr > 265umol/L, REDUCE to 50% dose.

Hepatic Dysfunction
1. If T.Bili = 26-51umol/L, or AST 60-180 IU/L, REDUCE to 75% dose.
2. If T.Bili = 52-85umol/L, REDUCE to 50% dose.
3. If T.Bili > 85umol/L, or AST > 180 IU/L, OMIT dose.

SUGGESTED ACTION

CLINICAL MONITORING:
- Clinical exam for symptoms of CHF.
- Periodic cardiac tests for all patients with cardiac risk factors and patients at or above the threshold dose levels.

LV Systolic Dysfunction:
1. Asymptomatic, resting ejection fraction (EF) < 60 - 50%; shortening fraction (SF) < 30 - 24%
2. Asymptomatic, resting EF < 50 - 40%; SF < 24 - 15%
3. Symptomatic CHF responsive to intervention; EF < 40 - 20% SF < 15%
4. Refractory CHF or poorly controlled; EF < 20%; intervention such as ventricular assist device, ventricular reduction surgery, or heart transplant indicated
5. Death

For Cardiac Toxicity Ratings:
First rating at the cumulative dose threshold of 450mg/m² and repeat ratings at each cumulative dose increment of 100mg/m² above threshold. (Cumulative dose sooner for high risk patients, eg. pre-existing cardiac disease, prior chest irradiation). Note: Threshold Cumulative dose reduced proportionately if other anthracycline or anthracenedione drugs have been given; cardiotoxicity is additive.

RATED AT EACH CLINIC VISIT

REFERENCES:

CCO Eligibility Form Required □ Non-Formulary Form Required □ Date revised: 07/16/2008

Gynecological
DOXORUBICIN-CISPLATIN Chemotherapy
Endometrial Cancer

DOXORUBICIN
50mg/m² IV Day 1 Round to nearest 1mg
- Slow push through sidearm of free flowing IV; Give 2 to 4mg (1-2mL) per minute.

CISPLATIN
50mg/m² IV Day 1 Round to nearest 1mg
- Mix in 500mL bag Normal Saline; Infuse over 60 minutes.

HYDRATION:
Pre
- Infuse 1000mL Normal Saline with 20mEq Potassium Chloride IV over 2 hours.
Concurrent
- May give 250mL of 20% Mannitol solution (50G) IV; Infuse through side arm concurrent with Cisplatin (if diuresis is required).
Post
- Infuse 500mL Normal Saline with 10mEq Potassium Chloride IV; (2G Magnesium sulfate may also be added) over 1 hour.
- Increase fluids if poor oral intake.

TESTS:
Baseline Tests WBC HB PLT ANC 24Hr CrCl T.Bili AST ALT GGT AlkPhosphatase
Day 1 WBC HB PLT ANC Cr Urea

ANTIEMETIC PRE-CHEMO REGIMEN:
Level C Day 1
- Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
- Dexamethasone 8mg PO/IV

PATIENT VISITS and APPOINTMENT TYPE:
⇒ Day 1 5hrs Type D

ANCILLARY:
- Oral hydration is strongly encouraged; poorly hydrated patients may need more IV hydration.

SUGGESTED ACTION
Gynecological
DOXORUBICIN-CISPLATIN Chemotherapy

CLINICAL MONITORING:
- Clinical exam for symptoms of CHF.
- Periodic cardiac tests for all patients with cardiac risk factors and patients at or above the threshold dose levels (Doxorubicin 450mg/m²).
- Periodic Urinalysis (for RBCs) for low IV dose or patient complaint.

Sensory
1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function
2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL
3. Sensory alteration or paresthesia interfering with ADL
4. Disabling
5. Death

Hearing
1. Asymptomatic, detected on exam/testing only
2. Symptomatic, not interfering with ADL
3. Symptomatic, interfering with ADL
4. Life-threatening; disabling
5. Death

- Clinical exam for symptoms of CHF.
- Periodic cardiac tests for all patients with cardiac risk factors at or above the threshold dose levels.

LV Systolic Dysfunction
1. Asymptomatic, resting ejection fraction (EF) < 60 - 50%; shortening fraction (SF) < 30 - 24%
2. Asymptomatic, resting EF < 50 - 40%; SF < 24 - 15%
3. Symptomatic CHF responsive to intervention; EF < 40 - 20% SF < 15%
4. Refractory CHF or poorly controlled; EF < 20%; intervention such as ventricular assist device, ventricular reduction surgery, or heart transplant indicated
5. Death

- For Cardiac Toxicity Ratings: First rating at the cumulative dose threshold of 450mg/m², and repeat ratings at each cumulative dose increment of 100mg/m² above threshold. (Cumulative dose sooner for high risk patients, eg. pre-existing cardiac disease, prior chest irradiation).
- Note: Threshold Cumulative dose reduced proportionately if other anthracycline or anthracenedione drugs have been given; cardiotoxicity is additive.

RATED AT EACH CLINIC VISIT

FORMULAE:

Creatinine Cl (mL/min) mL/min = 60 x CrCl mL/sec
CrCl - Cockcroft & Gault (mL/sec) Female: \[ 140 \times \text{age(years)} \times \text{TBW(Kg)} / [50 \times \text{SCr(umol/L)}] \times 0.85 \]

REFERENCES:
DOXORUBICIN Low Dose Chemotherapy  
Advanced Ovarian or Endometrial Carcinoma

DOXORUBICIN  30mg  IV  Day 1, 8 & 15  Round to nearest 1mg
- Slow push through sidearm of free flowing IV
- Give 2 to 4mg (1-2mL) per minute.

REPEAT EVERY 28 DAYS (weekly administration for 3 out of 4 weeks)

TESTS:
Baseline Tests  WBC  HB  PLT  ANC  Cr  Urea  T.Bili  AST  ALT  AlkPhosphatase
Day 1  WBC  HB  PLT  ANC
Test Notes  - Repeat lytes, urea, Cr, LFTs every 3 months or prn.

ANTIEMETIC PRE-CHEMO REGIMEN:
Level B  Day 1  - Dexamethasone 4mg PO/IV
- May add or substitute Prochlorperazine 10mg PO/IV prn

ANTIEMETIC TAKE-HOME REGIMEN:
Level A  Day 1  - Prochlorperazine 10mg PO q4-6h prn

PATIENT VISITS and APPOINTMENT TYPE:
- Day 1: 30min Type B

ANCILLARY:
- Port recommended.

TOXICITIES:
Hematologic
1. If ANC < 1.5 x 10^9/L, or if PLT < 100 x 10^9/L, HOLD Doxorubicin dose for 1 week.

Renal Failure
1. If SrCr > 265umol/L, REDUCE Doxorubicin dose to 50%.

Hepatic Dysfunction
1. If T.Bili = 26-51umol/L, or AST = 60-180 IU/L, REDUCE Doxorubicin to 25% dose.
2. If T.Bili = 52-85umol/L, or AST > 180 IU/L, REDUCE Doxorubicin to 50% dose.
3. If T.Bili > 85umol/L, OMIT Doxorubicin.

SUGGESTED ACTION
CLINICAL MONITORING:
- Clinical exam for symptoms of CHF.
- Periodic cardiac tests for all patients with cardiac risk factors at or above the threshold dose levels.

LV Systolic Dysfunction:
1. Asymptomatic, resting ejection fraction (EF) < 60 - 50%; shortening fraction (SF) < 30 - 24%
2. Asymptomatic, resting EF < 50 - 40%; SF < 24 - 15%
3. Symptomatic CHF responsive to intervention; EF < 40 - 20%; intervention such as ventricular assist device, ventricular reduction surgery, or heart transplant indicated
4. Refractory CHF or poorly controlled; EF < 20%; intervention such as ventricular assist device, ventricular reduction surgery, or heart transplant indicated
5. Death
- For Cardiac Toxicity Ratings: First rating at the cumulative dose threshold of 450mg/m², and repeat ratings at each cumulative dose increment of 100mg/m² above threshold. (Cumulative dose sooner for high risk patients, eg. pre-existing cardiac disease, prior chest irradiation).
- Note: Threshold Cumulative dose reduced proportionately if other anthracycline or anthracenedione drugs have been given; cardiotoxicity is additive.
RATED AT EACH CLINIC VISIT

INTERNAL CODE:
OPIS CODE: DOXO-LO

REFERENCES:

CCO Eligibility Form Required  □  Non-Formulary Form Required  □  Date revised: 10/28/2008
**LIPOSOMAL DOXORUBICIN Chemotherapy**

*Advanced Ovarian Carcinoma*

### DOXORUBICIN LIPOSOMAL

- **Dose:** 40mg/m² IV Day 1 Round to nearest 1mg

#### Administration

- **If dose < 90mg,** mix in **250mL Dextrose 5%** or **If dose > 90mg,** mix in **500mL Dextrose 5%**

#### Administration Details

- **Test dose:** 20mg admix into 100mL D5W and infuse over 1 hour.
- **If no reaction occurs,** admix the remaining dose into a 250mL D5W and infuse at 150mL/hr for 10 minutes then 200mL/hr for 10 minutes then if tolerated full rate.
- **For the subsequent infusions:**
  - **Infuse 250mL over 1 hour.**

#### Repeat

- **Repeat every 28 days**

### Tests

<table>
<thead>
<tr>
<th>Baseline Tests</th>
<th>WBC HB PLT ANC Cr Urea T.Bili AST ALT GGT AlkPhosphatase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1</td>
<td>WBC HB PLT ANC</td>
</tr>
</tbody>
</table>

#### Antiemetic Pre-Chemo Regimen

**Level B**

- **Day 1**
  - Dexamethasone 8mg PO/IV
  - May add or substitute Prochlorperazine 10mg PO/IV prn

#### Antiemetic Take-Home Regimen

**Level A**

- **Day 1**
  - Prochlorperazine 10mg PO q4-6h prn

### Patient Visits and Appointment Type

- **Day 1**
  - 1.5hrs
  - Type B

### Toxicities

**Hematologic**

1. If **ANC < 1.5 x 10⁹/L,** or if **PLT < 100 x 10⁹/L,** HOLD dose for 1 week.

**Renal Failure**

1. If **SrCr > 265umol/L,** REDUCE dose to **50%**.

**Hepatic Dysfunction**

1. If **T.Bili = 26-51umol/L,** or **AST = 60-180 IU/L,** GIVE **75%** dose.
2. If **T.Bili = 52-85umol/L,** or **AST > 180 IU/L,** GIVE **50%** dose.
3. If **T.Bili > 85umol/L,** OMIT dose.

**Suggested Action**

- Observation for infusion reaction (back pain, flushing, chest tightness) during and for 30 minutes after first injection.
- Emergency treatment must be available, eg. antihistamine injection.

### hypersensitivity

**Management of Hypersensitivity Reactions During Doxorubicin Liposomal (CAELYX™) Infusion:**

**Mild** (mild flushing, rash, pruritis)
- Complete infusion. Supervise at bedside. No treatment required.

**Moderate** (moderate rash, flushing, mild dyspnea, chest discomfort, mild hypotension, back pain)
- Stop infusion; Give IV Diphenhydramine 25-50mg and IV Dexamethasone 10mg.
- After recovery of symptoms, resume infusion at a rate of 50% of the initial rate of infusion.

**Severe** (one or more of respiratory distress requiring treatment, generalized urticaria, angioedema, hypotension requiring therapy)
- Stop infusion.
- Give IV antihistamine and steroid as above. Add Epinephrine or bronchodilators if indicated.

### Internal Code

**OPIS CODE: DOXORUBICIN LIPO**

### References


**Date revised: 07/16/2008**

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**Gynecological**
ETOPOSIDE

50-100mg PO Days 1-14 (or Days 1-21) 50mg capsule

- Daily for 14-21 days.
- Outpatient prescription available as 50mg capsules.
- Trade name is Vepesid™

REPEAT EVERY 28 DAYS

TESTS:
Baseline Tests: WBC HB PLT ANC T.Bili AST ALT GGT AlkPhosphatase
Day 1: WBC HB PLT ANC

ANTEMETIC TAKE-HOME REGIMEN:
Level A: Days 1-14 (or 21) - Prochlorperazine 10mg PO q4-6h prn

TOXICITIES:
Hematologic
1. If ANC < 1.5 x 10⁹/L, or if PLT < 100 x 10⁹/L, HOLD dose for 1 week.

Hepatic Dysfunction
1. If T.Bili = 26-51umol/L, or AST = 60-180 IU/L, REDUCE Etoposide to 50% dose.
2. If T.Bili = 52-85umol/L, REDUCE Etoposide to 25% dose.
3. If T.Bili > 85umol/L, or AST > 180 IU/L, OMIT Etoposide.

SUGGESTED ACTION

CLINICAL MONITORING:
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.

INTERNAL CODE:
OPIS CODE: ETOP*PO GY

REFERENCES:

Date revised: 07/16/2008
GEMCITABINE Chemotherapy
Recurrent Ovarian Carcinoma

GEMCITABINE 1000mg/m² IV Days 1, 8 Round to nearest 19mg
- Admix in 250mL bag 5% Dextrose or Normal Saline; Infuse over 30 minutes.

REPEAT EVERY 21 DAYS

TESTS:
Baseline Tests: WBC HB PLT ANC Ca K Na Chloride Glucose T.Bili Albumin AST ALT GGT AlkPhosphatase
Test Notes: Baseline & periodic renal function tests (if failure suspected).

ANTIEMETIC PRE-CHEMO REGIMEN:
Level A Days 1,8 - Prochlorperazine 10mg PO/IV pm

ANTIEMETIC TAKE-HOME REGIMEN:
Level A Days 1,8 - Prochlorperazine 10mg PO q4-6h pm

PATIENT VISITS and APPOINTMENT TYPE:
Days 1, 8 45min Type A

TOXICITIES:
Hematologic
1. If ANC < 1.5 x 10⁹/L, or if PLT = 75-100 x 10⁹/L, REDUCE to 50% dose.
2. If ANC < 1.0 x 10⁹/L, or if PLT < 75 x 10⁹/L, HOLD dose for 1 week.

Gastrointestinal
1. If Mucositis or Diarrhea > Grade 3 in previous course, REDUCE to 2/3 dose.

CLINICAL MONITORING:

Edema limb
1. 5 - 10% inter-limb discrepancy in volume or circumference at point of greatest visible difference; swelling or obscuration of anatomic architecture on close inspection; pitting edema 2. >10 - 30% inter-limb discrepancy in volume or circumference at point of greatest visible difference; readily apparent obscuration of anatomic architecture; obliteration of skin folds; readily apparent deviation from normal anatomic contour 3. >30% inter-limb discrepancy in volume; lymphorrhea; gross deviation from normal anatomic contour; interfering with ADL 4. Progression to malignancy (i.e., lymphangiosarcoma); amputation indicated; disabling 5. Death

Mucositis
1. Erythema of the mucosa 2. Patchy ulcerations or pseudomembranes 3. Confluent ulcerations or pseudomembranes; bleeding with minor trauma 4. Tissue necrosis; significant spontaneous bleeding; life-threatening consequences 5. Death

Diarrhea
1. Increase of < 4 stools per day over baseline; mild increase in ostomy output compared to baseline 2. Increase of 4 - 6 stools per day over baseline; IV fluids indicated < 24hrs; moderate increase in ostomy output compared to baseline; not interfering with ADL 3. Increase of ≥7 stools per day over baseline; incontinence; IV fluids >24 hrs; hospitalization; severe increase in ostomy output compared to baseline; interfering with ADL 4. Life-threatening consequences (e.g., hemodynamic collapse) 5. Death

RATED AT EACH CLINIC VISIT

INTERNAL CODE:
OPIS CODE: GEMCIT-GYN

REFERENCES:

Date revised: 10/28/2008
MEDROXYPROGESTERONE Chemotherapy

Endometrial Cancer

MEDROXYPROGESTERONE 100mg
PO Daily treatment 100mg tablet

- BID to QID
- Outpatient prescription available in 2.5mg, 5mg, 10mg and 100mg tablets.
- Trade name is Provera™

CLINICAL MONITORING:
- Medroxyprogesterone is contraindicated in patients with a history of significant thromboembolic disease.

INTERNAL CODE:
OPIS CODE: MEDROXY

REFERENCES:

Date revised: 07/16/2008
MELPHALAN Chemotherapy
Ovarian Cancer

MELPHALAN

- Daily for 4 days.
- Outpatient prescription available in 2mg tablets.
- Trade name is Alkeran™

MELPHALAN 0.25mg/Kg PO Days 1-4 2mg tablet

REPEAT EVERY 28 DAYS

TESTS:
Baseline Tests WBC HB PLT ANC
Day 1 WBC HB PLT ANC

TOXICITIES:
Hematologic
1. If ANC < 1.5 x 10⁹/L, or if PLT < 100 x 10⁹/L, HOLD dose for 1 week.

SUGGESTED ACTION

Date revised: 07/16/2008
METHOTREXATE Chemotherapy
Gestational Trophoblast Disease- Low Risk

METHOTREXATE
50-75mg/m² IM Day 1 Round to nearest 5mg
- IM administration.

REPEAT EVERY 7 DAYS for a Usual Total of 1-2 Cycles after Normal HCG Titre

TESTS:
Baseline Tests
Day 1
WBC HB PLT ANC Cr Urea T.Bili AST ALT GGT AlkPhosphatase
WBC HB PLT ANC

ANTIEMETIC PRE-CHEMO REGIMEN:
Level A
Day 1
- Prochlorperazine 10mg PO pm

ANTIEMETIC TAKE-HOME REGIMEN:
Level A
Day 1
- Prochlorperazine 10mg PO q4-6h pm

PATIENT VISITS and APPOINTMENT TYPE:
⇒ Day 1: 15min Type A

TOXICITIES:
Hematologic
1. If ANC < 1.5 x 10⁹/L, or if PLT < 100 x 10⁹/L, HOLD dose for 1 week.

Renal Failure
1. If CrCl = 0.2-0.8mL/sec, or SrCr = 100-180umol/L, GIVE 50% of Methotrexate dose.
2. If CrCl < 0.2mL/sec, or SrCr > 180umol/L, OMIT Methotrexate dose.

Hepatic Dysfunction
1. If T.Bili = 52-85umol/L, or AST > 180 IU/L, GIVE 75% Methotrexate dose.
2. If T.Bili > 85umol/L, OMIT Methotrexate dose.

SUGGESTED ACTION

REFERENCES:
- Society of Gynecologists and Obstetricians of Canada Clinical Practice Guidelines.

Date revised: 07/17/2008
PACLITAXEL Chemotherapy  
**Advanced Ovarian Cancer (recurrent)**

**PACLITAXEL**  
175mg/m² IV Day 1  
- Mix in **500mL** bag **Normal Saline** (dilution concentration 0.3-1.2 mg/mL).  
- Use non-PVC equipment, including 0.22 micron in-line filter.  
- Infuse over **3 hours**.

**DEXAMETHASONE**  
20mg PO Day 1  
- 12 and 6 hours before Paclitaxel administration (if not taken at home, give 20mg Dexamethasone IV **30-60 minutes** before Paclitaxel).

**DIPHENHYDRAMINE**  
50mg PO Day 1  
- Administer at least **30 minutes** before Paclitaxel.

**RANITIDINE**  
150mg PO Day 1  
- Administer at least **30 minutes** before Paclitaxel.

**TESTS:**

| Test Notes |  
| Baseline Tests | WBC | HB | PLT | ANC | 24Hr CrCl | T.Bili | AST | ALT | GGT | AlkPhosphatase |
| Test Notes |  
| Day 1 | WBC | HB | PLT | ANC |  

**ANTIEMETIC PRE-CHEMO REGIMEN:**

- Dexamethasone -see regimen information re pre-medications.  
- May add Prochlorperazine 10mg PO/IV prn

**ANTIEMETIC TAKE-HOME REGIMEN:**

- Day 1 - Prochlorperazine 10mg PO q4-6h prn

**PATIENT VISITS and APPOINTMENT TYPE:**

- Day 1 5hrs  
  
**ANCILLARY:**

- Take a baseline blood pressure measurement, if prior hypotension.
- Observe patient for the first 5 minutes of the Paclitaxel infusion, then periodically for the remainder of the infusion.

**SUGGESTED ACTION**

**CLINICAL MONITORING:**

- Watch for symptoms of fever and infection.  
- Blood pressure and pulse rate monitoring during drug administration & for the following hour.

**Sensory**

1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function.  
2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL.  
3. Sensory alteration or paresthesia interfering with ADL.  
4. Disabling.  
5. Death

**Flu-like Symptoms**

1. Symptoms present but not interfering with function  
2. Moderate or causing difficulty performing some ADL  
3. Severe symptoms interfering with ADL  
4. Disabling  
5. Death

**Allergic Reaction**

1. Transient flushing or rash; drug fever < 38 degrees C  
2. Rash; flushing; urticaria; dyspnea; drug fever > 38 degrees C  
3. Symptomatic bronchospasm, with or without urticaria; parenteral medication(s) indicated; allergy-related edema/angiokeratoma; hypotension  
4. Anaphylaxis  
5. Death

**RATED AT EACH CLINIC VISIT**

Gynecological
**HYPERSENSITIVITY:**

**PACLITAXEL Chemotherapy**

Retreatment for Paclitaxel Hypersensitivity Reaction:

1. Discontinue Paclitaxel immediately if there are signs or symptoms of hypersensitivity.
2. Rapid IV administration of Diphenhydramine 50mg direct IV push over 1 minute and Hydrocortisone 100mg in 100ml Normal Saline over 5-10 minutes.
3. Reinitiate Paclitaxel infusion after 30 minutes, or when signs of reaction are resolved. Resume Paclitaxel infusion at 17mL/hr (10% of original rate) for 15 minutes, then at 42mL/hr (25% of original rate) for 15 minutes. If no further symptoms develop, continue at original rate until infusion complete.
4. If reaction recurs, STOP Paclitaxel for this dose and treat patient symptoms.

Desensitization for Paclitaxel Hypersensitivity Reactions:

1. Dexamethasone 20mg PO 36 hours and 12 hours before chemotherapy, and 20mg PO morning of chemotherapy.
2. Dexamethasone 20mg IV, Diphenhydramine 50mg IV & Ranitidine 50mg IV about 30min before infusion.
3. Paclitaxel Infusion: 2mg in 100mL Normal Saline over 30min; if no reaction, 10mg in 100mL Normal Saline over 30min; if no reaction, remainder of dose in 500mL Normal Saline over 3 hours.
4. If reaction occurs, discontinue infusion; Diphenhydramine 50mg direct IV push over 1 minute and Hydrocortisone 100mg in 100ml Normal Saline over 5-10 minutes.
5. Restart Paclitaxel infusion after 30 minutes.

**REFERENCES:**

PACLITAXEL-CARBOPLATIN Chemotherapy

Gynecological Ovarian Cancer

PACLITAXEL 175mg/m² IV Day 1 Round to nearest 3mg
- Mix in 500mL bag Normal Saline (dilution concentration 0.3-1.2 mg/mL).
- Use non-PVC equipment, including 0.22 micron in-line filter.
- Infuse over 3 hours, before Carboplatin.

DEXAMETHASONE 20mg PO Day 0 & 1 4mg tablet
- To be administered at home 12 and 6 hours before Paclitaxel (if not taken at home, Dexamethasone 20mg IV 30-60 minutes before Paclitaxel).

DIPHENHYDRAMINE 50mg PO Day 1
- Administer at least 30 minutes before Paclitaxel.

RANITIDINE 150mg PO Day 1
- Administer at least 30 minutes before Paclitaxel.

CARBOPLATIN AUC = 5 to 7.5 IV Day 1 Round to nearest 5mg
- Mix in 250mL 5% Dextrose.
- Infuse over 30 to 60 minutes, after Paclitaxel.

TESTS:
- WBC HB PLT ANC 24Hr CrCl T.Bili Albumin AST ALT GGT AlkPhosphatase
- WBC HB PLT ANC Cr Urea

ANTIEMETIC PRE-CHEMO REGIMEN:
Level C Day 1
- Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
- Dexamethasone 20mg PO/IV (if patient has not taken PO dexamethasone at home)

ANTIEMETIC TAKE-HOME REGIMEN:
Level B/C Day 1
- Ondansetron 8mg PO BID for 2-3 days, or
- Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days
- Dexamethasone 8 mg PO BID for 2-3 days
- Prochlorperazine 10 mg PO q4-6h prn

PATIENT VISITS and APPOINTMENT TYPE:
⇒ Day 1 6hrs Type D

ANCILLARY:
- Take a baseline blood pressure measurement, if prior hypotension.

TOXICITIES:
Hematologic
1. If ANC < 1.5 x 10^9/L, or if PLT < 100 x 10^9/L, HOLD dose for 1 week.

Hepatic Dysfunction
1. If AST > 70 IU/L, or T.Bili < 25umol/L, give MAXIMUM Paclitaxel dose of 135mg/m².
2. If T.Bili = 25-50umol/L, give MAXIMUM Paclitaxel dose of 75mg/m².
3. If T.Bili > 50umol/L, give MAXIMUM Paclitaxel dose of 50mg/m².

SUGGESTED ACTION
Renal Failure
1. Adjust Carboplatin dose if estimated CrCl changes > 20%.

SUGGESTED ACTION

CLINICAL MONITORING:
- Watch for symptoms of fever and infection.
- Blood pressure and pulse rate monitoring during drug administration and for the following hour.

Sensory
1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function. 2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL. 3. Sensory alteration or paresthesia interfering with ADL. 4. Disabling. 5. Death

Flu-like Symptoms

Allergic Reaction
1. Transient flushing or rash; drug fever < 38 degrees C 2. Rash; flushing; urticaria; dyspnea; drug fever > 38 degrees C 3. Symptomatic bronchospasm, with or without urticaria; parenteral medication(s) indicated; allergy-related edema/angioedema; hypotension 4. Anaphylaxis 5. Death

RATED AT EACH CLINIC VISIT
PACLITAXEL-CARBOPLATIN Chemotherapy

HYPERSENSITIVITY:

Paclitaxel Procedures

Retreatment for Paclitaxel Hypersensitivity Reaction:

If Paclitaxel hypersensitivity reaction occurs during administration:

1. Discontinue Paclitaxel immediately if there are signs or symptoms of hypersensitivity.
2. Rapid IV administration of Diphenhydramine 50mg direct IV push over 1 minute and Hydrocortisone 100mg in 100ml Normal Saline over 5-10 minutes.
3. Reinitiate Paclitaxel infusion after 30 minutes, or when signs of reaction are resolved. Resume Paclitaxel infusion at 17ml/hr (10% of original rate) for 15 minutes, then at 42ml/hr (25% of original rate) for 15 minutes. If no further symptoms develop, continue at original rate until infusion complete.
4. If reaction recurs, STOP Paclitaxel for this dose and treat patient symptoms.

Desensitization for Paclitaxel Hypersensitivity Reactions:

If Paclitaxel hypersensitivity recurs during previous administration despite retreatment plan:

1. Dexamethasone 20mg PO 36 hours and 12 hours before chemotherapy, and 20mg PO morning of chemotherapy.
2. Dexamethasone 20mg IV, Diphenhydramine 50mg IV & Ranitidine 50mg IV about 30min before infusion.
3. Paclitaxel Infusion: 2mg in 100mL Normal Saline over 30min; if no reaction, 10mg in 100mL Normal Saline over 30min; if no reaction, remainder of dose in 500mL Normal Saline over 3 hours. 4. If reaction occurs, discontinue infusion; Diphenhydramine 50mg direct IV push over 1 minute and Hydrocortisone 100mg in 100ml Normal Saline over 5-10 minutes. 5. Restart Paclitaxel infusion after 30 minutes.

FORMULAE:

CrCl - Cockcroft & Gault (mL/sec)
Player: \[\text{[140-age(yrs)] x TBW(Kg) / [50 x SCr(umol/L)] x 0.85}\]

Creatinine Cl (mL/min) mL/min = 60 x CrCl mL/sec

Calvert Formula Dose (in mg) = target AUC x (GFR + 25) GFR in mL/min

INTERNAL CODE:

OP/S CODE:
- PACLI-CARB 5
- PACLI-CARB 6

REFERENCES:

- CCO Practice Guideline4-1-2: First-line Chemotherapy for Postoperative Patients with Stage II, III or IV Epithelial Ovarian Cancer, Fallopian Tube Cancer, or Primary Peritoneal .
- Draft Evidence summary pending: 4-14 ES.

Date revised: 07/17/2008
**PACLITAXEL-CISPLATIN** Intraperitoneal Chemotherapy

*Advanced Ovarian Cancer*

**PACLITAXEL** 175mg/m² IV Day 1 Round to nearest 3mg
- Mix in **500mL** bag **Normal Saline** (dilution concentration 0.3-1.2 mg/mL).
- Use non-PVC equipment, including 0.22 micron in-line filter.
- Infuse over **3 hours**.

**DEXAMETHASONE** 20mg PO Day 1 4mg tablet
- To be administered at home 12 and 6 hours before Paclitaxel (if not taken at home, Dexamethasone 20mg IV **30-60 minutes** before Paclitaxel).

**DIPHENHYDRAMINE** 50mg PO Day 1
- Administer at least **30 minutes** before Paclitaxel.

**RANITIDINE** 150mg PO Day 1
- Administer at least **30 minutes** before Paclitaxel.

**CISPLATIN** 75-100mg/m² IP Day 1 Round to nearest 1mg
- Warm solution to body temperature to reduce cramping.
- Infuse the following (in sequential order) through implanted intraperitoneal port into peritoneum by gravity (NO PUMPS):
  - **500mL** of **Normal Saline**.
  - Cisplatin mixed in **500mL** bag of **Normal Saline**.
  - Flush port with **10mL** **Normal Saline**, followed by **500Units of Heparin**.

**HYDRATION:**
*Pre*
- Infuse **500mL** (up to 1000mL) Normal Saline with 10mEq Potassium Chloride/0.5L + 1G Magnesium Sulfate/0.5L IV at **500mL/hr**, starting 1 hour pre IP Cisplatin.

*Concurrent*
- Give **50mL** of **20% Mannitol** solution (10G) IV (if diuresis is required)

*Post*
- Infuse **1000mL** Normal Saline with 20mEq Potassium Chloride/L + 2G Magnesium Sulfate/L IV at **500mL/hr**, after the completion of IP Cisplatin.
- Home hydration: **1000mL** Normal Saline over 5 hours on Days 2 and 3.

**TESTS:**
- Baseline Tests: WBC HB PLT ANC K Na Chloride Mg Cr Urea T.Bili Albumin AST ALT GGT AlkPhosphatase
- Day 1: WBC HB PLT ANC K Na Chloride Mg Cr Urea AST ALT GGT AlkPhosphatase

**ANTIEMETIC PRE-CHEMO REGIMEN:**
- Level C Day 1 - Granisetron 1mg IV

**ANTIEMETIC TAKE-HOME REGIMEN:**
- Level B/C Day 1 - Granisetron 1mg IV for 2 days (home care to administer)
  - Dexamethasone 4mg PO BID for 3 days starting the morning of Day 2
  - Prochlorperazine 10mg PO q4-6h prn

**PATIENT VISITS and APPOINTMENT TYPE:**
- Day 1 6-8hrs Type L

**ANCILLARY:**
- Take a baseline blood pressure measurement, if prior hypotension.

**TOXICITIES:**

**Hematologic**
1. If ANC < 1.5 x 10⁹/L, or if PLT < 100 x 10⁹/L, **HOLD** dose for 1 week.

**Hepatic Dysfunction**
1. If AST > 70 IU/L, or T.Bili < 25umol/L, give MAXIMUM Paclitaxel dose of **135mg/m²**.
2. If T.Bili = 25-50umol/L, give MAXIMUM Paclitaxel dose of **75mg/m²**.
3. If T.Bili > 50umol/L, give MAXIMUM Paclitaxel dose of **50mg/m²**.

**SUGGESTED ACTION**

**Renal Failure**
1. If CrCl = 0.5-1.0mL/sec, or SrCr = 136-185umol/L, REDUCE Cisplatin to **50%** dose.
2. If CrCl < 0.5mL/sec, or SrCr > 185umol/L, **OMIT** Cisplatin dose.

**SUGGESTED ACTION**

Gynecological
PACLITAXEL-CISPLATIN Intraperitoneal Chemotherapy

CLINICAL MONITORING:
- Watch for symptoms of fever and infection.
- Blood pressure and pulse rate monitoring during drug administration and for the following hour.

Sensory
1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function.
2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL.
3. Sensory alteration or paresthesia interfering with ADL.
4. Disabling.
5. Death

Flu-like Symptoms
1. Symptoms present but not interfering with function
2. Moderate or causing difficulty performing some ADL
3. Severe symptoms interfering with ADL
4. Disabling
5. Death

Allergic Reaction
1. Transient flushing or rash; drug fever < 38 degrees C
2. Rash; flushing; urticaria; dyspnea; drug fever ≥ 38 degrees C
3. Symptomatic bronchospasm, with or without urticaria; parenteral medication(s) indicated; allergy-related edema/angioedema; hypotension
4. Anaphylaxis
5. Death

RATED AT EACH CLINIC VISIT

HYPERSENSITIVITY:
Paclitaxel Procedures
Retreatment for Paclitaxel Hypersensitivity Reaction:
If Paclitaxel hypersensitivity reaction occurs during administration:
1. Discontinue Paclitaxel immediately if there are signs or symptoms of hypersensitivity.
2. Rapid IV administration of Diphenhydramine 50mg direct IV push over 1 minute and Hydrocortisone 100mg in 100ml Normal Saline over 5-10 minutes.
3. Reinitiate Paclitaxel infusion after 30 minutes, or when signs of reaction are resolved. Resume Paclitaxel infusion at 17mL/hr (10% of original rate) for 15 minutes, then at 42mL/hr (25% of original rate) for 15 minutes. If no further symptoms develop, continue at original rate until infusion complete.
4. If reaction recurs, STOP Paclitaxel for this dose and treat patient symptoms.

Desensitization for Paclitaxel Hypersensitivity Reactions:
If Paclitaxel hypersensitivity recurs during previous administration despite retreatment plan:
1. Dexamethasone 20mg PO 36 hours and 12 hours before chemotherapy, and 20mg PO morning of chemotherapy.
2. Dexamethasone 20mg IV, Diphenhydramine 50mg IV & Ranitidine 50mg IV about 30min before infusion.
3. Paclitaxel Infusion: 2mg in 100mL Normal Saline over 30min; if no reaction, 10mg in 100mL Normal Saline over 30min; if no reaction, remainder of dose in 500mL Normal Saline over 3 hours.
4. If reaction occurs, discontinue infusion; Diphenhydramine 50mg direct IV push over 1 minute and Hydrocortisone 100mg in 100ml Normal Saline over 5-10 minutes.
5. Restart Paclitaxel infusion after 30 minutes.

FORMULAE:
CrCl - Cockcroft & Gault (mL/sec) Female: \[140\text{-age(yrs)} x \text{TBW(Kg)} / [50 x \text{SCr(umol/L)}] x 0.85\] 
Creatinine Cl (mL/min) \(\text{mL/min} = 60 \times \text{CrCl mL/sec}\)

INTERNAL CODE:
OPIS CODES:
- PACLI-CISP*IP 75
- PACLI-CISP*IP 100

REFERENCES:

Date revised: 07/17/2008
**GY-TAM*HD**
Gynecological

**TAMOXIFEN Therapy**
**Advanced (Platinum-Resistant) Ovarian Cancer- Palliative Intent**

<table>
<thead>
<tr>
<th>TAMOXIFEN</th>
<th>40mg</th>
<th>PO</th>
<th>Daily</th>
<th>10 &amp; 20mg tablets</th>
</tr>
</thead>
</table>

- 40mg PO daily or 20mg PO BID.
- Outpatient prescription available as 10mg and 20mg tablets.
- Trade names is Nolvadex-D™

**CONTINUOUS TREATMENT**

**TESTS:**
Baseline Tests: WBC HB PLT ANC LVEF

**CLINICAL MONITORING:**
- Clinical assessment for gynecological symptoms (endometrial hyperplasia/neoplasia).
- Tamoxifen is contraindicated in patients with a history of significant thromboembolic disease.

**REFERENCES:**

CCO Eligibility Form Required [ ] Non-Formulary Form Required [ ] Date revised: 07/17/2008
ETYXOL 24H
Gynecological

PACLITAXEL-CARBOPLATIN Chemotherapy (Inpatient Regimen)
Ovarian Cancer- for hypersensitivity reactions

DEXAMETHASONE 20 mg IV Day 1
- Infuse 30 minutes prior to Paclitaxel.

PACLITAXEL 135 mg/m² IV 24 hour infusion Round to nearest 3mg
- Mix in 500mL bag Normal Saline (Concentration 0.5 mg/mL).
- Use non-PVC equipment, including 0.22 micron in-line filter.
**Infuse over 24 hours as follows:**
1. 20% of final rate x 2 hours.
2. If no reaction, then give 40% of final rate x 2 hours.
3. If no reaction, then give 60% of final rate x 2 hours.
4. If no reaction, then give 80% of final rate x 2 hours.
5. Then infuse at the final rate until infusion complete.
   - (To calculate the final rate, use total volume divided by 20 hours).
   - For neuropathy, no need for graduated infusion.

DIPHENHYDRAMINE 50 mg IV Day 1
- Infuse 30 minutes prior to Paclitaxel.

RANITIDINE 50 mg IV Day 1
- Infuse 30 minutes prior to Paclitaxel.

LORAZEPAM 1-2 mg PO Day 1
- Give 1-2mg prior to chemo.

DEXAMETHASONE 4 mg PO Q6H
- Start 4 hours after Paclitaxel infusion begins.

CARBOPLATIN AUC range 5-7 IV Day 2 Round to nearest 5 mg
- Mix in 250mL bag D5W; Infuse over 30-60 minutes.

**REPEAT EVERY 21 DAYS**

HYDRATION:
Pre
- IV Normal Saline 100mL/hr until discharge.

TESTS:
Baseline Tests: WBC HB PLT ANC Cr 24Hr CrCl T.Bili Albumin AST AlkPhosphatase
Test Notes: Baseline CBC & diff, PLT, Cr, LFTs. Chest X ray
   - Before each treatment : CBC & diff, Cr, LFTs (if clinically indicated)

ANTIEMETIC PRE-CHEMO REGIMEN:
Level C Days 1-3
- Ondansetron 8mg PO/IV pre-chemo, then BID or Granisetron 1-2mg PO/IV daily
   - Dexamethasone 20mg PO/IV

INPATIENT ANTIEMETICS:
- Ondansetron 8mg pre-chemo, then BID x 3 days
- Ondansetron can be substituted with Granisetron 1-2 mg daily

ANCILLARY:
- Take a baseline blood pressure measurement, if prior hypotension.

TOXICITIES:
Hematologic
1. If ANC < 1.5 x 10^9/L, or if PLT < 100 x 10^9/L, HOLD dose for 1 week.

Hepatic Dysfunction
1. If T.Bili = 26-51umol/L, or AST = 60-180 IU/L, GIVE Paclitaxel maximum dose of 75mg/m².
2. If T.Bili = 52-85umol/L, GIVE Paclitaxel maximum dose of 50mg/m².

Renal Failure
1. If SrCr = 136-150 umol/L, REDUCE Carboplatin dose by 50mg/m².
2. If SrCr = 151-180 umol/L, REDUCE Carboplatin dose by 100mg/m².
3. If SrCr > 181 umol/L, OMIT Carboplatin dose.

SUGGESTED ACTION

Gynecological
PACLITAXEL-CARBOPLATIN Chemotherapy (Inpatient Regimen)

**CLINICAL MONITORING:**
- Watch for symptoms of fever and infection.
- Blood pressure and pulse rate monitoring during drug administration and for the following hour.

**Sensory**
1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function. 2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL. 3. Sensory alteration or paresthesia interfering with ADL. 4. Disabling. 5. Death

**Flu-like Symptoms**

**Allergic Reaction**
1. Transient flushing or rash; drug fever < 38 degrees C 2. Rash; flushing; urticaria; dyspnea; drug fever > 38 degrees C 3. Symptomatic bronchospasm, with or without urticaria; parenteral medication(s) indicated; allergy-related edema/angioedema; hypotension 4. Anaphylaxis 5. Death

RATED AT EACH CLINIC VISIT

**HYPERSENSITIVITY:**

**Paclitaxel Hypersensitivity Procedures**

**Retreatment for Paclitaxel Hypersensitivity Reaction:**
1. Discontinue Paclitaxel immediately if there are signs or symptoms of hypersensitivity.
2. Rapid IV administration of Diphenhydramine 50mg and Hydrocortisone 100mg.
3. Reinitiate Paclitaxel infusion after 30 minutes, or when signs of reaction are resolved. Resume Paclitaxel infusion at 17mL/hr (10% of original rate) for 15 minutes, then at 42mL/hr (25% of original rate) for 15 minutes. If no further symptoms develop, continue at original rate until infusion complete.
4. If reaction recurs, STOP Paclitaxel for this dose and treat patient symptoms.

**Desensitization for Paclitaxel Hypersensitivity Reactions:**
1. Dexamethasone 20mg PO 36 hours and 12 hours before chemotherapy, and 20mg PO morning of chemotherapy.
2. Dexamethasone 20mg IV, Diphenhydramine 50mg IV and Ranitidine 50mg IV about 30 minutes before infusion.
3. Paclitaxel Infusion: 2mg in 100mL Normal Saline over 30 minutes; if no reaction, 10mg in 100mL Normal Saline over 30 minutes; if no reaction, remainder of dose in 500mL Normal Saline over 3 hours.
4. If reaction occurs, discontinue infusion; Diphenhydramine 50mg IV and Hydrocortisone 100mg IV.
5. Restart Paclitaxel infusion after 30 minutes.

**Date revised:** 03/07/2005
TOPOTECAN Chemotherapy (daily)
Advanced Ovarian Cancer

TOPOTECAN 1.25mg/m² IV Days 1-5 Round to nearest 0.1mg
- Mix in 50-100mL minibag Normal Saline; Infuse over 30 minutes.
- Final concentration should be 10mcg-500mcg/mL.

REPEAT EVERY 21 DAYS

TESTS:
Baseline Tests WBC HB PLT ANC
Day 1 WBC HB PLT ANC

ANTIEMETIC PRE-CHEMO REGIMEN:
Level B Days 1-5 - Prochlorperazine 10mg PO if needed.

ANTIEMETIC TAKE-HOME REGIMEN:
Level A Day 5 - Prochlorperazine 10mg PO q4-6h prn

PATIENT VISITS and APPOINTMENT TYPE:
Days 1-5: 20min Type B

TOXICITIES:
Hematologic
1. If ANC < 1.5 x 10⁹/L, or if PLT <100 x 10⁹/L, HOLD dose for 1 week.

Renal Failure
1. If CrCl 0.3-0.6ml/sec, REDUCE to 50% dose of Topotecan.
2. If CrCl < 0.3ml/sec, OMIT dose of Topotecan.

SUGGESTED ACTION

CLINICAL MONITORING:
- Baseline renal function tests (esp. if failure suspected).
- Pulmonary toxicity ratings at each visits (SOB).
- Watch for symptoms of fever and infection.
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.

Dyspnea (shortness of breath)
1. Dyspnea on exertion, but can walk 1 flight of stairs without stopping
2. Dyspnea on exertion but unable to walk 1 flight of stairs or 1 city block (0.1km) without stopping
3. Dyspnea with ADL
4. Dyspnea at rest; intubation/ventilator indicated
5. Death

Fever
1. 38.0 - 39.0°C (100.4 - 102.2°F)
2. >39.0 - 40.0°C (102.3 - 104.0°F)
3. >40.0°C (>104.0°F) for ≤24 hrs
4. >40.0°C (>104.0°F) for >24 hrs
5. Death

RATED AT EACH CLINIC VISIT

INTERNATIONAL CODE:
OPIS CODE: TOPOTEC

CCO Eligibility Form Required ✔ Non-Formulary Form Required ☐ Date revised: 02/11/2009
TOPOTECAN Chemotherapy (weekly)

**TOPOTECAN**

3-4mg/m² IV Days 1, 8, 15 Round to nearest 0.1mg

- Mix in 50mL bag Normal Saline; Infuse over 30 minutes.
- Final concentration should be 20mcg-500mcg/mL.

**REPEAT EVERY 28 DAYS**

**TESTS:**

<table>
<thead>
<tr>
<th>Baseline Tests</th>
<th>WBC HB PLT ANC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1</td>
<td>WBC HB PLT ANC</td>
</tr>
</tbody>
</table>

**Antiemetic Pre-Chemo Regimen:**

**Level B**

- Days 1, 8 & 15 - Dexamethasone 8mg PO
- Prochlorperazine 10mg PO if needed.

**Level A**

- Days 1, 8, 15 - Prochlorperazine 10mg PO q4-6h prn

**Patient Visits and Appointment Type:**

- Days 1, 8, 15
- 45min Type B

**Toxicities:**

**Hematologic**

1. If ANC < 1.5 x 10⁹/L, or if PLT < 100 x 10⁹/L, **hold** dose for 1 week.

**Renal Failure**

1. If CrCl 0.3-0.6ml/sec, **reduce** to 50% dose of Topotecan.
2. If CrCl < 0.3ml/sec, **omit** dose of Topotecan.

**Suggested Action**

**Clinical Monitoring:**

- Baseline renal function tests (esp. if failure suspected).
- Watch for symptoms of fever and infection.
- Dyspnea (shortness of breath)
  1. Dyspnea on exertion, but can walk 1 flight of stairs without stopping
  2. Dyspnea on exertion but unable to walk 1 flight of stairs or 1 city block (0.1km) without stopping
  3. Dyspnea with ADL
  4. Dyspnea at rest; intubation/ventilator indicated
  5. Death

**Fever**

1. 38.0 - 39.0°C (100.4 - 102.2°F) 2. >39.0 - 40.0°C (102.3 - 104.0°F) 3. >40.0°C (>104.0°F) for ≤24 hrs 4. >40.0°C (>104.0°F) for >24 hrs 5. Death

**Rated at Each Clinic Visit**

**References:**


**Opis Code:** TOPO*W

| Date Revised: 10/21/2008 | Non-Formulary Form Required | CCO Eligibility Form Required | Gynecological |
CARBOPLATIN Chemotherapy weekly
Carcinoma- Head & Neck

**CARBOPLATIN**
- **AUC= 3**
- Round to nearest 5mg
  - **IV**
  - **Day 1**
  - **Mix in 250mL bag 5% Dextrose.**
  - **Infuse over 30 to 60 minutes.**

**REPEAT EVERY 7 DAYS**

**TESTS:**
- **Baseline Tests**
  - WBC HB PLT ANC Cr Urea 24Hr CrCl T.Bili Albumin AST ALT GGT
  - AlkPhosphatase
- **Day 1**
  - WBC HB PLT ANC Cr Urea
**Test Notes**
- Baseline & routine renal function tests, especially if there are other concurrent nephrotoxic drugs.

**ANTIEMETIC PRE-CHEMO REGIMEN:**
- **Level C**
  - **Day 1**
    - Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
    - Dexamethasone 20mg PO/IV

**ANTIEMETIC TAKE-HOME REGIMEN:**
- **Level B/C**
  - **Day 1**
    - Ondansetron 8mg PO BID for 2-3 days, or Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days
    - Dexamethasone 8mg PO OD for 2-3 days
    - Prochlorperazine 10mg PO q4-6h prn

**PATIENT VISITS and APPOINTMENT TYPE:**
- **Day 1**
  - 1.5hrs Type B

**ANCILLARY:**
- Oral hydration is strongly encouraged, poorly hydrated patients may need more IV hydration.

**TOXICITIES:**
- **Hematologic**
  - If ANC < 1.5 x 10⁹/L, or if PLT < 100 x 10⁹/L, **HOLD** dose for 1 week.
  - **Renal Failure**
  - Adjust Carboplatin dose if estimated CrCl changes > 20%.

**SUGGESTED ACTION**

**CLINICAL MONITORING:**
- **Sensory**
  - Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function.
  - Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL.
  - Sensory alteration or paresthesia interfering with ADL.
  - Disabling.
  - Death

**RATED AT EACH CLINIC VISIT**

**FORMULAE:**
- **CrCl - Cockcroft & Gault (mL/sec)**
  - Male: \[(140-age(yrs)) \times TBW(Kg) / [50 \times SCr(umol/L)]\]
  - Female: \[(140-age(yrs)) \times TBW(Kg) / [50 \times SCr(umol/L)] \times 0.85\]
- **Creatinine Cl (mL/min)**
  - \[mL/min = 60 \times CrCl mL/sec\]
- **Calvert Formula**
  - \[Dose (in mg) = target AUC \times (GFR + 25)\]
  - \[GFR \text{ in mL/min}\]

**INTERNAL CODE:**
- **OPIS CODE:**
  - **CARBO*3**

**REFERENCES:**
CETUXIMAB Chemotherapy + Radiation

For the initial treatment of locally or regionally advanced squamous cell head and neck cancer (without distant metastases, curative intent).

**DIPHENHYDRAMINE** 50mg IV Pre Cetuximab
- Admix in **50-100mL** minibag 5% Dextrose or **Normal Saline**.
- Give over **10-15 minutes** 30 minutes before Cetuximab dose started.

**CETUXIMAB** 400mg/m² IV LOADING DOSE Round to nearest 1mg
- Add into an empty IV bag and infuse undiluted over **2 hours** with 0.2 micron in-line filter. (Maximum infusion rate is 5mL/min).
- **DO NOT ADMINISTER AS IV PUSH OR BOLUS.**
- Give **one week** before starting radiation therapy. For the first dose, observe patients for 1 hour for infusion reactions after completion of the infusion.
- Complete Cetuximab administration 1 hour prior to radiation therapy.
- Use with caution in patients with known cardiac disease.
- Only patients > 70 years with Karnofsky Performance Score > 90 eligible for NDFP funding.

**LOADING DOSE - ADMINISTER ON DAY -7 ONLY (1 week prior to RT)**

**CETUXIMAB** 250mg/m² IV MAINTENANCE Round to nearest 1mg
- Add into an empty IV bag and infuse undiluted over **1 hour** with 0.2 micron in-line filter. (Maximum infusion rate is 5mL/min). Infuse weekly during radiation therapy.
- **DO NOT ADMINISTER AS IV PUSH OR BOLUS.**
- For the first and second doses, observe patients for 1 hour for infusion reactions after completion of the infusion.
- Complete Cetuximab administration 1 hour prior to radiation therapy.
- **REPEAT EVERY 7 DAYS** during radiotherapy (6-7) weeks unless unacceptable toxicities

**RADIATION** IV Daily Round to nearest 1mg
- Technique: IMRT
- Modality: 6MV photons
- Total Dose: 6996/33 or 7000/35
- Fraction Dose: 212 or 200cGy
- Pattern: Daily

**TESTS:**
- Baseline Tests: WBC, HB, PLT, ANC, Ca, K, Mg, Cr, Urea
- Weekly: WBC, HB, PLT, ANC, Ca, K, Mg

**PATIENT VISITS and APPOINTMENT TYPE:**
- Day -7 Cetuximab Loading Dose 3.5hrs Type C
- Day 1 Cetuximab Maintenance 2.5hrs Type C
- Day 1 Cetuximab subsequent doses 2hrs Type C

**ANCILLARY:**
- Patients should limit sun exposure (sunscreen and hats) as it may exacerbate Cetuximab induced skin reactions.

**TOXICITIES:**

**Cutaneous**
1. If first occurrence of severe acneform rash, **DELAY** infusion 1-2 weeks until improvement, then continue Cetuximab at 250mg/m². If no improvement, discontinue Cetuximab.
2. If second occurrence of severe acneform rash, delay infusion 1-2 weeks until improvement, then **REDUCE** Cetuximab to 200mg/m². If no improvement, discontinue Cetuximab.
3. If third occurrence of severe acneform rash, delay infusion 1-2 weeks until improvement, then **REDUCE** Cetuximab to 150mg/m². If no improvement, discontinue Cetuximab.
4. If fourth occurrence of severe acneform rash, **DISCONTINUE** Cetuximab.

SUGGESTED ACTION
CETUXIMAB Chemotherapy + Radiation

**CLINICAL MONITORING:**
- Hold Cetuximab if patient experiences acute onset or worsening of pulmonary symptoms. If Interstitial Lung Disease confirmed, discontinue Cetuximab.
- Rash:
  1. Macular or papular eruption or erythema without associated symptoms  
  2. Macular or papular eruption or erythema with pruritus or other associated symptoms; localized desquamation or other lesions covering <50% of body surface area (BSA)  
  3. Severe, generalized erythoderma or macular, papular or vesicular eruption; desquamation covering ≥50% BSA  
  4. Generalized exfoliative, ulcerative, or bullous dermatitis  
  5. Death  
- Usually will improve with time but early intervention with steroid cream and antibiotic cream (clindamycin) is recommended.
- If severe rash, may consider oral antibiotics such as minocycline or doxycycline. If severe rash despite appropriate management, may require treatment interruption and/or dose modification.
- Allergic Reaction
  1. Transient flushing or rash; drug fever < 38 degrees C  
  2. Rash; flushing; urticaria; dyspnea; drug fever ≥ 38 degrees C  
  3. Symptomatic bronchospasm, with or without urticaria; parenteral medication(s) indicated; allergy-related edema/angioedema; hypotension  
  4. Anaphylaxis  
  5. Death
- If the patient experiences a mild or moderate (Grade 1 or 2) infusion reaction, the infusion rate should be decreased by 50% on all subsequent Cetuximab infusions (ie 2.5mL/min)
- If the patient experiences a severe (Grade 3 or 4) infusion reaction, discontinue Cetuximab treatment.

**INTERNAL CODE:**

- CETUX-RT LOAD
- CETUX-RT MAINT

**REFERENCES:**
- CCO Evidence-Based Series: Epidermal Growth Factor Receptor (EGFR) Targeted Therapy in Stage III and IV Head and Neck Cancer.

**Date revised:** 06/01/2009
Daily CISPLATIN Combination Chemotherapy + Radiotherapy
Locally Advanced Nonresectable Squamous Cell Cancer of the Head & Neck (Stages III-IV)

CISPLATIN 6mg/m² IV Daily during radiotherapy Round to nearest 1mg
- Mix in 250mL bag Normal Saline; Infuse over 30-60 minutes.
- Administer within 30-90 minutes before radiation treatment.
- May be for a longer or shorter duration of treatment if the radiotherapy dosing is adjusted.

RADIATION
Technique: IMRT (Intensity-Modulated Radiotherapy)
Modality: 6 MV
Dose Specification: Individually Planned
Total Dose: 6996 cGy
Fraction Dose: 212 cGy per day
Pattern: Daily

CONTINUOUS TREATMENT (concurrent with radiation)

HYDRATION:
Pre - NO PRE HYDRATION IS NEEDED
Post - May give 100-250mL Normal Saline as post-hydration.

TESTS:
Baseline Tests WBC HB PLT ANC K Na Chloride Mg Cr Urea
Weekly (Mondays) WBC HB PLT ANC K Na Chloride Mg Cr Urea
Test Notes - Baseline & routine renal function tests, especially if there are other concurrent nephrotoxic drugs.

ANTIEMETIC PRE-CHEMO REGIMEN:
Level A Daily concurrent - Prochlorperazine 10mg PO/IV pm
- with radiation - Adjust antiemetics per patient need as treatment progresses.

ANTIEMETIC TAKE-HOME REGIMEN:
Level A Daily concurrent - Prochlorperazine 10mg PO q4-6h pm
- with radiation

PATIENT VISITS and APPOINTMENT TYPE:
Daily during radiotherapy: 60min Type B

ANCILLARY:
- Oral hydration is strongly encouraged; poorly hydrated patients may need more IV hydration (to prevent renal toxicity).

TOXICITIES:
Hematologic
1. If ANC < 1.5 x 10⁹/L, or if PLT < 100 x 10⁹/L, HOLD dose for 1 week.

Renal Failure
1. If CrCl = 0.5-1.0mL/sec, or SrCr = 136-185umol/L, REDUCE Cisplatin to 50% dose.
2. If CrCl < 0.5mL/sec, or SrCr > 185umol/L, OMIT dose.

CLINICAL MONITORING:
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.
- Sensory
  1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function.
  2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL.
  3. Sensory alteration or paresthesia interfering with ADL.
  4. Disabling.
  5. Death
- Hearing
  1. Asymptomatic, detected on exam/testing only.
  2. Symptomatic, not interfering with ADL.
  3. Symptomatic, interfering with ADL.
  4. Life-threatening; disabling.
  5. Death
RATED AT EACH CLINIC VISIT

FORMULAE:
CrCl - Cockcroft & Gault (mL/sec)
Male: [140-age(ys)] x TBW(Kg) / [50 x SCR(umol/L)]
CrCl - Cockcroft & Gault (mL/sec)
Female: [140-age(ys)] x TBW(Kg) / [50 x SCR(umol/L)] x 0.85
Daily CISPLATIN Combination Chemotherapy + Radiotherapy

REFERENCES:

- CCO Practice Guideline 5-6a: Concomitant Chemotherapy and Radiotherapy in Squamous Cell Head and Neck Cancer (Excluding Nasopharynx).

Several other platinum-based or 5-fluorouracil/platinum-based regimens are acceptable to be administered in combination with radiotherapy. Selected examples:

- Carboplatin 70mg/m²/day iv bolus x 4 days; 5FU 600mg/m²/day continuous iv infusion x 4 days; total of 3 cycles during conventional radiotherapy starting days 1, 22 and 43 (Reference: Calais G, Alfonsi M, Bardet E, et al. Randomized trial of radiation therapy versus concomitant chemotherapy and radiation therapy for advanced-stage oropharynx carcinoma. J Natl Cancer Inst 1999; 91: 2081-2086)

- Cisplatin 20mg/m²/day continuous iv infusion 4 days; 5FU 1000mg/m²/day continuous iv infusion x 4 days; total of 2 cycles during conventional radiotherapy starting days 1 and 22 (Reference: Adelstein DJ, Lavertu P, Saxton JP, et al. Mature results of a phase III randomized trial comparing concurrent chemoradiotherapy with radiation therapy alone in patients with stage III and IV squamous cell carcinoma of the head and neck. Cancer 2000;88: 876-883)

- Cisplatin 12mg/m²/day iv bolus x 5 days; 5FU 600mg/m²/day continuous iv infusion x 5 days; total of 2 cycles during hyperfractionated radiotherapy starting weeks 1 and 6; 2 additional cycles of cisplatin and 5FU post radiotherapy (Reference: Brizel DM, Albers ME, Fisher SR, et al. Hyperfractionated irradiation with or without concurrent chemotherapy for locally advanced head and neck cancer. N Engl J Med 1998; 338: 1798-1804)
CISPLATIN Concurrent Chemoradiotherapy Followed by 5-FLUOROURACIL Infusion/CISPLATIN

**Combined Modality; Carcinoma of Nasopharynx**

**Head and Neck**

**Order Group 1**

**CISPLATIN** 100mg/m² IV Days 1,22 & 43 Round to nearest 1mg
- Mix drug in 500mL Normal Saline; Infuse over 60 minutes.

**RADIATION**

**Daily**
- Technique: IMRT (Intensity-Modulated Radiotherapy)
- Modality: 6 MV
- Dose Specification: Individually Planned
- Total Dose: 6996 cGy
- Fraction Dose: 212 cGy per day
- Pattern: Daily

**REPEAT EVERY 21 DAYS DURING RADIOTHERAPY**

**Order Group 2**
- To follow Days 1,22 & 43 of Cisplatin therapy

**CISPLATIN** 80mg/m² IV Day 1 Round to nearest 1mg
- Mix drug in 500mL Normal Saline; Infuse over 60 minutes.
- Maximum dose = 150mg.

**5-FLUOROURACIL** 1000mg/m²/day IV Day 1-4 (96 hours) Round to nearest 25mg
- Continuous infusion using ambulatory infusion pump (2mL/hr).
- Maximum dose = 2G/day.

**REPEAT EVERY 28 DAYS for 3 Cycles**

**HYDRATION:**

- Pre: Infuse 1000mL Normal Saline with 20mEq Potassium Chloride IV over 2 hours before Cisplatin.
- Concurrent: May give 250mL of 20% Mannitol solution (50G) IV; Infuse through sidearm concurrent with Cisplatin.
- Post: Infuse 500mL Normal Saline with 10mEq Potassium Chloride IV over 1 hour after Cisplatin.

**TESTS:**

<table>
<thead>
<tr>
<th>Baseline Tests</th>
<th>Days 1, 22 &amp; 43 (Cisplatin)</th>
<th>Day 1 (Cisplatin &amp; 5-FU)</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC HB PLT ANC Mg Cr Urea</td>
<td>WBC HB PLT ANC Mg Cr Urea</td>
<td>WBC HB PLT ANC Mg Cr Urea T.Bili AST ALT GGT AlkPhosphatase</td>
</tr>
</tbody>
</table>

**Test Notes**
- Baseline & routine renal function tests, especially if there are other concurrent nephrotoxic drugs.

**ANTIEMETIC PRE-CHEMO REGIMEN:**

**Level C**
- Days 1,22 & 43 (Cisp only)
  - Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
  - Dexamethasone 20mg PO/IV
  - May add Aprepitant 125mg PO before chemo (reduce PO Dexamethasone by 50%)

**Level C**
- Day 1 (Cisp & 5-FU)
  - Same as above

**ANTIEMETIC TAKE-HOME REGIMEN:**

**Level B/C**
- Days 1,22 & 43 (Cisp only)
  - Ondansetron 8mg PO BID for 2-3 days, or Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days.
  - Dexamethasone 8mg PO BID for 2-3 days.
  - May add Aprepitant 80mg PO on Days 2&3 (reduce PO Dexamethasone by 50%)
  - Prochlorperazine 10mg PO q4-6h prn

**Level B/C**
- Day 1 (Cisp & 5-FU)
  - Same as above

**PATIENT VISITS and APPOINTMENT TYPE:**
- Days 1,22 & 43 (Cisp only) 4-6hrs Type D
- Day 1 (Cisp & 5-FU) 4-6hrs Type D
- Day 5 (5-FU pump disconnect) 10min Type A

**ANCILLARY:**
- Increase fluids if poor oral intake.

**TOXICITIES:**

**Hematologic**
1. If ANC = 1.0-1.5 x 10⁹/L, or if PLT = 75-100 x 10⁹/L, REDUCE 5FU to 50% dose.
2. If ANC < 1.0 x 10⁹/L, or if PLT < 75 x 10⁹/L, HOLD dose for one week.
CISPLATIN Concurrent Chemoradiotherapy Followed by 5-FLUOROURACIL Infusion/CISPLATIN

Renal Failure
1. If renal function has not returned to normal (CrCl > 1.0mL/sec or SrCr < 136umol/L) by day 1 of cycle, DISCONTINUE CISPLATIN.

Gastrointestinal
1. If Mucositis or diarrhea ≥ Grade 3 in previous course, REDUCE to 2/3 dose of 5FU.

SUGGESTED ACTION

CLINICAL MONITORING:
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.
- Skin assessment, especially extremities.

Sensory
1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function. 2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL. 3. Sensory alteration or paresthesia interfering with ADL. 4. Disabling. 5. Death.

Hearing
1. Asymptomatic, detected on exam/testing only. 2. Symptomatic, not interfering with ADL.

Diarrhea
1. Increase of < 4 stools per day over baseline; mild increase in ostomy output compared to baseline.
2. Increase of 4 - 6 stools per day over baseline; IV fluids indicated < 24hrs; moderate increase in ostomy output compared to baseline; not interfering with ADL. 3. Increase of ≥7 stools per day over baseline; incontinence; IV fluids >=24 hrs; hospitalization; severe increase in ostomy output compared to baseline; interfering with ADL. 4. Life-threatening consequences (e.g., hemodynamic collapse).
5. Death

Mucositis
1. Erythema of the mucosa. 2. Patchy ulcerations or pseudomembranes. 3. Confluent ulcerations or pseudomembranes; bleeding with minor trauma. 4. Tissue necrosis; significant spontaneous bleeding; life-threatening consequences. 5. Death.

RATED AT EACH CLINIC VISIT

FORMULAE:

CrCl - Cockcroft & Gault (mL/sec)
Male: \[140 \text{(-age(years))} \times \text{TBW(Kg)} / [50 \times \text{Scr(umol/L)}] \]
Female: \[140 \text{(-age(years))} \times \text{TBW(Kg)} / [50 \times \text{Scr(umol/L)}] \times 0.85 \]

INTERNAL CODE:
OPIS CODES:
- CISP-FC DAYS 1,22 + 43
- CISP-FC CIS+FU CIV

REFERENCES:
- CCO Practice Guideline 5-7: The Role of Chemotherapy with Radiotherapy in the Management of Patients with Newly Diagnosed Locally Advanced Squamous Cell or Undifferentiated Nasopharyngeal Cancer.

Date revised: 07/14/2008
5-FLUOROURACIL Infusion/CISPLATIN

Combined Modality: Head and Neck Carcinoma

5-FLUOROURACIL

1000mg/m²/day IV Days 1-4 Round to nearest 25mg
- Continuous Infusion for 4 days using ambulatory infusion pump (Infusor 2mL/hr).
- Maximum dose = 2G/day.

CISPLATIN

75-100mg/m² IV Day 1 Round to nearest 1mg
- Admix in 500mL Normal Saline; Infuse over 60 minutes.
- Maximum dose = 150mg.

DURING WEEKS 1 & 5 of RADIOTHERAPY; then REPEAT EVERY 21 DAYS

RADIATION

Daily

Technique: IMRT (Intensity-Modulated Radiotherapy)
Modality: 6 MV
Dose Specification: Individually Planned
Total Dose: 6996 cGy
Fraction Dose: 212 cGy per day
Pattern: Daily

HYDRATION:

Pre
- Infuse 1000-2000mL Normal Saline with 20mEq Potassium Chloride IV over 2 hours before Cisplatin.

Concurrent
- May give 250mL of 20% Mannitol solution (50G) IV; Infuse through sidearm concurrent with Cisplatin.

Post
- Infuse 500mL Normal Saline with 10mEq Potassium Chloride IV; (2G Magnesium Sulfate may also be added) over 1 hour after Cisplatin.
- Increase fluids if poor oral intake.

TESTS:

Baseline Tests
WBC HB PLT ANC Mg Cr Urea T.Bili AST ALT

Day 1
WBC HB PLT ANC Mg Cr Urea AST ALT

Test Notes
- Baseline & routine renal function tests, especially if there are other concurrent nephrotoxic drugs.

ANTIEMETIC PRE-CHEMO REGIMEN:

Level C Day 1
- Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
- Dexamethasone 20mg PO/IV
- May add Aprepitant 125mg PO before chemo (reduce PO Dexamethasone by 50%)

ANTIEMETIC TAKE-HOME REGIMEN:

Level B/C Day 1
- Ondansetron 8mg PO BID for 2-3 days, or Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days
- Dexamethasone 8mg PO BID for 2-3 days
- May add Aprepitant 80mg PO on Days 2&3 (reduce PO Dexamethasone by 50%)
- Prochlorperazine 10mg PO q4-6h prn

PATIENT VISITS and APPOINTMENT TYPE:

- Day 1 4-6hrs Type D
- Day 5 (Pump disconnect) 10min Type A

ANCILLARY:
- Oral hydration is strongly encouraged; poorly hydrated patients may need more IV hydration.

TOXICITIES:

Hematologic
1. If ANC < 1.5 x 10⁹/L, or if PLT = 75-100 x 10⁹/L, REDUCE 5FU to 50% dose.
2. If ANC < 1.0 x 10⁹/L, or if PLT < 75 x 10⁹/L, HOLD dose for 1 week.

Renal Failure
1. If renal function has not returned to normal (CrCl > 1.0mL/sec or SrCr < 136umol/L) by Day 1 of cycle, DISCONTINUE CISPLATIN.

Gastrointestinal
1. If Mucositis or Diarrhea > Grade 3 in previous course, REDUCE to 2/3 dose of 5-FU.

SUGGESTED ACTION
5-FLUOROURACIL Infusion/CISPLATIN

CLINICAL MONITORING:
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.
- Skin assessment, especially extremities.

Sensory
1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function. 2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL. 3. Sensory alteration or paresthesia interfering with ADL. 4. Disabling. 5. Death.

Hearing

Diarrhea
1. Increase of < 4 stools per day over baseline; mild increase in ostomy output compared to baseline. 2. Increase of 4 - 6 stools per day over baseline; IV fluids indicated < 24hrs; moderate increase in ostomy output compared to baseline; not interfering with ADL. 3. Increase of >=7 stools per day over baseline; incontinence; IV fluids >=24 hrs; hospitalization; severe increase in ostomy output compared to baseline; interfering with ADL. 4. Life-threatening consequences (e.g., hemodynamic collapse). 5. Death.

Mucositis
1. Erythema of the mucosa. 2. Patchy ulcerations or pseudomembranes. 3. Confluent ulcerations or pseudomembranes; bleeding with minor trauma. 4. Tissue necrosis; significant spontaneous bleeding; life-threatening consequences. 5. Death.

RATED AT EACH CLINIC VISIT

FORMULAE:
- Cockcroft & Gault (mL/sec) Male: \[\frac{140 - \text{age(yrs)}}{50 \times \text{SCr(umol/L)}} \times \text{TBW(Kg)}\]
- Cockcroft & Gault (mL/sec) Female: \[\frac{140 - \text{age(yrs)}}{50 \times \text{SCr(umol/L)}} \times 0.85 \times \text{TBW(Kg)}\]

INTERNAL CODE:
- OPIS CODE: FU-CISP HN

REFERENCES:
- Browman GP, Cronin L. Standard chemotherapy in squamous cell head and neck cancer: what we have learned from randomized trials. Semin Oncol, 1994; 21: 311-319

Date revised: 07/14/2008
METHOTREXATE Chemotherapy
Carcinoma- Head & Neck

METHOTREXATE 40mg/m² IV Day 1 Round to nearest 5mg
- Inject by direct IV push, followed by a Normal Saline flush (if no IV line has been set up).
- May give by slow push through sidearm of free flowing IV (D5W, Normal Saline).
- Rate of administration ≤ 10mg per minute.
- Doses > 100mg, mix in 50-100mL Normal Saline and infuse over 30-60 minutes.

REPEAT EVERY 7 DAYS

TESTS:
Baseline Tests  WBC  HB  PLT  ANC  Cr  Urea  T.Bili  AST  ALT
Day 1          WBC  HB  PLT  ANC  Cr  Urea  T.Bili  AST  ALT

ANTIEMETIC PRE-CHEMO REGIMEN:
Level A  Day 1 - Prochlorperazine 10mg PO prn

ANTIEMETIC TAKE-HOME REGIMEN:
Level A  Day 1 - Prochlorperazine 10mg PO q4-6h prn

PATIENT VISITS and APPOINTMENT TYPE:
⇒ Day 1 10min Type A

TOXICITIES:
Hematologic
1. If ANC < 1.5 x 10⁹/L, or if PLT < 100 x 10⁹/L, HOLD dose for 1 week.

Renal Failure
1. If CrCl = 0.2-0.8mL/sec, or SrCr = 100-180umol/L, REDUCE Methotrexate to 50% dose.
2. If CrCl < 0.2mL/sec, or SrCr >180umol/L, OMIT Methotrexate dose.

Hepatic Dysfunction
1. If T.Bili = 50-85umol/L, or AST > 180 IU/L, REDUCE Methotrexate to 75% dose.
2. If T.Bili > 85umol/L, OMIT Methotrexate dose.

SUGGESTED ACTION
CLINICAL MONITORING:
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.

REFERENCES:

Date revised: 03/07/2005

CCO Eligibility Form Required  Non-Formulary Form Required
DAUNORUBICIN-CYTARABINE AML
Induction/Consolidation Treatment (Inpatient Regimen)

**Acute Myeloid Leukemia - Curative intent**

**DAUNORUBICIN**
60mg/m² IV Days 1 to 3 Round to nearest 1mg
- Slow push through sidearm of free flowing IV; Give 2-4mg per minute.
  May be mixed in 50mL minibag (5% Dextrose, Normal Saline). Infuse through central catheter over 15-30 minutes.

**CYTARABINE**
100mg/m² IV Days 1 to 7 Round to nearest 1mg
- Mix in **500mL bag 5% Dextrose**; Infuse over 7 days by continuous infusion through central venous access device.
  *Cycle may be repeated once, if bone marrow shows persistent leukemia*

**HYDRATION:**
- Pre
  - IV Normal Saline

**ANTIMICROBIAL PROPHYLAXIS:**
1. Fluconazole 400mg Daily (induction prophylaxis)

**TESTS:**

<table>
<thead>
<tr>
<th>Baseline Tests</th>
<th>WBC</th>
<th>HB</th>
<th>PLT</th>
<th>Ca</th>
<th>K</th>
<th>Na</th>
<th>Chloride</th>
<th>Phosphate</th>
<th>Glucose</th>
<th>Cr</th>
<th>Urea</th>
<th>T.Bili</th>
<th>Albumin</th>
<th>ALT</th>
<th>AlkPhosphatase</th>
<th>Urate</th>
<th>LVEF</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Test Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Every Monday and Thursday: Calcium, protein, albumin, T.Bili, ALT, alkaline phosphatase.</td>
</tr>
<tr>
<td>INR and PTT when clinically indicated.</td>
</tr>
</tbody>
</table>

**ANTIEMETIC PRE-CHEMO REGIMEN:**
- Level B/C
- Day 1-7 - Ondansetron 8mg q8h PO/IV or Granisetron 1-2mg daily PO/IV
  - Prochlorperazine 10 mg PO/IV q4h prn

**INPATIENT ANTIEMETICS:**
- Ondansetron 8mg q8h PO/IV can be substituted with Granisetron 1-2mg daily PO/IV

**TOXICITIES:**

**Hematologic**
1. If ANC < 1.0 x 10⁹ /L; PLT < 75 x 10⁹/L
  - Parameters may be changed at the discretion of the clinician if cytopenias presumed to be due to underlying disease.

**Renal Failure**
1. Hyperuricemia - can be minimized with Allopurinol and hydration.
2. Renal failure (recommended action)
  - If CrCl < 10 mL/min, administer 75% of normal Daunorubicin dose.

**Hepatic Dysfunction**
1. Hepatic dysfunction ( Suggested action )
  - If T.Bili 26-51 umol/L or AST = 60-180 IU/L, REDUCE Daunorubicin to 75% dose
    - 52-85 umol/L or AST > 180 IU/L, REDUCE Daunorubicin to 50% dose.
    - > 85 umol/L, OMIT dose.

**Cardiac**
1. Daunorubicin cardiotoxicity manifested by fatigue, dyspnea on exertion and arrhythmias.
  - Cardiomyopathy may be dose dependant (life time dose 550mg/m²).

**CLINICAL MONITORING:**
- Clinical exam for symptoms of CHF.
- Periodic cardiac tests for all patients with cardiac risk factors.
- Baseline and regular liver function test.
- Baseline cardiac function test (Echo and/or RNA) for all patients with cardiac risk factors.

**REFERENCES:**
HE-ABVD

Hematological

DOXORUBICIN-BLEOMYCIN-VINBLASTINE-DACARBAZINE

Chemotherapy

Hodgkin’s Lymphoma-Curative Intent (Standard First-line Therapy)

DOXORUBICIN

25mg/m² IV Days 1 & 15 Round to nearest 1mg

- Slow push through sidearm of free flowing IV: Give 2 to 4mg (1-2mL) per minute.
- Cap BSA at 2.2m²

BLEOMYCIN

10units/m² IV Days 1 & 15 Round to nearest 1unit

- Slow push through sidearm of free flowing IV over 10 minutes.
- May be given by direct IV push, followed by a Normal Saline flush.
- Cap BSA at 2.2m²

VINBLASTINE

6mg/m² IV Days 1 & 15 Round to nearest 0.1mg

- Slow push through sidearm of free flowing IV: Inject over 1 minute.
- Cap BSA at 2.2m²

DACARBAZINE

375mg/m² IV Days 1 & 15 Round to nearest 10mg

- Mix in 250-500mL bag Normal Saline.
- Infuse through main IV line, with an additional 500mL Normal Saline run at same time by piggyback, to reduce vein irritation.
- Infuse over 30-120 minutes: If vein irritation, infuse slowly. Protect from light.
- Cap BSA at 2.2m²

REPEAT EVERY 28 DAYS for 6-8 Cycles

TESTS:

Baseline Tests

WBC HB PLT ANC Ca Glucose Cr T.Bili ALT AlkPhosphatase

Day 1

WBC HB PLT ANC Cr T.Bili ALT AlkPhosphatase

Day 15

WBC HB PLT ANC

Test Notes: Protein electrophoresis and direct antiglobulin test (Coombs test) to be added to Baseline testing.

ANTIEMETIC PRE-CHEMO REGIMEN:

Level C Days 1 & 15

- Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
- Dexamethasone 20mg PO/IV

ANTIEMETIC TAKE-HOME REGIMEN:

Level B/C Days 1 & 15

- Ondansetron 8mg PO BID for 2-3 days, or Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days
- Dexamethasone 8mg PO BID for 2-3 days
- Prochlorperazine 10mg PO q4-6h prn

PATIENT VISITS and APPOINTMENT TYPE:

- Days 1 & 15 2.5hrs Type D

ANCILLARY:

- Oral hydration is strongly encouraged; poorly hydrated patients may need more IV hydration.

TOXICITIES:

Hematologic

1. If ANC < 1.0 x 10⁹/L, DELAY therapy 1 week and give G-CSF with next cycle.
2. If PLT < 75 x 10⁹/L, DELAY therapy 1 week.
- Dose attenuations may be over-ridden if cytopenias presumed to be due to underlying disease.

Renal Failure

1. If CrCl = 0.2-1.0mL/sec, REDUCE Bleomycin to 75% dose.
2. If CrCl < 0.2mL/sec, REDUCE Bleomycin to 50% dose.
3. If SrCr > 265umol/L, REDUCE Doxorubicin to 50% dose.
4. Consider dose reduction of Dacarbazine if renal function is reduced (eg. reduced CrCl or SrCr).

Hepatic Dysfunction

1. If T.Bili = 26-51umol/L, or AST = 60-180 IU/L, REDUCE Doxorubicin to 75% dose & Vinblastine to 50% dose.
2. If T.Bili = 52-85umol/L, or AST > 180 IU/L, REDUCE Doxorubicin to 50% dose & Vinblastine to 25% dose.
3. If T.Bili > 85umol/L, OMIT Doxorubicin & Vinblastine doses.

Neurologic

1. If peripheral neuropathy ≥ 2, OMIT Vinblastine.

SUGGESTED ACTION
DOXORUBICIN-BLEOMYCIN-VINBLASTINE-DACARBAZINE
Chemotherapy

CLINICAL MONITORING:
- Clinical pulmonary exam, including auscultation, pulmonary toxicity ratings (Cough, SOB).
- Clinical exam for symptoms of CHF.
- Periodic cardiac tests for all patients with cardiac risk factors and patients at or above the threshold dose levels (Doxorubicin 450mg/m²).
- Neurologic toxicity ratings (Sensory, Constipation) at each visit.

Sensory
1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function 2.
Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL 3.
Sensory alteration or paresthesia interfering with ADL 4. Disabling 5. Death

Constipation
1. Occasional or intermittent symptoms: occasional use of stool softeners, laxatives, dietary modification, or enema
2. Persistent symptoms with regular use of laxatives or enemas indicated 3. Symptoms interfering with ADL;
obstipation with manual evacuation indicated 4. Life-threatening consequences (e.g., obstruction, toxic megacolon)
5. Death

Dyspnea
1. Dyspnea on exertion, but can walk 1 flight of stairs without stopping 2. Dyspnea on exertion but unable to walk 1
   flight of stairs or 1 city block (0.1km) without stopping 3. Dyspnea with ADL 4. Dyspnea at rest; intubation/ventilator
   indicated 5. Death

Cough
1. Symptomatic, non-narcotic medication only indicated 2. Symptomatic and narcotic medication
   indicated 3. Symptomatic and significantly interfering with sleep or ADL

REFERENCES:
- Bonadonna G, Valagussa P, Santoro A. Alternating non-cross-resistant combination chemotherapy or MOPP in
- Canellos GP, Anderson JR, Propert KJ, et al, Chemotherapy of advanced Hodgkin’s disease with MOPP, ABVD,
- Duggan DB, Petroni GR, Johnson JL, Glick JH, Fisher RI, Connors JM, Canellos GP, Peterson BA. Randomized
  comparison of ABVD and MOPP/ABV hybrid for the treatment of advanced Hodgkin’s disease: Report of an

Date revised: 10/08/2008
DOXORUBICIN-BLEOMYCIN-VINBLASTINE-DACARBAZINE
Chemotherapy (Inpatient Regimen)
Standard first-line therapy for patients with Hodgkin’s lymphoma

DOXORUBICIN
25mg/m² IV Day 1 & 15 Round to nearest 1mg
- Slow push through sidearm of free flowing IV fluid; Give 2-4mg (1-2mL) per minute.
- Cap BSA at 2.2 m². Doses < 100mg may be mixed in 50mL minibag 5% Dextrose, doses > 100mg may be mixed in 100mL minibag 5% Dextrose and infused through central venous access device.

BLEOMYCIN
10units/m² IV Day 1 & 15 Round to nearest 1unit
- Slow push through sidearm of free flowing IV. Give test dose of Bleomycin 1unit with first dose.
- Cap BSA at 2.2 m²
- May be mixed in 50mL minibag (Normal Saline or 5% Dextrose). Infuse over 10-15 minutes.

VINBLASTINE
6mg/m² IV Day 1 & 15 Round to nearest 0.1mg
- Quick push through sidearm of free flowing IV (5% Dextrose, NS or 2/3-1/3 IV solution). Inject over 1 minute.
- Do not mix with solution that will change pH (lactate containing solutions).
- May mix in 50mL minibag (NS or D5W); Infuse over 20-30 minutes.
- Cap BSA on 2.2 m²

DACARBAZINE
375mg/m² IV Day 1 & 15 Round to nearest 10mg
- Mix in 250-500mL bag Normal Saline; Infuse through main IV line, with an additional 500mL Normal Saline run at same time by piggyback, to reduce vein irritation.
- Infuse over 30-120 minutes; If vein irritation, inject slowly; Protect from light
- Cap BSA at 2.2 m²

REPEAT EVERY 28 DAYS for 6-8 Cycles

TESTS:
Baseline Tests WBC HB PLT ANC Ca Glucose Cr T.Bili ALT
Days 1 & 15 WBC HB PLT ANC
Test Notes
- Baseline CBC, Cr, glucose, calcium, LFTs, protein electrophoresis, direct antiglobulin test (Coombs test)
- Day 1 : CBC, Cr, LFTs
- Day 15 : CBC

ANTIEMETIC PRE-CHEMO REGIMEN:
Level C Day 1 & 15 - Ondansetron 8mg PO/IV q12h or Granisetron 1mg PO/IV Daily
- Dexamethasone 20mg PO/IV pre-chemo

INPATIENT ANTIEMETICS:
- Ondansetron 8 mg PO/IV q12h can be substituted with Granisetron 1-2 mg PO/IV daily.

ANCILLARY:
- Oral hydration is strongly encouraged; Poorly hydrated patients may need more IV hydration.
- Inadequate total hydration may result in dose-related hemorrhagic cystitis.

TOXICITIES:
Hematologic
1. If ANC < 1.0 x 10⁹/L, DELAY therapy 1 week and give G-CSF with next cycle.
2. If PLT < 75 x 10⁹/L, DELAY therapy 1 week.
- Dose attenuation may be over-ridden if cytopenias presumed to be due to underlying disease.

Renal Failure
1. If CrCl = 0.2-1.0mL/sec, REDUCE Bleomycin to 75% dose.
2. If CrCl < 0.2 mL/sec, REDUCE Bleomycin to 50% dose.
3. If SrCr > 265μmol/L, REDUCE Doxorubicin to 50% dose.
4. Consider dose reduction of Dacarbazine if renal function is reduced (reduced SrCr or CrCl).

Hepatic Dysfunction
1. If T.Bili = 26-51μmol/L or AST = 60-180 IU/L, REDUCE Doxorubicin to 75% dose & Vinblastine to 50% dose.
2. If T.Bili = 52-85μmol/L or AST > 180 IU/L, REDUCE Doxorubicin to 50% dose & Vinblastine to 25% dose.
3. If T.Bili > 85μmol/L, OMIT Doxorubicin & Vinblastine doses.

Neurologic
1. If peripheral neuropathy ≥ 2, OMIT Vinblastine.
SUGGESTED ACTION
DOXORUBICIN-BLEOMYCIN-VINBLASTINE-DACARBAZINE
Chemotherapy (Inpatient Regimen)

CLINICAL MONITORING:
- Clinical pulmonary exam, including auscultation, pulmonary toxicity ratings (Cough, SOB).
- Clinical exam for symptoms of CHF.
- Periodic cardiac tests for all patients with cardiac risk factors and at or above the threshold dose levels (Doxorubicin 450mg/m²).
- Neurologic toxicity ratings (Sensory, Constipation) at each visit.

Sensory
1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function.
2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL.
3. Sensory alteration or paresthesia interfering with ADL.
4. Disabling.
5. Death

Constipation
1. Occasional or intermittent symptoms: occasional use of stool softeners, laxatives, dietary modification, or enemas.
2. Persistent symptoms with regular use of laxatives or enemas indicated.
3. Symptoms interfering with ADL; obstruction with manual evacuation indicated.
4. Life-threatening consequences (e.g., obstruction, toxic megacolon).
5. Death

Dyspnea
1. Dyspnea on exertion, but can walk 1 flight of stairs without stopping.
2. Dyspnea on exertion but unable to walk 1 flight of stairs or 1 city block (0.1km) without stopping.
3. Dyspnea with ADL.
4. Dyspnea at rest; intubation/ventilator indicated.
5. Death

Cough
1. Symptomatic, non-narcotic medication only indicated.
2. Symptomatic and narcotic medication indicated.
3. Symptomatic and significantly interfering with sleep or ADL.

REFERENCES:

Date revised: 10/08/2008
Dana Farber Cancer Institute (DFCI) Consortium Protocol
2000-01, CNS Therapy
First-Line Treatment of Acute Lymphoblastic Leukemia in Adults

VINCRISTINE
2mg IV Day 1 Round to nearest 0.1mg
- Mix in 50mL bag Normal Saline; infuse over 10 minutes.

DOXORUBICIN
30mg/m² IV Day 1 Round to nearest 1mg
- Slow push through sidearm of free flowing IV. Give 2 to 4mg (1-2mL) per minute.

6-MERCAPTOPURINE
50mg/m²/day PO Days 1-14 Round to nearest 25mg
- Take at bedtime (without milk) for 14 consecutive days.

METHOTREXATE
12mg IT Days 1, 3, 8 & 10
- Prepared by hematologist and give as intrathecal injection, concurrent with radiation.
- All IT doses are flat dose and are NOT adjusted for body surface area.
- To be administered twice weekly x 4 doses (days may vary).

CYTARABINE
40mg IT Days 1, 3, 8 & 10
- Prepared by hematologist and give as intrathecal injection, concurrent with radiation.
- All IT doses are flat dose and are NOT adjusted for body surface area.
- To be administered twice weekly x 4 doses (days may vary).

HYDROCORTISONE SODIUM SUCCINATE
50mg IT Days 1, 3, 8 & 10
Optional Administration:
- Prepared by hematologist and give as intrathecal injection, concurrent with radiation.
- All IT doses are flat dose and are NOT adjusted for body surface area.
- To be administered twice weekly x 4 doses (days may vary).

RADIATION
- For patients who present without CNS disease at diagnosis:
  Total Dose: 1800 cGy
  Fraction Dose: 180 cGy (10 fractions)
- For patients who present with CNS disease at diagnosis:
  Total Dose: 2400 cGy
  Fraction Dose: 240 cGy (10 fractions)
- Radiation should start as close to Day 1 as possible.

ANTIMICROBIAL PROPHYLAXIS:
- Trimethoprim/Sulfamethoxazole DS PO BID for 3 days per week. If not tolerated, Atovaquone 750mg PO BID (with food). Prophylaxis should be instituted for all patients from the time they enter complete remission and continued until 6 months after cessation of treatment.
- Trimethoprim/Sulfamethoxazole should not be given on the same day as Methotrexate, but can be given later the same week.

ANTIEMETIC PRE-CHEMO REGIMEN:
Level C Day 1
- Ondansetron 8mg PO/IV

ANTIEMETIC TAKE-HOME REGIMEN:
Level B/C Day 1
- Ondansetron 8mg PO Q8H for 2 days
- Prochlorperazine 10mg PO q4-6h prn

PATIENT VISITS and APPOINTMENT TYPE:
- Day 1 2hrs Type C
- Days 3, 8 & 10 1.5hrs Type B

TOXICITIES:
Hematologic
Starting Criteria: ANC> 1.0 x 10⁹/L and PLT >100 x 10⁹/L
Intrathecal Medications:
1. If ANC < 0.5 x 10⁹/L, or if PLT < 50 x 10⁹/L, and/or moderate mucositis, DECREASE Methotrexate IT by 50%.
2. If ANC < 0.3 x 10⁹/L, or if PLT < 25 x 10⁹/L, and/or severe mucositis, OMIT Methotrexate IT and ADMINISTER Cytarabine IT.
6-Mercaptopurine:
1. If ANC < 0.5 x 10⁹/L, or if PLT < 50 x 10⁹/L, and/or moderate/severe mucositis HOLD 6-Mercaptopurine.

Hepatic Dysfunction
Starting Criteria: Direct Bili < 26 umol/L and AST < 8 x normal.
Intrathecal Medications:
1. If Direct Bili > 26 umol/L, and/or AST ≥ 8 x normal; OMIT Methotrexate IT and ADMINISTER Cytarabine IT.
6-Mercaptopurine:
1. If Direct Bili > 26 umol/L, and/or AST ≥ 8 x normal; HOLD 6-Mercaptopurine.

SUGGESTED ACTION

CCO Eligibility Form Required [ ] Non-Formulary Form Required [ ] Date revised: 10/08/2008
Hematological

Dana Farber Cancer Institute (DFCI) Consortium Protocol
2000-01, Continuation Therapy
First-Line Treatment of Acute Lymphoblastic Leukemia in Adults

VINCRISTINE 2mg IV Week 1 Round to nearest 0.1mg
- Administer once on Week 1
- Mix in 50mL bag Normal Saline; infuse over 10 minutes.

DEXAMETHASONE 6mg/m²/day PO Week 1 Round up to the nearest whole number
- Divide into BID dosing x 5 days in Week 1 of cycle.

6-MERCAPTOPURINE 50mg/m²/day PO Weeks 1-2 Round to nearest 25mg
- Take at bedtime (without milk) for 14 consecutive days beginning on week 1 of cycle.
- Begin Methotrexate after Doxorubicin is discontinued.

METHOTREXATE 30mg/m² IV Weeks 1-3 Round to nearest 5mg
- Slow push through sidearm of free flowing IV at a rate of ≤ 10mg per minute once each week.
- Doses > 100mg, mix in 50-100mL Normal Saline and infuse over 30-60 minutes.
- Maximum dose for previously irradiated patients is 40mg/m².
- Hold IV Methotrexate on the day that IT Methotrexate is given.

REPEAT UNTIL 2 YEARS FROM DATE OF REMISSION

METHOTREXATE 12mg IT Every 18 weeks
- Prepared by hematologist and give as intrathecal injection.
- All IT doses are flat dose and are NOT adjusted for body surface area.

CYTARABINE 40mg IT Every 18 weeks
- Prepared by hematologist and give as intrathecal injection.
- All IT doses are flat dose and are NOT adjusted for body surface area.
- First dose is given approximately 18 weeks after start of CNS treatment.

HYDROCORTISONE SODIUM SUCCINATE 50mg IT Every 18 weeks
Optional Administration:
- Prepared by hematologist and give as intrathecal injection.
- All IT doses are flat dose and are NOT adjusted for body surface area.

REPEAT EVERY 18 WEEKS

ANTIMICROBIAL PROPHYLAXIS:
- Trimethoprim/Sulfamethoxazole DS PO BID for 3 days per week. If not tolerated, Atovaquone 750mg PO BID (with food). Prophylaxis should be instituted for all patients from the time they enter complete remission and continued until 6 months after cessation of treatment.
- Trimethoprim/Sulfamethoxazole should not be given on the same day as Methotrexate, but can be given later the same week.

PATIENT VISITS and APPOINTMENT TYPE:
⇒ Weeks 1-3 15min Type A
⇒ Every 18 weeks 1.5hrs Type B

TOXICITIES:
Hematologic
Starting Criteria: ANC > 1.0 x 10⁹/L and PLT ≥ 100 x 10⁹/L
Desired Hematologic Nadirs:
- ANC = 0.5-0.75 x 10⁹/L; PLT = 75-100 x 10⁹/L
- All potentially myelosuppressive non-chemotherapeutic agents should be stopped prior to reducing doses of any chemotherapy.
1. If ANC < 0.5 x 10⁹/L, HOLD Methotrexate and 6-Mercaptopurine, and then reduce both agents by 20% at start of the next cycle.
2. Re-escalate Methotrexate and 6-Mercaptopurine in 20% increments according to patient tolerance to maintain the desired hematologic nadirs. Dose adjustments should be made once for each cycle (every 3 weeks)

Hepatic Dysfunction
1. Hold start of intensification cycle if AST > 8 times normal or a direct bilirubin ≥ 26 umol/L. Begin cycle when levels have fallen below these values, adjusting doses of chemotherapy as follows:
   - REDUCE Methotrexate by 20%.
   - If elevation of AST/direct bilirubin recurs, then reduce 6-Mercaptopurine by 20% with subsequent cycles. Alternate 20% reductions of Methotrexate and 6-Mercaptopurine with subsequent cycles if elevation of AST/direct bilirubin recurs.
   - Re-escalate chemotherapy by 20% increments as tolerated if LFTs remain within normal range on dose-reduced chemotherapy after 2 cycles.
2. - HOLD 6-Mercaptopurine and weeks 2 and/or 3 Methotrexate for an AST > 8 times normal or a direct bilirubin ≥ 26 umol/L. At start of next cycle, dose reduce Methotrexate and 6-Mercaptopurine.

SUGGESTED ACTION

Date revised: 10/08/2008
Dana Farber Cancer Institute (DFCI) Consortium Protocol
2000-01, Induction Protocol
First-Line Treatment of Acute Lymphoblastic Leukemia in Adults

**CYTARABINE**
50mg IT Day 0
- Prepared by hematologist and give as intrathecal injection.
- All IT doses are flat dose and are NOT adjusted for body surface area.

**PREDNISONE**
40mg/m²/day PO Days 1-28 Round up to nearest 5mg
- Divide daily dose into q6h intervals.
- May substitute Methylprednisolone 32mg/m²/day IV divided into q6h dosing.
- It is recommended that the steroids be given every 6 hours as indicated above.

**VINCRISTINE**
2mg IV Days 1, 8, 15 & 22 Round to nearest 0.1mg
- Mix in 50mL bag Normal Saline; infuse over 10 minutes.

**DOXORUBICIN**
30mg/m² IV Days 1 & 2 Round to nearest 0.5mg
- Give as IV push or bolus over 15 minutes via central line.

**SODIUM BICARBONATE**
100mEq/L IV Day 3
- Admix Sodium Bicarbonate in 1000mL Dextrose 5% and prehydrate at 250mL/hr for at least 4 hours or until urine pH is > 7.0 (do not give Methotrexate until urine PH is >7.0).

**METHOTREXATE**
4G/m² IV Day 3
- Give on Day 3, at least 8 hours but not more than 24 hours after last Doxorubicin dose.
- Admix in 500mL D5W and infuse over 1 hour.
- Direct Bilirubin must be < 26umol/L to administer full dose.

**SODIUM BICARBONATE**
100mEq/L IV Day 3
- Admix Sodium Bicarbonate in 1000mL Dextrose 5% and posthydrate at 150mL/hr until Methotrexate level is < 0.1 micromolar.

**LEUCOVORIN**
IV Day 4 Round to nearest 1mg
Start 36 hours after the start of high dose Methotrexate:
- Give 200mg/m² IV bolus, then continue with the following:
- Give 24mg/m² IV/PO (PO dose is rounded up to the nearest 5mg dose) every 6 hours until Methotrexate level ≤ 0.1 micromolar.
- Check Methotrexate level 36 hours after Methotrexate and then daily.
- If 36 hour Methotrexate level ≥ 2, but < 10, administer 25mg/m² Leucovorin IV/PO every 3 hours.
- If 36 hour Methotrexate ≥ 10 administer 100mg/m² PO/IV every 3 hours.
- If 36 hour level ≥ 10 or renal failure develops call the study chair.
- If 48 hour Methotrexate level ≥ 2.0, give 100mg/m² Leucovorin PO/IV every 3 hours.
- Continue all Leucovorin dosing until Methotrexate level < 0.1 micromolar.
- Leucovorin will always continue regardless of Methotrexate level for a minimum of 6 doses.

**L-ASPARAGINASE**
25,000IU/m² IM Day 5 Round to nearest 1000 IU
- Administer (e-coli L-asparaginase) intramuscularly x 1 dose only.
- If platelets are < 50K, give platelets prior to administering IM.
- If patient receives full dose of Methotrexate with Leucovorin, give 12 hours after first dose of Leucovorin is administered. If low dose Methotrexate (40mg/m²) is given, give 24 hours after dose of Methotrexate.
- Hold if amylase ≥ 3 x normal, or if fibrinogen levels < 2.94umol/L.
- Epinephrine and Diphenhydramine should be available during treatment.

**METHOTREXATE**
12mg IT Days 15 & 29
- Prepared by hematologist and give as intrathecal injection.
- All IT doses are flat dose and are NOT adjusted for body surface area.
- OMIT if patient has any mucositis.

**HYDROCORTISONE**
50mg IT Days 15 & 29
- Prepared by hematologist and give as intrathecal injection.
- All IT doses are flat dose and are NOT adjusted for body surface area.

**CYTARABINE**
- Prepared by hematologist and give as intrathecal injection.
- All IT doses are flat dose and are NOT adjusted for body surface area.

**ANTIMICROBIAL PROPHYLAXIS**:
- Trimethoprim/Sulfamethoxazole DS PO BID for 3 days per week. If not tolerated, Atovaquone 750mg PO BID (with food). Prophylaxis should be continued for all patients from the time they enter complete remission and continued until 6 months after cessation of treatment.
- Trimethoprim/Sulfamethoxazole should not be given on the same day as Methotrexate, but can be given later the same week.

Hematological
Dana Farber Cancer Institute (DFCI) Consortium Protocol  
2000-01, Induction Protocol

PATIENT VISITS and APPOINTMENT TYPE:
- Days 1-7 In-patient
- Days 8 & 22 15min Type A
- Days 15 & 29 1.5hrs Type B

TOXICITIES:

Hepatic Dysfunction

Starting Criteria: Direct Bili < 26 umol/L.
1. If T.Bili > 26umol/L, HOLD Doxorubicin until less than 26umol/L. OMIT induction Doxorubicin if bilirubin is still > 26umol/L on Day 10.
2. If T.Bili > 26umol/L after Doxorubicin but before Methotrexate administered on Day 2, delay high dose Methotrexate no more than 24 hours after completion of Doxorubicin. If bilirubin still > 26umol/L at that point, check bilirubin daily until it is < 26umol/L, then give Methotrexate 40mg/m² iv push (no Leucovorin). No Methotrexate if bilirubin is not < 26umol/L by Day 10.
3. If T.Bili = 51-102 umol/L, REDUCE Vincristine to 50% dose.
4. If T.Bili > 103 umol/L, HOLD Vincristine.

Neurologic

1. If peripheral neuropathy > 2, OMIT Vincristine.

SUGGESTED ACTION

CLINICAL MONITORING:
- Starting with Day 3 Methotrexate, patients should have daily weights and urine output documented in order to avoid symptoms of fluid overload. Diuretics may be used as needed to maintain proper fluid balance.
- Neurologic toxicity ratings (Sensory, Constipation) at each visit.

Sensory
1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function
2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL
3. Sensory alteration or paresthesia interfering with ADL
4. Disabling
5. Death

Constipation
1. Occasional or intermittent symptoms; occasional use of stool softeners, laxatives, dietary modification, or enema
2. Persistent symptoms with regular use of laxatives or enemas indicated
3. Symptoms interfering with ADL; obstipation with manual evacuation indicated
4. Life-threatening consequences (e.g., obstruction, toxic megacolon)
5. Death

RATED AT EACH CLINIC VISIT

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**HEAL 4 INTEN**

**Hematological**

**Dana Farber Cancer Institute (DFCI) Consortium Protocol**

**2000-01, Intensification Therapy**

**First-Line Treatment of Acute Lymphoblastic Leukemia in Adults**

**VINCRISTINE** 2mg IV Week 1 Round to nearest 0.1mg
- Administer once on Week 1
- Mix in 50mL bag Normal Saline; infuse over 10 minutes.
- Give Vincristine 12-24 hours before L-Asparaginase.

**DEXAMETHASONE** 18mg/m²/day PO Week 1 Round up to the nearest whole number
- Divide into BID dosing x 5 days in Week 1 of cycle.
- If additional cycles (greater than ten 3 week cycles) are needed to complete 30 doses of L-asparaginase, decrease Dexamethasone dose to 6mg/m²/day.

**6-MERCAPTOPURINE** 50mg/m²/day PO Weeks 1-2 Round to nearest 25mg
- Take at bedtime (without milk) for 14 consecutive days.

**DOXORUBICIN** 30mg/m² IV Week 1 Round to nearest 1mg
- Administer once on Week 1 of cycle.
- Slow push through sidearm of free flowing IV. Give 2 to 4mg (1-2mL) per minute.
- Continue Doxorubicin to a total cumulative (Induction plus Intensification) dose of 300mg/m² or until 9 months from the date of CR, whichever comes sooner.
- After maximum dose reached, begin weekly Methotrexate at the start of the next cycle.
- Begin Methotrexate after Doxorubicin is discontinued.

**METHOTREXATE** 30mg/m² IV Weeks 1-3 Round to nearest 5mg
- Inject by direct IV push, followed by a Normal Saline flush (if no IV line has been set up).
- May give by slow push through sidearm of free flowing IV (D5W, Normal Saline).
- Rate of administration ≤ 10mg per minute.
- Doses > 100mg, mix in 50-100mL Normal Saline and infuse over 30-60 minutes.
- Administer 1 day after l-asparaginase.
- Hold IV Methotrexate on the day that IT Methotrexate is given.

**L-ASPARAGINASE** 12,500 IU/m²/dose IM Weeks 1-3 Round to nearest 1000 IU
- Administer once per week x 30 doses, starting at 12,500 IU/m²/dose.
- Doses will be adjusted based on the most recent L-asparaginase enzyme level result. The minimum dose is 6,000 IU/m² and the maximum dose is 25,000 IU/m².
- Epinephrine and Diphenhydramine should be available during treatment.
- Patients should be observed for 1 hour after each L-asparaginase dose.

**ANTIMICROBIAL PROPHYLAXIS:**
- Trimethoprim/Sulfamethoxazole DS PO BID for 3 days per week. If not tolerated, Atovaquone 750mg PO BID (with food). Prophylaxis should be instituted for all patients from the time they enter complete remission and continued until 6 months after cessation of treatment.
- Trimethoprim/Sulfamethoxazole should not be given on the same day as Methotrexate, but can be given later the same week.

**PATIENT VISITS and APPOINTMENT TYPE:**
- Weeks 1-3 1.5hrs Type A
- Every 18 weeks 1.5hrs Type B
**HEMATOLOGICAL TOXICITIES:**

**Hematologic**

Starting Criteria: ANC > 1.0 x 10^9/L and PLT > 100 x 10^9/L

Desired Hematologic Nadirs:
- ANC = 0.5-0.75 x 10^9/L; PLT = 75-100 x 10^9/L
- All potentially myelosuppressive non-chemotherapeutic agents should be stopped prior to reducing doses of any chemotherapy.

1. If ANC < 0.5 x 10^9/L, HOLD Methotrexate and 6-Mercaptopurine, and then reduce both agents by 20% at start of the next cycle.
2. Re-escalate Methotrexate and 6-Mercaptopurine in 20% increments according to patient tolerance to maintain the desired hematologic nadirs. Dose adjustments should be made once for each cycle (every 3 weeks).
3. Doxorubicin doses should be reduced by 20% only if appropriate reductions of 6-Mercaptopurine do not result in an ANC nadir of 0.5-0.75 x 10^9/L. **Do not reduce Doxorubicin doses beyond 80% for myelosuppression.**

**Hepatic Dysfunction**

1. Hold start of intensification cycle if AST > 8 times normal or a direct bilirubin > 26 umol/L. Begin cycle when levels have fallen below these values, adjusting doses of chemotherapy as follows:
   - REDUCE 6-Mercaptopurine by 20%.
   - If elevation of AST/direct bilirubin recurs, then reduce Doxorubicin by 20%. **Do not reduce Doxorubicin doses beyond 80%**.
   - If elevation of AST/direct bilirubin recurs with 80% dose Doxorubicin, continue to reduce doses of 6-Mercaptopurine with subsequent cycles by 20% each cycle.
2. - HOLD 6-Mercaptopurine and weeks 2 and/or 3 Methotrexate for an AST > 8 times normal or a direct bilirubin > 26 umol/L. At start of next cycle, dose reduce Methotrexate, 6-Mercaptopurine, Doxorubicin as above, depending upon phase of therapy.
3. - L-asparaginase should be given regardless of AST, but HOLD if direct bilirubin > 52 umol/L.

**SUGGESTED ACTION**

- CCO Eligibility Form Required □
- Non-Formulary Form Required □

**Date revised:** 10/08/2008
**DAUNORUBICIN-CYTARABINE -ATRA AML - M3 Induction (Inpatient regimen)**

**DAUNORUBICIN**
- **50mg/m²** IV Days 3 to 6 Round to nearest 1 mg
- Slow push through sidearm of free flowing IV; Give 2-4mg per minute. (Total 4 doses)
- May be mixed in **50mL minibag (5% Dextrose, Normal Saline)**. Infuse through central catheter over 15-30 minutes.

**CYTARABINE**
- **200mg/m²** IV Days 3 to 9 Round to nearest 1 mg
- Mix in **500mL bag 5% Dextrose**; Infuse over 7 days by continuous infusion through central venous access device.

**ALL-TRANS RETINONIC ACID**
- **45mg/m²** PO Day 1 to CR Round to nearest 10mg
- Divide daily dose into q12h intervals, continue until complete remission.

**HYDRATION:**
- IV Normal Saline

**TESTS:**
- **Baseline Tests**
  - WBC, HB, PLT, ANC, Ca, K, Na, Chloride, Phosphate, Mg, Cr, T.Bili, AST, ALT, Urate, LVEF
- **Daily**
  - WBC, HB, PLT, ANC, K, Na, Chloride, Cr, Urate
- **Monday & Thursday**
  - T.Bili, AST, ALT, Alk Phosphatase, Urate

**Test Notes:**
- On Admission: Serum HcG (for female) if not done in previous 30 days, INR, PTT, CBC, Lytes, Cr, Glucose, T.bili, Alk phos, LDH, AST, ALT, GST, Protein, Albumin, Uric Acid, Calcium, Phosphate, Magnesium, Zinc, Chest X-ray, EKG when needed, LVEF, Cholesterol, Triglycerides,
- Daily: CBC, Cr, BUN, Na*, Cl, K
- **Monday & Thursday:** T.bili, AST, ALT, LDH, PT, PTT, Fibrinogen, Alk phosphate, Uric acid
- **Weekly:** Cholesterol, Triglycerides, CXR

**ANTIEMETIC PRE-CHEMO REGIMEN:**
- **Level B/C**
  - Day 1-7 Ondansetron 8mg q8h PO/IV or Granisetron 1-2mg daily PO/IV
  - Prochlorperazine 10 mg PO/IV

**INPATIENT ANTIEMETICS:**
- Ondansetron 8mg q8h PO/IV can be substituted with Granisetron 1-2mg daily PO/IV

**TOXICITIES:**

**Hematologic**
1. If ANC < 1.0 x 10^9/L; PLT < 75 x 10^9/L
   - Parameters may be changed at the discretion of the clinician if cytopenias presumed to be due to underlying disease.

**Renal Failure**
1. Hyperuricemia - can be minimized with Allopurinol and hydration.
2. Renal failure (recommended action)
   - If CrCl < 10 mL/min, administer 75% of normal Daunorubicin dose.

**Hepatic Dysfunction**
1. Hepatic dysfunction (Suggested action)
   - If T.Bili 26-51 umol/L or AST = 60-180 IU/L, **REDUCE** Daunorubicin to 75% dose
     - 52-85 umol/L or AST > 180 IU/L, **REDUCE** Daunorubicin to 50% dose.
     - > 85 umol/L, **OMIT** dose.

**CLINICAL MONITORING:**
- Rating of Hypervitaminosis A syndrome

**REFERENCES:**
- C9710 Trial Phase III Randomised study of concurrent Tretinoin and Chemotherapy with or without Arsenic Trioxide (As2O3) as initial consolidation therapy followed by maintenance therapy with intermittent Tretinoin versus intermittent Tretinoin plus Mercaptopurine and Methotrexate for patients with untreated Acute Promyelocytic Leukemia

**Date revised:** 03/17/2008
Carmustine (BCNU)-Etoposide-Cytarabine-Melphalan - High dose therapy (Non Hodgkins lymphoma and Hodgkins lymphoma) (Inpatient Regimen)

High dose therapy with autologous hematopoetic stem cell transplantation for Hodgkin's disease

CARMUSTINE
300mg/m² IV Day - 6
- Mix in 250mL Normal Saline in polyolefin bag, use non-PVC equipment, no in-line filter; protect from light.
- Infuse over 2 hours. Cap BSA=2.2m²

ETOPOSIDE
200mg/m² IV Day - 5 to Day - 2 Round to nearest 10mg
- Mix in 1000mL bag Normal Saline; infuse over 3 hours daily. Cap BSA=2.2m²

CYTARABINE
200mg/m² IV Day - 5 to Day - 2 q12h Round to nearest 10mg
- Mix in 100mL bag 5% Dextrose; infuse over 1 hour. Total 8 doses. Cap BSA=2.2m²

MELPHALAN
140mg/m² IV Day -1 Round to nearest 5mg
- Mix in 250mL bag Normal Saline; infuse over 30 minutes.
- Complete infusion within 60 minutes of preparation. Cap BSA=2.2m²

ACETAMINOPHEN
650mg PO Day 0
- Give 2 tablets of Acetaminophen (325mg) prior to stem cell transplant.

HYDROCORTISONE SODIUM SUCCINATE
100mg IV Day 0
- Infuse Hydrocortisone 100mg 30 minutes prior to stem cell transplant.

HYDRATION:
Pre
- Run IV Normal Saline with 20mmol/L KCl at 150mL/hr. Reassess after Stem Cell Reinfusion.

ANTIMICROBIAL PROPHYLAXIS:
- Start on day of Stem Cell Reinfusion
  1. Ciprofloxacin 500mg PO bid
  2. Acyclovir 400mg PO/IV q8h

TESTS:
Baseline Tests WBC HB PLT ANC Ca K Na Chloride Phosphate Mg Cr Urea T.Bili AST ALT AlkPhosphatase Urate
Test Notes - CBC, baseline and regular liver function test. Baseline and regular renal function tests and urinalysis.

ANTIEMETIC PRE-CHEMO REGIMEN:
Level C Day-6 to Day+1 - Ondansetron 8mg PO/IV q8h
Level B Day-6 to Day-1 - Dexamethasone 8mg prior to each dose of Carmustine, Etoposide and Melphalan.
Level A Day-6 - Start Prochlorperazine on Day-6 and continue q4h prn

INPATIENT ANTIEMETICS:
- Ondansetron 8mg q8h can be substituted with Granisetron 1-2mg PO/IV daily.

TOXICITIES:
Hematologic
1. If ANC < 1.0 x 10⁹/L or if PLT < 75 x 10⁹/L, HOLD dose for 1 week.

Renal Failure
1. If CrCl < 1.0mL/sec, REDUCE Carmustine dose by 25-50%.
2. If CrCl = 0.2-0.8mL/sec or SrCr > 130μmol/L, REDUCE Melphalan and Etoposide to 75% dose.
3. If CrCl < 0.2mL/sec, REDUCE Melphalan and Etoposide to 50% dose.

Hepatic Dysfunction
1. If T.Bili = 25-51μmol/L or AST = 60-180 IU/L, REDUCE Etoposide to 50% dose.
2. If T.Bili = 52-85μmol/L, REDUCE Etoposide to 25% dose.
3. If T.Bili > 85μmol/L or AST > 180 IU/L, OMIT Etoposide dose.

Pulmonary
1. Clinical pulmonary exam, pulmonary toxicity rating.

SUGGESTED ACTION

CLINICAL MONITORING:
- Clinical toxicity assessment (including stomatitis, gastrointestinal, pulmonary toxicity). Baseline and regular liver function tests. Baseline and renal function test and urinalysis.

REFERENCES:

Date revised: 10/08/2008
BORTEZOMIB Therapy
Multiple Myeloma

BORTEZOMIB 1.3mg/m² IV Days 1,4,8 & 11 Round to nearest 0.1mg

Standard regimen:
- Give as an IV bolus over 3-5 seconds through an intravenous catheter followed by a flush with Normal Saline. At least 72 hours should elapse between consecutive doses.
- Trade name Velcade™

REPEAT EVERY 21 DAYS

Alternate weekly regimen started at discretion of hematologist.

BORTEZOMIB 1.3mg/m² IV Days 1,8,15 & 22 Round to nearest 0.1mg

Weekly regimen:
- Give as an IV bolus over 3-5 seconds through an intravenous catheter followed by a flush with Normal Saline.

REPEAT EVERY 35 DAYS

TESTS:
Baseline Tests WBC HB PLT ANC Ca Cr ALT GGT AlkPhosphatase Urate
Once Weekly WBC HB PLT ANC

Test Notes - Additional baseline tests: Protein electrophoresis (SPEP), Quantitative immunoglobulins (QIs)

PATIENT VISITS and APPOINTMENT TYPE:
- Days 1,4,8 & 11 (Standard) 15min Type A
- Days 1,8,15 & 22 (Weekly) 15min Type A

TOXICITIES:
Hematologic
1. If ANC < 0.5 x 10⁹/L, HOLD treatment until AGC level is reached.
2. If PLT < 30 x 10⁹/L, HOLD treatment until PLT level is reached.
3. If HB < 70, HOLD treatment until HB level is reached.
- Once the symptoms of the toxicity have resolved, Bortezomib therapy may be reinitiated at a 25% reduced dose: 1.0mg/m², then 0.7mg/m² (lowest dose to be administered).

Neurologic
1. Grade 1 without pain or loss of function (paresthesia and/or loss of reflexes): No action.
2. Grade 1 with pain or Grade 2 (interfering with function but not ADL): Reduce to 1mg/m².
3. Grade 2 with pain or Grade 3 (interfering with ADL): HOLD until toxicity resolves. When resolved change dose to 0.7mg/m² and change treatment schedule to once a week.
If the toxicity does not resolve after dosing has been withheld for 2 weeks, then the patient must be discontinued from treatment.

CLINICAL MONITORING:
- Therapy is commonly associated with orthostatic/postural hypotension which is not an acute reaction, and is observed throughout treatment. Use with caution in patients with a history of syncope or patients using medications associated with hypotension.
- Patients with risk factors for, or existing heart disease should be closely monitored. Acute development or exacerbation of congestive heart failure and decreased LVEF has been reported.
- Bortezomib is metabolized by liver enzymes, therefore clearance may decrease in patients with hepatic impairment. Patients should be treated with extreme caution, monitored for toxicity and a dose reduction should be considered (dose level not specified by Ortho Biotech). No formal studies have been done with Bortezomib in liver dysfunction.

INTERNAL CODE:
- OPIS CODES:
  - BORTEZOMIB STANDARD
  - BORTEZOMIB WEEKLY

REFERENCES:
BORTEZOMIB-MELPHALAN-PREDNISONE Therapy

Multiple Myeloma; Previously untreated multiple myeloma patients who are unsuitable for stem cell transplantation

Group 1: Initial - Cycle 1-4 (every 6 weeks)
BORTEZOMIB 1.3mg/m² IV Days 1,4,8,11,22,25,29,32 Round to nearest 0.1mg
- Give as an IV bolus over 3-5 seconds through an intravenous catheter followed by a flush with Normal Saline. At least 72 hours should elapse between consecutive doses.

Group 2: Maintenance - Cycle 5-9 (every 6 weeks)
BORTEZOMIB 1.3mg/m² IV Days 1, 8, 22, 29 Round to nearest 0.1mg
- Give as an IV bolus over 3-5 seconds through an intravenous catheter followed by a flush with Normal Saline.

Cycles 1-9
MELPHALAN 9mg/m²/day PO Days 1-4 2mg tablets
- Daily for 4 days.
- Outpatient available in 2mg tablets.
- Trade name Alkeran™

Cycles 1-9
PREDNISONE 60mg/m²/day PO Days 1-4 50mg tablets
- Daily for 4 days.
- Dose capped at 100mg daily.
- Outpatient prescription available as 5mg and 50mg tablets.

EVERY 6 WEEKS for a usual total dose of 9 cycles (4 cycles of Initial Phase and 5 cycles of Maintenance Phase), in the absence of disease progression or unacceptable toxicities

TESTS:
Baseline Tests
WBC HB PLT ANC Ca Glucose Cr Urea T.Bili AST ALT GGT AlkPhosphatase Urate
Day 15 (first 3 cycles of therapy)
WBC HB PLT ANC Ca Glucose Cr Urea T.Bili Albumin ALT AlkPhosphatase
Once Weekly
WBC HB PLT ANC
- Additional baseline tests: Protein electrophoresis (SPEP), Quantitative immunoglobulins (QIs) and 24-hour urine for UPEP.
- Additional tests on therapy:
  Day 1: Protein electrophoresis (SPEP)
  Selected patients, especially those with IgA or IgD myeloma, may be better followed by specific measurement of relevant immunoglobulin level - in these cases repeating of SPEP is not necessary.
  Routine duplication measurement of SPEP and QIs should be avoided.
- 24-hour urine for UPEP should be repeated with every cycle if positive and every 3 cycles if negative.

ANTIEMETIC PRE-CHEMO REGIMEN:
Level A Days 1-4 - Prochlorperazine 10mg PO pm

ANTIEMETIC TAKE-HOME REGIMEN:
Level A Days 1-4 - Prochlorperazine 10mg PO q4-6h pm

PATIENT VISITS and APPOINTMENT TYPE:
⇒ Days 1,4,8,11,22,25,29 & 32 15min (Initial) Type A
⇒ Days 1,8,22 & 29 (Maintenance) 15min Type A

ANCILLARY:
- Allopurinol and hydration to reduce the risk of tumour lysis syndrome are recommended, especially for patients with high tumour load.

TOXICITIES:
Hematologic
1. If ANC < 0.75 x 10⁹/L, HOLD treatment until ANC level is reached.
2. If PLT < 30 x 10⁹/L, HOLD treatment until PLT level is reached.
3. If HB < 70, HOLD treatment until HB level is reached.
- Once the symptoms of the toxicity have resolved, Bortezomib therapy may be reinitiated at a 25% reduced dose: 1.0mg/m², then 0.7mg/m² (lowest dose to be administered).
Hematological

BORTEZOMIB-MELPHALAN-PREDNISONE Therapy

**Neurologic**

1. Grade 1 without pain or loss of function (paresthesia and/or loss of reflexes): No action.
2. Grade 1 with pain or Grade 2 (interfering with function but not ADL): Reduce to 1mg/m².
3. Grade 2 with pain or Grade 3 (interfering with ADL): Hold until toxicity resolves. When resolved change dose to 0.7mg/m² and change treatment schedule to once a week.

If the toxicity does not resolve after dosing has been withheld for 2 weeks, then the patient must be discontinued from treatment.

**Renal Failure**

1. If CrCl = 0.2-0.8mL/sec or SrCr > 130μmol/L, REDUCE Melphalan to 75% dose.
2. If CrCl < 0.2mL/sec, REDUCE Melphalan to 50% dose.

**CLINICAL MONITORING:**

- Therapy is commonly associated with orthostatic/postural hypotension which is not an acute reaction, and is observed throughout treatment. Use with caution in patients with a history of syncope or patients using medications associated with hypotension.
- Patients with risk factors for, or existing heart disease should be closely monitored. Acute development or exacerbation of congestive heart failure and decreased LVEF has been reported.
- Bortezomib is metabolized by liver enzymes, therefore clearance may decrease in patients with hepatic impairment. Patients should be treated with extreme caution, monitored for toxicity and a dose reduction should be considered (dose level not specified by Ortho Biotech). No formal studies have been done with Bortezomib in liver dysfunction.
- Patients with compromised renal function should be monitored carefully when treated with Bortezomib, especially if creatinine clearance is less than 30mL/min.

**REFERENCES:**


**INTERNAL CODE:**

- BORT-MELPH-PRED

**OPIS CODE:**

- BORT-MELPH-PRED

**CCO Eligibility Form Required** ✔️ **Non-Formulary Form Required** ☐

*Date revised: 05/13/2009*
Hematological

MODIFIED BOSTON PROTOCOL (Pegylated L-Asparaginase) Chemotherapy

Acute Lymphoblastic Leukemia- High-risk Consolidation and Maintenance (in case of allergy to L-Asparaginase)

6-MERCAPTOPURINE 100mg PO Week 1 (14 days) 50mg tablet
- Daily for 14 days (decrease if hepatotoxicity).
- Outpatient prescription.

DOXORUBICIN 300mg/m² IV Week 1 (1 day) Round to nearest 1mg
- Slow push through sidearm of free-flowing IV; Rate = 2mL (4mg) per minute.
- May be deleted due to cumulative dose.

PEG-L-ASPARAGINASE 2,500 IU/m² IM Week 1 (1 day) Round to nearest 375 IU
- Give intramuscularly (Dose divided into 2 syringes).

VINCristine 2mg IV Week 1 (1 day) Round to nearest 0.1mg
- Mix in 50mL bag Normal Saline; infuse over 10 minutes.

PREDNISONE 75-150mg PO Week 1 (5 days) 5mg & 50mg tablets
- Daily for 5 days.
- Outpatient prescription.

DOXORUBICIN 300mg/m² IV Week 3 (1 day) Round to nearest 1mg
- Slow push through sidearm of free-flowing IV; Rate = 2mL (4mg) per minute.
- May be deleted due to cumulative dose.

PEG-L-ASPARAGINASE 2,500 IU/m² IM Week 3 (1 day) Round to nearest 375 IU
- Give intramuscularly (Dose divided into 2 syringes).

VINCristine 2mg IV Week 3 (1 day) Round to nearest 0.1mg
- Mix in 50mL bag Normal Saline; infuse over 10 minutes.

PREDNISONE 75-150mg PO Week 3 (5 days) 5mg & 50mg tablets
- Daily for 5 days.
- Outpatient prescription.

6-MERCAPTOPURINE 100mg PO Week 4 (14 days) 50mg tablet
- Daily for 14 days (decrease if hepatotoxicity).
- Outpatient prescription.

PEG-L-ASPARAGINASE 2,500 IU/m² IM Week 5 (1 day) Round to nearest 375 IU
- Give intramuscularly (dose divided into 2 syringes).

VINCristine 2mg IV Week 7 (1 day) Round to nearest 0.1mg
- Mix in 50mL bag Normal Saline; infuse over 10 minutes.

PREDNISONE 75-150mg PO Week 7 (5 days) 5mg & 50mg tablets
- Daily for 5 days.
- Outpatient prescription.

METHOTREXATE 300mg/m² IV Week 7 (1 day) Round to nearest 5mg
- Inject by direct IV push, followed by a Normal Saline flush (if no IV line has been set up).
- May give by slow push through sidearm of free flowing IV (D5W, Normal Saline).
- Rate of administration ≤ 10mg per minute.
- Doses > 100mg, mix in 50-100mL Normal Saline and infuse over 30-60 minutes.

METHOTREXATE 300mg/m² IV Week 8 (1 day) Round to nearest 5mg
- Inject by direct IV push, followed by a Normal Saline flush (if no IV line has been set up).
- May give by slow push through sidearm of free flowing IV (D5W, Normal Saline).
- Rate of administration ≤ 10mg per minute.

METHOTREXATE 12mg IT Week 9 (1 day)
- Prepared by hematologist and give as intrathecal injection.
- All IT doses are flat dose and are NOT adjusted for body surface area.

TESTS:
Baseline Tests WBC HB PLT ANC Ca K Na Chloride Glucose Cr Urea T.Bili Albumin ALT AlkPhosphatase

Hematological
MODIFIED BOSTON PROTOCOL (Pegylated L-Asparaginase) Chemotherapy

**Weekly Tests**
- WBC, HB, PLT, ANC, Cr, T.Bili, ALT, AlkPhosphatase
- Note if PLT < 50 x 10^9/L consider PLT transfusion prior to IM injection.
- LVEF if clinically indicated.

**Test Notes**
- INR, PTT and Fibrinogen added to both baseline and weekly tests while on L-asparaginase.

**ANTIEMETIC PRE-CHEMO REGIMEN:**
- Level A
  - Weeks 1, 2, 3, 4, 5, 6, 7 & 8
  - Prochlorperazine 10mg PO prn

**ANTIEMETIC TAKE-HOME REGIMEN:**
- Level A
  - Weeks 1, 2, 3, 4, 6, 7 & 8
  - Prochlorperazine 10mg PO q4-6h prn
- Level B/C
  - Week 5
  - Ondansetron 8mg PO BID for 2-3 days, or
  - Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days
  - Dexamethasone 8mg PO BID for 2-3 days
  - Prochlorperazine 10mg PO q4-6h prn

**PATIENT VISITS and APPOINTMENT TYPE:**
- Weeks 1 & 3: 1h Type C
- Weeks 5, 7 & 8: 15min Type A
- Week 9: 45min Type B

**TOXICITIES:**

**Hematologic**
1. If INR > 1.4, or PTT > 42 sec, or Fibrinogen < 1.0 G/L **HOLD** L-asparaginase.

**Hepatic Dysfunction**
1. If T.Bili = 26-51umol/L, or AST = 60-180 IU/L **REDUCE** Vincristine to 25% dose.
2. If T.Bili = 52-85umol/L, or AST > 180 IU/L **REDUCE** Vincristine to 50% dose & **OMIT** L-asparaginase.

**CLINICAL MONITORING:**
- Observation for hypersensitivity reaction during and for 30 minutes after L-asparaginase injection (emergency treatment available).
- Neurologic toxicity ratings (Sensory, Constipation) at each visit.

**Allergic Reaction**
1. Transient flushing or rash; drug fever < 38 degrees C
2. Rash; flushing; urticaria; dyspnee; drug fever ≥ 38 degrees C
3. Symptomatic bronchospasm, with or without urticaria; parenteral medication(s) indicated; allergy-related edema/angioedema; hypotension
4. Anaphylaxis
5. Death

**RATED IN RESPONSE TO PATIENT REACTION**

**Sensory**
1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function 2.
2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL 3. Sensory alteration or paresthesia interfering with ADL 4. Disabling 5. Death

**Constipation**
1. Occasional or intermittent symptoms; occasional use of stool softeners, laxatives, dietary modification, or enema
2. Persistent symptoms with regular use of laxatives or enemas indicated
3. Symptoms interfering with ADL; obstruction with manual evacuation indicated
4. Life-threatening consequences (e.g., obstruction, toxic megacolon)
5. Death

**RATED AT EACH CLINIC VISIT**

**INTERNAL CODE:**
- OPIS CODES:
  - BOSTON MOD PEG-ASP 1
  - BOSTON MOD PEG-ASP 3-5
  - BOSTON MOD PEG-ASP 7-9

**REFERENCES:**

CCO Eligibility Form Required [ ] Non-Formulary Form Required [ ] Date revised: 10/08/2008
6-MERCAPTOPURINE  
- 100mg PO Week 1 (14 days)  
- Daily for 14 days (decrease if hepatotoxicity).  
- Outpatient prescription.

DOXORUBICIN  
- 30mg/m² IV Week 1 (1 day)  
- Slow push through sidearm of free-flowing IV; rate = 2mL (4mg) per minute.  
- May be deleted due to cumulative dose.

L-ASPARAGINASE  
- 25,000 IU/m² IM Week 1 (1 day)  
- Give intramuscularly (Dose divided into 2 syringes).

VINCISTINE  
- 2mg IV Week 1 (1 day)  
- Mix in 50mL bag Normal Saline; infuse over 10 minutes.
- Give Vincristine 12-24 hours before L-Asparaginase.

PREDNISONE  
- 75-150mg PO Week 1 (5 days)  
- Daily for 5 days.  
- Outpatient prescription.

L-ASPARAGINASE  
- 25,000 IU/m² IM Week 2 (1 day)  
- Give intramuscularly (dose divided into 2 syringes).

L-ASPARAGINASE  
- 25,000 IU/m² IM Week 3 (1 day)  
- Give intramuscularly (dose divided into 2 syringes).

L-ASPARAGINASE  
- 25,000 IU/m² IM Week 4 (1 day)  
- Give intramuscularly (dose divided into 2 syringes).

6-MERCAPTOPURINE  
- 100mg PO Week 4 (14 days)  
- Daily for 14 days (decrease if hepatotoxicity).  
- Outpatient prescription.

DOXORUBICIN  
- 30mg/m² IV Week 4 (1 day)  
- Slow push through sidearm of free-flowing IV; rate = 2mL (4mg) per minute.  
- May be deleted due to cumulative dose.

VINCISTINE  
- 2mg IV Week 4 (1 day)  
- Mix in 50mL bag Normal Saline; infuse over 10 minutes.

PREDNISONE  
- 75-150mg PO Week 4 (5 days)  
- Daily for 5 days.  
- Outpatient prescription.

L-ASPARAGINASE  
- 25,000 IU/m² IM Week 5 (1 day)  
- Give intramuscularly (dose divided into 2 syringes).

L-ASPARAGINASE  
- 25,000 IU/m² IM Week 6 (1 day)  
- Give intramuscularly (dose divided into 2 syringes).

6-MERCAPTOPURINE  
- 100mg PO Week 7 (14 days)  
- Daily for 14 days (decrease if hepatotoxicity).  
- Outpatient prescription.

VINCISTINE  
- 2mg IV Week 7 (1 day)  
- Mix in 50mL bag Normal Saline; infuse over 10 minutes.

PREDNISONE  
- 75-150mg PO Week 7 (5 days)  
- Daily for 5 days.  
- Outpatient prescription.

METHOTREXATE  
- 30mg/m² IV Week 7 (1 day)  
- Slow push through sidearm of free flowing IV at a rate of ≤ 10mg per minute.  
- Doses > 100mg, mix in 50-100mL Normal Saline and infuse over 30-60 minutes.

METHOTREXATE  
- 30mg/m² IV Week 8 (1 day)  
- Slow push through sidearm of free flowing IV at a rate of ≤ 10mg per minute.  
- Doses > 100mg, mix in 50-100mL Normal Saline and infuse over 30-60 minutes.

METHOTREXATE  
- 12mg IT Week 9 (1 day)  
- Prepared by hematologist and give as intrathecal injection.  
- All IT doses are flat dose and are NOT adjusted for body surface area.
Hematological

MODIFIED BOSTON PROTOCOL  Chemotherapy

**TESTS:**

**Baseline Tests**
- WBC  HB  PLT  ANC  Ca  K  Na  Chloride  Phosphate  Glucose  Cr  Urea  T.Bili  Albumin  ALT  AlkPhosphatase  Urate

**Weekly**
- WBC  HB  PLT  ANC  Cr  T.Bili  ALT  AlkPhosphatase

**Test Notes**
- INR, PTT and Fibrinogen- added to both baseline and weekly tests while on L-asparaginase.
- Note if Platelets < 50 x 10^9/L, consider PLT transfusion prior to IM injection.
- LVEF if clinically indicated.

**ANTIEMETIC PRE-CHEMO REGIMEN:**

<table>
<thead>
<tr>
<th>Level</th>
<th>Weeks</th>
<th>Regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>1,2,3,4,5,6,7,8 &amp; 9</td>
<td>Prochlorperazine 10mg PO pm</td>
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**ANTIEMETIC TAKE-HOME REGIMEN:**

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<tr>
<th>Level</th>
<th>Weeks 1,4,7,8 &amp; 9</th>
<th>Regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td></td>
<td>Prochlorperazine 10mg PO q4-6h pm</td>
</tr>
<tr>
<td>B/C</td>
<td>2,3,5,6 &amp; 8</td>
<td>Ondansetron 8mg PO BID for 2-3 days, or</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Dexamethasone 8mg PO BID for 2-3 days</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Prochlorperazine 10mg PO q4-6h pm</td>
</tr>
</tbody>
</table>

**PATIENT VISITS and APPOINTMENT TYPE:**

- Weeks 1 & 4: 1h Type C
- Weeks 2,3,5,6,7 & 8: 15min Type A
- Week 9: 45min Type C

**TOXICITIES:**

**Hematologic**
1. If INR > 1.4, or PTT > 42 sec, or Fibrinogen < 1.0 G/L, HOLD L-asparaginase.

**Hepatic Dysfunction**
1. If T.Bili = 26-51umol/L, or AST = 60-180 IU/L, REDUCE Vincristine to 25% dose.
2. If T.Bili = 52-85umol/L, or AST > 180 IU/L, REDUCE Vincristine to 50% dose & OMIT L-asparaginase.

**Cardiac**
1. OMIT Doxorubicin if cumulative dose>450mg/m² reached (including prior chemotherapy regimens) OR if LVEF<50%.

**CLINICAL MONITORING:**
- Observation for hypersensitivity reaction during and for 30 minutes after L-asparaginase injection (emergency treatment available).
- Neurologic toxicity ratings (Sensory, Constipation) at each visit.

**Allergic Reaction**
- Transient flushing or rash; drug fever < 38 degrees C
- Rash; flushing; urticaria; dyspnea; drug fever ≥ 38 degrees C
- Symptomatic bronchospasm, with or without urticaria; parenteral medication(s) indicated; allergy-related edema/angioedema; hypotension
- Anaphylaxis
- Death

**Sensory**
1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function
2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL
3. Sensory alteration or paresthesia interfering with ADL
4. Disabling
5. Death

**Constipation**
1. Occasional or intermittent symptoms; occasional use of stool softeners, laxatives, dietary modification, or enema
2. Persistent symptoms with regular use of laxatives or enemas indicated
3. Symptoms interfering with ADL
4. Life-threatening consequences (e.g., obstruction, toxic megacolon)
5. Death

**REFERENCES:**

**INTERNAL CODE:**
- BOSTON MODIFIED WK 1
- BOSTON MODIFIED WK 2-3
- BOSTON MODIFIED WK 4
- BOSTON MODIFIED WK 5-6
- BOSTON MODIFIED WK 7
- BOSTON MODIFIED WK 8-9

**CCO Eligibility Form Required** ☐  **Non-Formulary Form Required** ☐  **Date revised:** 10/08/2008
LOMUSTINE-ETOPOSIDE-PREDNISONE-CHLORAMBUCIL
Chemotherapy

Patient refractory to autologous stem cell transplantation and disease not controlled with single agent Vinblastine

**LOMUSTINE**
- **80mg/m²** PO Day 1
- Cap BSA at 2.2m²
- Outpatient prescription.

**ETOPOSIDE**
- **100mg/m²** PO Days 1-5
- Cap BSA at 2.2m²
- Outpatient prescription.

**PREDNISONE**
- **40mg/m²** PO Days 1-5
- Cap BSA at 2.2m²
- Outpatient prescription.

**CHLORAMBUCIL**
- **6mg/m²** PO Days 1-5
- Cap BSA at 2.2m²
- Outpatient prescription.

REPEAT EVERY 42 DAYS for 6-8 cycles

**TESTS:**
Baseline Tests: WBC HB PLT ANC Ca Glucose Cr T.Bili ALT AlkPhosphatase
Day 1: WBC HB PLT ANC Ca T.Bili Albumin ALT AlkPhosphatase
Test Notes: Additional Baseline test (Staging): Protein electrophoresis
- Additional Day 1 test: Protein
- Monitoring of CBC every 2-3 weeks while on therapy should be considered.

**ANTIEMETIC PRE-CHEMO REGIMEN:**
Level C
- Day 1: Ondansetron 8mg PO or Granisetron 2mg PO
- Prednisone: see regimen information.

**ANTIEMETIC TAKE-HOME REGIMEN:**
Level B/C
- Days 2-5: Ondansetron 8mg PO BID for 2-3 days, or Granisetron 2mg PO OD for 2-3 days
- Prednisone: see regimen information.
- Prochlorperazine 10mg PO q4-6h prn

**TOXICITIES:**

**Hematologic**
1. If ANC < 1.0 x 10⁹/L, DELAY therapy 1 week.
2. If PLT < 75 x 10⁹/L, DELAY therapy 1 week.
   - If after 1 week delay, cytopenias remain, dose attenuate as follows:
     1. If ANC = 0.5-0.99 x 10⁹/L, REDUCE all doses except Prednisone by 50%.
     2. If PLT = 50-74 x 10⁹/L, REDUCE all doses except Prednisone by 50%.
     OR
     1. If ANC < 0.5 x 10⁹/L, consider continued delay of therapy.
     2. If PLT = 50-99 x 10⁹/L, consider continued delay of therapy.
     Dose attenuations may be over-ridden if cytopenias presumed to be due to underlying disease. Patients who are heavily pretreated have varying risk/benefit profiles with respect to choice and dose of therapy. Doses may require reduction in patients with poor bone marrow function. Dose attenuations may be over-ridden if need for disease control warrants.

**Renal Failure**
1. If CrCl < 10mL/min, REDUCE Lomustine to 25-50% dose.
2. If CrCl = 0.2-0.8mL/sec, or SrCr > 130umol/L, REDUCE Etoposide to 75% dose.
3. If CrCl < 0.2mL/sec, REDUCE Etoposide to 50% dose.
4. Consider dose reduction of Procarbazine if renal function is reduced (eg. reduced CrCl or SrCr).

**Hepatic Dysfunction**
1. If T.Bili = 26-51umol/L, or AST = 60-180 IU/L, REDUCE Etoposide to 50% dose.
2. If T.Bili = 52-85umol/L, or AST > 180 IU/L, REDUCE Etoposide to 25% dose.
3. If T.Bili > 85umol/L, OMIT Etoposide.
4. Consider Chlorambucil dose reduction if LFTs elevated (eg. Bilirubin or AST).

**SUGGESTED ACTION**

**CLINICAL MONITORING:**

Dyspnea (shortness of breath)
1. Occasional or intermittent symptoms; occasional use of stool softeners, laxatives, dietary modification, or enema
2. Persistent symptoms with regular use of laxatives or enemas indicated
3. Symptoms interfering with ADL; obstipation with manual evacuation indicated
4. Life-threatening consequences (e.g., obstruction, toxic megacolon)
5. Death
RATED AT EACH CLINIC VISIT

**REFERENCES:**
**CYCLOPHOSPHAMIDE-ETOPOSIDE-PREDNISONE- (RITUXIMAB) Chemotherapy**

Non-Hodgkin’s Lymphoma- Salvage therapy, patient unable to receive anthracycline due to cardiac disease. Regimen chosen over CEPP because of unavailability or intolerance of Procarbazine

### CYCLOPHOSPHAMIDE
- 750mg/m² IV Days 1 & 8 Round to nearest 10mg
- Mix in 250mL bag Normal Saline; Infuse over 10-20 minutes.
- Cap BSA at 2.2m²

### ETOPOSIDE
- 70mg/m² IV Day 1 Round to nearest 10mg
- Mix in 500mL bag of Normal Saline; connect piggyback to IV line; Infuse over 30-60 minutes.

### ETOPOSIDE
- 140mg/m² PO Days 2 & 3 50mg capsule
- Daily for 2 days.
- OR may continue IV Etoposide on Days 2 & 3 (70mg/m²).
- Outpatient prescription.

### PREDNISONE
- 100mg PO Days 1-10 50mg tablet
- Daily for 10 days starting the morning of Day 1 of CEPP(MOD)-Rituximab treatment.
- Outpatient prescription.

### ACETAMINOPHEN
- 650mg PO Day 1 325mg tablet
- Administer 30 minutes before Rituximab infusion.

### DIPHENHYDRAMINE
- 50mg PO Day 1 50mg capsule
- Administer 30 minutes before Rituximab infusion.

### RITUXIMAB
- 375mg/m² IV Day 1 Round to nearest 1mg
- Add to CEPP regimen provided eligibility criteria are met.
- Mix in Normal Saline or 5% Dextrose to a final concentration 1-4 mg/mL (concentration used at JCC is 2mg/mL).

**First infusion**
- Infuse IV at 50mg/hr, after 60 minutes increase rate by increments of 50mg/hr every 30 minutes, as tolerated to a final rate 400 mg/hr for the first dose.

**Subsequent infusions**
- Subsequent infusion may be initiated at 100mg/hr and increased by increments of 100mg/hr every 30 minutes to a maximum rate 400mg/hr as tolerated by the patient.
- For eligible patients * Rituximab may be given as a Rapid infusion:
  - Mix Rituximab in 250mL (or 500mL) Normal Saline; infuse 75mL (or 100mL of 500mL bag) over 30 minutes, then infuse the remaining volume over 60 minutes.
  - Take complete vital signs prior to and after treatment.
  - Do Not administer as IV push or bolus
  - Caution using Rituximab with bulky disease (10cm diameter) or circulating lymphoma cells (> 50 x 10⁹/L).
  - * Eligible patients show no reaction with first infusion.

REPEAT EVERY 21-28 DAYS for 6-8 cycles

### TESTS:
- **Baseline Tests:**
  - WBC HB PLT ANC Ca Glucose Cr T.Bili ALT AlkPhosphatase
- **Day 1:**
  - WBC HB PLT ANC Cr T.Bili ALT AlkPhosphatase
- **Day 8:**
  - WBC HB PLT ANC Glucose

**Test Notes:** Additional Baseline tests: Protein electrophoresis and direct antiglobulin test (Coombs test)

### ANTIEMETIC PRE-CHEMO REGIMEN:
- **Level C**
- Days 1 & 8 - Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
- Dexamethasone 20mg PO/IV

### ANTIEMETIC TAKE-HOME REGIMEN:
- **Level B/C**
- Days 1 & 8 - Ondansetron 8mg PO BID for 2-3 days, or Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days
- Prochlorperazine 10mg PO q4-6h prn

### PATIENT VISITS and APPOINTMENT TYPE:
- **Day 1** (90 minute infusion) 5hrs Type E
- or **Day 1** (6-8h-if reaction to Rituximab) 6-8hrs Type H
- **Day 8** 45min Type B
**TOXICITIES:**

**Hematologic**

**Day 1**
1. If ANC < 1.0 x 10^9/L, **DELAY** therapy 1 week.
2. If PLT < 75 x 10^9/L, **DELAY** therapy 1 week.

**Day 8**
1. If ANC < 1.0 x 10^9/L, **OMIT** therapy.
2. If PLT < 75 x 10^9/L, **OMIT** therapy.

- Dose attenuations may be over-ridden if cytopenias presumed to be due to underlying disease.

**Renal Failure**
1. If CrCl = 0.2-0.8mL/sec, or SrCr > 130umol/L, **REDUCE** Etoposide to 75% dose.
2. If CrCl < 0.2mL/sec, **REDUCE** Etoposide to 50% dose & **OMIT** Cyclophosphamide.

**Hepatic Dysfunction**
1. If T.Bili = 26-51umol/L, or AST = 60-180 IU/L, **REDUCE** Etoposide to 50% dose.
2. If T.Bili = 52-85umol/L, or AST > 180 IU/L, **REDUCE** Etoposide to 25% dose.
3. If T.Bili > 85umol/L, **OMIT** Etoposide.

**SUGGESTED ACTION**

**CLINICAL MONITORING:**
- Urinalysis (RBCs) & Cystitis toxicity ratings - only in response to patient complaint.
- Clinical pulmonary exam, including auscultation, pulmonary toxicity ratings (Cough, SOB).
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.
- Baseline blood pressure at each treatment visit: Monitor for hypotension.

**Dyspnea**
1. Dyspnea on exertion, but can walk 1 flight of stairs without stopping
2. Dyspnea on exertion but unable to walk 1 flight of stairs or 1 city block (0.1km) without stopping
3. Dyspnea with ADL
4. Dyspnea at rest; intubation/ventilator indicated
5. Death

**Cough**
1. Symptomatic, non-narcotic medication only indicated
2. Symptomatic and narcotic medication indicated
3. Symptomatic and significantly interfering with sleep or ADL

**RATED AT EACH CLINIC VISIT**

**Rituximab**
- Close observation for infusion related symptoms including: fever, chills, pain, asthenia and other flu-like symptoms.
- Clinical cardiac monitoring for all patients with cardiac risk factors or previous cardiac conditions (eg. arrhythmia, angina). Observe for symptoms of hypersensitivity including: hypotension, bronchospasm and angioedema.
- **Fatal Cytokine Release Syndrome** has been reported. It usually occurs within 1-2 hours of initiating the first infusion. Initially, it is characterized by severe dyspnea (often with bronchospasm and hypoxia) in addition to fever, chills, rigors, urticaria and angioedema. There may be features of tumor lysis syndrome and pulmonary infiltration. Aggressive symptomatic treatment is required.
- **Rituximab is possibly associated with Hepatitis B reactivation.** All patients should be tested for HBsAg and HBcAb. If either test is positive, such patients should be treated with Lamivudine 100mg/day orally, for the entire duration of chemotherapy and for two months afterwards. Such patients should be monitored with frequent liver tests and hepatitis B virus DNA (at least every two months) up to one year following Rituximab therapy.

**HYPERSENSITIVITY:**
- **Rituximab can cause allergic type reaction during infusion.** If an allergic reaction occurs, stop infusion and the physician in charge should determine a safe time and rate to resume infusion. After recovery of symptoms, restart Rituximab infusion one infusion rate below the rate at which the reaction occurred and continue with escalation of infusion rates on the appropriate schedule.

**Hypersensitivity**
0. None  1. Transient rash ; fever < 38°C  2. Urticaria ; fever > 38°C
3. Serum sickness ; bronchospasm, requires parenteral medications  4. Anaphylaxis

**INTERNAL CODE:**
OPIS CODE: CEPP (R) MODIFIED

**REFERENCES:**
**CHLORAMBUCIL Chemotherapy**

**Chronic Lymphocytic Leukemia (Active or Indolent Disease)**

**CHLORAMBUCIL**
- 6mg/m² PO Days 1-21
- 2mg tablet
- Daily for 21 days.
- Outpatient prescription.

**PREDNISONE**
- 50mg PO Day 1
- 5mg & 50mg tablets
- May also add Prednisone to regimen, dosage may vary.
- Daily for 5-10 days.
- Outpatient prescription.

**TESTS:**
- Baseline Tests: WBC HB PLT ANC Ca K Na Chloride Phosphate Glucose Cr Urea T.Bili AST ALT AlkPhosphatase Urate
- Day 1: WBC HB PLT ANC Ca K Na Chloride Phosphate Glucose Cr Urea T.Bili AST ALT AlkPhosphatase Urate

**Test Notes:** Follow-up blood work:
- CBC three times weekly until recovery and transfusion support as necessary.
- Chemistry to be repeated once weekly.

**ANTIEMETIC PRE-CHEMO REGIMEN:**
- Level A Chlorambucil: Prochlorperazine 10mg PO prn treatment days

**ANTIEMETIC TAKE-HOME REGIMEN:**
- Level A Chlorambucil: Prochlorperazine 10mg PO q4-6h prn treatment days

**TOXICITIES:**

**Hematologic**
1. If ANC < 1.0 x 10⁹/L, or if PLT < 100 x 10⁹/L, HOLD dose for 1 week.

**Hepatic Dysfunction**
1. Consider dose reduction if LFTs elevated (eg. T.Bili or AST).

**SUGGESTED ACTION**

**CLINICAL MONITORING:**
- Clinical pulmonary exam, including auscultation, pulmonary toxicity ratings (Cough, SOB).

**Dyspnea**
1. Dyspnea on exertion, but can walk 1 flight of stairs without stopping 2. Dyspnea on exertion but unable to walk 1 flight of stairs or 1 city block (0.1km) without stopping 3. Dyspnea with ADL 4. Dyspnea at rest; intubation/ventilator indicated 5. Death

RATED AT EACH CLINIC VISIT

**INTERNAL CODE:**
- OPIS CODE: CHLORAM 21D

**REFERENCES:**

**Date revised:** 10/08/2008
**Hematological**

**CHLORAMBUCIL-(RITUXIMAB) Chemotherapy**

*Non-Hodgkin's Lymphoma; Indolent histologies; up-front or salvage therapy*

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Days</th>
<th>Frequency</th>
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</thead>
<tbody>
<tr>
<td>CHLORAMBUCIL</td>
<td>6mg/m²</td>
<td>PO</td>
<td>Days 1-14</td>
<td>2mg tablet</td>
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<td>ACETAMINOPHEN</td>
<td>650mg</td>
<td>PO</td>
<td>Day 1</td>
<td>325mg tablet</td>
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<td>DIPHENHYDRAMINE</td>
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<td>PO</td>
<td>Day 1</td>
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<tr>
<td>RITUXIMAB</td>
<td>375mg/m²</td>
<td>IV</td>
<td>Day 1</td>
<td>Round to nearest 1mg</td>
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</tbody>
</table>

- **First Infusion**
  - Infuse IV at 50mg/hr, then increase by increments of 50mg/hr every 30 minutes as tolerated, to a final rate of 400mg/hr for the first dose.

- **Subsequent Infusions**
  - Subsequent infusion may be initiated at 100mg/hr and increased by increments of 100mg/hr every 30 minutes to a maximum rate of 400mg/hr, as tolerated by the patient.
  - Take complete vital signs prior to and after treatment.
  - Observe for 30-60 minutes after infusion. **DO NOT ADMINISTER AS IV PUSH OR BOLUS.**
  - Caution using Rituximab with bulky disease (10cm diameter) or circulating lymphoma cells (>50x10⁹/L).

**TESTS:**

- Baseline Tests: WBC HB PLT ANC Ca Glucose Cr T.Bili ALT AlkPhosphatase
- Every 2 Months: WBC HB PLT ANC Ca Cr T.Bili Albumin ALT AlkPhosphatase
- With Each Treatment: WBC HB PLT ANC
- **Test Notes:**
  - Additional Baseline tests: Protein electrophoresis and direct antiglobulin test (Coombs test).
  - Every 2 months: add protein electrophoresis.

**ANTIEMETIC PRE-CHEMO REGIMEN:**

- **Level A Chlorambucil treatment days**
  - Prochlorperazine 10mg PO prn

**ANTIEMETIC TAKE-HOME REGIMEN:**

- **Level A Chlorambucil treatment days**
  - Prochlorperazine 10mg PO q4-6h prn

**PATIENT VISITS and APPOINTMENT TYPE:**

- **Type H**

**TOXICITIES:**

**Hematologic**

1. If ANC < 1.0 x 10⁹/L, or if PLT < 75 x 10⁹/L, **DELAY** therapy 1 week.
2. Dose attenuations may be over-ridden if cytopenias presumed to be due to underlying disease.

**Hepatic Dysfunction**

1. Consider dose reduction if LFTs elevated (eg. T.Bili or AST).

**SUGGESTED ACTION**

**CLINICAL MONITORING:**

- Clinical pulmonary exam, including auscultation, pulmonary toxicity ratings (Cough, SOB).

**Dyspnea**

- Dyspnea on exertion, but can walk 1 flight of stairs without stopping 2. Dyspnea on exertion but unable to walk 1 flight of stairs or 1 city block (0.1km) without stopping 3. Dyspnea with ADL 4. Dyspnea at rest; intubation/ventilator indicated 5. Death

**RATED AT EACH CLINIC VISIT**

**Rituximab:**

- Close observation for infusion related symptoms including: fever, chills, pain, asthenia and other flu-like symptoms.
- If treatment is well tolerated during loading dose and early maintenance doses, observation time may be reduced.
- Clinical cardiac monitoring for all patients with cardiac risk factors or previous cardiac conditions (eg. arrhythmia, angina). Observe for symptoms of hypersensitivity including: hypotension, bronchospasm and angioedema.

**Fatal Cytokine Release Syndrome** has been reported. It usually occurs within 1-2 hours of initiating the first infusion. Initially, it is characterized by severe dyspnea (often with bronchospasm and hypoxia) in addition to fever, chills, rigors, urticaria and angioedema. There may be features of tumor lysis syndrome and pulmonary infiltration.

**Aggressive symptomatic treatment is required.**

**Rituximab is possibly associated with Hepatitis B reactivation.** All patients should be tested for HBsAg and HBeAb. If either test is positive, such patients should be treated with Lamivudine 100mg/day orally, for the entire duration of chemotherapy and for two months afterwards. Such patients should be monitored with frequent liver tests and hepatitis B virus DNA (at least every two months) up to one year following Rituximab therapy.
Hematological

CHLORAMBUCIL-(RITUXIMAB) Chemotherapy

**HYPERSENSITIVITY:**
- Rituximab can cause allergic type reaction during infusion.
- If an allergic reaction occurs, stop infusion and the physician in charge should determine a safe time and rate to resume infusion. After recovery of symptoms, restart Rituximab infusion one infusion rate below the rate at which the reaction occurred and continue with escalation of infusion rates on the appropriate schedule.

**Hypersensitivity**
0. None  1. Transient rash; fever < 38°C  2. Urticaria; fever > 38°C  3. Serum sickness; bronchospasm, requires parenteral medications  4. Anaphylaxis

**REFERENCES:**

Date revised: 10/08/2008
CYCLOPHOSPHAMIDE-DOXORUBICIN-VINCRISTINE- 
PREDNISONE Chemotherapy

Non-Hodgkin’s Lymphoma - Standard first-line Therapy

CYCLOPHOSPHAMIDE  750mg/m²  IV  Day 1  Round to nearest 10mg
- Mix in 250mL bag Normal Saline; Infuse over 10-20 minutes.
- Cap BSA at 2.2m²

DOXORUBICIN  50mg/m²  IV  Day 1  Round to nearest 1mg
- Slow push through sidearm of free flowing IV; Give 2 to 4mg (1-2mL) per minute.
- Cap BSA at 2.2m²

VINCRISTINE  1.4mg/m²  IV  Day 1  Round to nearest 0.1mg
- Maximum dose = 2mg
- Mix in 50mL bag Normal Saline; Infuse over 10 minutes.

PREDNISONE  75-150mg PO  Days 1-5  50mg tablet
- Daily for 5 days.
- If patient greater than 60 years old, decrease Prednisone dose to 75mg per day.
- Outpatient prescription.

REPEAT EVERY 21 DAYS  For a Usual 6 to 8 cycles

TESTS:
Baseline Tests  WBC  HB  PLT  ANC  Ca  Glucose  Cr  T.Bili  ALT  AlkPhosphatase
Day 1  WBC  HB  PLT  ANC  Cr  T.Bili  ALT  AlkPhosphatase
Test Notes  - Additional Baseline tests: Protein electrophoresis and direct antiglobulin test (Coombs test).

ANTIEMETIC PRE-CHEMO REGIMEN:
Level C  Day 1  - Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
- Dexamethasone 20mg PO/IV

ANTIEMETIC TAKE-HOME REGIMEN:
Level B/C  Day 1  - Ondansetron 8mg PO BID for 2-3 days, or Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days
- Prochlorperazine 10mg PO q4-6h prn

PATIENT VISITS and APPOINTMENT TYPE:
⇒ Day 1  2hrs  Type D

ANCILLARY:
- Oral hydration is strongly encouraged; poorly hydrated patients may need more IV hydration.

TOXICITIES:
Hematologic
1. If ANC < 1.0 x 10⁹/L, DELAY therapy 1 week and give G-CSF with next cycle.
2. If PLT < 75 x 10⁹/L, DELAY therapy 1 week.
- Dose attenuations may be over-ridden if cytopenias presumed to be due to underlying disease.

Renal Failure
1. If SrCr > 265umol/L, REDUCE Doxorubicin to 50% dose.
2. If CrCl < 0.2mL/sec, OMIT Cyclophosphamide dose.

Hepatic Dysfunction
1. If T.Bili = 26-51umol/L, or AST = 60-180 IU/L, REDUCE Doxorubicin to 75% dose and Vincristine to 50% dose.
2. If T.Bili = 52-85umol/L, or AST > 180 IU/L, REDUCE Doxorubicin to 50% dose and Vincristine to 25% dose.
3. If T.Bili > 85umol/L, OMIT ALL drugs.

Neurologic
1. If peripheral neuropathy > 2, OMIT Vincristine.

SUGGESTED ACTION
CLINICAL MONITORING:
- Urinalysis (RBCs) & Cysitis toxicity ratings - only in response to patient complaint.
- Periodic cardiac tests for all patients with cardiac risk factors and patients at or above the threshold dose levels Doxorubicin 450mg/m².
- Neurologic toxicity ratings (Sensory, Constipation) at each visit.

Sensory
1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function 2.
2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL 3. Sensory alteration or paresthesia interfering with ADL 4. Disabling 5. Death

Constipation
1. Occasional or intermittent symptoms; occasional use of stool softeners, laxatives, dietary modification, or enema
2. Persistent symptoms with regular use of laxatives or enemas indicated 3. Symptoms interfering with ADL; obstipation with manual evacuation indicated 4. Life-threatening consequences (e.g., obstruction, toxic megacolon)
5. Death

RATED AT EACH CLINIC VISIT

REFERENCES:

Date revised: 10/08/2008
**HE - CHOP (FRENCH)**

**Hematological**

**CYCLOPHOSPHAMIDE-DOXORUBICIN-VINCRISTINE-PREDNISONE Chemotherapy**

**Chronic Lymphocytic Leukemia**

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<th>CYCLOPHOSPHAMIDE</th>
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<th>PO</th>
<th>Days 1-5</th>
<th>25mg &amp; 50mg tablets</th>
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<tr>
<td><strong>DOXORUBICIN</strong></td>
<td>25mg/m²</td>
<td>IV</td>
<td>Day 1</td>
<td>Round to nearest 1mg</td>
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<tr>
<td><strong>VINCRISTINE</strong></td>
<td>1.0mg/m²</td>
<td>IV</td>
<td>Day 1</td>
<td>Round to nearest 0.1mg</td>
</tr>
<tr>
<td><strong>PREDNISONE</strong></td>
<td>75-150mg</td>
<td>PO</td>
<td>Days 1-5</td>
<td>50mg tablet</td>
</tr>
</tbody>
</table>

**TESTS:**

- **Baseline Tests:**
  - WBC HB PLT ANC Ca Glucose Cr T.Bili ALT AlkPhosphatase
- **Day 1:**
  - WBC HB PLT ANC Ca Cr T.Bili ALT AlkPhosphatase

**Test Notes:**
- Additional Baseline tests: Protein electrophoresis and direct antiglobulin test (Coombs test).

**ANTIEMETIC PRE-CHEMO REGIMEN:**

**Level C**
- Day 1
  - Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
  - Dexamethasone 20mg PO/IV

**ANTIEMETIC TAKE-HOME REGIMEN:**

**Level B/C**
- Day 1
  - Ondansetron 8mg PO BID for 2-3 days, or Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days
  - Prochlorperazine 10mg PO q4-6h pm

**PATIENT VISITS and APPOINTMENT TYPE:**

- **Day 1**: 30min Type B

**ANCILLARY:**
- Oral hydration is strongly encouraged; Poorly hydrated patients may need more IV hydration.

**TOXICITIES:**

**Hematologic**
1. If ANC < 1.0 x 10⁹/L, DELAY therapy 1 week and give G-CSF with next cycle.
2. If PLT < 75 x 10⁹/L, DELAY therapy 1 week.
- Dose attenuations may be over-riden if cytopenias presumed to be due to underlying disease.

**Renal Failure**
1. If SrCr > 265umol/L, REDUCE Doxorubicin to 50% dose.
2. If CrCl < 0.2mL/sec, OMIT Cyclophosphamide dose.

**Hepatic Dysfunction**
1. If T.Bili = 52-85umol/L, or AST > 180 IU/L, REDUCE Doxorubicin to 75% dose and Vincristine to 50% dose.
2. If T.Bili = 26-51umol/L, or AST > 180 IU/L, REDUCE Doxorubicin to 50% dose and Vincristine to 25% dose.
3. If T.Bili > 85umol/L, OMIT ALL drugs.

**Neurologic**
1. If peripheral neuropathy > 2, OMIT Vincristine.

**SUGGESTED ACTION**

**CLINICAL MONITORING:**
- Urinalysis (RBCs) & Cystitis toxicity ratings - only in response to patient complaint.
- Periodic cardiac tests for all patients with cardiac risk factors and patients at or above the threshold dose levels (Doxorubicin 450mg/m²).
- Neurologic toxicity ratings (Sensory, Constipation) at each visit.

**Sensory**
1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function
2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL
3. Sensory alteration or paresthesia interfering with ADL
4. Disabling
5. Death

**Constipation**
1. Occasional or intermittent symptoms; occasional use of stool softeners, laxatives, dietary modification, or enema
2. Persistent symptoms with regular use of laxatives or enemas indicated
3. Symptoms interfering with ADL; obstipation with manual evacuation indicated
4. Life-threatening consequences (e.g., obstruction, toxic megacolon)
5. Death

**RATED AT EACH CLINIC VISIT**

**REFERENCES:**

**Date revised:** 10/08/2008

**HE**
HEMATOLOGICAL CYCLOPHOSPHAMIDE-DOXORUBICIN-VINCRISTINE-
PREDNISONE Chemotherapy (Inpatient Regimen)

Non Hodgkin’s Lymphoma

CYCLOPHOSPHAMIDE 750mg/m² IV Day 1 Round to nearest 10mg
- Mix in 250mL bag Normal Saline (0.45% Sodium Chloride, 5% Dextrose). Infuse over 1 hour.
- Cap BSA at 2.2m²

DOXORUBICIN 50mg/m² IV Day 1 Round to nearest 1mg
- Slow push through sidearm of free flowing IV at rate 2-4mg (1-2mL) per minute. Cap BSA at 2.2m²
- Doses ≤ 100mg may be mixed in 50mL minibag 5% Dextrose, doses > 100mg may be mixed in 100mL minibag 5% Dextrose and infuse through central venous access device.

VINCRISTINE 1.4mg/m² IV Day 1
- Mix in 50mL bag Normal Saline; infuse over 10 minutes.
- Maximum dose = 2mg.

PREDNISONE 75-150mg PO Day 1 to 5
- Daily for 5 days.
- If patient greater than 60 years old, decrease Prednisone dose to 75mg per day. May be given tid.

REPEAT EVERY 21 DAYS For a Usual 6 to 8 cycles

HYDRATION:
Pre
- IV Normal Saline at 125mL/hr

TESTS:
Baseline Tests WBC HB PLT ANC Ca K Glucose Cr T.Bili AST Urate
Test Notes - Baseline CBC, Cr, glucose, calcium, LFTs, protein electrophoresis, direct antiglobulin test (Coombs test).
- Clinical exam for symptoms of CHF, LVEF for all patients with cardiac risk factors or patients at or above the threshold dose levels.

ANTIEMETIC PRE-CHEMO REGIMEN:
Level C Day 1 - Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
- Dexamethasone 20mg PO/IV

INPATIENT ANTIEMETICS:
- Ondansetron can be substituted with Granisetron 1mg PO/IV

TOXICITIES:
Hematologic
1. If ANC < 1.0 x 10⁹/L, DELAY therapy 1 week and give G-CSF with next cycle.
2. If PLT < 75 x 10⁹/L, DELAY therapy 1 week.
- Dose attenuations may be over-ridden if cytopenias presumed to be due to underlying disease.

Renal Failure
1. If SrCr > 265umol/L, REDUCE Doxorubicin to 50% dose.
2. If CrCl < 0.2mL/sec, OMIT Cyclophosphamide dose.

Hepatic Dysfunction
1. If T.Bili = 26-51umol/L, or AST = 60-180 IU/L, REDUCE Doxorubicin to 75% dose, and Vincristine to 50% dose.
2. If T.Bili = 52-85umol/L, or AST > 180 IU/L, REDUCE Doxorubicin to 50% dose and Vincristine to 25% dose.
3. If T.Bili > 85umol/L, OMIT ALL drugs.

Neurologic
1. If peripheral neuropathy > 2, OMIT Vincristine.

SUGGESTED ACTION
CLINICAL MONITORING:
- Urinalysis (RBCs) & Cystitis toxicity ratings - only in response to patient complaint.
- Periodic cardiac tests for all patients with cardiac risk factors and patients at or above the threshold dose levels (Doxorubicin 450mg/m²).
- Neurologic toxicity ratings (Sensory, Constipation) at each visit.

Sensory
1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function 2.
2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL 3.
3. Sensory alteration or paresthesia interfering with ADL 4.
4. Disabling 5.

Constipation
1. Occasional or intermittent symptoms; occasional use of stool softeners, laxatives, dietary modification, or enema
2. Persistent symptoms with regular use of laxatives or enemas indicated 3.
4. Life-threatening consequences (e.g., obstruction, toxic megacolon)
5. Death

REFERENCES:

CCO Eligibility Form Required ☑ | Non-Formulary Form Required ☑ Date revised: 10/08/2008
**CYCLOPHOSPHAMIDE-DOXORUBICIN-VINCRISTINE-PREDNISONE-RITUXIMAB Chemotherapy**

*Non-Hodgkin’s Lymphoma- Standard first-line Therapy*

**CYCLOPHOSPHAMIDE**  750mg/m² IV Day 1 Round to nearest 10mg
- Mix in 250mL bag **Normal Saline**; Infuse over 10-20 minutes.
- Cap BSA at 2.2m²

**DOXORUBICIN**  50mg/m² IV Day 1 Round to nearest 1mg
- Slow push through sidearm of free flowing IV; Give 2 to 4mg (1-2mL) per minute.
- Cap BSA at 2.2m²

**VINCRISTINE**  1.4mg/m² IV Day 1 Round to nearest 0.1mg
- Maximum dose = 2mg
- Mix in 50mL bag **Normal Saline**; infuse over 10 minutes.

**PREDNISONE**  75-150mg PO Days 1-5 50mg tablet
- Daily for 5 days starting the morning of Day 1 of CHOP-Rituximab treatment.
- If patient greater than 60 years old, decrease Prednisone dose to 75mg per day.
- Outpatient prescription.

**ACETAMINOPHEN**  650mg PO Day 1 325mg tablet
- Administer 30 minutes before Rituximab infusion.

**DIPHENHYDRAMINE**  50mg PO Day 1 50mg capsule
- Administer 30 minutes before Rituximab infusion.

**RITUXIMAB**  375mg/m² IV Day 1 Round to nearest 1mg
- Add to CHOP regimen provided eligibility criteria are met.
- Mix in **Normal Saline** or 5% Dextrose to a final concentration 1-4mg/mL (concentration used at JCC is 2mg/mL).

First infusion
- Infuse IV at 50mg/hr, after 60 minutes increase rate by increments of 50mg/hr every 30 minutes as tolerated, to a final rate 400mg/hr for the first dose.

Subsequent infusions
- Subsequent infusion may be initiated at 100mg/hr and increased by increments of 100mg/hr every 30 minutes to a maximum rate of 400mg/hr, as tolerated by the patient.
- For eligible patients * Rituximab may be given as a Rapid infusion:
  - Mix Rituximab in 250mL (or 500mL) Normal Saline; infuse 75mL (or 100mL of 500mL bag) over 30 minutes, then infuse the remaining volume over 60 minutes.
  - Take complete vital signs prior to and after treatment.
  - Observe for 30-60 minutes after infusion. **DO NOT ADMINISTER AS IV PUSH OR BOLUS**
  - Caution using Rituximab with bulky disease (10cm diameter) or circulating lymphoma cells (> 50 x 10⁹/L).
  - * Eligible patients show no reaction with first infusion.

**TESTS:**

<table>
<thead>
<tr>
<th>Baseline Tests</th>
<th>WBC HB PLT ANC Ca Glucose Cr T.Bili ALT AlkPhosphatase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1</td>
<td>WBC HB PLT ANC Cr T.Bili ALT AlkPhosphatase</td>
</tr>
</tbody>
</table>

**ANTIEMETIC PRE-CHEMO REGIMEN:**

<table>
<thead>
<tr>
<th>Level C Day 1</th>
<th>Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Dexamethasone 20mg PO/IV</td>
</tr>
</tbody>
</table>

**ANTIEMETIC TAKE-HOME REGIMEN:**

<table>
<thead>
<tr>
<th>Level B/C Day 1</th>
<th>Ondansetron 8mg PO BID for 2-3 days, or Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Prochlorperazine 10mg PO q4-6h pm</td>
</tr>
</tbody>
</table>

**PATIENT VISITS and APPOINTMENT TYPE:**

- **Day 1 (90 minute infusion)** 5hrs  Type F
- or Day 1 (6-8h if reaction to Rituximab) 6-8hrs  Type J

**ANCILLARY:**
- Oral hydration is strongly encouraged; poorly hydrated patients may need more IV hydration.

**TOXICITIES:**

**Hematologic**
1. If ANC < 1.0 x 10⁹/L, DELAY therapy 1 week and give G-CSF with next cycle.
2. If PLT < 75 x 10⁹/L, DELAY therapy 1 week.
- Dose attenuations may be over-ridden if cytopenias presumed to be due to underlying disease.

**Renal Failure**
1. If SrCr > 265umol/L, REDUCE Doxorubicin to 50% dose.
2. If CrCl < 0.2mL/sec, OMIT Cyclophosphamide dose.
**HEMOPHILIC RENAL DISEASE**

**HEPATIC DYSFUNCTION**

1. If T.Bili = 26-51umol/L, or AST = 60-180 IU/L, **REDUCE** Doxorubicin to 75% dose and Vincristine to 50% dose.
2. If T.Bili = 52-85umol/L, or AST > 180 IU/L, **REDUCE** Doxorubicin to 50% dose and Vincristine to 25% dose.
3. If T.Bili > 85umol/L, **OMIT** ALL drugs.

**NEUROLOGIC**

1. If peripheral neuropathy > 2, **OMIT** Vincristine.

**SUGGESTED ACTION**

**REFERENCES:**

- **HYPERSENSITIVITY:**

  - **Fatal Cytokine Release Syndrome** has been reported. It usually occurs within 1-2 hours of initiating the first infusion. Initially, it is characterized by severe dyspnea (often with bronchospasm and hypoxia) in addition to fever, chills, rigors, urticaria and angioedema. There may be features of tumor lysis syndrome and pulmonary infiltration. Aggressive symptomatic treatment is required.

  - **Rituximab** can cause allergic type reaction during infusion. If an allergic reaction occurs, stop infusion and the physician in charge should determine a safe time and rate to resume infusion. After recovery of symptoms, restart rituximab infusion one infusion rate below the rate at which the reaction occurred and continue with escalation of infusion rates on the appropriate schedule.

  - Hypersensitivity

    0. None
    1. Transient rash; fever < 38°C
    2. Urticaria; fever > 38°C
    3. Serum sickness; bronchospasm, requires parenteral medications
    4. Anaphylaxis

**CLINICAL MONITORING:**

- Urinalysis (RBCs) & Cystitis toxicity ratings - only in response to patient complaint.
- Periodic cardiac tests for all patients with cardiac risk factors and patients at or above the threshold dose levels Doxorubicin 450mg/m².
- Neurologic toxicity ratings (Sensory, Constipation) at each visit.

**Sensory**

1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function 2.

2. Persistent symptoms with regular use of laxatives or enemas indicated

3. Symptoms interfering with ADL: obstipation with manual evacuation indicated

4. Life-threatening consequences (e.g., obstruction, toxic megacolon)

5. Death

RATED AT EACH CLINIC VISIT

**Rituximab:**

- Close observation for infusion related symptoms including: fever, chills, pain, asthenia and other flu-like symptoms. If treatment is well tolerated during loading dose and early maintenance doses, observation time may be reduced.
- Clinical cardiac monitoring for all patients with cardiac risk factors or previous cardiac conditions (eg. arrhythmia, angina). Observe for symptoms of hypersensitivity including: hypotension, bronchospasm and angioedema.
- Rituximab is contraindicated in patients with known anaphylactic reaction to murine protein.

**URINALYSIS (RBCs) & CYSTITIS TOXICITY RATINGS:**

- Only in response to patient complaint.

**REFERENCES:**


**Constipation:**

- Occasional or intermittent symptoms; occasional use of stool softeners, laxatives, dietary modification, or enema

- Persistent symptoms with regular use of laxatives or enemas indicated

- Symptoms interfering with ADL: obstipation with manual evacuation indicated

- Life-threatening consequences (e.g., obstruction, toxic megacolon)

- Death

RATED AT EACH CLINIC VISIT

**Rituximab infusion one infusion rate below the rate at which the reaction occurred and continue with escalation of infusion rates on the appropriate schedule.**

**REFERENCES:**


CCO Eligibility Form Required ✔ Non-Formulary Form Required  Date revised: 10/08/2008

**HEMOPHILIC RENAL DISEASE**

**HEPATIC DYSFUNCTION**

1. If T.Bili = 26-51umol/L, or AST = 60-180 IU/L, **REDUCE** Doxorubicin to 75% dose and Vincristine to 50% dose.
2. If T.Bili = 52-85umol/L, or AST > 180 IU/L, **REDUCE** Doxorubicin to 50% dose and Vincristine to 25% dose.
3. If T.Bili > 85umol/L, **OMIT** ALL drugs.

**NEUROLOGIC**

1. If peripheral neuropathies > 2, **OMIT** Vincristine.
**CLADRIBINE Chemotherapy**

**Hairy Cell Leukemia - Curative Intent**

**CLADRIBINE** 0.14mg/kg/day IV Days 1-5 Round to nearest 0.01mg

- Admix in 500mL Normal Saline, infuse over 2 hours daily for 5 days.
- Please complete blood bank form for irradiated products.

**SINGLE COURSE ONLY**

**TESTS:**

<table>
<thead>
<tr>
<th>Baseline Tests</th>
<th>WBC HB PLT ANC Ca K Na Chloride Phosphate Mg Glucose Cr Urea T.Bili Albumin ALT AlkPhosphatase Urate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1</td>
<td>WBC HB PLT ANC Ca Cr Urea T.Bili Albumin ALT AlkPhosphatase Urate</td>
</tr>
</tbody>
</table>

**ANTIEMETIC TAKE-HOME REGIMEN:**

**Level A**  
Days 1-5 - Prochlorperazine 10mg PO q4-6h prn

**PATIENT VISITS and APPOINTMENT TYPE:**

- **Days 1-5**  
  2.25hrs Type C

**ANCILLARY:**

**Hepatitis B Reactivation:** All lymphoma patients should be tested for both HBsAg and HBcoreAb. If either test is positive, such patients should be treated with Lamivudine 100 mg/day orally, for the entire duration of chemotherapy and for six months afterwards. Such patients should also be monitored with frequent liver function tests and hepatitis B virus DNA at least every two months. If the hepatitis B virus DNA level rises during this monitoring, management should be reviewed with a hepatologist and consideration given to halting chemotherapy.

**TOXICITIES:**

**Hematologic**  
- No limitations to treatment.

**Renal Failure**  
- Creatinine clearance should be measured for all patients with a serum creatinine above normal and all patients greater than 60 years of age. Adjust dosing as needed:
  1. If CrCl = 30-70mL/min, REDUCE to 60% dose for 3 days only.
  2. If CrCl < 30mL/min, NO treatment.

**SUGGESTED ACTION**

**CLINICAL MONITORING:**

- Febrile episodes are common in hairy cell leukemia patients, but may not be a side effect of Cladribine.
- Infections are common in patients receiving Cladribine.

**FORMULAE:**

- Male: \[
\text{CrCl} = \frac{(140-\text{age(yrs)}) \times \text{TBW(Kg)}}{\left(\frac{50 \times \text{SCr(umol/L)}}{\text{TBW(Kg)}}\right)}
\]

- Female: \[
\text{CrCl} = \frac{(140-\text{age(yrs)}) \times \text{TBW(Kg)}}{\left(\frac{50 \times \text{SCr(umol/L)}}{\text{TBW(Kg)}}\right) \times 0.85}
\]

**REFERENCES:**


**Date revised: 10/08/2008**
**C-MOPP Chemotherapy**

Hodgkin’s Lymphoma: Patient unable to receive anthracycline due to cardiac disease OR patient refractory to ABVD and unable to receive or refractory to autologous stem cell transplantation. Regimen chosen over MOPP because of unavailability of, OR patient intolerance to Mechlorethamine.

### CYCLOPHOSPHAMIDE

650mg/m² IV Days 1 & 8
- Mix in 250mL bag Normal Saline; Infuse over 20 minutes.
- Cap BSA at 2.2m²

### VINCRIStINE

1.4mg/m² IV Days 1 & 8
- Mix in 50mL bag Normal Saline; infuse over 10 minutes.
- Maximum dose = 2mg

### PROCARBAZINE

100mg/m² PO Days 1-14
- Outpatient prescription.

### PREDNISONE

40mg/m² PO Days 1-14
- Outpatient prescription.

Repeat every 28 days for a usual total of 6-8 cycles

### Baseline Tests

<table>
<thead>
<tr>
<th>Test</th>
<th>WBC</th>
<th>HB</th>
<th>PLT</th>
<th>ANC</th>
<th>Ca</th>
<th>Glucose</th>
<th>Cr</th>
<th>T.Bili</th>
<th>ALT</th>
<th>AlkPhosphatase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 0</td>
<td>WBC</td>
<td>HB</td>
<td>PLT</td>
<td>ANC</td>
<td>Ca</td>
<td>Glucose</td>
<td>Cr</td>
<td>T.Bili</td>
<td>ALT</td>
<td>AlkPhosphatase</td>
</tr>
<tr>
<td>Day 1</td>
<td>WBC</td>
<td>HB</td>
<td>PLT</td>
<td>ANC</td>
<td>Ca</td>
<td>Glucose</td>
<td>Cr</td>
<td>T.Bili</td>
<td>ALT</td>
<td>AlkPhosphatase</td>
</tr>
</tbody>
</table>

**Test Notes:** Protein electrophoresis and direct antiglobulin test (Coombs test) to be added to Baseline testing.

### ANTIEMETIC PRE-CHEMO REGIMEN:

<table>
<thead>
<tr>
<th>Level</th>
<th>Days</th>
<th>Regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>C</td>
<td>1 &amp; 8</td>
<td>Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Dexamethasone: see Prednisone in regimen detail.</td>
</tr>
</tbody>
</table>

### ANTIEMETIC TAKE-HOME REGIMEN:

<table>
<thead>
<tr>
<th>Level</th>
<th>Days</th>
<th>Regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>B/C</td>
<td>1 &amp; 8</td>
<td>Ondansetron 8mg PO BID for 2-3 days, or Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Dexamethasone: see Prednisone in regimen detail.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Prochlorperazine 10mg PO q4-6h prn</td>
</tr>
</tbody>
</table>

### PATIENT VISITS and APPOINTMENT TYPE:

- Days 1 & 8 1hr Type B

### TOXICITIES:

#### Hematologic

**Day 1**
- If ANC < 1.0 x 10⁹/L, **DELAY** therapy 1 week and give G-CSF with next cycle.
- If PLT < 75 x 10⁹/L, **DELAY** therapy 1 week.

**Day 8**
- If AGC < 1.0 x 10⁹/L, **OMIT** therapy and consider G-CSF.
- If PLT < 50 x 10⁹/L, **OMIT** therapy.
- Dose attenuations may be over-ridden if cytopenias presumed to be due to underlying disease.

#### Renal Failure

- Consider dose reduction of Procarbazine if renal function is reduced (eg. reduced CrCl or SrCr).

#### Hepatic Dysfunction

- If T.Bili = 25-50umol/L, or AST = 60-180 IU/L, **REDUCE** Vincristine to 50% dose.
- If T.Bili > 50umol/L, or AST > 180 IU/L, **REDUCE** Vincristine to 25% dose.

#### Neurologic

- If peripheral neuropathy > 2, **OMIT** Vincristine (Days 1 & 8).
- SUGGESTED ACTION:
C-MOPP Chemotherapy

CLINICAL MONITORING:
- Periodic clinical pulmonary exam, including auscultation, pulmonary toxicity ratings (Cough, SOB).
- Neurologic toxicity ratings at each visit.
  
Sensory
1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function 2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL 3. Sensory alteration or paresthesia interfering with ADL 4. Disabling 5. Death

Constipation
1. Occasional or intermittent symptoms; occasional use of stool softeners, laxatives, dietary modification, or enema 2. Persistent symptoms with regular use of laxatives or enemas indicated 3. Symptoms interfering with ADL; obstipation with manual evacuation indicated 4. Life-threatening consequences (e.g., obstruction, toxic megacolon) 5. Death

Dyspnea
1. Dyspnea on exertion, but can walk 1 flight of stairs without stopping 2. Dyspnea on exertion but unable to walk 1 flight of stairs or 1 city block (0.1km) without stopping 3. Dyspnea with ADL 4. Dyspnea at rest; intubation/ventilator indicated 5. Death

Cough
1. Symptomatic, non-narcotic medication only indicated 2. Symptomatic and narcotic medication indicated 3. Symptomatic and significantly interfering with sleep or ADL

RATED AT EACH CLINIC VISIT

REFERENCES:

Date revised: 10/08/2008
HEMATOLOGICAL

CYCLOPHOSPHAMIDE PO or IV-VINCRISTINE-PREDNISONE-(RITUXIMAB) Chemotherapy

Non-Hodgkin’s Lymphoma; Patient unable to receive anthracycline due to cardiac disease OR salvage therapy with or without Rituximab, depending on histology

CYCLOPHOSPHAMIDE 300-450mg PO Days 1-5 25 & 50mg tablets
- If BSA is at least 1.6m², Cyclophosphamide dose = 450mg daily for 5 days.
- If BSA is less than 1.6m², Cyclophosphamide dose = 300mg daily for 5 days.
- Outpatient prescription.
OR
- If unable to tolerate PO Cyclophosphamide:
  Cyclophosphamide 750mg/m² IV on Day 1
  - Mix in 250mL bag Normal Saline; Infuse over 10-20 minutes.
VINCRISTINE 1.4mg/m² IV Day 1 Round to nearest 0.1mg
- Maximum dose of 2mg.
- Mix in 50mL bag Normal Saline; infuse over 10 minutes.
PREDNISONE 150mg PO Days 1-5 5mg & 50mg tablets
- Daily for 5 days starting the morning of Day 1 of CVP-Rituximab treatment.
- If patient greater than 60 years old, decrease Prednisone dose to 75mg per day.
- Outpatient prescription.
ACETAMINOPHEN 650mg PO Day 1 325mg tablet
- Administer 30 minutes before Rituximab infusion.
DIPHENHYDRAMINE 50mg PO Day 1 50mg capsule
- Administer 30 minutes before Rituximab infusion.
RITUXIMAB 375mg/m² IV Day 1 Round to nearest 1mg
- Add to CVP regimen provided eligibility criteria are met.
- Mix in Normal Saline or 5 % Dextrose to a final concentration 1-4 mg/mL (concentration used at JCC is 2mg/mL).
  First infusion
  - Infuse IV at 50mg/hr, after 60 minutes increase rate by increments of 50mg/hr every 30 minutes as tolerated, to a final rate 400mg/hr for the first dose.
  Subsequent infusions
  - Subsequent infusion may be initiated at 100mg/hr and increased by increments of 100mg/hr every 30 minutes to a maximum rate 400mg/hr as tolerated by the patient.
  - For eligible patients * Rituximab may be given as a Rapid infusion
  - Mix Rituximab in 250mL (or 500mL) Normal Saline; infuse 75mL (or 100mL of 500mL bag) over 30 minutes, then infuse the remaining volume over 60 minutes.
  - Take complete vital signs prior to and after treatment.
  - Observe for 30-60 minutes after infusion. DO NOT ADMINISTER AS IV PUSH OR BOLUS
  - Caution using Rituximab with bulky disease (10cm diameter) or circulating lymphoma cells (> 50 x 10⁹/L).
  * Eligible patients show no reaction with first infusion.
  REPEAT EVERY 21 DAYS for 6-8 cycles

TESTS:
Baseline Tests WBC HB PLT ANC Ca Glucose Cr T.Bili ALT AlkPhosphatase
Day 1 WBC HB PLT ANC Cr T.Bili ALT AlkPhosphatase

Test Notes - Additional Baseline tests: Protein electrophoresis and direct antiglobulin test (Coombs test).

ANTIEMETIC PRE-CHEMO REGIMEN:
Level A Days 1-5 - Prochlorperazine 10mg PO prn

ANTIEMETIC TAKE-HOME REGIMEN:
Level A Days 1-5 - Prochlorperazine 10mg PO q4-6h prn

PATIENT VISITS and APPOINTMENT TYPE:
  ➔ Day 1 (oral cyclo + 90 minute infusion) 3.25hrs Type C
  ➔ Day 1 (IV cyclo + 90 minute infusion) 3.75hrs Type D
  ➔ Day 1 (oral cyclo + 6-8 hour infusion) 6-8hrs Type H
  ➔ Day 1 (IV cyclo + 6-8 hour infusion) 6-8hrs Type J

TOXICITIES:
Hematologic
1. If ANC < 1.0 x 10⁹/L, DELAY therapy 1 week and consider G-CSF with next cycle.
2. If PLT < 75 x 10⁹/L, DELAY therapy 1 week.
- Dose attenuations may be over-ridden if cytopenias presumed to be due to underlying disease.
Hepatic Dysfunction
1. If T.Bili = 25-50umol/L, or AST = 60-180 IU/L, REDUCE Vincristine to 50% dose.
2. If T.Bili = 51-85umol/L, or AST > 180 IU/L, REDUCE Vincristine to 25% dose.
3. If T.Bili > 85umol/L, OMIT Vincristine.

Neurologic
1. If peripheral neuropathy > 2, OMIT Vincristine.

SUGGESTED ACTION

CLINICAL MONITORING:
- Urinalysis (RBCs) & Cystitis toxicity ratings - only in response to patient complaint.
- Neurologic toxicity ratings (Sensory, Constipation) at each visit.

Sensory
1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function.
2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL.
3. Sensory alteration or paresthesia interfering with ADL.
4. Disabling
5. Death

Constipation
1. Occasional or intermittent symptoms; occasional use of stool softeners, laxatives, dietary modification, or enema
2. Persistent symptoms with regular use of laxatives or enemas indicated
3. Symptoms interfering with ADL; obstipation with manual evacuation indicated
4. Life-threatening consequences (e.g., obstruction, toxic megacolon)
5. Death

RATED AT EACH CLINIC VISIT

Rituximab:
- Close observation for infusion related symptoms including: fever, chills, pain, asthenia and other flu-like symptoms.
- If treatment is well tolerated during loading dose and early maintenance doses, observation time may be reduced.
- Clinical cardiac monitoring for all patients with cardiac risk factors or previous cardiac conditions (e.g. arrhythmia, angina).
- Observe for symptoms of hypersensitivity including: hypotension, bronchospasm and angioedema.
- Rituximab is contraindicated in patients with known anaphylactic reaction to murine protein.
- Fatal Cytokine Release Syndrome has been reported. It usually occurs within 1-2 hours of initiating the first infusion. Initially, it is characterized by severe dyspnea (often with bronchospasm and hypoxia) in addition to fever, chills, rigors, urticaria and angioedema. There may be features of tumor lysis syndrome and pulmonary infiltration. Aggressive symptomatic treatment is required.
- Rituximab is possibly associated with Hepatitis B reactivation. All patients should be tested for HBsAg and HBeAb. If either test is positive, such patients should be treated with Lamivudine 100mg/day orally, for the entire duration of chemotherapy and for two months afterwards. Such patients should be monitored with frequent liver tests and hepatitis B virus DNA (at least every two months) up to one year following Rituximab therapy.

HYPERSENSITIVITY:
- Rituximab can cause allergic type reaction during infusion. If an allergic reaction occurs, stop infusion and the physician in charge should determine a safe time and rate to resume infusion. After recovery of symptoms, restart Rituximab infusion one infusion rate below the rate at which the reaction occurred and continue with escalation of infusion rates on the appropriate schedule.
- Allergic Reaction
  1. Transient flushing or rash; drug fever < 38 degrees C
  2. Rash; flushing; urticaria; dyspnea; drug fever > 38 degrees C
  3. Symptomatic bronchospasm, with or without urticaria; parenteral medication(s) indicated; allergy-related edema/angioedema; hypotension
  4. Anaphylaxis
  5. Death

RATED AT EACH CLINIC VISIT

INTERNAL CODE:
- CVP*IV (R)
- CVP*PO (R)

CCO Eligibility Form Required ☑ Non-Formulary Form Required □ Date revised: 10/08/2008
CYCLOPHOSPHAMIDE PO or IV-VINCRISTINE-PREDNISONE Chemotherapy

**Chronic Lymphocytic Leukemia**

**CYCLOPHOSPHAMIDE** 300-450mg PO Days 1-5 25 & 50mg tablets
- If BSA is at least 1.6m², Cyclophosphamide dose = 450mg daily for 5 days.
- If BSA is less than 1.6m², Cyclophosphamide dose = 300mg daily for 5 days.
- Outpatient prescription.
  OR
  - If unable to tolerate PO Cyclophosphamide:
    - Cyclophosphamide 750-800mg/m² IV on Day 1.
    - Mix in 250mL bag Normal Saline; infuse over 10-20 minutes.

**VINCRISTINE** 1.4mg/m² IV Day 1 Round to nearest 0.1mg
- Maximum dose of 2mg.
- Mix in 50mL bag Normal Saline; infuse over 10 minutes.

**PREDNISONE** 40mg/m² PO Days 1-5 5mg & 50mg tablets
- Daily for 5 days.
- Outpatient prescription.

**TESTS:**
- Baseline Tests WBC HB PLT ANC Ca Glucose Cr T.Bili ALT AlkPhosphatase
- Day 1 WBC HB PLT ANC Cr T.Bili ALT AlkPhosphatase
- Test Notes - Additional Baseline tests: Protein electrophoresis and direct antiglobulin test (Coombs test).

**ANTIEMETIC PRE-CHEMO REGIMEN:**
- Level C Day 1 - Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
- Dexamethasone 20mg PO/IV

**ANTIEMETIC TAKE-HOME REGIMEN:**
- Level B/C Days 4-5 - Ondansetron 8mg PO BID for 2-3 days, or Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days
- Dexamethasone 8mg PO BID for 2-3 days
- Prochlorperazine 10mg PO q4-6h prn

**PATIENT VISITS and APPOINTMENT TYPE:**
- Day 1- oral cyclo 15min Type A
- Day 1- IV cyclo 45min Type B

**ANCILLARY:**
- Oral hydration is strongly encouraged; poorly hydrated patients may need more IV hydration.

**TOXICITIES:**

**Hematologic**
1. If ANC < 1.0 x 10⁹/L, DELAY therapy 1 week and consider G-CSF with next cycle.
2. If PLT < 75 x 10⁹/L, DELAY therapy 1 week.
  - Dose attenuations may be over-ridden if cytopenias presumed to be due to underlying disease.

**Hepatic Dysfunction**
1. If T.Bili = 25-50umol/L, or AST = 60-180 IU/L, REDUCE Vincristine to 50% dose.
2. If T.Bili = 51-85umol/L, or AST > 180 IU/L, REDUCE Vincristine to 25% dose.
3. If T.Bili > 85umol/L, OMIT Vincristine.

**Neurologic**
1. If peripheral neuropathy > 2, OMIT Vincristine.

**SUGGESTED ACTION**

**CLINICAL MONITORING:**
- Urinalysis (RBCs) & Cystitis toxicity ratings - only in response to patient complaint.
- Neurologic toxicity ratings (Sensory, Constipation) at each visit.

**Sensory**
1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function 2.
2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL 3. Sensory alteration or paresthesia interfering with ADL 4. Disabling 5. Death

**Constipation**
1. Occasional or intermittent symptoms; occasional use of stool softeners, laxatives, dietary modification, or enema
2. Persistent symptoms with regular use of laxatives or enemas indicated
3. Symptoms interfering with ADL; obstipation with manual evacuation indicated
4. Life-threatening consequences (e.g., obstruction, toxic megacolon)
5. Death

**RATED AT EACH CLINIC VISIT**

**INTERNAL CODE:**
- CVP*IV
- CVP*PO

**REFERENCES:**

**Date revised: 10/08/2008**
CYCLOPHOSPHAMIDE*IV Chemotherapy
Multiple Myeloma- Palliative Intent

CYCLOPHOSPHAMIDE 750-1000mg flat dose IV Day 1 Round to nearest 10mg
- Mix in 250mL bag Normal Saline; Infuse over 10-20 minutes.

REPEAT EVERY 14 DAYS

TESTS:
Baseline Tests: WBC HB PLT ANC Ca K Na Chloride Phosphate Glucose Cr Urea T.Bili Albumin ALT AlkPhosphatase Urate

Day 1 WBC HB PLT ANC Ca Cr Urea T.Bili Albumin ALT AlkPhosphatase

ANTIEMETIC PRE-CHEMO REGIMEN:
Level C Day 1
- Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
- Dexamethasone 20mg PO/IV

ANTIEMETIC TAKE-HOME REGIMEN:
Level B/C Day 1
- Ondansetron 8mg PO BID for 2-3 days, or Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days
- Dexamethasone 8mg PO BID for 2-3 days
- Prochlorperazine 10mg PO q4-6h prn

PATIENT VISITS and APPOINTMENT TYPE:
- Day 1 45min Type A

ANCILLARY:
- Oral hydration is strongly encouraged; poorly hydrated patients may need more IV hydration.

CLINICAL MONITORING:
- Urinalysis (RBCs) & Cystitis toxicity ratings - only in response to patient complaint.

TOXICITIES:
Hematologic
1. If ANC < 1.0 x 10^9/L, or if PLT < 100 x 10^9/L, HOLD dose for 1 week.
SUGGESTED ACTION

CCO Eligibility Form Required ☐ Non-Formulary Form Required ☐ Date revised: 10/08/2008
CYCLOPHOSPHAMIDE*PO-PREDNISONE Chemotherapy

**Multiple Myeloma- Palliative Intent**

**CYCLOPHOSPHAMIDE**
- 200mg/m² PO Days 1-4
- 25mg & 50mg tablets
- Outpatient prescription.

**PREDNISONE**
- 100mg/day flat dose PO Days 1-4
- 50mg tablet
- Daily for 4 days.
- Outpatient prescription.

**REPEAT EVERY 28 DAYS**

**TESTS:**
- Baseline Tests: WBC HB PLT ANC Ca K Na Chloride Phosphate Glucose Cr Urea T.Bili Albumin AST ALT AlkPhosphatase Urate
- Day 1: WBC HB PLT ANC Ca Chloride Cr Urea T.Bili Albumin ALT AlkPhosphatase

**ANTIEMETIC PRE-CHEMO REGIMEN:**
- Level A: Days 1-14 - Prochlorperazine 10mg PO/IV prn

**ANTIEMETIC TAKE-HOME REGIMEN:**
- Level A: Days 1-14 - Prochlorperazine 10mg PO q4-6h prn

**TOXICITIES:**

**Hematologic**
1. If ANC < 1.0 x 10⁹/L, or if PLT < 100 x 10⁹/L, HOLD dose for 1 week.

**CLINICAL MONITORING:**
- Urinalysis (RBCs) and Cystitis toxicity ratings - only in response to patient complaint.

| CCO Eligibility Form Required | Non-Formulary Form Required | Date revised: 10/08/2008 |
CYCLOPHOSPHAMIDE*IV + PAMIDRONATE Chemotherapy

**Multile Myeloma - Palliative Intent**

**CYCLOPHOSPHAMIDE**

750-1000mg flat dose IV Day 1
- Mix in 250mL bag **Normal Saline**; Infuse over 10-20 minutes.
- Round to nearest 10mg

**PAMIDRONATE**

90mg IV Day 1

**FOR ALL DOSES**
- Admix into 250mL Intravenous LV50 pump (50mL/hr) and infuse over 5 hours at home for subsequent doses.
- **All first dose** patients are required to remain in the chemotherapy suite for 30 minutes after the start of the Pamidronate pump, in case of any potential reactions.
- Presently the Centre Pharmacy dispenses the premixed Pamidronate Intrameta prepared by Baxter.

**REPEAT EVERY 14 DAYS**

**TESTS:**

- **Baseline Tests**
  - WBC HB PLT ANC Ca K Na Chloride Phosphate Glucose Cr Urea T.Bili Albumin AST ALT AlkPhosphatase Urate
- **Day 1**
  - WBC HB PLT ANC Ca Cr Urea T.Bili Albumin ALT AlkPhosphatase

**ANTIEMETIC PRE-CHEMO REGIMEN:**

- **Level C**
  - Day 1 (Cyclo) - Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
  - Dexamethasone 20mg PO/IV

**ANTIEMETIC TAKE-HOME REGIMEN:**

- **Level B/C**
  - Day 1 (Cyclo) - Ondansetron 8mg PO BID for 2-3 days, or
  - Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days
  - Dexamethasone 8mg PO BID for 2-3 days
  - Prochlorperazine 10mg PO q4-6h pm

PATIENT VISITS and APPOINTMENT TYPE:

- Day 1 (first dose Pamidronate) 30 min Type B
- Day 1 subsequent doses 15 min Type B

**TOXICITIES:**

**Hematologic**

1. If ANC < 1.0 x 10⁹/L, or if PLT < 100 x 10⁹/L, **HOLD** Cyclophosphamide for 1 week.
2. If Corrected Serum Calcium < 2.10mmol/L, **HOLD** Pamidronate for 1 week, or until Serum Calcium levels within normal range.

**CLINICAL MONITORING:**

- Monitor serum electrolytes, including calcium.
- Urinalysis (RBCs) & Cystitis toxicity ratings - only in response to patient complaint.
- Creatinine should be monitored regularly.
- Consider a reduced initial dose or an infusion time of at least 4 hours in patients with pre-existing renal impairment (CrCl<30ml/min).
- Use is not recommended for the treatment of bone metastases in patients with severe renal impairment.

**FORMULAE:**

**Corrected Serum Calcium (mmol/L)**

\[
\text{Corrected Serum Calcium} = \frac{\text{Measured Serum Calcium} + [(40 - \text{serum albumin}) \times 0.02]}{1}
\]

**CrCl - Cockcroft & Gault (mL/sec)**

- Male: \(\frac{\text{[140-age(yrs)]} \times \text{TBW(Kg)}}{[50 \times \text{SCr(umol/L)}]}\)
- Female: \(\frac{\text{[140-age(yrs)]} \times \text{TBW(Kg)}}{[50 \times \text{SCr(umol/L)}]} \times 0.85\)

**INTERNAL CODE:**

OPIS CODE: CYCLO-PAMI

- CCO Eligibility Form Required ☑️
- Non-Formulary Form Required ☐

Date Revised: 10/08/2008
HE CYTAR/CONS

Hematological

CYTARABINE CONSOLIDATION >60 years

Acute Myeloid Leukemia

CYTARABINE

100mg/m²/day IV Days 1 to 5 Round to nearest 10mg

- Admix in Normal Saline to 240mL. Infuse over 5 days via Infusor LV2 pump (2mL/hr).
- Infusion through central venous access device (PICC) is recommended.

REPEAT EVERY 28 DAYS

TESTS:

Baseline Tests

| WBC | HB | PLT | ANC | Cr | Urea | T.Bili | AST | ALT |

Day 1

| WBC | HB | PLT | ANC |

Test Notes

- Baseline and periodic liver function tests (especially if poor performance status).
- Baseline and regular renal function including uric acid.
- Regular bone marrow assessments.
- Elevation in liver function test can cause hepatotoxicity, significant liver function abnormalities may require discontinuation of the drug.

ANTIEMETIC PRE-CHEMO REGIMEN:

Level A Day 1

- Prochlorperazine 10mg PO prn.
- NO DEXAMETHASONE WITH THIS REGIMEN

ANTIEMETIC TAKE-HOME REGIMEN:

Level A Day 1

- Prochlorperazine 10mg PO Q4-6H prn.

ANCILLARY:

- Hyperuricemia during periods of active cell lysis, which is caused by cytotoxic chemotherapy of highly proliferative tumours of massive burden (e.g., some leukemias and lymphomas), can be minimized with Allopurinol and hydration.

TOXICITIES:

Hematologic

1. If ANC < 1.0 x 10⁹ /L; PLT < 75 x 10⁹/L

- Parameters may be changed at the discretion of the clinician if cytopenias presumed to be due to underlying disease.

CLINICAL MONITORING:

- Fever may occur during the administration of Cytarabine in the absence of an infection. If fever occurs, the patient should be examined for a potential infectious source.

Nausea

1. Loss of appetite without alteration in eating habits
2. Oral intake decreased without significant weight loss, dehydration or malnutrition; IV fluids indicated < 24 hrs
3. Inadequate oral caloric or fluid intake; IV fluids, tube feedings, or TPN indicated ≥24 hrs
4. Life-threatening consequences
5. Death

Vomiting

1. 1 episode in 24 hrs
2. 2 - 5 episodes in 24 hrs; IV fluids indicated < 24 hrs
3. ≥6 episodes in 24 hrs; IV fluids, or TPN indicated ≥24 hrs
4. Life-threatening consequences
5. Death

Diarrhea

1. Increase of < 4 stools per day over baseline; mild increase in ostomy output compared to baseline
2. Increase of 4 - 6 stools per day over baseline; IV fluids indicated < 24hrs; moderate increase in ostomy output compared to baseline; not interfering with ADL
3. Increase of ≥ 7 stools per day over baseline; incontinence; IV fluids ≥ 24 hrs; hospitalization; severe increase in ostomy output compared to baseline; interfering with ADL
4. Life-threatening consequences (e.g., hemodynamic collapse)
5. Death

Mucositis

1. Erythema of the mucosa
2. Patchy ulcerations or pseudomembranes
3. Confluent ulcerations or pseudomembranes; bleeding with minor trauma
4. Tissue necrosis; significant spontaneous bleeding; life-threatening consequences
5. Death

RATED AT EACH CLINIC VISIT

INTERNAL CODE:

OPIS CODE: CYTAR/CONS>60

REFERENCES:

- Compendium of Pharmaceuticals and Specialties. 2007. Cytosar™
- Canadian Pharmacists Association.
- CCO Formulary, Cytarabine drug monograph. Revised 2006-2007

Date revised: 01/13/2009

Hematological
Hematological

**DASATINIB Therapy**

**Chronic Myeloid Leukemia - Palliative Intent**

**Chronic Phase** - 100mg po daily
**Accelerated Phase or Blast Crisis** - 140mg po daily

<table>
<thead>
<tr>
<th>DASATINIB</th>
<th>100-140mg</th>
<th>PO</th>
<th>Daily</th>
<th>20mg tablets</th>
</tr>
</thead>
</table>
- Treatment of adult patients with chronic, accelerated, or blast phase chronic myeloid leukemia (CML) with resistance or intolerance to prior therapy including Imatinib.
- Discontinue with disease progression or unacceptable toxicities.
- Use of antacid therapy (2 hrs pre or 2 hrs post Dasatinib) should be considered in place of H2-blockers or proton pump inhibitors.
- May be taken with or without food, avoid grapefruit juice/grapefruits.
- Take with water, avoid all other juices 2 hours before and 2 hours post Dasatinib.
- Exceptional Access Program (Section 16) with specific criteria
- Outpatient prescription available in 20mg, 50mg and 70mg tablets.
- Trade name= Sprycel™

**CONTINUOUS TREATMENT**

**TESTS:**

- **Baseline Tests**
  - WBC, HB, PLT, ANC, Ca, K, Na, Chloride, Phosphate, Mg, Cr, Urea, T.Bili, Albumin
  - AST, ALT, AlkPhosphatase, LVEF

- **Monthly**
  - WBC, HB, PLT, ANC, Ca, K, Na, Chloride, Phosphate, Mg, Cr, Urea, T.Bili, Albumin
  - AST, ALT

- **Weekly for first 2 months**
  - WBC, HB, PLT, ANC

**Test Notes**

- Periodic LVEF evaluation if patient has cardiac risk factors (consider for all patients)
- Periodic ECG during therapy, may prolong QT interval; caution in patients who have or may develop QT prolongation.
- Regular liver function tests and electrolytes (Ca, Ph, K, Mg)

**ANTIEMETIC TAKE-HOME REGIMEN:**

**Level A**
- Day 1 - Prochlorperazine 10mg PO q4-6h prn.

**ANCILLARY:**

- CYP3A4 substrate, avoid blood thinners, ASA and NSAIDS to reduce chance of bleeding.

**TOXICITIES:**

**Hematologic**

- Chronic Phase CML: (100mg daily)
  1. If ANC < 0.5 x 10⁹/L and/or PLT < 50 x 10⁹/L, HOLD Dasatinib until ANC > 1.0x10⁹/L and PLT > 50x10⁹/L.
  2. Resume treatment with Dasatinib at the original starting dose.
  3. If recurrence of ANC < 0.5 x 10⁹/L and/or PLT < 25 x 10⁹/L for > 7 days, repeat step 1 and resume Dasatinib at a reduced dose.

- Accelerated Phase CML and Blast Crisis: (140mg daily)
  1. If ANC < 0.5 x 10⁹/L and/or PLT < 10 x 10⁹/L check if cytopenia is leukemia related (marrow aspirate or biopsy)
  2. If unrelated, STOP Dasatinib and resume at original dose once ANC ≥ 1.0x10⁹/L and PLT ≥ 20x10⁹/L
  3. If recurrence of cytopenia, repeat step 1 and resume at reduced dose for second episode and further reduced dose for third episode.
  4. If leukemia related consider dose escalation

**SUGGESTED ACTION**

**Hepatic Dysfunction**

1. Not studied; hepatically metabolized/excreted significantly; consider dose reduction or interruption.

**SUGGESTED ACTION**

Hematological
**HE DASATINIB**

**Hematological**

**DASATINIB Therapy**

**CLINICAL MONITORING:**
- Toxicity assessment including fluid retention, neutropenia, thrombocytopenia, bleeding (gastrointestinal and cerebral hemorrhage)
- Weight assessment - monitor for fluid retention.

**Diarrhea**
1. Increase of < 4 stools per day over baseline; mild increase in ostomy output compared to baseline
2. Increase of 4 - 6 stools per day over baseline; IV fluids indicated < 24hrs; moderate increase in ostomy output compared to baseline; not interfering with ADL
3. Increase of ≥7 stools per day over baseline; incontinence; IV fluids >24 hrs; hospitalization; severe increase in ostomy output compared to baseline; interfering with ADL
4. Life-threatening consequences (e.g., hemodynamic collapse)
5. Death

**Nausea**
1. Loss of appetite without alteration in eating habits
2. Oral intake decreased without significant weight loss, dehydration or malnutrition; IV fluids indicated < 24 hrs
3. Inadequate oral caloric or fluid intake; IV fluids, tube feedings, or TPN indicated >24 hrs
4. Life-threatening consequences
5. Death

**Dyspnea**
1. Dyspnea on exertion, but can walk 1 flight of stairs without stopping
2. Dyspnea on exertion but unable to walk 1 flight of stairs or 1 city block
3. Dyspnea with ADL
4. Dyspnea at rest; intubation/ventilator indicated
5. Death

**Fatigue**
1. Mild fatigue over baseline
2. Moderate or causing difficulty performing some ADL
3. Severe fatigue interfering with ADL
4. Disabling

**Pleural effusion**
1. Asymptomatic
2. Symptomatic, intervention such as diuretics or up to 2 therapeutic thoracenteses indicated
3. Symptomatic and supplemental oxygen; >2 therapeutic thoracenteses, tube drainage, or pleurodesis indicated
4. Life-threatening (e.g., causing hemodynamic instability or ventilatory support indicated)
5. Death

**Fever**
1. 38.0 - 39.0°C (100.4 - 102.2°F)
2. >39.0 - 40.0°C (102.3 - 104.0°F)
3. >40.0°C (>104.0°F) for < 24 hours
4. >40.0°C (>104.0°F) for > 24 hours
5. Death

**INTERNAL CODE:**
- OPIS CODE: DASATINIB-HE

**REFERENCES:**
6. BCCA protocol summary for treatment of chronic myeloid leukemia (CML) using Dasatinib (SPRYCEL™)

**Date revised:** 01/16/2009
# DEXAMETHASONE*PO Therapy

**Multiple Myeloma**

**DEXAMETHASONE** 40mg/day PO Days 1-4 4mg tablet

- Daily for 4 days, with food.
- Outpatient prescription.

**TESTS:**

<table>
<thead>
<tr>
<th>Baseline Tests</th>
<th>WBC  HB  PLT  ANC  Ca  K  Na Chloride Phosphate Glucose Cr Urea T.Bili Albumin AST ALT AlkPhosphatase Urate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1</td>
<td>WBC  HB  PLT  ANC  Ca  Glucose Cr Urea T.Bili Albumin AST ALT AlkPhosphatase</td>
</tr>
</tbody>
</table>

**CLINICAL MONITORING:**

- Clinical exam for proximal muscle myopathy.

**Date revised:** 10/08/2008
HEMATOLOGICAL

CISPLATIN-CYTARABINE (High Dose)-DEXAMETHASONE
Chemotherapy (Inpatient Regimen)

Non-Hodgkin’s Lymphoma - Salvage therapy prior to autologus stem cell transplantation.

CISPLATIN
100 mg/m² IV D-1 Continuous infusion Round to nearest 1mg
- Capped BSA= 2.2m²
- Start Cisplatin six hours after Mannitol commenced. Mix Cisplatin in 500mL Normal Saline, infuse over 24 hours.

Repeat cycle every 28 days x 2 cycles

CYTARABINE
2000mg/m² IV D-2 q12h x 2 doses
- Capped BSA= 2.2m²
- Start Cytarabine infusion when Mannitol completed. Mix Cytarabine in 500mL 5% Dextrose and infuse over 3 hours, q12h two doses.

Repeat cycle every 28 days x 2 cycles

DEXAMETHASONE
2gtt OU OPH q6h
- Start 0.1% Dexamethasone eye drops - 2 drops in each eye q6h at least one hour prior to first dose of Cytarabine and continue for 24 h after last dose of Cytarabine.

DEXAMETHASONE
20mg IV D-1 to D-4 q12h
- Give Dexamethasone 20mg IV or PO x 8 doses beginning one hour before Cisplatin

HYDRATION:
Pre
- IV Normal Saline with 50 grams of Mannitol mixed to a volume of 1000mL. Run for 36 hours. Usual rate is 250mL/hr. Rate is to be assessed individually for each patient. (At MUMC run Mannitol 20% at 63ml/hr with Normal Saline at 187ml/hr to give a total rate of 250ml/hr as hydration is not prepeared by Pharmacy)

Post
- When Mannitol through, run IV Normal Saline at 125mL/hr.

TESTS:
Baseline Tests
WBC HB PLT ANC Ca K Na Chloride Phosphate Mg Glucose Cr Urea T.Bili Albunim ALT GGT AlkPhosphatase Urate

Test Notes
- Baseline protein electrophoresis, CBC, Cr, electrolytes, Glucose -daily; Alk.phos., Ca, Uric acid, Mg, T & conjugated bilirubin, Protein electrophoresis, INR PTT Q Monday and Thursday or at physician discretion.

ANTIEMETIC PRE-CHEMO REGIMEN:
Level C Days 1-3 Give Ondansetron pre-chemo and q8h, continue 24 hours after last chemo treatment.

INPATIENT ANTIEMETICS:
- Ondansetron can be substituted to Granisetron 1-2mg daily.

TOXICITIES:
Hematologic
1. If ANC < 1 x 10⁹/L or if PLT < 75 x 10⁹/L, DELAY therapy for 1 week,
2. Dose attenuations may be over-ridden if cytopenias presumed to be due to underlying disease.

Renal Failure
1. Cr Cl = 0.5-1ml/sec or SrCr = 136-185umo/L, REDUCE Cisplatin to 50 % dose.
2. CrCl < 0.5ml/sec or SrCr >185umo/L, OMIT Cisplatin dose (recommended action).

Pulmonary

Neurologic
1. Cerebellar and sensory toxicity monitoring prior each dose of Cytarabine and for the first few weeks after treatment.

CLINICAL MONITORING:
- Clinical toxicity assessment (including CNS toxicity, neurotoxicity, gastrointestinal, stomatitis, conjunctivitis, pulmonary toxicity and ototoxicity).
- Routine glucose test, CBC, renal function (including electrolytes, magnesium) test and urinalysis before each cycle.

FORMULAE:
CrCl - Cockcroft & Gault (mL/sec) Male: [140-age(yrs)] x TBW(Kg) / [50 x SCR(umo/L)]
CrCl - Cockcroft & Gault (mL/sec) Female: [140-age(yrs)] x TBW(Kg) / [50 x SCR(umo/L)] x 0.85

REFERENCES:

Date revised: 03/07/2005

CCO Eligibility Form Required ☐ Non-Formulary Form Required ☐
ETOPOSIDE

- 50-100mg
- PO
- Daily
- 50mg capsule
- Take on an empty stomach; may be taken with food if needed.
- Take with water; avoid grapefruit and grapefruit juice.
- Outpatient prescription available as 50mg capsules.
- Trade name: Vepesid™

REPEAT EVERY 14-21 DAYS

TESTS:

Baseline Tests
WBC  HB  PLT  ANC  Ca  K  Na  Chloride  Glucose  Cr  Urea  T.Bili  Albumin  AST  ALT  GGT  AlkPhosphatase

Day 1
WBC  HB  PLT  ANC  K  Na  Chloride  Cr  Urea  T.Bili  Albumin  AST  ALT  GGT  AlkPhosphatase

Test Notes:
- Monitor for hypotension; blood pressure at each clinic visit.
- Periodic renal and hepatic function tests.

ANTIEMETIC TAKE-HOME REGIMEN:

Level A
Day 1
- Prochlorperazine 10mg PO q4-6h prn

ANCILLARY:
- Etoposide is a major substrate of CYP3A4 levels may be reduced by CYP3A4 inducers and increased by CYP3A4 inhibitors.

TOXICITIES:

Hematologic
1. If ANC < 1.0 x 10^9/L, or PLT < 75 x 10^9/L, HOLD dose.

Hepatic Dysfunction
1. If T.Bili = 26-51umol/L, or AST = 60-180 IU/L, REDUCE Etoposide to 50% dose.
2. If T.Bili = 52-85umol/L, REDUCE Etoposide to 25% dose.
3. If T.Bili > 85umol/L, or AST > 180 IU/L, OMIT Etoposide.

- Minor alterations in liver function, such as transaminase elevations, do not require dose reductions if renal function is normal.

Renal Failure
1. If CrCl 10-50 mL/min, REDUCE to 75% of dose
2. If CrCl < 10 mL/min, REDUCE to 50% of dose

SUGGESTED ACTION

CLINICAL MONITORING:
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.

Nausea
1. Loss of appetite without alteration in eating habits 2. Oral intake decreased without significant weight loss, dehydration or malnutrition; IV fluids indicated < 24 hrs 3. Inadequate oral caloric or fluid intake; IV fluids, tube feedings, or TPN indicated > 24 hrs 4. Life-threatening consequences   5. Death

Vomiting
1. 1 episode in 24 hrs 2. 2 - 5 episodes in 24 hrs; IV fluids indicated < 24 hrs 3. >6 episodes in 24 hrs; IV fluids, or TPN indicated > 24 hrs 4. Life-threatening consequences   5. Death

Diarrhea
1. Increase of < 4 stools per day over baseline; mild increase in ostomy output compared to baseline
2. Increase of 4 - 6 stools per day over baseline; IV fluids indicated < 24hrs; moderate increase in ostomy output compared to baseline; not interfering with ADL 3. Increase of >7 stools per day over baseline; incontinence; IV fluids >24 hrs; hospitalization; severe increase in ostomy output compared to baseline; interfering with ADL 4. Life-threatening consequences (e.g., hemodynamic collapse)   5. Death

Mucositis
1. Erythema of the mucosa 2. Patchy ulcerations or pseudomembranes 3. Confluent ulcerations or pseudomembranes; bleeding with minor trauma 4. Tissue necrosis; significant spontaneous bleeding; life-threatening consequences   5. Death

RATED AT EACH CLINIC VISIT

INTERNAL CODE:
OPIS CODE: ETOP*PO HE

REFERENCES:
- Compendium of Pharmaceuticals and Specialties. 2004. Vepesid™
  Canadian Pharmacists Association.
**FLUDARABINE IV Chemotherapy**

*Chronic Lymphocytic Leukemia- Palliative Intent*

**FLUDARABINE** 25mg/m² IV Days 1-5 Round to nearest 2.5mg

- Mix in 50-100mL minibag **Normal Saline**: Infuse over 15-30 minutes.
- Please complete blood bank form for irradiated products.

**REPEAT EVERY 28 DAYS**

**TESTS:**
- Baseline Tests: WBC HB PLT ANC Ca K Na Chloride Phosphate Glucose Cr Urea T.Bili Albumin ALT AlkPhosphatase Urate
- Day 1: WBC HB PLT ANC Ca Cr Urea T.Bili Albumin ALT AlkPhosphatase

**ANTIEMETIC PRE-CHEMO REGIMEN:**
- Level A Days 1-5: Prochlorperazine 10mg PO pm

**ANTIEMETIC TAKE-HOME REGIMEN:**
- Level A Days 1-5: Prochlorperazine 10mg PO q4-6h pm

**PATIENT VISITS and APPOINTMENT TYPE:**
- Days 1-5: 30-45min Type B

**TOXICITIES:**

**Hematologic**
1. If ANC < 1.0 x 10⁹/L, or if PLT < 100 x 10⁹/L or PLT < baseline, **HOLD** dose for 1 week.

**CLINICAL MONITORING:**
- Watch for symptoms of fever and infection.
- Clinical pulmonary exam, including auscultation, pulmonary toxicity ratings (Cough, SOB).

**Dyspnea**
1. Dyspnea on exertion, but can walk 1 flight of stairs without stopping
2. Dyspnea on exertion but unable to walk 1 flight of stairs or 1 city block (0.1km) without stopping
3. Dyspnea with ADL
4. Dyspnea at rest; intubation/ventilator indicated
5. Death

**RATED AT EACH CLINIC VISIT**

**REFERENCES:**
- CCO Practice Guideline 6-1: Fludarabine in Intermediate- and High-Risk Chronic Lymphocytic Leukemia.

**Date revised:** 10/08/2008
FLUDARABINE Oral Chemotherapy
Chronic Lymphocytic Leukemia - Palliative Intent

FLUDARABINE
- Daily for 5 days.
- Outpatient prescription.
- Please complete blood bank form for irradiated products.

**TESTS:**
Baseline Tests: WBC HB PLT ANC Ca K Na Chloride Phosphate Glucose Cr Urea T.Bili Albumin ALT AlkPhosphatase Urate
Day 29: WBC HB PLT ANC Ca Cr Urea T.Bili Albumin ALT AlkPhosphatase

**ANTIEMETIC PRE-CHEMO REGIMEN:**
Level A Days 1-5
- Prochlorperazine 10mg PO prn

**TOXICITIES:**
Hematologic
1. If ANC < 1.0 x 10^9/L, or if PLT < 100 x 10^9/L, or PLT < baseline, HOLD dose for 1 week.

**REFERENCES:**
- CCO Practice Guideline 6-1: Fludarabine in Intermediate- and High-Risk Chronic Lymphocytic Leukemia.
FLUDARABINE- RITUXIMAB Chemotherapy
Non-Hodgkin’s Lymphoma

**FLUDARABINE**  
- 40mg/m² PO Days 1-5  
- 10mg tablet

**DIPHENHYDRAMINE**  
- 50mg PO Day 1  
- 50mg capsule

**ACETAMINOPHEN**  
- 650mg PO Day 1  
- 325mg tablet

**HYDROCORTISONE SODIUM SUCCINATE**  
- 100mg IV Day 1  
- Protect from light

**RITUXIMAB**  
- 375mg/m² IV Day 1  
- Round to nearest 1mg

**Tests:**
- Baseline CBC & diff., CR, T.bili, ALT, alkaline phosphatase, LDH, HBsAg, HBcAb (suggestion).
- Additional Baseline Tests: Protein electrophoresis and direct antiglobulin test (Coombs Test).

**Antiemetic Pre-Chemo Regimen:**
- Days 1-5  
- Prochlorperazine 10mg PO pm

**Antiemetic Take-Home Regimen:**
- Days 1-5  
- Prochlorperazine 10mg PO q4-6h pm

**Patient Visits and Appointment Type:**
- Day 1 (PO fludara + 90 minute infusion)  
  - 3hrs Type C
- Day 1 (IV fludara + 90 minute infusion)  
  - 3.5hrs Type D

**Toxicities:**
- Hematologic  
  1. If ANC < 1.0 x 10⁹/L, or if PLT < 75 x 10⁹/L or PLT < baseline, *HOLD* dose for 1 week.
- Renal Failure  
  1. If CrCl = 0.5-1.0mL/sec, *REDUCE* Fludarabine to 50% dose.
  2. If CrCl < 0.5mL/sec, *OMIT* Fludarabine dose.

**Suggested Action**

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HE-FLUDAR- RITUX HEM

**FLUDARABINE- RITUXIMAB Chemotherapy**

**HEMATOLOGICAL**

**FLUDARABINE**  
- 40mg/m² PO Days 1-5  
- 10mg tablet

**DIPHENHYDRAMINE**  
- 50mg PO Day 1  
- 50mg capsule

**ACETAMINOPHEN**  
- 650mg PO Day 1  
- 325mg tablet

**HYDROCORTISONE SODIUM SUCCINATE**  
- 100mg IV Day 1  
- Protect from light

**RITUXIMAB**  
- 375mg/m² IV Day 1  
- Round to nearest 1mg

**Tests:**
- Baseline CBC & diff., CR, T.bili, ALT, alkaline phosphatase, LDH, HBsAg, HBcAb (suggestion).
- Additional Baseline Tests: Protein electrophoresis and direct antiglobulin test (Coombs Test).

**Antiemetic Pre-Chemo Regimen:**
- Days 1-5  
- Prochlorperazine 10mg PO pm

**Antiemetic Take-Home Regimen:**
- Days 1-5  
- Prochlorperazine 10mg PO q4-6h pm

**Patient Visits and Appointment Type:**
- Day 1 (PO fludara + 90 minute infusion)  
  - 3hrs Type C
- Day 1 (IV fludara + 90 minute infusion)  
  - 3.5hrs Type D

**Toxicities:**
- Hematologic  
  1. If ANC < 1.0 x 10⁹/L, or if PLT < 75 x 10⁹/L or PLT < baseline, *HOLD* dose for 1 week.
- Renal Failure  
  1. If CrCl = 0.5-1.0mL/sec, *REDUCE* Fludarabine to 50% dose.
  2. If CrCl < 0.5mL/sec, *OMIT* Fludarabine dose.

**Suggested Action**
HEMATOLOGICAL

FLUDARABINE-RITUXIMAB Chemotherapy

CLINICAL MONITORING:
- Watch for symptoms of fever and infection.
- Clinical pulmonary exam, including auscultation, pulmonary toxicity ratings (Cough, SOB).
- Dyspnea (Shortness of Breath)
  1. Dyspnea on exertion, but can walk 1 flight of stairs without stopping
  2. Dyspnea on exertion but unable to walk 1 flight of stairs or 1 city block (0.1km) without stopping
  3. Dyspnea with ADL
  4. Dyspnea at rest;
  5. Death

SUGGESTED ACTION

Rituximab:
- Close observation for infusion related symptoms including: fever, chills, pain, asthenia and other flu-like symptoms.
- If treatment is well tolerated during loading dose and early maintenance doses, observation time may be reduced.
- Clinical cardiac monitoring for all patients with cardiac risk factors or previous cardiac conditions (eg. arrhythmia, angina). Observe for symptoms of hypersensitivity including: hypotension, bronchospasm and angioedema.
- Rituximab is contraindicated in patients with known anaphylactic reaction to murine protein.
- Fatal Cytokine Release Syndrome has been reported. It usually occurs within 1-2 hours of initiating the first infusion. Initially, it is characterized by severe dyspnea (often with bronchospasm and hypoxia) in addition to fever, chills, rigors, urticaria and angioedema. There may be features of tumor lysis syndrome and pulmonary infiltration. Aggressive symptomatic treatment is required.
- Rituximab is possibly associated with Hepatitis B reactivation. All patients should be tested for HBsAg and HBCAb. If either test is positive, such patients should be treated with Lamivudine 100mg/day orally, for the entire duration of chemotherapy and for two months afterwards. Such patients should be monitored with frequent liver tests and hepatitis B virus DNA (at least every two months) up to one year following Rituximab therapy.

HYPERSENSITIVITY:
- Rituximab can cause allergic type reaction during infusion. If an allergic reaction occurs, stop infusion and the physician in charge should determine a safe time and rate to resume infusion. After recovery of symptoms, restart Rituximab infusion one infusion rate below the rate at which the reaction occurred and continue with escalation of infusion rates on the appropriate schedule.
- Hypersensitivity
  1. Transient flushing or rash; drug fever < 38 degrees C
  2. Rash; flushing; urticaria; dyspnea; drug fever ≥ 38 degrees C
  3. Symptomatic bronchospasm, with or without urticaria; parenteral medication(s) indicated; allergy-related edema/angioedema; hypotension
  4. Anaphylaxis
  5. Death

INTERNAL CODE:
OPIS CODES:
- FLUDAR*IV-RITUX
- FLUDAR*PO-RITUX

REFERENCES:

Date revised: 03/10/2008
FLUDARABINE-CYCLOPHOSPHAMIDE Chemotherapy

Chronic Lymphocytic Leukemia - Palliative Intent

FLUDARABINE
25-30mg/m² IV Days 1-3 Round to nearest 2.5mg
- Mix in 50-100mL minibag Normal Saline; Infuse over 15-30 minutes.
OR
- Fludarabine 24mg/m² PO on Days 1-5.
- Outpatient prescription available in 10mg tablets.
- Take PO tablets 3-4 hours after Cyclophosphamide.
- Please complete blood bank form for irradiated products.

CYCLOPHOSPHAMIDE
250mg/m² IV Days 1-3 Round to nearest 10mg
- Cyclophosphamide 250mg/m² IV on Days 1-3.
- Mix in 250mL bag Normal Saline; Infuse over 10-20 minutes.
OR
- Cyclophosphamide 150mg/m² PO Days 1-5.
- Out-patient prescription available in 25mg & 50mg tablets.
- Wait 3-4 hours then take PO Fludarabine.

REPEAT EVERY 28 DAYS

TESTS:
Baseline Tests
Day 1
Test Notes

ANTIEMETIC PRE-CHEMO REGIMEN:
Level A
Days 1-3 (IV only) - Prochlorperazine 10mg PO prn

Level A
Days 1-5 (PO only) - Prochlorperazine 10mg PO prn

ANTIEMETIC TAKE-HOME REGIMEN:
Level A
Days 1-3 (IV only) - Prochlorperazine 10mg PO q4-6h prn

Level A
Days 1-5 (PO only) - Prochlorperazine 10mg PO q4-6h prn

PATIENT VISITS and APPOINTMENT TYPE:
Days 1-3 1 hr Type C

ANCILLARY:
- Oral hydration is strongly encouraged; poorly hydrated patients may need more IV hydration.

TOXICITIES:
Hematologic
1. If ANC < 1.0 x 10⁹/L, or if PLT < 75 x 10⁹/L or PLT < baseline, HOLD dose for 1 week.

Renal Failure
1. If CrCl = 0.5-1.0mL/sec, REDUCE Fludarabine to 50% dose.
2. If CrCl < 0.5mL/sec, OMIT Fludarabine dose.

SUGGESTED ACTION

CLINICAL MONITORING:
- Watch for symptoms of fever and infection.
- Clinical pulmonary exam, including auscultation, pulmonary toxicity ratings (Cough, SOB).
- Urinalysis (RBCs) & Cystitis toxicity ratings - only in response to patient complaint.

Dyspnea (Shortness of Breath)
1. Dyspnea on exertion, but can walk 1 flight of stairs without stopping 2. Dyspnea on exertion but unable to walk 1 flight of stairs or 1 city block (0.1km) without stopping 3. Dyspnea with ADL 4. Dyspnea at rest; intubation/ventilator indicated 5. Death

Cough
1. Symptomatic, non-narcotic medication only indicated 2. Symptomatic and narcotic medication indicated 3. Symptomatic and significantly interfering with sleep or ADL

SUGGESTED ACTION

INTERNAL CODE:
OPIS CODES:
- FLUDAR-CYCLO*IV
- FLUDAR-CYCLO*PO

REFERENCES:
- CCO Practice Guideline 6-1: Fludarabine in Intermediate- and High-Risk Chronic Lymphocytic Leukemia.
- D Catovsky, S Richards, E Matutes et al. Assessment of fludarabine plus cyclophosphamide for patients with chronic lymphocytic leukaemia (the LRF/FLUDARABINE CLL4 Trial): a randomized controlled trial. Lancet 2007; 370: 230-9

Date revised: 01/13/2009
Hematological

GEMCITABINE-DEXAMETHASONE-CISPLATIN
Chemotherapy

Hodgkin’s Lymphoma; Standard second-line therapy for patients who are intended to proceed to autologous stem cell transplantation. This regimen may also be used in patients refractory to autologous stem cell transplantation when disease not controlled with single agent Vinblastine.

**GEMCITABINE**
- 1000mg/m² IV Days 1 & 8
  - Admix in 250mL bag *Normal Saline*, infuse over 30 minutes through free-flowing IV.
  - Cap BSA at 2.2m²

**CISPLATIN**
- 75mg/m² IV Day 1
  - Admix in 500mL bag *Normal Saline*, infuse over 60 minutes.
  - Cap BSA at 2.2m²

**DEXAMETHASONE**
- 20mg PO Days 1-4
  - q12h for 4 days (8 doses).
  - Out-patient prescription.

**REPEAT EVERY 21 DAYS for 2-3 cycles**

**HYDRATION:**

**Pre**
- Pre-chemo hydrate with 250mL 5% Dextrose/Normal Saline over 30 minutes before Cisplatin.

**Concurrent**
- 250mL of Mannitol 20% (50G) IV concurrent with Cisplatin.

**Post**
- 1000mL Normal Saline with 10mEq Potassium Chloride. Infuse at 125mL/m²/hr for 4 hours after Cisplatin.
  - IV rate = 125 x BSA = ____ mL/hr
  - BSA is normally capped at 2.2m²
  - Maximum IV rate should not exceed 275mL/hr.

**TESTS:**

Baseline Tests
- WBC  HB  PLT  ANC  Ca  K  Na  Chloride  Mg  Glucose  Cr  T.Bili  ALT
- AlkPhosphatase

Day 8
- WBC  HB  PLT  ANC  K  Na  Chloride  Mg  Glucose  Cr

Day 1
- WBC  HB  PLT  ANC  K  Na  Chloride  Mg  Glucose  Cr
- T.Bili
- Albumin
- ALT
- AlkPhosphatase

**Test Notes**
- Additional Baseline tests: CO₂, protein electrophoresis and direct antiglobulin test (Coombs test)
- Additional Day 1 tests: CO₂ and protein
- Additional Day 8 test: CO₂

**ANTIEMETIC PRE-CHEMO REGIMEN:**

**Level C**
- Day 1
  - Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
  - Dexamethasone: see regimen information

**Level B**
- Day 8
  - May add or substitute Prochlorperazine 10mg PO/IV prn

**ANTIEMETIC TAKE-HOME REGIMEN:**

**Level B/C**
- Day 1
  - Ondansetron 8mg PO BID for 2-3 days, or Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days
  - Dexamethasone: see regimen information
  - Prochlorperazine 10mg PO q4-6h prn

**Level A**
- Day 8
  - Prochlorperazine 10mg PO q4-6h prn

**PATIENT VISITS and APPOINTMENT TYPE:**

- Day 1: 6hrs
- Day 8: 45min

**ANCILLARY:**
- Oral hydration is strongly encouraged; poorly hydrated patients may need more IV hydration (to prevent renal toxicity).

**TOXICITIES:**

**Hematologic**

**Day 1**
1. If ANC < 1.0 x 10⁹/L, DELAY therapy 1 week and give G-CSF with next cycle.
2. If PLT < 75 x 10⁹/L, DELAY therapy 1 week.

**Day 8**
1. If ANC = 0.5-0.99 x 10⁹/L, give full doses and add G-CSF
2. If ANC < 0.5 x 10⁹/L, OMIT therapy and add G-CSF.
3. If PLT < 50 x 10⁹/L, OMIT all therapy.
- Dose attenuations may be over-ridden if cytopenias presumed to be due to underlying disease.

**Renal Failure**
1. If SrCr > 120umol/L, HOLD therapy.

**Neurologic**
1. If peripheral neuropathy > 2, HOLD therapy.

**SUGGESTED ACTION**
HEMATOLOGICAL

GEMCITABINE-DEXAMETHASONE-CISPLATIN
Chemotherapy

CLINICAL MONITORING:
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.

Hearing
1. Asymptomatic, detected on exam/testing only
2. Symptomatic, not interfering with ADL
3. Symptomatic, interfering with ADL
4. Life-threatening; disabling
5. Death

Sensory
1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function
2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL
3. Sensory alteration or paresthesia interfering with ADL
4. Disabling
5. Death

RATED AT EACH CLINIC VISIT

Edema limb
1. 5 - 10% inter-limb discrepancy in volume or circumference at point of greatest visible difference; swelling or obscuration of anatomic architecture on close inspection; pitting edema
2. >10 - 30% inter-limb discrepancy in volume or circumference at point of greatest visible difference; readily apparent obscuration of anatomic architecture; obliteration of skin folds; readily apparent deviation from normal anatomic contour
3. >30% inter-limb discrepancy in volume; lymphorrhea; gross deviation from normal anatomic contour; interfering with ADL
4. Progression to malignancy (i.e., lymphangiosarcoma); amputation indicated; disabling
5. Death

RATED IF EDEMA NOTED ON ROUTINE VISITS

FORMULAE:

CrCl - Cockcroft & Gault (mL/sec)
Male: \[\frac{[140\text{-age(yrs)}] \times TBW(Kg)}{[50 \times SCr(umol/L)]}\]
Female: \[\frac{[140\text{-age(yrs)}] \times TBW(Kg)}{[50 \times SCr(umol/L)] \times 0.85}\]

REFERENCES:

Date revised: 10/08/2008
Harvest Regimen for Gianni Stem Cell Transplant Protocol
(Inpatient Regimen)
Intermediate or High Grade Non-Hodgkin’s Lymphoma - Stem Cell Transplant Phase II

**CYCLOPHOSPHAMIDE** 1400mg/m² IV D-1 q3h x 5 doses Round to nearest 10mg
- Mix each dose of Cyclophosphamide 1400mg/m² in Normal Saline at a concentration 20mg/mL.
- Infuse each dose of Cyclophosphamide 1400mg/m² q3h over 1 hour x 5 doses.
- Total dose of Cyclophosphamide is 7000 mg/m²
- Cap BSA=2.2m²

**MESNA** 1500mg IV Day 1 q3h
- Starting after each dose of Cyclophosphamide, infuse Mesna 1500mg diluted in 100mL bag 5% Dextrose over 5-10 minutes q3h x 5 doses.

**MESNA** 1000mg IV Day 2 q3h
- Admix Mesna 1000mg in 100mL bag 5% Dextrose, infuse over 5-10 minutes q3h x 7 doses.

**HYDRATION:**

**Pre**
- Beginning at 2300 of Day 0 start hydration with following IV fluids:
  - Bag #1 IV 2/3 and 1/3 solution with 10mmol KCL and 1G Magnesium Sulfate each per litre.
  - Bag #2 IV 2/3 and 1/3 solution with 10mmol KCL and 100mEq Sodium Bicarbonate each per litre.
  - Run IV at 125mL/m²/hr begin with bag #1 and alternate with bag #2.
- Reassess IV on Day 2.

**ANTIMICROBIAL PROPHYLAXIS:**
- Antimicrobial prophylaxis to begin on Day 1 and continue until AGC > 1.2 x 10⁹/L
  1. Ciprofloxacin 500mg PO bid
  2. Acyclovir 800mg PO bid
  3. Fluconazole 200mg daily

**TESTS:**

Baseline Tests: WBC HB PLT ANC Ca K Na Chloride Phosphate Mg Glucose Cr T.Bili AST ALT AlkPhosphatase Urate

**ANTIEMETIC PRE-CHEMO REGIMEN:**

**Level C** Days 1-2 - Ondansetron 8mg pre Cyclophosphamide and q8h x 48hr, may be given with Magnesium hydration bags (not compatible with Sodium Bicarbonate).

**Level B** Days 1-2 - Prochlorperazine 10mg IV/ PO q4h prn, can be given with Sodium Bicarbonate hydration bags or Normal saline (not compatible with Magnesium).

**INPATIENT ANTIEMETICS:**
- Ondansetron can be substituted with Granisetron 1-2mg PO/IV daily.

**TOXICITIES:**

**Hematologic**
1. Leukopenia is the dose-limiting toxicity.

**Renal Failure**
1. Hemorrhagic or nonhemorrhagic cystitis most reversible with discontinuation of the drug.
2. Urinalysis for RBCs repeated frequently following treatment.

**Pulmonary**
1. Pulmonary toxicity is usually characterized by pneumonitis.

**Cardiac**
1. Cardiac toxicity occurs with high doses of Cyclophosphamide.

**CLINICAL MONITORING:**
- Routine cardiac and pulmonary function, Cr, urinalysis for RBC’s repeated frequently following treatment.
- Routine check for symptoms of Cystitis:

**FORMULAE:**

\[ \text{CrCl - Cockcroft & Gault (ml/sec)} = \frac{[140-age(yrs)] \times TBW(Kg)}{[50 \times SCr(umol/L)]} \]
\[ \text{CrCl - Cockcroft & Gault (ml/sec)} = \frac{[140-age(yrs)] \times TBW(Kg)}{[50 \times SCr(umol/L)] \times 0.85} \]

**REFERENCES:**
- Alessandro M.Gianni,M.D., Marco Bregini,M.D., Salvatore Siena, M.D., Cristina Brambilla, M.D., Massimo Di Nicola, M.D., Fabrizio Lombardi, M.D.,Lorenza Gandola, M.D., Corrado Tarell, M.D., Alessandro Pileri, M.D., Fenando Ravagnani, M.D.,

CCO Eligibility Form Required ☐ Non-Formulary Form Required ☐ Date revised: 03/07/2005

Hematological
STEM CELL TRANSPLANT CHEMOTHERAPY (GIANNI PROTOCOL PHASE V) (Inpatient Regimen)

Intermediate or High grade Non-Hodgkin’s Lymphoma - Stem Cell Transplant Phase

**MITOXANTRONE** 20mg/m² IV Day - 4 q2h x 3 doses
- Mix in 250mL bag 5% Dextrose; infuse through central line over 1 hour q2h x 3 doses (total dose 60mg/m²).

**MELPHALAN** 60mg/m² IV Day -1 q2h x 3 doses
- Mix in 250mL bag Normal Saline; infuse through central line over 30min q2h x 3 doses (total dose 180mg/m²).
  Complete each infusion within 60 minutes of preparation.

**ACETAZOLAMIDE** 250mg PO qid
- Give 250mg qid on Days -4,-1,1,1

**HYDROCORTISONE SODIUM SUCCINATE**
- Give one dose prior to stem cell reinfusion.

**ACETAMINOPHEN** 650mg PO Pre Stem Cell Reinfusion
- Give 2 tablets prior to stem cell reinfusion.

**HYDRATION:**
Pre
- Start hydration on Day -5 (evening) with IV fluids as follows:
  - Bag #1 2/3 and 1/3 solution with 10mmol KCL and 1G Magnesium Sulfate each per litre
  - Bag #2 2/3 and 1/3 solution with 10mmol KCL and 50mEq Sodium Bicarbonate each per litre
  - Run IV at rate 125mL/m²/hr. Begin IV fluids with Bag #1 and alternate Bag #1 with Bag #2 after each litre through.
  - Continue above hydration until 24 hours after completion of Melphalan infusion.

Post
- IV Normal Saline with 20mmol KCL at rate 125mL/hr

**ANTIMICROBIAL PROPHYLAXIS:**
- Start 24 hours post MELPHALAN:
  1. Cipro 500mg PO bid
  2. Fluconazole 200mg PO/IV daily
  3. Acyclovir 400mg PO/IV q8h

**TESTS:**
Baseline Tests WBC HB PLT ANC Ca K Na Chloride Phosphate Mg Cr Urea T.Bili Albumin AST ALT AlkPhosphatase Urate LVEF
Test Notes - Routine hematology orders, BUN, Cr and electrolytes (Bicarb, Magnesium) - daily.

**ANTIEMETIC PRE-CHEMO REGIMEN:**
Level C Day -4 to Day-0 - Ondansetron 8mg PO/IV q8h
Level C Day -4 to Day -1 - Dexamethasone 8mg before first dose of Mitoxantrone and Melphalan

**INPATIENT ANTIEMETICS:**
- Start Ondansetron 1 hour before first dose of Mitoxantrone. Ondansetron can be substituted with Granisetron 1-2mg PO/IV daily.

**TOXICITIES:**

**Hematologic**
1. Myelosuppression
   1. Patients with impaired hepatic functioning may require a dose reduction of Mitoxantrone.
   - If T. Bili > 50umol/L, REDUCE Mitoxantrone to 50% dose.

**Pulmonary**
1. Interstitial pneumonitis

**Cardiac**
1. Cardiac monitoring of EKGs and LVEF is recommended before treatment.

**CLINICAL MONITORING:**
- Baseline liver and renal function test.
- Clinical exam for symptoms of CHF for patients with cardiac risk.

**FORMULAE:**
CrCl - Cockcroft & Gault (mL/sec)
Male: \[\frac{[140\text{-age(yrs)}] \times TBW(Kg)}{[50 \times SCr(umol/L)]}\]
CrCl - Cockcroft & Gault (mL/sec)
Female: \[\frac{[140\text{-age(yrs)}] \times TBW(Kg)}{[50 \times SCr(umol/L)] \times 0.85}\]

**REFERENCES:**
- Alessandro M. Gianni, M.D., Marco Bregini, M.D., Salvatore Siena, M.D., Cristina Brambilla, M.D., Massimo Di Nicola, M.D.,
  Fabrizio Lombardi, M.D., Lorenzo Gandola, M.D., Corrado Tarell, M.D., Alessandro Pileri, M.D., Fenando Ravagnani, M.D.,

CCO Eligibility Form Required
Non-Formulary Form Required
Date revised: 03/07/2005
ETOPOSIDE (High Dose) Chemotherapy (Gianni Protocol Phase IV) (Inpatient Regimen)

Intermediate of High Grade Non-Hodgkin’s Lymphoma - Stem Cell Transplant Phase IV

ETOPOSIDE

- Give Etoposide undiluted through dedicated central line over 12 hours. Etoposide concentration is 20mg/mL, infusion rate 8.3mL/hr.
- Do not run any IV fluids or drugs through same line as Etoposide.
- Flush line with Normal Saline at the same rate as Etoposide for one hour.

METHYLPREDNISOLON 60mg

E SODIUM SUCCINATE
- Give Methylprednisolone 60mg IV x 3 doses starting 6 hours prior to Etoposide.

HYDRATION:
- Pre
- Beginning at least 6 hours prior chemotherapy run IV fluids as follows:
  1. Bag #1 IV 2/3 and 1/3 solution with 10mmol KCL and 1G Magnesium Sulfate each per litre.
  2. Bag #2 IV 2/3 and 1/3 solution with 10mmol KCL and 50mEq of Sodium Bicarbonate each per litre. Run IV solution at 125mL/m²/hr; Begin IV fluids with Bag #1, and alternate Bag #1 with Bag #2 after each litre through.

- Post
- On Day 2 change IV to Normal Saline with 20 mmol KCL/L at 125mL/hr.

ANTIMICROBIAL PROPHYLAXIS:
- Start on Day 1 and continue until AGC > 1.0 x10⁹/L for 3 days:
  1. Ciprofloxacin 500mg bid
  2. Fluconazole 200mg PO/IV daily
  3. Acyclovir 400mg PO/IV q8h

TESTS:
- Baseline Tests: WBC HB PLT ANC Ca K Na Chloride Phosphate Mg Cr Urea T.Bili AST ALT
- Test Notes: CBC, baseline and regular liver function test daily.

ANTIEMETIC PRE-CHEMO REGIMEN:
- Level C: Day 1 to 2 - Ondansetron 8mg PO/IV q8h x 4 doses
- Level B: Start on day 1 - Prochlorperazine 10mg q4h prn, PO/IV

INPATIENT ANTIEMETICS:
- Ondansetron can be substituted with Granisetron 1-2mg PO/IV daily.
- Ondansetron is compatible with the Magnesium hydration.

TOXICITIES:
Cardiac
1. Myocardial infarction and congestive heart failure in patients with pre-existing heart disease.

Hematologic
1. Myelosuppression (dose limiting)

Hepatic Dysfunction
1. Hepatotoxic at high doses
- If T.Bili = 26-51umol/L, or AST 60-180 IU/L, REDUCE Etoposide 50% dose.
- If T.Bili = 52-85umol/L, REDUCE Etoposide to 25% dose.
2. Gastrointestinal
   - Nausea, vomiting, stomatitis, metallic taste during infusion.

Pulmonary
1. Bronchospasm with severe wheezing during administration, usually responsive to antihistamines and corticosteroids.

CLINICAL MONITORING:
- Baseline Blood pressure. Check blood pressure q2h during Etoposide infusion.
- Etoposide has an appreciable risk of causing hypersensitivity reaction. Treatment consists of stopping the drug and administering antihistamines, corticosteroids and pressor agents.

INTERNAL CODE:
Gianni Protocol - Phase IV

REFERENCES:

CCO Eligibility Form Required ☐ Non-Formulary Form Required ☐ Date revised: 03/07/2005
METHOTREXATE (High dose) , VINCristine - GIANNI
PROTOlCOL PHASE III (Inpatient Regimen)
Intermediate or High Grade Non Hodgkin's Lymphoma - Stem cell Transplant Phase III

VINCristine
1.4mg/m² IV Day 1
- Mix in 50mL bag Normal Saline; infuse over 10 minutes.
- Max dose cap at 2mg

METHOTREXATE
8Gm/m² IV Day 1
- Admix Methotrexate in 1000mL bag Normal Saline; infuse over 6 hours, start 30 minutes after Vincristine.

SODIUM BICARBONATE
500mg PO q3h
- Give Sodium Bicarbonate tablet (500mg) to provide proper pH of urine; 2 tablets if urine pH <7.4; increase by 1 tablet q3h if urine pH stays below 7.4; decrease by 1 tablet q3h if urine pH > 8. If urine pH is between 7.4 and 8, do not adjust Sodium Bicarbonate dose.

CHOLESTYRAMINE
2Gm PO q6h
- Give Cholestyramine 2gm x 4 doses on day 3.

LEUCOVORIN
9mg/m² IV q6h
- Start Leucovorin (Folinic Acid) q6h 24 hours after Methotrexate commenced and continue until Methotrexate level < 0.05umol/L.

HYDRATION:
Pre
- Beginning on admission, start IV 2/3 and 1/3 solution with 100mEq of Sodium Bicarbonate per litre at rate 125mL/m²/hr.
- Give IV fluids for at least 6 hours prior to Methotrexate and urine pH > 7.4.
Post
- Continue pre chemo alkalinization until Methotrexate level < 0.05umol/L.

TESTS:
Baseline Tests
WBC HB PLT ANC Ca K Na Chloride Phosphate Mg Cr Urea T.Bili AST ALT AlkPhosphatase
Test Notes - BUN, Cr, electrolytes daily. Baseline liver function test. Methotrexate level with daily blood work beginning day after medication commenced.

ANTIEMETIC PRE-CHEMO REGIMEN:
Level A
- Prochlorperazine 10mg IV q4h prn, can be run with the Sodium Bicarbonate IV solution.

TOXICITIES:
Hematologic
1. Myelosuppresion; If ANC < 1.5 x 10⁹/L, or PLT < 100 x10⁹/L, HOLD dose for 1 week.
Gastrointestinal
1. Nausea and vomiting are dose dependent and may occur during drug administration.
2. Stomatitis
3. Hepatotoxicity can lead to cirrhosis in severe cases.
Renal Failure
1. Acute renal tubular necrosis, urinary retention, renal failure can be decreased by alkalinization of the urine.

Pulmonary
1. Pulmonary toxicity - pneumonitis, pulmonary infiltrates

CLINICAL MONITORING:
- Monitor renal & liver function test and serum electrolytes before and during treatment. Monitor and record input and output of fluids and urine.

FORMULAE:
CrCl - Cockcroft & Gault (mL/sec)
Male: [140-age(yrs)] x TBW(Kg) / [50 x SCr(umol/L)]
CrCl - Cockcroft & Gault (mL/sec)
Female: [140-age(yrs)] x TBW(Kg) / [50 x SCr(umol/L)] x 0.85

INTERNAL CODE:
Gianni Protocol Phase III - High Dose Methotrexate

REFERENCES:

CCO Eligibility Form Required □ Non-Formulary Form Required □ Date revised: 03/07/2005
HIGH DOSE CYTARABINE - INDUCTION THERAPY
(Inpatient Regimen) for patient with cardiac risk
Acute Myeloid Leukemia - Curative intent

CYTARABINE 2000mg/m² IV q12h
- Admix in 500mL bag 5% Dextrose and infuse over 3 hours every 12 hours for total of 12 doses.
- Induction therapy for patient with cardiac risk (suboptimal RNA or echocardiogram).

DEXAMETHASONE 2gtt OU OPH q6h
- Commence Dexamethasone 0.1% eye drops in each eye at least 1 hr prior to Cytarabine and continue for 24 hours post last dose of Cytarabine.

HYDRATION:
- IV Normal Saline

TESTS:
- Baseline Tests: WBC HB PLT ANC Ca K Na Chloride Phosphate Mg Glucose Cr Urea T.Bili Albumin ALT AlkPhosphatase Urate
- Test Notes: Baseline and frequent CBC, baseline and regular renal function including uric acid, INR, PTT and fibrinogen during the first 3 days of induction - where clinically indicated.

ANTIEMETIC PRE-CHEMO REGIMEN:
Level C Days 1 to 7 - Ondansetron 8mg PO/IV q8h can be substituted with Granisetron 1-2mg PO/IV daily.

INPATIENT ANTIEMETICS:
- Ondansetron can be substituted with Granisetron 1-2mg PO/IV daily.

TOXICITIES:
Hematologic
1. If ANC < 1.0 x 10⁹/L; PLT < 75 x 10⁹/L, parameters may be changed at the discretion of the clinician if cytopenias presumed to be due to underlying disease.

Hepatic Dysfunction
1. Elevation in liver function tests, significant liver function abnormalities may require discontinuation of the drug.

Neurologic
1. Cerebellar toxicity, cerebellar dysfunction manifests as somnolence, confusion, cognitive dysfunction, memory loss, psychosis or seizures. In most patients, neurologic dysfunction resolve in 5-10 days, but in some patients toxicity may be irreversible.

Renal Failure
1. Hyperuricemia (during periods of active cell lysis) can be minimized with Allopurinol and hydration. In hospitalized patients the urine can be alkalinized by addition of Sodium Bicarbonate in the IV fluids, if tumour lysis is expected.

CLINICAL MONITORING:
- Baseline and frequent CBC, baseline and regular renal function, clinical assessment of GI and CNS toxicity (cerebellar testing).
- Renal insufficiency increases the likelihood of CNS toxicity.
- For patients over 60 years of age, adjust Cytarabine dose to 1500mg/m².
- Guidelines for dosing also include consideration of white blood cell count.
- Dosage may be reduced and/or delayed with bone marrow depression due to cytotoxic therapy.

INTERNAL CODE:
HIGH DOSE CYTARABINE - FOR ACUTE MYELOID LEUKEMIA

REFERENCES:

Date revised: 03/07/2005
HEMATOLOGICAL

HIGH DOSE CYTARABINE - CONSOLIDATION THERAPY
(Inpatient Regimen) For patients over 60 years of age

Acute Myeloid Leukemia - Consolidation therapy

CYTARABINE
1.5G/m² IV q12h
- Admix in 500mL bag 5% Dextrose; infuse over 3 hours every 12 hours for total of 8 doses.

DEXAMETHASONE
2gtt OU OPH q6h
- Commence Dexamethasone 0.1% eye drops in each eye at least 1 hour prior to Cytarabine and continue for 24 hours post last dose of Cytarabine.

HYDRATION:
Pre
- IV Normal Saline TKVO.

TESTS:
Baseline Tests
WBC HB PLT ANC Ca K Na Chloride Phosphate Mg Glucose Cr Urea T.Bili Albumin ALT AlkPhosphatase Urate
Test Notes
- Baseline CBC, baseline and regular renal function including uric acid, INR, PTT where clinically indicated.
- CBC, lytes, Cr, urea, LFT’s 3 times a week.

ANTIEMETIC PRE-CHEMO REGIMEN:
Level C Days 1 to 5 - Ondansetron q8h PO/IV, can be substituted with Granisetron 1-2mg PO/IV daily.

INPATIENT ANTIEMETICS:
- Ondansetron may be substituted with Granisetron 1-2mg PO/IV daily.

TOXICITIES:
Hematologic
1. Myelosuppression

Hepatic Dysfunction
1. Elevation of liver function tests, significant liver function abnormalities may require discontinuation of the drug.

Neurologic
1. Cerebellar toxicity, cerebellar dysfunction manifests as somnolence, confusion, cognitive dysfunction, memory loss, psychosis or seizures. In most patients, neurologic dysfunction resolve in 5-10 days, but in some patients toxicity may be irreversible.

Renal Failure
1. Hyperuricemia (during period of active cell lysis) can be minimized with Allopurinol and hydration. In hospitalized patients the urine can be alkalized by addition of sodium bicarbonate in the IV fluids, if tumour lysis is expected.

CLINICAL MONITORING:
- Baseline and frequent CBC, baseline and regular renal function, clinical assessment of GI and CNS toxicity (cerebellar testing). Renal insufficiency increases the likelihood of CNS toxicity.
- Guidelines for dosing also include consideration of white blood cell count.
- Dosage may be reduced and/or delayed with bone marrow depression due to cytotoxic therapy.

INTERNAL CODE:
HIGH DOSE CYTARABINE - CONSOLIDATION THERAPY

CCO Eligibility Form Required
Non-Formulary Form Required

Date revised: 09/20/2006
HIGH DOSE CYTARABINE - CONSOLIDATION THERAPY (Inpatient Regimen)
Acute Myeloid Leukemia - Consolidation therapy for patients in complete remission age 60 years and under

CYTARABINE 3Gm/m² IV Day 1,3,5 q12h Round to nearest 10mg
- Admix in 500mL bag 5% Dextrose; infuse over 3 hours every 12 hours on Day 1,3,5 (total 6 doses).

REPEAT EVERY 28 DAYS TIMES 3 CYCLES

DEXAMETHASONE 2gtt OU OPH q6h
- Commence Dexamethasone 0.1% eye drops in each eye at least 1 hour prior to Cytarabine and continue for 24 hours post last dose of Cytarabine.

HYDRATION:
Pre
IV Normal Saline TKVO.

TESTS:
Baseline Tests WBC HB PLT ANC Ca K Na Phosphate Mg Glucose Cr Urea T.Bili Albumin AST ALT AlkPhosphatase Urate
Test Notes Baseline CBC, baseline and regular renal function including uric acid, INR, PTT where clinically indicated.
- CBC, lytes, Cr, urea, LFT's 3 times a week.

ANTIEMETIC PRE-CHEMO REGIMEN:
Level C Day 1-5 -Ondansetron q8h PO/IV, can be substituted with Granisetron 1-2mg PO/IV daily.

INPATIENT ANTIEMETICS:
- Ondansetron may be substituted with Granisetron 1-2mg PO/IV daily.

TOXICITIES:
Hematologic
1. Myelosuppression
Hepatic Dysfunction
1. Elevation of liver function tests, significant liver function abnormalities may require discontinuation of the drug.
Neurologic
1. Cerebellar toxicity, cerebellar dysfunction manifests as somnolence, confusion, cognitive dysfunction, memory loss, psychosis or seizures. In most patients, neurologic dysfunction resolve in 5-10 days, but in some patients toxicity may be irreversible.
Renal Failure
1. Hyperuricemia (during period of active cell lysis) can be minimized with Allopurinol and hydration. In hospitalized patients the urine can be alkalized by addition of sodium bicarbonate in the IV fluids, if tumour lysis is expected.

CLINICAL MONITORING:
- Baseline and frequent CBC, baseline and regular renal function, clinical assessment of GI and CNS toxicity (cerebellar testing). Renal insufficiency increases the likelihood of CNS toxicity.
- Guidelines for dosing also include consideration of white blood cell count.
- Cerebellar testing prior each dose of Cytarabine

INTERNAL CODE:
HIGH DOSE CYTARABINE - CONSOLIDATION THERAPY FOR PATIENTS 60 YEARS OF AGE AND YOUNGER

REFERENCES:

Date revised: 11/07/2006
HIGH DOSE CYTARABINE with Amsacrine - (Inpatient Regimen) Re-Induction salvage refractory AML

Acute Myeloid Leukemia - Curative intent

**CYTARABINE**
2000mg/m² IV q12h
- Admin in 500mL bag 5% Dextrose and infuse over 3 hours every 12 hours for total of 12 doses.

**AMSA CRINE**
100mg/m² IV Daily x 3 days
- Admin in 500mL bag 5% Dextrose and infuse over 60-90 minutes on days 7, 8, and 9.

**DEXAMETHASONE**
2gt OU OPH q6h
- Commence Dexamethasone 0.1% eye drops in each eye at least 1 hr prior to Cytarabine and continue for 24 hours post last dose of Cytarabine.

**HYDRATION:**
Pre - IV Normal Saline

**TESTS:**

Baseline Tests: WBC HB PLT ANC Ca K Na Chloride Phosphate Mg Glucose Cr Urea T.Bili Albumin ALT AlkPhosphatase Urate

Test Notes:
- Baseline and frequent CBC, baseline and regular renal function including uric acid, INR, PTT and fibrinogen during the first 3 days of induction - where clinically indicated.
- Serum potassium levels should be at least 4.2mg/dl prior to Amsacrine administration.
- Day 6 bone marrow optional with this regimen.

**ANTIEMETIC PRE-CHEMO REGIMEN:**

Level C Days 1 to 7
- Ondansetron 8mg PO/IV q8h can be substituted with Granisetron 1-2mg PO/IV daily.
- Dexamethasone 8mg PO daily.
- Prochlorperazine 10mg PO/IV prn.

Level B/C Days 7, 8, & 9
- Ondansetron 8mg PO q12h prn for 3 days
- Prochlorperazine 10mg PO q6h prn for 5 days

**INTERNAL CODE:**

High Dose Cytarabine with Amsacrine - FOR ACUTE MYELOID LEUKEMIA

**REFERENCES:**

CCO Eligibility Form Required ☐ Non-Formulary Form Required ☐ Date revised: 12/08/2008
**HE - HIGH DOSE MTX**

**Hematological**

**High Dose METHOTREXATE Chemotherapy (Inpatient Regimen)**

**CNS LYMPHOMA**

**METHOTREXATE** 3G/m² IV Day 1 Round to nearest 10mg
- Admix Methotrexate in **500mL of Normal Saline;** infuse over 6 hours. Check urine pH q3h after first litre of IV fluid.

**SODIUM BICARBONATE** 500mg PO q3h 500mg tablet
- Give Sodium Bicarbonate tablet (500mg), two tablets orally if urine pH < 7.4. Increase by one tablet q3h if urine pH stays below 7.4. Decrease by one tablet q3h if urine pH > 8.0. **If urine pH between 7.4-8.0, do not adjust bicarbonate dose.**

**LEUCOVORIN** 20mg IV q6h
- Start Leucovorin (Folinic Acid) q6h exactly 24 hours after Methotrexate commenced and continue until Methotrexate level < 0.05umol/L.

**HYDRATION:**
- IV fluid 2/3 and 1/3 with 100mEq Sodium Bicarbonate per litre at rate 250mL/hr, starting 6-12h prior to Methotrexate. Check urine pH q3h after first litre of IV through. After first litre of IV fluid through and provided urine pH > 7.4, start Methotrexate. Measure in and out q4h.

**TESTS:**
- CBC, BUN, Cr, Electrolytes daily. Baseline liver function test.
- Methotrexate level with daily blood work beginning 24 hours after medication commenced.

**ANTIEMETIC PRE-CHEMO REGIMEN:**
- Prochlorperazine 10mg IV q4h prn, can be run with the Sodium Bicarbonate IV solution.

**TOXICITIES:**

**Hematologic**
1. If ANC < 1.5 x 10^9/L, or PLT < 100 x 10^9/L, HOLD dose for 1 week.
   - Dose attenuations may be over-ridden if cytopenias presumed to be due to underlying disease.

**Gastrointestinal**
1. Nausea, vomiting are dose dependent and may occur during drug administration.
2. Stomatitis
3. Hepatotoxicity can lead to cirrhosis in severe cases.

**Renal Failure**
1. Acute renal tubular necrosis, urinary retention, renal failure can be decreased by alkalinization of the urine.

**Pulmonary**
1. Pulmonary toxicity - pneumonitis, pulmonary infiltrates.

**CLINICAL MONITORING:**
- Monitor renal & hepatic function test and serum electrolytes before and during treatment.
- Monitor and record input and output of fluids and urine, measure in and out every 4 hours.
- Observe skin colour and condition, especially around pressure points, for 5 days after each dose.

**FORMULAE:**
- CrCl - Cockcroft & Gault (mL/sec) Male: \[\frac{140 - \text{age(yrs)}}{50} \times \text{TBW(Kg)} / \text{50 x SCR(umol/L)}\]
- CrCl - Cockcroft & Gault (mL/sec) Female: \[\frac{140 - \text{age(yrs)}}{50} \times \text{TBW(Kg)} / \text{50 x SCR(umol/L)} \times 0.85\]

**REFERENCES:**
HYDROXYUREA Chemotherapy

Hematological

HYDROXYUREA:

<table>
<thead>
<tr>
<th>Increments of</th>
<th>PO</th>
<th>Daily</th>
<th>500mg capsule</th>
</tr>
</thead>
<tbody>
<tr>
<td>500mg/m²</td>
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</tr>
</tbody>
</table>

- Titrate dose as needed to reduce WBC to $10 \times 10^9$/L or lower, or as tolerated. When WBC in acceptable range, reduce or maintain dose (500-1000mg/m²).
- Begin full dose treatment when WBC > $50 \times 10^9$/L, titrate to lower dose or hold treatment when WBC < $10 \times 10^9$/L.
- Discontinue if disease enters accelerated phase; treat as ALL or AML (depending on the transformation phenotype).
- Outpatient prescription available as 500mg capsule.

CONTINUOUS TREATMENT TO RESPONSE:

TESTS:
Baseline Tests: WBC HB PLT ANC Ca K Na Chloride Phosphate Glucose Cr Urea T.Bili Albumin ALT AlkPhosphatase

Day 1: WBC HB PLT ANC Ca

Test Notes: - Periodic renal function tests
- Regular liver function tests

ANTIEMETIC PRE-CHEMO REGIMEN:
Level A Daily: Prochlorperazine 10mg PO pm

ANTIEMETIC TAKE-HOME REGIMEN:
Level A Daily: Prochlorperazine 10mg PO q4-6h pm

ANCILLARY:
- Handle with gloves.
- Minimize hyperuricemia with hydration and Allopurinol.

TOXICITIES:
Renal Failure
1. If CrCl >0.8 mL/sec, GIVE 100% of dose
2. If CrCl 0.2-0.8 mL/sec, REDUCE to 50% of dose
3. If CrCl <0.2 mL/sec, REDUCE to 10-20% of dose

SUGGESTED ACTION:
CLINICAL MONITORING:
- Recommend clinical toxicity assessment of rash, gastrointestinal and neurologic symptoms.
- Myelosuppression, primarily leucopenia.
- Megaloblastic erythropoiesis, early stages, may treat prophylactically with folic acid.

Rash
1. Macular or papular eruption or erythema without associated symptoms
2. Macular or papular eruption or erythema with pruritus or other associated symptoms; localized desquamation or other lesions covering <50% of body surface area (BSA)
3. Severe, generalized erythroderma or macular, papular or vesicular eruption; desquamation covering ≥50% BSA
4. Generalized exfoliative, ulcerative, or bullous dermatitis
5. Death

Mucositis
1. Erythema of the mucosa
2. Patchy ulcerations or pseudomembranes
3. Confluent ulcerations or pseudomembranes; bleeding with minor trauma
4. Tissue necrosis; significant spontaneous bleeding; life-threatening consequences
5. Death

RATED AT EACH CLINIC VISIT

REFERENCES:
- Compendium of Pharmaceuticals and Specialties. 2006. Hydrea™, Canadian Pharmacists Association
- Health Canada Endorsed Important Safety Information on Hydrea™ (Hydroxyurea capsules) March 1st, 2006

Date revised: 01/16/2009
Therapy for Lymphoblastic Lymphoma and Acute Lymphoid leukemia (for patients previously treated with AL-4 if there is failure to achieve remission)

**6-MERCAPTOPURINE** 50mg PO tid
- Administer 1 tab tid on an empty stomach

**METHOTREXATE** 20mg/m² PO Weekly

**VINCRIStINE** 2mg IV Monthly
- Mix in **50mL bag Normal Saline**; infuse over 10 minutes.
- Maximum dose = 2mg

**PREDNISONE** 200mg PO Daily
- Daily for 5 days each month.

**ANTIMICROBIAL PROPHYLAXIS:**
Antibiotics prophylaxis for first 6 months
1. Acyclovir 200mg PO daily or Valcyclovir 500mg PO daily or three times weekly.
2. Co-Trimoxazole 1 tablet bid on weekends

**TESTS:**
Baseline Tests: WBC HB PLT ANC Ca K Na Chloride Phosphate Mg Cr Urea T.Bili AST ALT AlkPhosphatase Urate LVEF

**INTERNAL CODE:**
Maintenance phase.

**REFERENCES:**
- Hagop M. Kantarjian, Susan O’Brien, Terry L. Smith, Jorge Cortes, Francis J. Giles, Miloslav beran, Sherry Pierce, Yang Huh, Michael Andreeff, Charles Koller, Chul S.Ha, Michael J. Keating, Sharon Murphy, and Emil J. Freireich, Result of Treatment With Hyper-CVAD, a Dose Intensive Regimen, in Adult Acute Lymphocytic Leukemia, J Clin Oncol, Vol 18, No 3 (February), 2000: pp 547-561.

**Date revised:** 07/31/2006
### Hematological

**CYCLOPHOSPHAMIDE-VINCRISTINE-DOXORUBICIN-DEXAMETHASONE Chemotherapy and HIGH DOSE METHOTREXATE/CYTARABINE-DOSE INTENSIVE PHASE**

Therapy for Lymphoblastic Lymphoma and Acute Lymphoid leukemia (for patients previously treated with AL-4 if there is failure to achieve remission)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
<th>Route</th>
<th>Days</th>
<th>Course</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CYCLOPHOSPHAMIDE</strong></td>
<td>300mg/m²</td>
<td>IV</td>
<td>Day 1, 2, 3 q12h</td>
<td>A</td>
</tr>
<tr>
<td>- Mix in 250mL bag Normal Saline</td>
<td>(0.45% Sodium Chloride, 5% Dextrose)</td>
<td></td>
<td>Infuse over 3 hours every 12 hours (total 6 doses).</td>
<td></td>
</tr>
<tr>
<td><strong>MESNA</strong></td>
<td>300mg/m²</td>
<td>IV</td>
<td>Day 1,2,3 cont. infusion</td>
<td>A</td>
</tr>
<tr>
<td>- Mesna may be given as an uroprotectant at the same total dose as Cyclophosphamide but given by continuous infusion starting with Cyclophosphamide and ending 6 hours after the last dose.</td>
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<tr>
<td>- Mix total daily dose in 1000 ml bag Normal Saline, inuse continuously over 24 hours on day 1,2,3.</td>
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<td></td>
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</tr>
<tr>
<td><strong>METHOTREXATE</strong></td>
<td>12mg IT</td>
<td>Day 2</td>
<td>Course A</td>
<td></td>
</tr>
<tr>
<td>- Prepared by hematologist and give as intrathecal injection.</td>
<td></td>
<td></td>
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</tr>
<tr>
<td><strong>DOXORUBICIN</strong></td>
<td>50mg/m²</td>
<td>IV</td>
<td>Day 4 Course A</td>
<td>Round to nearest 1mg</td>
</tr>
<tr>
<td>- Slow push through sidearm of free flowing IV at rate 2-4mg (1-2mL) per minute.</td>
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</tr>
<tr>
<td>- Doses &lt; 100mg may be mixed in 50mL minibag 5% Dextrose, doses &gt; 100mg may be mixed in 100mL minibag 5% Dextrose and infuse through central venous access device.</td>
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<tr>
<td><strong>VINCRISTINE</strong></td>
<td>2mg</td>
<td>IV</td>
<td>Day 4, 11 Course A</td>
<td></td>
</tr>
<tr>
<td>- Mix in 50mL bag Normal Saline; infuse over 10 minutes.</td>
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</tr>
<tr>
<td><strong>DEXAMETHASONE</strong></td>
<td>40mg</td>
<td>IV</td>
<td>Day 1 to 4, 11 to 14</td>
<td>A</td>
</tr>
<tr>
<td>- Give Dexamethasone 40 mg PO/IV daily on days 1-4 and 11-14</td>
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<tr>
<td><strong>CYTARABINE</strong></td>
<td>70mg IT</td>
<td>Day 11</td>
<td>Course A</td>
<td></td>
</tr>
<tr>
<td>- Prepared by hematologist and give as intrathecal injection.</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>METHOTREXATE</strong></td>
<td>200mg/m²</td>
<td>IV</td>
<td>Day 1 Course B</td>
<td>Round to nearest 5mg</td>
</tr>
<tr>
<td>- Mix Methotrexate in 500mL bag Normal Saline, infuse over 2 hours.</td>
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<td></td>
<td></td>
</tr>
<tr>
<td><strong>METHOTREXATE</strong></td>
<td>800mg/m²</td>
<td>IV</td>
<td>Day 1 Course B</td>
<td>Round to nearest 10mg</td>
</tr>
<tr>
<td>- Mix in 1000mL bag Normal Saline, infuse over 22 hours after completion of Methotrexate 200mg/m²</td>
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</tr>
<tr>
<td><strong>LEUCOVORIN</strong></td>
<td>15mg</td>
<td>IV</td>
<td>q6h Course B</td>
<td></td>
</tr>
<tr>
<td>- Administer Leucovorin 15mg q6h x 8 doses starting 24 hours after completion of Methotrexate infusion.</td>
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<tr>
<td>- Increase Leucovorin to 50mg q6h if Methotrexate levels were more than 20umol/L at the end of the infusion, more than 1umol/L 24h later, or more than 0.1umol/L 48h after the end of Methotrexate infusion.</td>
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<tr>
<td>- Continue Leucovorin until Methotrexate level &lt; 0.1umol/L</td>
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<td></td>
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</tr>
<tr>
<td><strong>CYTARABINE</strong></td>
<td>3gm/m²</td>
<td>IV</td>
<td>Day 2, 3 q12h Course B</td>
<td>Round to nearest 10mg</td>
</tr>
<tr>
<td>- Admix in 500mL bag 5% Dextrose; infuse over 2 hours every 12 hours for total of 4 doses, on days 2 and 3</td>
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<td></td>
<td></td>
</tr>
<tr>
<td><strong>METHYLPR Nednisolon</strong></td>
<td>50mg</td>
<td>IV</td>
<td>Days 1, 2, 3 BID Course B</td>
<td></td>
</tr>
<tr>
<td>- Give Methylprednisolone twice a day on days 1 through 3.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>METHOTREXATE</strong></td>
<td>12mg IT</td>
<td>Day 2</td>
<td>Course B</td>
<td></td>
</tr>
<tr>
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<tr>
<td><strong>CYTARABINE</strong></td>
<td>70mg IT</td>
<td>Day 11</td>
<td>Course B</td>
<td></td>
</tr>
<tr>
<td>- Prepared by hematologist and given as intrathecal injection.</td>
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</tr>
</tbody>
</table>

**HYDRATION:**

| Pre Course A Hydration | IV Normal Saline TKVO |
| Pre Course B Hydration | IV fluid 2/3 and 1/3 with 150mmEq Sodium Bicarbonate per litre at rate 150mL/hr (80mL/kg) |

**ANTIMICROBIAL PROPHYLAXIS:**

1. Acyclovir 400mg BID

**TESTS:**

| Baseline Tests | WBC HB PLT ANC Ca K Na Chloride Phosphate Mg Glucose Cr Urea T.Bili Albumin AST ALT AlkPhosphatase Urate |

Hematological
HC - HYPERCVAD/MT
X-Ara-C

Hematological

CYCLOPHOSPHAMIDE-VINCRISTINE-DOXORUBICIN-DEXAMETHASONE Chemotherapy and HIGH DOSE METHOTREXATE/ CYTARABINE-DOSE INTENSIVE PHASE

Test Notes
On Admission: Serum HcG (for females). If not done in previous 30 days, INR, PTT, CBC, Lytes, Cr, Glucose, T.bili, Alk phos, LDH, AST, Protein, Albumin, Uric Acid, Calcium, Phosphate, Magnesium, Zinc, Chest X-ray, LVEF
Daily: CBC, Cr, BUN, Na+, Cl-, K+, Glucose
Monday, Wednesday, Friday: Bilirubin, Alk Phos, Protein, Albumin

ANTIEMETIC PRE-CHEMO REGIMEN:
Level C Day 1-5: Ondansetron 8mg PO/IV q8h or Granisetron 1mg PO/IV bid

TOXICITIES:
Renal Failure
1. If SrCr 137-154 umol/L REDUCE Methotrexate dose to 75%
   If SrCr 155-246 umol/L REDUCE Methotrexate dose to 50%

Hepatic Dysfunction
(Suggested action)
1. If T.Bili < 34 umol/L give 100% dose of Methotrexate
   If T.Bili 34-51 umol/L REDUCE Methotrexate dose to 50%
   If T.Bili 52-86 umol/L REDUCE Methotrexate dose to 25%
2. If T.Bili = 26-51umol/L, or AST = 60-180 IU/L, REDUCE Doxorubicin to 75% dose and Vincristine to 50% dose
3. If T.Bili = 52-85umol/L, or AST > 180 IU/L, REDUCE Doxorubicin to 50% dose and Vincristine to 25% dose.

INTERNAL CODE:
The dose intensive phase consisted of 8 cycles of dose - intensive therapy courses of Hyper-CVAD therapy (Course A) alternating with High-dose Methotrexate /Ara-C therapy (Course B).

REFERENCES:

CCO Eligibility Form Required ☐ Non-Formulary Form Required ☐ Date revised: 09/20/2006
IFOSFAMIDE, CARBOPLATIN and ETOPOSIDE - for the treatment of relapsed or refractory advanced stage Aggressive B-Cell non Hodgkin’s Lymphoma

**AGGRESSIVE HISTOLOGY LYMPHOMA**

**IFOSFAMIDE**

- 1667mg/m² IV Days 1,2,3 Round to nearest 10 mg
- Mix in **1000ml bag Normal Saline** or 5% Dextrose with Mesna: Infuse over 2 hours on days 1,2,3.
- Total dose per cycle = 5000mg/m²

**MESNA**

- 1667mg/m² IV Day 1,2,3 Round to nearest 10mg
- Mix in **1000ml bag Normal Saline or 5% Dextrose** with Ifosfamide: Infuse over 2 hours on day 1,2,3.
- Total dose per cycle = 5000mg/m²

**ETOPOSIDE**

- 100mg/m² IV Days 1,2,3 Round to nearest 1mg
- Mix in 500ml bag Normal Saline, infuse over 60 minutes

**CARBOPLATIN**

- 5 x (25+CrCl) max 800mg IV Days 1 Round to nearest 1 mg
- Mix in **250ml bag 5% Dextrose**, infuse over 1 hour on day 1 ONLY (max dose 800mg)

**TESTS:**

- Baseline Tests: WBC HB PLT ANC Ca Cr Urea 24Hr CrCl T.Bili ALT AlkPhosphatase
- Before each treatment: WBC HB PLT ANC Cr T.Bili

**Test Notes:**

- Baseline (required before first treatment): CBC & diff, platelets, total bilirubin, alkaline phosphate, LDH, creatinine, calcium.
- Before each treatment: CBC & diff, platelets, total bilirubin, LDH, creatinine

**ANTIEMETIC PRE-CHEMO REGIMEN:**

- **level C**
- Days 1,2,3
- Ondansetron 8mg PO/IV q8h can be substituted with Granisetron 1-2mg PO/IV daily.

**INPATIENT ANTIEMETICS:**

- Ondansetron can be substituted with Granisetron 1-2mg PO/IV daily.

**ANCILLARY:**

- Calculate CrCl prior to each cycle and calculate dose of Carboplatin accordingly.

**TOXICITIES:**

**Hematologic**

1. If ANC < 1.5 x 10⁹/L, or if PLT < 100 x 10⁹/L, **HOLD** dose for 1 week.
2. SUGGESTED ACTION - Filgrastim 300mcg daily x 5-10 days to allow full dose treatment on schedule

**Renal Failure**

1. ADJUST Carboplatin dose if estimated CrCl changes > 20%.
2. SUGGESTED ACTION

**HYPERSENSITIVITY:**

- Hypersensitivity reaction including anaphylactic shock has been reported with etoposide.
- Monitor etoposide infusion for 15 minutes for signs of hypotension.

**FORMULAE:**

- Creatinine Cl (mL/min) mL/min = 60 x CrCl mL/sec
- CrCl - Cockcroft & Gault (mL/sec) Female: [140-age(ys)] x TBW(Kg) / [50 x SCr(umol/L)] x 0.85
- Calvert Formula Dose (in mg) = target AUC x (GFR + 25) GFR in mL/min

**REFERENCES:**


**Date revised:** 09/04/2008

**HEMATOLOGICAL**
**IMATINIB Therapy**  
*Chronic Myelogenous Leukemia*

<table>
<thead>
<tr>
<th>IMATINIB</th>
<th>400-800mg</th>
<th>PO</th>
<th>Daily</th>
<th>100mg tablets</th>
</tr>
</thead>
</table>
| Dosing:  | - Once daily with food.  
|          | - CML chronic phase = 400mg/day.  
|          | - CML accelerated phase or blast crisis or Ph+ acute leukemias = 600mg/day.  
|          | - Above doses may be increased to 600-800mg respectively, in order to achieve a response.  
|          | - 800mg dose should be administered in two divided doses.  
|          | - Out-patient prescription available as 100mg and 400mg tablets.  
|          | - Trade name = Gleevec™ |

### CONTINUOUS TREATMENT

**TESTS:**
- **Baseline Tests:** WBC, HB, PLT, ANC, Ca, K, Na, Chloride, Phosphate, Mg, Glucose, Cr, Urea, T.Bili, Albumin, ALT, AlkPhosphatase
- **Every 2-4 weeks:** WBC, HB, PLT, ANC, Ca, K, Na, Chloride, Phosphate, Mg, Glucose, Cr, Urea, T.Bili, Albumin, ALT

**Test Notes:**
- LVEF in patients with known underlying heart disease and the elderly.
- EKG to be done.
- FISH or RT-PCR q3-6months

**ANTIEMETIC PRE-CHEMO REGIMEN:**
- Level A Daily
  - Prochlorperazine 10mg PO prn

**ANTIEMETIC TAKE-HOME REGIMEN:**
- Level A Daily
  - Prochlorperazine 10mg PO q4-6h prn

### TOXICITIES:
#### Hematologic
**Chronic Phase CMS:** (starting dose 400mg)
1. If ANC < 1.0 x 10^9/L and/or PLT < 50 x 10^9/L, **STOP** Imatinib until ANC=1.5 x 10^9/L and PLT > 75 x 10^9/L.  
2. Resume treatment with Imatinib at 400mg dose.
3. If recurrence of ANC < 1.0 x 10^9/L and/or PLT < 50 x 10^9/L, repeat step 1 and resume Imatinib at a reduced dose of 300mg.

**Accelerated Phase CML and Blast Crisis and Ph+:** (starting dose 600mg)
1. If ANC < 0.5 x 10^9/L and/or PLT < 10 x 10^9/L, check if cytopenia is related to leukemia (marrow aspirate or biopsy).
2. If cytopenia is unrelated to leukemia, reduce dose of Imatinib to 400mg.
3. If cytopenia persists for 2 weeks, reduce further to 300mg.
4. If cytopenia persists for 4 weeks and is still unrelated to leukemia, STOP Imatinib until ANC>1.0 x 10^9/L and PLT > 20 x 10^9/L and then resume treatment at 300mg.

**Hepatic Dysfunction**
1. If T.Bili is > 3 x ULN or liver transaminases are > 5 x ULN, **HOLD** Imatinib until T.Bili has returned to <1.5 x ULN and/or liver transaminase levels to <2.5 x ULN. Continue treatment at a reduced daily dose (eg. 300mg if treated at 400mg or 400mg if treated at 600mg).

### SUGGESTED ACTION
- Monitor patients for edema and fluid retention (patients > 65 years of age and for doses > 600mg).
- Imatinib is metabolized by CYP3A4 and has many drug-drug interactions (eg. Warfarin).
- Monitor for myalgia and arthralgia.

### INTERNAL CODE:
- OPIS CODE: IMATINIB-HE

### REFERENCES:
- BCCA: Protocol summary for treatment of chronic myeloid leukemia using Imatinib (Gleevec™)  

**Date revised:** 01/16/2009
L17 PROTOCOL (Modified)-Consolidation #1
Chemotherapy

Acute Lymphocytic Leukemia; Lymphoblastic Lymphoma - Modified for Magrath Consolidation Cycle

DAUNORUBICIN 60mg/m² IV Day 1 Round to nearest 1mg
- Slow push through sidearm of free flowing IV; give 10mg/2mL per minute.

CYTARABINE 25mg/m² IV Day 1 Round to nearest 10mg
- Admix in 100mL Normal Saline; Infuse over 15 minutes.

CYTARABINE 200mg/m²/day IV Days 1-5 Round to nearest 10mg
- Admix in Normal Saline to 240mL; Infuse over 5 days via Infusor LV2 pump (2mL/hr).

METHOTREXATE 12mg IT Day 1
- Prepared by hematologist and give as intrathecal injection.
- All IT doses are flat dose and are NOT adjusted for body surface area.

THIOGUANINE 200mg/m² PO Days 1-5 Round to nearest 10mg
- Daily for 5 days.
- Outpatient prescription.

DAUNORUBICIN 60mg/m² IV Day 2 Round to nearest 1mg
- Slow push through sidearm of free flowing IV; give 10mg/2mL per minute.

DAUNORUBICIN 60mg/m² IV Day 3 Round to nearest 1mg
- Slow push through sidearm of free flowing IV; give 10mg/2mL per minute.

METHOTREXATE 12mg IT Day 3
- Prepared by hematologist and give as intrathecal injection.
- All IT doses are flat dose and are NOT adjusted for body surface area.

START CONSOLIDATION #2, 21 to 28 DAYS AFTER CONSOLIDATION # 1

TESTS:
Baseline Tests
- WBC HB PLT ANC Ca K Na Chloride Phosphate Glucose Cr Urea T.Bili Albumin ALT AlkPhosphatase Urate

Day 1
- WBC HB PLT ANC Ca K Na Chloride Phosphate Glucose Cr Urea T.Bili Albumin ALT AlkPhosphatase Urate

Test Notes Baseline:
- Bone marrow aspirate and biopsy done prior to each consolidation and maintenance course.
- INR and PTT to be added to each test day.
- Day 1:
- During period of aplasia, CBC to be done 2 to 3 times per week for blood product support.

ANTIEMETIC PRE-CHEMO REGIMEN:
Level C Days 1-5
- Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
- Dexamethasone 20mg PO/IV

ANTIEMETIC TAKE-HOME REGIMEN:
Level B/C Day 5
- Ondansetron 8mg PO BID for 2-3 days, or Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days
- Dexamethasone 8mg PO BID for 2-3 days
- Prochlorperazine 10mg PO q4-6h pm

PATIENT VISITS and APPOINTMENT TYPE:
- Day 1 1.5hrs Type C
- Day 2: 45min Type B
- Day 3 1.5hrs Type C

TOXICITIES:
Hematologic
1. If ANC < 1.0 x 10⁹/L, or if PLT < 100 x 10⁹/L, HOLD dose for 1 week.

Renal Failure
1. If SrCr > 265 umol/L, reduce Daunorubicin to 50% dose.

Hepatic Dysfunction
1. If T.Bili = 18-36umol/L, REDUCE Daunorubicin to 75% dose.
2. If T.Bili = 36-72umol/L, REDUCE Daunorubicin to 50% dose.
3. If T.Bili > 72umol/L, OMIT Daunorubicin.
4. If evidence of hepatotoxicity or biliary stasis, HOLD Thioguanine.

SUGGESTED ACTION

CLINICAL MONITORING:
- This regimen should only be given by Hematologists trained in the care of acute leukemia patients, and practicing in institutions with adequate acute care designed to support acute leukemia patients.
- All IT doses are flat dose and are NOT adjusted for body surface area.
- This regimen causes severe marrow suppression lasting 21-28 days with blood product support needed.
- Risk of infection high during period of marrow aplasia.

REFERENCES:

Date revised: 10/08/2008
HE \textbf{L17*C2}  
\textbf{Hematological}

**L17 PROTOCOL (Modified)-Consolidation #2 Chemotherapy**  
\textit{Acute Lymphocytic Leukemia; Lymphoblastic Lymphoma - Modified for Magrath}  
\textit{Consolidation Cycle}

**DOXORUBICIN**  
40mg/m\(^2\) IV Day 1  
- \textit{Slow push through sidearm of free-flowing IV}; rate = 2mL (4mg) per minute.

**CYCLOPHOSPHAMIDE**  
1200mg/m\(^2\) IV Day 1  
- Admix in 500mL Normal Saline; Infuse over 30 minutes.

**CYTARABINE**  
70mg IT Day 1  
- Prepared by hematologist and give as \textit{intrathecal} injection.  
- All IT doses are flat dose and are NOT adjusted for body surface area.

**VINCRISTINE**  
1.4mg/m\(^2\) IV Day 1  
- Maximum dose = 2mg  
- Mix in 50mL bag Normal Saline; infuse over 10 minutes.

**PREDNISONE**  
40mg/m\(^2\) PO Days 1-5  
- \text{5mg & 50mg tablets}  
- \text{Daily for 5 days (take with food).}  
- Outpatient prescription.

**CYTARABINE**  
70mg IT Day 2  
- Prepared by hematologist and give as \textit{intrathecal} injection.  
- All IT doses are flat dose and are NOT adjusted for body surface area.

**METHOTREXATE**  
12mg IT Day 3  
- Prepared by hematologist and give as \textit{intrathecal} injection.  
- All IT doses are flat dose and are NOT adjusted for body surface area.  
- May be given on Day 2.

**METHOTREXATE**  
2500mg/m\(^2\) IV Day 10  
- Admix in 1000mL Normal Saline; Infuse over 6 hours.  
- Administered as an \textit{in-patient with alkaline diuresis}.

**LEUCOVORIN**  
12mg/m\(^2\) IV Day 11  
- Admix in 50mL Normal Saline; Infuse over 10-20 minutes starting \textit{24 hours after START of Methotrexate infusion}.  
- Infuse every 6 hours; continue until Methotrexate level < 0.05.

**START CONSOLIDATION #3 , 21 to 28 DAYS AFTER CONSOLIDATION # 2**

**TESTS:**

<table>
<thead>
<tr>
<th>Baseline Tests</th>
<th>WBC HB PLT ANC Ca K Na Chloride Glucose Cr Urea T.Bili Albumin AST ALT AlkPhosphatase Urate</th>
</tr>
</thead>
</table>

**TESTS:**

<table>
<thead>
<tr>
<th>Day 1</th>
<th>WBC HB PLT ANC Cr Urea T.Bili Albumin ALT AlkPhosphatase</th>
</tr>
</thead>
</table>

**Test Notes**

- Bone marrow aspirate and biopsy done prior to each consolidation and maintenance course.  
- INR and PTT to be added to each test day.  
- During period of aplasia, CBC to be done 2 to 3 times per week for blood product support.

**ANTIEMETIC PRE-CHEMO REGIMEN:**

**Level C**

<table>
<thead>
<tr>
<th>Day 1</th>
<th>Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Dexmethasone 20mg PO/IV</td>
</tr>
</tbody>
</table>

| Days 10 & 11 | In-patient |

**ANTIEMETIC TAKE-HOME REGIMEN:**

**Level B/C**

<table>
<thead>
<tr>
<th>Day 1</th>
<th>Ondansetron 8mg PO BID for 2-3 days. or Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Dexmethasone 8mg PO BID for 2-3 days</td>
</tr>
<tr>
<td></td>
<td>Prochlorperazine 10mg PO q4-6h prn</td>
</tr>
</tbody>
</table>

| Days 10 & 11 | In-patient |

**PATIENT VISITS and APPOINTMENT TYPE:**

| ➡ Day 1 | 2hrs | Type C |
|         |      |       |
| ➡ Days 2 & 3 | 1.5hrs | Type C |
| ➡ Days 10 & 11: | In-patient |

**TOXICITIES:**

**Hematologic**

1. If ANC < 1.0 x 10\(^9\)/L, or if PLT < 100 x 10\(^9\)/L, \textbf{HOLD} dose for 1 week (Until ANC \geq 1 x 10\(^9\)/L).

**Renal Failure**

1. If SrCr > 265umol/L, \textbf{REDUCE} Doxorubicin to 50% dose.
2. If CrCl < 0.2mL/sec, \textbf{OMIT} Cyclophosphamide dose.

**Hematological**
Hematological

L17 PROTOCOL (Modified)-Consolidation #2 Chemotherapy

Hepatic Dysfunction
1. If T.Bili = 26-51umol/L, or AST = 60-180 IU/L, REDUCE Doxorubicin to 75% dose and Vincristine to 50% dose.
2. If T.Bili = 52-85umol/L, or AST > 180 IU/L, REDUCE Doxorubicin to 50% dose and Vincristine to 25% dose.
3. If T.Bili > 85umol/L, OMIT ALL drugs.

SUGGESTED ACTION

CLINICAL MONITORING:
- This regimen should only be given by Hematologists trained in the care of acute leukemia patients, and practicing in institutions with adequate acute care designed to support acute leukemia patients.
- All IT doses are flat dose and are NOT adjusted for body surface area.

REFERENCES:

CCO Eligibility Form Required □ Non-Formulary Form Required □ Date revised: 10/08/2008
## L17 PROTOCOL (Modified)-Consolidation #3 Chemotherapy

**Acute Lymphocytic Leukemia; Lymphoblastic Lymphoma - Modified for Magrath Consolidation Cycle**

### METHOTREXATE
- **12mg** IT Day 1
  - Prepared by hematologist and give as intrathecal injection.
  - All IT doses are flat dose and are NOT adjusted for body surface area.

### METHOTREXATE
- **15mg/m²** IV Day 1
  - Maximum dose of 25mg.
  - **Inject by direct IV push**, followed by a Normal Saline flush (if no IV line has been set up).
  - May give by slow push through sidearm of free flowing IV (D5W, Normal Saline).
  - Rate of administration ≤ 10mg per minute.

### CYTARABINE
- **200mg/m²/day** IV Days 1-4
  - Admix in Normal Saline to 192mL. Infuse over 4 days via Infusor LV2 pump (2mL/hr).

### METHOTREXATE
- **15mg/m²** IV Day 2
  - Maximum dose of 25mg.
  - **Slow push through sidearm of free flowing IV** at a rate of ≤ 10mg per minute.

### METHOTREXATE
- **15mg/m²** IV Day 3
  - Maximum dose of 25mg.
  - **Inject by direct IV push**, followed by a Normal Saline flush (if no IV line has been set up).
  - May give by slow push through sidearm of free flowing IV (D5W, Normal Saline).
  - Rate of administration ≤ 10mg per minute.

### METHOTREXATE
- **15mg/m²** IV Day 4
  - Maximum dose of 25mg.
  - **Inject by direct IV push**, followed by a Normal Saline flush (if no IV line has been set up).
  - May give by slow push through sidearm of free flowing IV (D5W, Normal Saline).
  - Rate of administration ≤ 10mg per minute.

### L-ASPARAGINASE
- **20,000 U/m²** IM Day 5
  - **IM injection**: Mix in 2 syringes.
  - Consider platelet transfusion prior to IM injections of l-asparaginase if PLT < 50 x 10⁹/L.

### EPINEPHRINE
- **1:1000** IV Days 5, 7, 9, 11, 13 & 15
  - Keep at bedside.
  - 0.5mL if allergic reaction.

### L-ASPARAGINASE
- **20,000 U/m²** IM Day 7
  - **IM injection**: Mix in 2 syringes.
  - Consider platelet transfusion prior to IM injections of l-asparaginase if PLT < 50 x 10⁹/L.

### L-ASPARAGINASE
- **20,000 U/m²** IM Day 9
  - **IM injection**: Mix in 2 syringes.
  - Consider platelet transfusion prior to IM injections of l-asparaginase if PLT < 50 x 10⁹/L.

### L-ASPARAGINASE
- **20,000 U/m²** IM Day 11
  - **IM injection**: Mix in 2 syringes.
  - Consider platelet transfusion prior to IM injections of l-asparaginase if PLT < 50 x 10⁹/L.

### L-ASPARAGINASE
- **20,000 U/m²** IM Day 13
  - **IM injection**: Mix in 2 syringes.
  - Consider platelet transfusion prior to IM injections of l-asparaginase if PLT < 50 x 10⁹/L.

### L-ASPARAGINASE
- **20,000 U/m²** IM Day 15
  - **IM injection**: Mix in 2 syringes.
  - Consider platelet transfusion prior to IM injections of l-asparaginase if PLT < 50 x 10⁹/L.

### CYCLOPHOSPHAMIDE
- **1200mg/m²** IV 2 weeks after recovery
  - Start 2 weeks after recovery (when AGC > 1 x 10⁹/L and PLT > 100 x 10⁹/L).
  - Admix in **500mL Normal Saline**: Infuse over 30 minutes.

### TESTS:

<table>
<thead>
<tr>
<th>Baseline Tests</th>
<th>WBC HB PLT ANC Ca K Na Chloride Glucose Cr Urea T.Bili Albumin ALT GGT AlkPhosphatase Urate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Days 8 &amp; 15</td>
<td>WBC HB PLT ANC Ca Cr Urea T.Bili Albumin ALT AlkPhosphatase</td>
</tr>
<tr>
<td>Day 1</td>
<td>WBC HB PLT ANC</td>
</tr>
</tbody>
</table>

**Hematological**
L17 PROTOCOL (Modified)-Consolidation #3 Chemotherapy

Test Notes
Baseline:
- Bone marrow aspirate and biopsy done prior to each consolidation and maintenance course.
- INR, PTT and Fibrinogen to be added to each test day.
  Days 1, 8 & 15
- During period of aplasia, CBC to be done 2 to 3 times per week for blood product support.

ANTIEMETIC PRE-CHEMO REGIMEN:
Level C
5, 7, 9, 11, 13, 15 & cyclo day
- Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
- Dexamethasone 20mg PO/IV

ANTIEMETIC TAKE-HOME REGIMEN:
Level B/C
- Ondansetron 8mg PO BID for 2-3 days, or
- Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days
- Dexamethasone 8mg PO BID for 2-3 days
- Prochlorperazine 10mg PO q4-6h prn

PATIENT VISITS and APPOINTMENT TYPE:
- Day 1 1.5hrs Type C
- Day 2-4: 30min Type B
- Days 5, 7, 9, 11, 13 & 15: 30min Type B
- Cyclo Day: 45min Type B

TOXICITIES:
Hematologic
1. If ANC < 1.0 x 10^9/L, or if PLT < 100 x 10^9/L, HOLD dose for 1 week (Until ANC ≥ 1.0 x 10^9/L).
2. If INR > 1.4, or PTT > 42sec, or Fibrinogen < 1.0 G/L, HOLD L-asparaginase.

Renal Failure
1. If CrCl < 0.2mL/sec, OMIT Cyclophosphamide dose.

Hepatic Dysfunction
1. If T.Bili > 85umol/L, OMIT L-asparaginase.

SUGGESTED ACTION
- This regimen should only be given by Hematologists trained in the care of acute leukemia patients, and practicing in institutions with adequate acute care designed to support acute leukemia patients.
- All IT doses are flat dose and are NOT adjusted for body surface area.
- L-asparaginase can cause anaphylactic reactions, therefore epinephrine should be kept at the bedside.

Allergic Reaction
1. Transient flushing or rash; drug fever < 38 degrees C
2. Rash; flushing; urticaria; dyspnea; drug fever ≥ 38 degrees C
3. Symptomatic bronchospasm, with or without urticaria; parenteral medication(s) indicated; allergy-related edema/angioedema; hypotension
4. Anaphylaxis
5. Death

RATED IN RESPONSE TO PATIENT REACTION

INTERNAL CODE:
OPIS CODES:
- L17*C3 DAYS 1-4
- L17*C3 DAYS 5-15

REFERENCES:
**L17 PROTOCOL-Induction Chemotherapy**  
*Acute Lymphocytic Leukemia; Lymphoblastic Lymphoma*

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
<th>Route</th>
<th>Day</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>VINCRISTINE</strong></td>
<td>2mg/m²</td>
<td>IV</td>
<td>Day 1</td>
<td>Round to nearest 0.1mg</td>
</tr>
<tr>
<td>- Maximum dose = 4mg if patient &lt; 60 years old &amp; 2.5mg if &gt; 60 years old.</td>
<td></td>
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</tr>
<tr>
<td>- May cap dose at 2mg if neuropathies.</td>
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<td></td>
</tr>
<tr>
<td>- Mix in <strong>50mL bag Normal Saline</strong>; infuse over 10 minutes.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>PREDNISONE</strong></td>
<td>60mg/m²</td>
<td>PO</td>
<td>Days 1-30</td>
<td>5mg &amp; 50mg tablets</td>
</tr>
<tr>
<td>- Daily for 30 days, then taper over 7 days.</td>
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<td></td>
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<tr>
<td>- Outpatient prescription.</td>
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<td></td>
</tr>
<tr>
<td><strong>METHOTREXATE</strong></td>
<td>12mg</td>
<td>IT</td>
<td>Day 2</td>
<td></td>
</tr>
<tr>
<td>- Prepared by hematologist and give as <strong>intrathecal</strong> injection.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- All IT doses are flat dose and are NOT adjusted for body surface area.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>METHOTREXATE</strong></td>
<td>12mg</td>
<td>IT</td>
<td>Day 4</td>
<td></td>
</tr>
<tr>
<td>- Prepared by hematologist and give as <strong>intrathecal</strong> injection.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- All IT doses are flat dose and are NOT adjusted for body surface area.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>VINCRISTINE</strong></td>
<td>2mg/m²</td>
<td>IV</td>
<td>Day 8</td>
<td>Round to nearest 0.1mg</td>
</tr>
<tr>
<td>- Maximum dose = 4mg if patient &lt; 60 years old &amp; 2.5mg if &gt; 60 years old.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- May cap dose at 2mg if neuropathies.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Mix in <strong>50mL bag Normal Saline</strong>; infuse over 10 minutes.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>METHOTREXATE</strong></td>
<td>12mg</td>
<td>IT</td>
<td>Day 13</td>
<td></td>
</tr>
<tr>
<td>- Prepared by hematologist and give as <strong>intrathecal</strong> injection.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- All IT doses are flat dose and are NOT adjusted for body surface area.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>METHOTREXATE</strong></td>
<td>12mg</td>
<td>IT</td>
<td>Day 15</td>
<td></td>
</tr>
<tr>
<td>- Prepared by hematologist and give as <strong>intrathecal</strong> injection.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- All IT doses are flat dose and are NOT adjusted for body surface area.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>VINCRISTINE</strong></td>
<td>2mg/m²</td>
<td>IV</td>
<td>Day 15</td>
<td>Round to nearest 0.1mg</td>
</tr>
<tr>
<td>- Maximum dose = 4mg if patient &lt; 60 years old &amp; 2.5mg if &gt; 60 years old.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- May cap dose at 2mg if neuropathies.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Mix in <strong>50mL bag Normal Saline</strong>; infuse over 10 minutes.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>DOXORUBICIN</strong></td>
<td>20mg/m²</td>
<td>IV</td>
<td>Day 16</td>
<td>Round to nearest 1mg</td>
</tr>
<tr>
<td>- <strong>Slow push through sidearm of free-flowing IV</strong>; rate = 2mL (4mg) per minute.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>DOXORUBICIN</strong></td>
<td>20mg/m²</td>
<td>IV</td>
<td>Day 17</td>
<td>Round to nearest 1mg</td>
</tr>
<tr>
<td>- <strong>Slow push through sidearm of free-flowing IV</strong>; rate = 2mL (4mg) per minute.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>DOXORUBICIN</strong></td>
<td>20mg/m²</td>
<td>IV</td>
<td>Day 18</td>
<td>Round to nearest 1mg</td>
</tr>
<tr>
<td>- <strong>Slow push through sidearm of free-flowing IV</strong>; rate = 2mL (4mg) per minute.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>VINCRISTINE</strong></td>
<td>2mg/m²</td>
<td>IV</td>
<td>Day 22</td>
<td>Round to nearest 0.1mg</td>
</tr>
<tr>
<td>- Maximum dose = 4mg if patient &lt; 60 years old &amp; 2.5mg if &gt; 60 years old.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- May cap dose at 2mg if neuropathies.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Mix in <strong>50mL bag Normal Saline</strong>; infuse over 10 minutes.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>VINCRISTINE</strong></td>
<td>2mg/m²</td>
<td>IV</td>
<td>Day 29</td>
<td>Round to nearest 0.1mg</td>
</tr>
<tr>
<td>- Maximum dose = 4mg if patient &lt; 60 years old &amp; 2.5mg if &gt; 60 years old.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- May cap dose at 2mg if neuropathies.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Mix in <strong>50mL bag Normal Saline</strong>; infuse over 10 minutes.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>METHOTREXATE</strong></td>
<td>12mg</td>
<td>IT</td>
<td>Day 31</td>
<td></td>
</tr>
<tr>
<td>- Prepared by hematologist and give as <strong>intrathecal</strong> injection.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- All IT doses are flat dose and are NOT adjusted for body surface area.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>METHOTREXATE</strong></td>
<td>12mg</td>
<td>IT</td>
<td>Day 33</td>
<td></td>
</tr>
<tr>
<td>- Prepared by hematologist and give as <strong>intrathecal</strong> injection.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- All IT doses are flat dose and are NOT adjusted for body surface area.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>DOXORUBICIN</strong></td>
<td>30mg/m²</td>
<td>IV</td>
<td>Day 34</td>
<td>Round to nearest 1mg</td>
</tr>
<tr>
<td>- <strong>Slow push through sidearm of free-flowing IV</strong>; rate = 2mL (4mg) per minute.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>CYCLOPHOSPHAMIDE</strong></td>
<td>600mg/m²</td>
<td>IV</td>
<td>Day 34</td>
<td>Round to nearest 10mg</td>
</tr>
<tr>
<td>- Admix in <strong>250mL in Normal Saline</strong>; Infuse over <strong>20 minutes</strong>.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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**START CONSOLIDATION ON DAY 48 OF INDUCTION CYCLE**
L17 PROTOCOL-Induction Chemotherapy

**TESTS:**

**Baseline Tests**
- WBC  HB  PLT  ANC  Ca  K  Na  Chloride  Phosphate  Glucose  Cr  Urea  T.Bili  Albumin  ALT  AlkPhosphatase  Urate

**Day 1**
- WBC  HB  PLT  ANC  Ca  K  Na  Chloride  Phosphate  Glucose  Cr  Urea  T.Bili  Albumin  ALT  AlkPhosphatase  Urate

**Days 8 to 34**
- WBC  HB  PLT  ANC  Ca  K  Na  Chloride  Phosphate  Glucose  Cr  Urea  T.Bili  Albumin  ALT  AlkPhosphatase  Urate

**Test Notes**
- Bone marrow aspirate and biopsy done prior to induction chemotherapy, Day 48 of induction chemotherapy, and prior to each consolidation and maintenance course.
- INR and PTT twice weekly (more often if abnormal).
- CBC, lytes, urea & creatinine usually done daily while in hospital.
- Calcium, phosphate & urea done daily for first 3 days if concern for tumour lysis syndrome.
- LVEF if clinically indicated.

**ANTIEMETIC PRE-CHEMO REGIMEN:**

| Level A | Days 16-18 | - Prochlorperazine 10mg PO prn |
| Level C | Day 34     | - Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV |
|         |            | - Dexamethasone 20mg PO/IV |

**ANTIEMETIC TAKE-HOME REGIMEN:**

| Level A | Days 16-18 | - Prochlorperazine 10mg PO q4-6h pm |
| Level B/C | Day 34   | - Ondansetron 8mg PO BID for 2-3 days, or Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days |
|          |          | - Dexamethasone 8mg PO BID for 2-3 days |
|          |          | - Prochlorperazine 10mg PO q4-6h pm |

**PATIENT VISITS and APPOINTMENT TYPE:**

- Days 1,8,22 & 29 30min Type B
- Days 2,4,13,15,31 & 33 1.5hrs Type C
- Days 16,17,18 & 34 45min Type B

**TOXICITIES:**

**Hematologic**

- Day 34 Only
  1. If ANC < 1.0 x 10^9/L, or if PLT < 100 x 10^9/L, HOLD dose for 1 week (until AGC > 1.0 x 10^9/L).

**Renal Failure**

1. If SrCr > 265 umol/L, REDUCE Doxorubicin to 50% dose.
2. If CrCl < 0.2mL/sec, OMIT Cyclophosphamide dose.

**Hepatic Dysfunction**

1. If T.Bili = 26-51 umol/L, or AST = 60-180 IU/L, REDUCE Doxorubicin to 75% dose, and Vincristine to 50% dose.
2. If T.Bili > 52-85 umol/L, or AST > 180 IU/L, REDUCE Doxorubicin to 50% dose and Vincristine to 25% dose.
3. If T.Bili > 85 umol/L, OMIT ALL drugs.

**CLINICAL MONITORING:**

- This regimen should only be given by Hematologists trained in the care of acute leukemia patients, and practicing in institutions with adequate acute care designed to support acute leukemia patients.
- Induction therapy may require hospitalization for supportive care.
- Initiation of induction therapy will require special measures to monitor and prevent complications of tumour lysis syndrome.
- Vincristine dose may be modified for autonomic and peripheral neuropathy. This will usually involve capping dose at 2.0mg as an initial step, and omitting dose for cases of severe toxicity.
- Doxorubicin and Cyclophosphamide doses are not generally delayed or modified for cytopenias. In cases where bone marrows done during induction show hypoplasia, Day 34 doses may be delayed until recovery of neutrophils and platelets.
- Protocol of IT doses of Methotrexate may be modified according to physician’s availability. Initiation of IT methotrexate should be deferred until stabilization of any coagulopathy and reduction of circulating blast count. Platelet transfusion to be done prior to IT injection if platelets < 50 x 10^9/L.
- All IT doses are flat dose and are NOT adjusted for body surface area.
- Protocols that lead to prolonged periods of marrow suppression have increased risks of serious infection and bleeding.
- Neurologic toxicity ratings (Sensory, Constipation) at each visit.

**Sensory**

1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function
2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL
3. Sensory alteration or paresthesia interfering with ADL
4. Disabling 5. Death

**Constipation**

1. Occasional or intermittent symptoms; occasional use of stool softeners, laxatives, dietary modification, or enema
2. Persistent symptoms with regular use of laxatives or enemas indicated
3. Symptoms interfering with ADL; obstipation with manual evacuation indicated
4. Life-threatening consequences (e.g., obstruction, toxic megacolon)
5. Death

**RATED AT EACH CLINIC VISIT**
GREEN STR
Hematological

L17 PROTOCOL-Induction Chemotherapy

INTERNAL CODE:
OPIS CODES:
- L17*I DAYS 1-4
- L17*I DAYS 8-15
- L17*I DAYS 16-18
- L17*I DAYS 22-29
- L17*I DAYS 31-34

REFERENCES:

CCO Eligibility Form Required ☐ Non-Formulary Form Required ☐ Date revised: 10/08/2008
**L17 PROTOCOL-MAINTENANCE Chemotherapy, Sequence #1**

**Acute Lymphocytic Leukemia; Lymphoblastic Lymphoma**

**VINCristine**
- Maximum dose = 2mg
- Mix in **50mL** bag **Normal Saline**; infuse over 10 minutes.

**Prednisone**
- **BID** for 7 days.
- Outpatient prescription.

**VINCristine**
- Maximum dose = 2mg
- Mix in **50mL** bag **Normal Saline**; infuse over 10 minutes.

**Doxorubicin**
- Daily for 3 days.
- Slow push through sidearm of free-flowing IV; rate = 2mL (4mg) per minute.

**6-Mercaptopurine**
- Daily for 28 days.
- May give a maximum daily dose of 100mg.
- Decrease if hepatotoxicity.
- Outpatient prescription.

**Methotrexate**
- Maximum dose = 25mg
- Daily for one day only, starting 3 days after first day of Mercaptopurine.
- Outpatient prescription.

**Methotrexate**
- Prepared by hematologist and give as **intrathecal** injection.
- Daily x 2 doses (Give IT Methotrexate doses 48 hours apart).
- All IT doses are flat dose and are NOT adjusted for body surface area.

**Methotrexate**
- Maximum dose = 25mg
- Daily for one day only.
- Outpatient prescription.

**Methotrexate**
- Maximum dose = 25mg
- Daily for one day only.
- Outpatient prescription.

**Methotrexate**
- Maximum dose = 25mg
- Daily for one day only.
- Outpatient prescription.

**Dactinomycin**
- Maximum dose = 2mg
- Daily for one day only.
- Outpatient prescription.

**Dactinomycin**
- Slow push through sidearm of free-flowing IV, then flush line.

**Tests:**
- **Baseline Tests**
  - WBC, HB, PLT, ANC, Ca, K, Na, Chloride, Glucose, Cr, Urea, T.Bili, Albumin, ALT, AlkPhosphatase
- **Weeks 1 to 10**
  - WBC, HB, PLT, ANC, Ca, K, Na, Chloride, Glucose, Cr, Urea, T.Bili, ALT, AlkPhosphatase

**Test Notes**
- Bone marrow aspirate and biopsy done prior to each maintenance course.

**ANTIEMETIC PRE-CHEMO REGIMEN:**
- **Level A**
  - Weeks 1, 2, 5, 6, 7 & 8 - Prochlorperazine 10mg PO pm
- **Level C**
  - Weeks 3 & 10 - Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
  - Dexamethasone 20mg PO/IV

**ANTIEMETIC TAKE-HOME REGIMEN:**
- **Level A**
  - Weeks 1, 2, 5, 6, 7, 8 - Prochlorperazine 10mg PO q4-6h PRN
- **Level B/C**
  - Weeks 3 & 10 - Ondansetron 8mg PO BID for 2-3 days, or Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days
  - Dexamethasone 8mg PO BID for 2-3 days
  - Prochlorperazine 10mg PO q4-6h pm
PATIENT VISITS and APPOINTMENT TYPE:

- Week 1 & 2: 30min  
  Type B
- Week 3 (3 days): 45min  
  Type B
- Week 5 (2 days): 1.5hrs  
  Type C
- Week 10: 30min  
  Type B

TOXICITIES:

Hematologic
1. If ANC < 1.0 x 10^9/L, or if PLT < 100 x 10^9/L, HOLD dose for 1 week (until AGC > 1 x 10^9/L).

Renal Failure
1. If SrCr > 265umol/L, REDUCE Doxorubicin to 50% dose.

Hepatic Dysfunction
1. If T.Bili = 26-51umol/L, or AST = 60-180 IU/L, REDUCE Doxorubicin to 75% dose, and Vincristine to 50% dose.
2. If T.Bili = 50-85umol/L, or AST > 180 IU/L, REDUCE Methotrexate to 75% dose.
3. If T.Bili > 85umol/L, OMIT ALL drugs.

SUGGESTED ACTION

CLINICAL MONITORING:
- This regimen should only be given by Hematologists trained in the care of acute leukemia patients, and practicing in institutions with adequate acute care designed to support acute leukemia patients.
- For patients age > 65 and for many other patients, week 1 Prednisone will need capping at 100mg total dose if there is persisting myopathy from induction therapy.
- For weeks 5-8 and 10, treatment each week should be delayed until AGC > 1.0 x 10^9/L, and PLT > 100 x 10^9/L.
- Periodic cardiac tests for all patients with cardiac risk factors or patients at or above the threshold dose levels (Doxorubicin 450mg/m^2).
- Neurologic toxicity ratings (Sensory, Constipation) at each visit.

Sensory
1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function 2.
2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL 3.
3. Sensory alteration or paresthesia interfering with ADL 4.
4. Disabling 5.
5. Death

Constipation
1. Occasional or intermittent symptoms; occasional use of stool softeners, laxatives, dietary modification, or enema
2. Persistent symptoms with regular use of laxatives or enemas indicated
3. Symptoms interfering with ADL; obstipation with manual evacuation indicated
4. Life-threatening consequences (e.g., obstruction, toxic megacolon)
5. Death

RATED AT EACH CLINIC VISIT

INTERNAL CODE:
- L17*M1 WKS 1-2
- L17*M1 WK 3
- L17*M1 WK 5-10

REFERENCES:

Date revised: 10/08/2008
**Hematological L17 PROTOCOL-MAINTENANCE Chemotherapy Sequence #2**

**Acute Lymphocytic Leukemia; Lymphoblastic Lymphoma**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
<th>Route</th>
<th>Week</th>
<th>Frequency</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>VINCRISTINE</td>
<td>2mg/m²</td>
<td>IV</td>
<td>1</td>
<td>1 day</td>
<td>Maximum dose = 2mg; Mix in 50mL bag Normal Saline; infuse over 10 minutes.</td>
</tr>
<tr>
<td>PREDNISONE</td>
<td>90mg/m²</td>
<td>PO</td>
<td>1</td>
<td></td>
<td>BID for 7 days. - Outpatient prescription.</td>
</tr>
<tr>
<td>VINCRISTINE</td>
<td>2mg/m²</td>
<td>IV</td>
<td>2</td>
<td>1 day</td>
<td>Maximum dose = 2mg; Mix in 50mL bag Normal Saline; infuse over 10 minutes.</td>
</tr>
<tr>
<td>CARMUSTINE</td>
<td>80mg/m²</td>
<td>IV</td>
<td>3</td>
<td>1 day</td>
<td>Admin in 250mL Normal Saline; Infuse over 60 minutes.</td>
</tr>
<tr>
<td>CYCLOPHOSPHAMIDE</td>
<td>800mg/m²</td>
<td>IV</td>
<td>3</td>
<td>1 day</td>
<td>Admin in 250mL Normal Saline; Infuse over 20 minutes.</td>
</tr>
<tr>
<td>6-MERCAPTOPURINE</td>
<td>90mg/m²</td>
<td>PO</td>
<td>5</td>
<td></td>
<td>Daily for 28 days. - May give a maximum daily dose of 100mg. - Decrease if hepatotoxicity. - Outpatient prescription.</td>
</tr>
<tr>
<td>METHOTREXATE</td>
<td>15mg/m²</td>
<td>PO</td>
<td>5</td>
<td>1 day</td>
<td>Maximum dose = 25mg; Daily for one day only; starting 3 days after first day of Mercaptopurine. - Outpatient prescription.</td>
</tr>
<tr>
<td>METHOTREXATE</td>
<td>12mg</td>
<td>IT</td>
<td>5</td>
<td>2 days</td>
<td>Prepared by hematologist and give as intrathecal injection. - Give IT Methotrexate doses 2 days apart. - All IT doses are flat dose and are NOT adjusted for body surface area.</td>
</tr>
<tr>
<td>METHOTREXATE</td>
<td>15mg/m²</td>
<td>PO</td>
<td>6</td>
<td>1 day</td>
<td>Maximum dose = 25mg; Daily for one day only. - Outpatient prescription.</td>
</tr>
<tr>
<td>METHOTREXATE</td>
<td>15mg/m²</td>
<td>PO</td>
<td>7</td>
<td>1 day</td>
<td>Maximum dose = 25mg; Daily for one day only. - Outpatient prescription.</td>
</tr>
<tr>
<td>METHOTREXATE</td>
<td>15mg/m²</td>
<td>PO</td>
<td>8</td>
<td>1 day</td>
<td>Maximum dose = 25mg; Daily for one day only. - Outpatient prescription.</td>
</tr>
<tr>
<td>DACTINOMYCIN</td>
<td>1mg/m²</td>
<td>IV</td>
<td>10</td>
<td>1 day</td>
<td>Slow push through sidearm of free-flowing IV, then flush line. Round to nearest 0.05mg</td>
</tr>
</tbody>
</table>

**TESTS:**
- Test Notes: Bone marrow aspirate and biopsy done prior to each maintenance course.

**ANTIEMETIC PRE-CHEMO REGIMEN:**
- **Level A** Weeks 1, 2, 5, 6, 7, 8: Prochlorperazine 10mg PO pm
  - Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
  - Dexamethasone 20mg PO/IV

**ANTIEMETIC TAKE-HOME REGIMEN:**
- **Level A** Weeks 1, 2, 5, 6, 7, 8: Prochlorperazine 10mg PO q4-6h pm
  - Ondansetron 8mg PO for 2-3 days, or Granisetron 1mg PO OD for 2-3 days
  - Dexamethasone 8mg PO for 2-3 days
  - Prochlorperazine 10mg PO q4-6h pm
PATIENT VISITS and APPOINTMENT TYPE:

- Weeks 1 & 2: 30min Type B
- Week 3: 2hrs Type C
- Week 5: 1.5hrs Type C
- Week 10: 30min Type B

TOLERANCES:

Hematologic
1. If ANC < 1.0 x 10^9/L, or if PLT < 100 x 10^9/L, HOLD dose for 1 week (until AGC > 1 x 10^9/L).

Renal Failure
1. If CrCl < 0.2mL/sec, REDUCE Carmustine by 50-75% and OMIT Cyclophosphamide.

Hepatic Dysfunction
1. If T.Bili = 26-51umol/L or AST = 60-180 IU/L, REDUCE Vincristine to 50% dose.
2. If T.Bili = 52-85umol/L or AST > 180 IU/L, REDUCE Vincristine to 25% dose.
3. If T.Bili > 85umol/L, OMIT ALL drugs.

SUGGESTED ACTION

CLINICAL MONITORING:
- This regimen should only be given by Hematologists trained in the care of acute leukemia patients, and practicing in institutions with adequate acute care designed to support acute leukemia patients.
- For patients age > 65 and for many other patients, week 1 Prednisone will need capping at 100mg total dose if there is persisting myopathy from induction therapy.
- For weeks 5-8 and 10, treatment each week should be delayed until AGC > 1.0 x 10^9/L, and PLT > 100 x 10^9/L.
- Neurologic toxicity ratings (Sensory, Constipation) at each visit.

Sensory
1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function
2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL
3. Sensory alteration or paresthesia interfering with ADL
4. Disabling
5. Death

Constipation
1. Occasional or intermittent symptoms; occasional use of stool softeners, laxatives, dietary modification, or enema
2. Persistent symptoms with regular use of laxatives or enemas indicated
3. Symptoms interfering with ADL; obstipation with manual evacuation indicated
4. Life-threatening consequences (e.g., obstruction, toxic megacolon)
5. Death

RATED AT EACH CLINIC VISIT

INTERNAL CODE:
OPIS CODES:
- L17*M2 WKS 1-2
- L17*M2 WK 3
- L17*M2 WK 5-10

REFERENCES:

CCO Eligibility Form Required [ ] Non-Formulary Form Required [ ] Date revised: 10/08/2008
**LENALIDOMIDE/ DEXAMETHASONE Therapy**

*Multiple Myeloma*

**Cycle 1-4**

### LENALIDOMIDE

- **Dosage:** 25mg PO Day 1-21, 5mg capsule
- **Instructions:**
  - Dose is 25mg daily Days 1-21 every 28 days with water, swallow whole and preferable on an empty stomach.
  - Indicated for the treatment of multiple myeloma patients who have received at least one prior therapy.
  - Trade name is Revlimid™ (Celgene)
  - Exceptional Access Program (Section 16) with specific criteria
  - Continue or modify treatment until disease progression or unacceptable toxicities.
  - Available as 5, 10, 15 and 25mg capsules.
  - Swallow capsule whole with a glass of water with or without food.

### DEXAMETHASONE

- **Dosage:** 40mg PO Day 1-4, 9-12 & 17-20, 0.5mg tablet
- **Instructions:**
  - Daily for 4 days starting Days 1, 9 & 17.
  - Outpatient prescription available in 0.5mg and 4mg tablets.
  - Trade name is Decadron™

**Repeat every 28 days x 4 cycles**

**Cycle 5 and subsequent cycles**

### LENALIDOMIDE

- **Dosage:** 25mg PO Day 1-21, 5mg capsule
- **Instructions:**
  - Dose is 25mg daily Days 1-21 every 28 days with water, swallow whole and preferable on an empty stomach.
  - Indicated for the treatment of multiple myeloma patients who have received at least one prior therapy.
  - Trade name is Revlimid™ (Celgene)
  - Exceptional Access Program (Section 16) with specific criteria
  - Continue or modify treatment until disease progression or unacceptable toxicities.
  - Available as 5, 10, 15 and 25mg capsules.
  - Swallow capsule whole with a glass of water with or without food.

### DEXAMETHASONE

- **Dosage:** 40mg PO Day 1-4, 0.5mg tablets
- **Instructions:**
  - Daily for 4 days starting Day 1
  - Outpatient prescription available in 0.5mg and 4mg tablets.
  - Trade name is Decadron™

**Repeat every 28 days until disease progression or unacceptable toxicities**

**TESTS:**

- **Baseline Tests**
  - WBC, Hb, PLT, ANC, Ca, K, Na, Chloride, Mg, Cr, Urea, T.Bili, Albumin, AST, ALT, AlkPhosphatase

- **Monthly Tests**
  - WBC, Hb, PLT, ANC, Ca, K, Na, Chloride, Cr, Urea, T.Bili, Albumin, AST, ALT

- **Test Notes**
  - Thyroid function tests TSH and T4 levels.
  - CBC q2weeks X 12 weeks then monthly.
  - Women of child bearing potential require serum pregnancy test 10-14 days and 24 hours before first dose; weekly tests during first month of treatment, then monthly and 4 weeks after discontinuing treatment.

**ANCILLARY:**

- **Contraception**
  - Women of child bearing potential require serum pregnancy test 10-14 days and 24 hours before first dose; then weekly for 1 month; then monthly and 4 weeks after discontinuing Lenalidomide.
  - Women must use 2 effective contraception methods for 1 month before, during and 1 month after Lenalidomide therapy.
  - Mandatory contraception for male patients even if they have undergone a successful vasectomy.
  - Risk of thromboembolism - give low dose ASA or LMWH if high risk; avoid Erythropoietin if possible
  - Breast feeding is contraindicated.
  - Lenalidomide is a human TERATOGEN and can cause life threatening birth defects or fetal death if taken during pregnancy.

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**Hematological**
LENALIDOMIDE/ DEXAMETHASONE Therapy

TOXICITIES:
Hematologic
Thrombocytopenia
1. If PLT < 30x10^9/L HOLD treatment until PLT > 30x10^9/L, then resume Lenalidomide at 15mg/day.
2. If PLT < 30x10^9/L with subsequent doses HOLD treatment until PLT > 30x10^9/L then resume treatment at 5mg
less than the previous dose. Minimm dose is 5mg daily.

Hematologic
Neutropenia
1. If ANC < 1.0x10^9/L HOLD treatment until ANC≥1.0x10^9/L, then add G-CSF and resume at 25mg/day if no other
toxicities. If other toxicities present, resume Lenalidomide therapy at 15mg/day.
2. For each subsequent drop, if ANC < 1.0x10^9/L HOLD treatment until ANC≥1.0x10^9/L and resume Lenalidomide at
5mg less than the previous dose. Do not dose below 5mg daily.

Renal Failure
1. If CrCl <0.8mL/sec REDUCE dose to 10mg daily (may increase to 15mg daily if not responding and tolerating
drug).
2. If CrCl <0.5mL/sec (not requiring dialysis) REDUCE dose to 15mg every other day.
3. If CrCl <0.5mL/sec (requiring dialysis) REDUCE dose to 15mg three times a week following each dialysis.

SUGGESTED ACTION

CLINICAL MONITORING:
Fatigue
1. Mild fatigue over baseline  2. Moderate or causing difficulty performing some ADL  3. Severe fatigue interfering
with ADL  4. Disabling
Diarrhea
1. Increase of < 4 stools per day over baseline; mild increase in ostomy output compared to baseline
2. Increase of 4 - 6 stools per day over baseline; IV fluids indicated < 24hrs; moderate increase in ostomy output
compared to baseline; not interfering with ADL
3. Increase of >=7 stools per day over baseline; incontinence; IV fluids >=24 hrs; hospitalization; severe increase in
ostomy output compared to baseline; interfering with ADL
4. Life-threatening consequences (e.g. hemodynamic collapse)  5. Death
Constipation
1. Occasional or intermittent symptoms; occasional use of stool softeners, laxatives, dietary modification, or enema
2. Persistent symptoms with regular use of laxatives or enemas indicated  3. Symptoms interfering with ADL;
obstipation with manual evacuation indicated  4. Life-threatening consequences (e.g., obstruction, toxic megacolon)
5. Death
RATED AT EACH CLINIC VISIT

FORMULAE:
CrCl - Cockcroft & Gault (mL/sec)  Male: [140-age(yrs)] x TBW(Kg) / [50 x SCr(umol/L)]
CrCl - Cockcroft & Gault (mL/sec)  Female: [140-age(yrs)] x TBW(Kg) / [50 x SCr(umol/L)] x 0.85

REFERENCES:
alone in relapsed or refractory multiple myeloma (MM): results of a phase 3 study (MM010). Blood, 2005; 106:106,
Abstract 6.
- Michael Wang, Meletios A. Dimopoulos, Christine Chen, M. Teresa Cibeira, Michel Attal, Andrew Spencer,
S. Vincent Rajkumar, Zhinuan Yu, Marta Olesnyckyj, Jerome B.Zeldis, Robert D.Knight, and Donna M. Weber,
Lenalidomide plus Dexamethasone is more effective than Dexamethasone alone in patients with relapsed or

Date revised: 01/21/2009
LENALIDOMIDE Therapy
Myelodysplastic Syndrome - Deletion 5q

LENALIDOMIDE 10mg PO Daily 5mg capsule
- Dose is 10mg daily with water, swallow whole and preferable on an empty stomach.
- Indicated (NOC/c) for the treatment of patients with transfusion-dependent anemia due to low- or intermediate-1-risk myelodysplastic syndromes (MDS) associated with a deletion 5q cytogenetic abnormality with or without additional cytogenetic abnormalities.
- Exceptional Access Program (Section 16) with specific criteria
- Trade name is Revlimid™ (Celgene)
- Continue treatment until disease progression or unacceptable toxicities.
- Available as 5mg and 10mg capsules.
- Swallow capsule whole with a glass of water with or without food.

CONTINUOUS TREATMENT

TESTS:
Baseline Tests WBC HB PLT ANC Ca K Na Chloride Mg Cr Urea T.Bili Albumin AST ALT AlkPhosphatase
Monthly WBC HB PLT ANC Ca K Na Chloride Cr Urea T.Bili Albumin AST ALT
Test Notes - Thyroid function tests TSH, T3 and T4 levels every 3 months.
- CBC weekly X 8 weeks then monthly.
- Women of child bearing potential require serum pregnancy test 10-14 days and 24 hours before first dose; weekly tests during first month of treatment, then monthly and 4 weeks after discontinuing treatment.

ANCILLARY:
Contraception
- Women of child bearing potential require serum pregnancy test 10-14 days and 24 hours before first dose; then weekly for 1 month; then monthly and 4 weeks after discontinuing Lenalidomide.
- Women must use 2 effective contraception methods for 1 month before, during and 1 month after Lenalidomide therapy.
- Mandatory contraception for male patients even if they have undergone a successful vasectomy.
- Risk of thromboembolism - give low dose ASA or LMWH if high risk; avoid Erythropoietin if possible
- Breast feeding is contraindicated.
- Lenalidomide is a human TERATOGEN and can cause life threatening birth defects or fetal death if taken during pregnancy.

TOXICITIES:
Hematologic
Thrombocytopenia
Within first 4 weeks of treatment
1. If baseline PLT>100x10^9/L and falls to PLT<50x10^9/L HOLD until PLT>50x10^9/L, then resume at 5mg/day.
2. If baseline PLT<100x10^9/L and PLT falls to <50% baseline HOLD until PLT >50% baseline, then resume at 5mg/day.
After first 4 weeks of treatment
3. If baseline PLT<100x10^9/L and falls to PLT<30-50x10^9/L despite platelet transfusion, HOLD until PLT>30x10^9/L and then resume at 5mg/day.
4. If patient already on 5mg/day and baseline PLT>100x10^9/L and falls to PLT<30-50x10^9/L despite platelet transfusion, HOLD until PLT>30x10^9/L and then resume at 5mg every other day.

Hematologic
Neutropenia
Within first 4 weeks of treatment
1. If baseline ANC>1.0x10^9/L and falls to ANC<0.75x10^9/L HOLD until ANC>1.0x10^9/L, then resume at 5mg/day.
2. If baseline ANC<1.0x10^9/L and falls to ANC<0.50x10^9/L HOLD until ANC>0.50x10^9/L, then resume at 5mg/day.
After first 4 weeks of treatment
3. If ANC<0.50x10^9/L for > 7days or ANC<0.50x10^9/L with fever >38.5°C, HOLD until ANC>0.50x10^9/L and then resume at 5mg/day.
SUGGESTED ACTION

Renal Failure
1. If CrCl <0.8mL/sec REDUCE dose to 5mg daily.
2. If CrCl <0.5mL/sec (not requiring dialysis) REDUCE dose to 5mg every other day.
3. If CrCl <0.5mL/sec (requiring dialysis) REDUCE dose to 5mg three times a week following each dialysis
SUGGESTED ACTION
LENALIDOMIDE Therapy

**Hematological**

**CLINICAL MONITORING:**

**Fatigue**
1. Mild fatigue over baseline  
2. Moderate or causing difficulty performing some ADL  
3. Severe fatigue interfering with ADL  
4. Disabling

**Rash**
1. Macular or papular eruption or erythema without associated symptoms  
2. Macular or papular eruption or erythema with pruritus or other associated symptoms; localized desquamation or other lesions covering < 50% of body surface area (BSA)  
3. Severe, generalized erythroderma or macular, papular or vesicular eruption; desquamation covering >=50% BSA  
4. Generalized exfoliative, ulcerative, or bullous dermatitis  
5. Death

- Rash on trunk, back and proximal extremities may appear 10-14 days after start of treatment.  
- Resolution occurs within 24 hours of discontinuation, but patient may be rechallenged at a lower dose.  
- Monitor for ongoing rash that may require discontinuation.

**Diarrhea**
1. Increase of < 4 stools per day over baseline; mild increase in ostomy output compared to baseline  
2. Increase of 4-6 stools per day over baseline; IV fluids indicated < 24hrs; moderate increase in ostomy output compared to baseline; not interfering with ADL  
3. Increase of >=7 stools per day over baseline; incontinence; IV fluids >=24 hrs; hospitalization; severe increase in ostomy output compared to baseline; interfering with ADL  
4. Life-threatening consequences (e.g. hemodynamic collapse)  
5. Death

**RATED AT EACH CLINIC VISIT**

**FORMULAE:**

\[
\text{CrCl - Cockcroft & Gault (mL/sec)} = \frac{140 - \text{age(yrs)}}{\text{TBW(Kg)}} \times \frac{\text{TBW(Kg)}}{50 \times \text{Scr(umol/L)}}
\]

\[
\text{CrCl - Cockcroft & Gault (mL/sec)} = \frac{140 - \text{age(yrs)}}{\text{TBW(Kg)}} \times \frac{\text{TBW(Kg)}}{50 \times \text{Scr(umol/L)}} \times 0.85
\]

**REFERENCES:**


CCO Eligibility Form Required ☐  Non-Formulary Form Required ☐  Date revised: 01/20/2009
HEMELP200

Hematological

High dose Melphalan for Myeloma - peripheral stem cell transplant (Inpatient Regimen)

Multiple Myeloma

MELPHALAN 200mg/m² IV Day -2 Round to nearest 10mg
- Admix in 250mL bag Normal Saline, infuse over 30 minutes. Complete infusion within 60 minutes of preparation.

FUROSEMIDE 0-40mg IV Post Melphalan
- Give one dose of Furosemide post Melphalan.

ACETAMINOPHEN 650mg PO Day 0
- Give 2 tablets of Acetaminophen 325mg pre stem cell reinfusion.

HYDROCORTISONE SODIUM SUCCINATE 100mg IV Day 0
- Give Hydrocortisone 100mg pre stem cell reinfusion.

HYDRATION:
Pre
- Normal Saline with 20mmol KCL and 4mmol MgSO₄ per litre, run at 200mL/hr beginning 6 hours prior to Melphalan, continuing for 24 hours after Melphalan.

Post
- At 24 hours post Melphalan, change IV solution to Normal Saline with 20mmol KCL per litre and infuse at rate 125mL/hr, post stem cells infusion decrease rate to 75mL/hr.

ANTIMICROBIAL PROPHYLAXIS:
- Start 24 hours post stem cell transplant and continue until AGC > 1.0 x 10⁹/L.
  1. Ciprofloxacin 500mg PO bid
  2. Acyclovir 400mg PO/IV q8h

TESTS:
Baseline Tests WBC HB PLT ANC Ca K Na Chloride Phosphate Mg Glucose Cr Urea 24Hr CrCl T.Bili AST ALT AlkPhosphatase Urate
Test Notes - CBC, diff, Cr, electrolytes, ALT, AST, T.Bili, alk.phos, magnesium, calcium.

ANTIEMETIC PRE-CHEMO REGIMEN:
Level C Day -2 to Day +1 - Ondansetron 8mg q8h IV prior Melphalan and continue q8h until stem cell transplant.
  1. Ondansetron 8mg q8h IV prior Melphalan and continue q8h until stem cell transplant.
  2. Dexamethasone 8mg IV pre Melphalan, then Dexamethasone 8mg x 3 doses in addition to Ondansetron if patient continues to be nauseated.

INPATIENT ANTIEMETICS:
- Ondansetron 8mg PO/IV q8h can be substituted with Granisetron 1-2mg PO/IV daily.

TOXICITIES:
Hematologic 1. If ANC < 1.5 x 10⁹/L or PLT < 100 x 10⁹/L, HOLD dose for one week.

Renal Failure 1. Consider dose reduction of IV Melphalan on patients with renal insufficiency:
  CrCl (mL/min)
  > 60  200mg/m²
  40-60  140mg/m²
  20-39  100mg/m²
  < 20  no transplant

Pulmonary
1. Interstitial pneumonitis

CLINICAL MONITORING:
- Baseline and regular renal function, baseline pulmonary function.
- There is cross sensitivity between Melphalan and Chlorambucil, which is manifested as a rash.
- IV Melphalan can cause anaphylaxis, diaphoresis, hypotension, tachycardia and cardiac arrest.

FORMULAE:
CrCl - Cockcroft & Gault (mL/sec)
  Male: [140-age(yrs)] x TBW(Kg) / [50 x SCR(umol/L)]
  Female: [140-age(yrs)] x TBW(Kg) / [50 x SCR(umol/L)] x 0.85

INTERNAL CODE:
HIGH DOSE CHEMOTHERAPY FOR MYELOMA, PERIPHERAL STEM CELL TRANSPLANT

REFERENCES:
- Comparison of 200mg/m² Melphalan and 8Gy total body irradiation plus 140mg/m² Melphalan as conditioning regimen for peripheral blood stem cell transplantation in patients with newly diagnosed multiple myeloma: Final analysis of the Intergroupe Francophone du Myelome 9502 randomized trial. Blood 2002; 99: 731-735.

Date revised: 03/07/2005

Hematological
**MELPHALAN-PREDNISONE Chemotherapy**

Multiple Myeloma; Standard first-line therapy when autologous stem cell transplantation is not planned. May be used as second-line therapy for patients previously treated with VAD who are no longer candidates for autologous stem cell transplantation.

**MELPHALAN**
- Daily for 4 days.
  - Cap BSA at 2.2m²
  - Out-patient prescription.

Dose Escalation:
CBC should be repeated on day 15 of the first 3 cycles of therapy. Patients with a day 15 neutrophil count of < 0.5 x 10^9/L, but day 29 ANC > 1.0 x 10^9/L and Platelets > 75 x 10^9/L AND those with a 50% or greater fall in the serum M protein or 90% or greater fall in the urine M protein, should not undergo dose escalation.

Patients with both a nadir neutrophil count of ≥ 0.5 x 10^9/L, and a day 29 ANC > 1.0 x 10^9/L and PLT > 75 x 10^9/L AND failing to meet the above serum and urine M protein criteria for a response, should have the dose of melphalan increased to 12mg/m² daily on days 1-4. If these above criteria are maintained after treatment with 12mg/m², further escalation of melphalan dose to 15mg/m² with subsequent treatment cycles can be considered.

**PREDNISONE**
- BID for 4 days (8 doses).
- Outpatient prescription.

REPEAT EVERY 28 DAYS for 12 cycles

**TESTS:**

**Baseline Tests**
- WBC Hb PLT ANC Ca Glucose Cr T.Bili AST ALT AlkPhosphatase Urate

**Day 1**
- WBC HB PLT ANC Ca Glucose Cr T.Bili Albumin AST ALT AlkPhosphatase

**Day 15**
(first 3 cycles of therapy)
- WBC HB PLT ANC Ca Glucose Cr Urea T.Bili Albumin ALT AlkPhosphatase

**Test Notes**
- Additional baseline tests: Protein electrophoresis (SPEP), Quantitative immunoglobulins (QIs) and 24-hour urine for UPEP.
- Additional tests on therapy:
  - Day 1: Protein electrophoresis (SPEP)
  - Selected patients, especially those with IgA or IgD myeloma, may be better followed by specific measurement of relevant immunoglobulin level - in these cases repeating of SPEP is not necessary.

Routine duplication measurement of SPEP and QIs should be avoided.
- 24-hour urine for UPEP should be repeated with every cycle if positive and every 3 cycles if negative.

**ANTIEMETIC PRE-CHEMO REGIMEN:**
Level A
- Prochlorperazine 10mg PO pm

**ANTIEMETIC TAKE-HOME REGIMEN:**
Level A
- Prochlorperazine 10mg PO q4-6h pm

**TOXICITIES:**

**Hematologic**
1. If ANC < 1.0 x 10^9/L, DELAY therapy 1 week.
2. If PLT < 75 x 10^9/L, DELAY therapy 1 week.
- If dose delay is required, commence next cycle of therapy with Melphalan dose at 75% of the previous dose and maintain this dose unless further dose delays are required. Continue to reduce to 75% of new dose level for any repeat dose delays.
- If after one week delay, blood counts remain below the above cut-off values, commence next cycle of therapy after a total of 2 weeks of delay and omit Melphalan with that cycle (i.e. give prednisone only). Reassess patient for next treatment cycle 4 weeks later and reduce Melphalan to 75% of previous dose.

**Date revised:** 03/07/2005
**Hematological**

**CARMUSTINE (BCNU)-ETOPOSIDE-CYTARABINE-MELPHALAN** (Hodgkins lymphoma - Advanced Stage)

**Salvage Therapy for Refractory Hodgkin’s lymphoma**

**CARMUSTINE**  
60mg/m² IV Day 1  
Round to nearest 3 mg  
Mix in **250mL Normal Saline** in polyolefin bag. Use non-PVC equipment. No in-line filter. Protect from light.  
- Infuse over 1 hour or longer. Cap BSA=2.2m²

**ETOPOSIDE**  
75mg/m² IV Day 2 to 5  
Round to nearest 10mg  
- Mix in **500mL bag Normal Saline**; infuse over 2 hours daily. Cap BSA=2.2m²

**CYTARABINE**  
100mg/m² IV Day 2 to 5  
Round to nearest 10mg  
- Mix in **100mL bag 5% Dextrose**; infuse over 1 hour q12h. Total 8 doses. Cap BSA=2.2m²

**MELPHALAN**  
30mg/m² IV Day 6  
Round to nearest 5mg  
- Mix in **100mL bag Normal Saline**; infuse over 30 minutes.  
- Complete infusion within 60 minutes of preparation. Cap BSA=2.2m²

**REPEAT CYCLE EVERY 28 DAYS when adequate marrow recovery**

**HYDRATION:**  
Pre  
- Run IV Normal Saline with 20mmol/L KCL at 150mL/hr.

**TESTS:**  
Baseline Tests  
- WBC  HB  PLT  ANC  Ca  K  Na  Chloride  Phosphate  Mg  Cr  Urea  T.Bili  AST  ALT  AlkPhosphatase

**Test Notes**  
- CBC, baseline and regular liver function test. Baseline and regular renal function tests and urinalysis.

**ANTIEMETIC PRE-CHEMO REGIMEN:**  
**Level C**  
Day 1 to 6  
- Ondansetron 8mg PO/IV q8h

**Level B**  
Day 1 to 6  
- Dexamethasone 8mg prior to each dose of Carmustine, Etoposide and Melphalan.

**Level A**  
Day 1  
- Start Prochlorperazine on Day 1 and continue q4h prn

**TOXICITIES:**  
**Hematologic**  
1. If ANC < 1.0 x 10⁹/L or if PLT < 75 x 10⁹/L, **HOLD** dose for 1 week.

**Renal Failure**  
1. If CrCl < 1.0 mL/sec, **REDUCE** Carmustine dose by 25-50%.
2. If CrCl = 0.2-0.8 mL/sec or SrCr > 130umol/L, **REDUCE** Melphalan and Etoposide to 75% dose.
3. If CrCl < 0.2 mL/sec, **REDUCE** Melphalan and Etoposide to 50% dose.

**Hepatic Dysfunction**  
1. If T.Bili = 25-51umol/L or AST = 60-180 IU/L, **REDUCE** Etoposide to 50% dose.
2. If T.Bili = 52-85umol/L, **REDUCE** Etoposide to 25% dose.
3. If T.Bili > 85umol/L or AST > 180 IU/L, **OMIT** Etoposide dose.

**Pulmonary**  
1. Clinical pulmonary exam, pulmonary toxicity rating.

**SUGGESTED ACTION**  
**CLINICAL MONITORING:**  
- Clinical toxicity assessment (including stomatitis, gastrointestinal, pulmonary toxicity ). Baseline and regular liver function tests. Baseline and renal function tests and urinalysis.

**REFERENCES:**  
Mitoxantrone-Etoposide-Cytarabine (Acute Myeloid Leukemia)

Salvage of Resistant/Refractory of Acute Myeloid Leukemia for patients under 60 years of age

Induction Regimen

**MITOXANTRONE** 10mg/m² IV Days 1 to 5 Round to nearest 1mg
- **Slow push through sidearm of free flowing IV.** Give 4mg/2mL per minute.
- Threshold dose of Mitoxantrone = 140mg/m²
- If LVEF 40-49%, substitute Amsacrine 100mg/m² IV day x 5 days for Mitoxantrone in induction and consolidation.
- If LVEF < 40%, delete both Mitoxantrone and Amsacrine.

**ETOPOSIDE** 100mg/m²² IV Days 1 to 5 Round to nearest 10mg
- Mix in **500mL** bag **Normal Saline;** infuse over 2 hours daily for 5 days.

**CYTARABINE** 1.5Gm/m²/day IV Days 1 to 3 Round to nearest 10mg
- **Admix in 500mL bag 5% Dextrose;** Administer as a 24 hour continuous IV infusion daily x 3 days starting on Day1.

**DEXAMETHASONE** 2 gtts OU OPH q6h
- QID to both eyes for 7 days with high-dose Cytarabine.

Consolidation Regimen (1-2 cycles)

**MITOXANTRONE** 12mg/m² IV Day 1-2 Round to nearest 1 mg
- **Slow push through sidearm of free flowing IV.** Give 4mg/2mL per minute daily for 2 days.
- Threshold dose of Mitoxantrone = 140mg/m²
- If LVEF 40-49%, or > 10% decrease in LVEF compared with baseline, substitute Amsacrine 120mg/m²/day IV daily x 2 days for mitoxantrone.
- If LVEF < 40%, ommit Mitoxantrone and Amsacrine.

**CYTARABINE** 1.5Gm/m²/day IV Days 1 to 3 Round to nearest 10mg
- Administer as 24 hour continuous IV infusion via LV2 pump (CADD pump).
- QS 96ml in a 100ml cassette with Normal Saline and set the pump rate at 32ml/day.

**TESTS:**

*Baseline Tests* WBC HB PLT ANC Ca K Na Chloride Phosphate Mg Cr Urea T.Bili AST ALT AlkPhosphatase

*Test Notes* - Baseline and frequent CBC, baseline and regular renal function including uric acid, INR, PTT and fibrinogen during the first 3 days of induction - where clinically indicated.
- **N.B.** MUGA scans should be done prior to induction chemotherapy.
- **N.B.** MUGA scans should be done prior to EACH consolidation cycle.
- Bone marrow at Day 28-35. If in CR, proceed to BMT/consolidation. If hypocellular with <5% blasts, wait for count recovery, then repeat marrow.

**ANTIEMETIC PRE-CHEMO REGIMEN:**

**Level B** Day 1 to 5 - Granisetron 1mg IV daily for 5 days

**INPATIENT ANTIEMETICS:**
- **Solumedrol 50mg IV daily x 4 days**

**TOXICITIES:**

**Hematologic**
1. If ANC < 1.0 x 10⁹/L or if PLT < 75 x 10⁹/L, **HOLD** dose for 1 week.

**Renal Failure**
2. If CrCl = 0.2-0.8mL/sec or SrCr > 130umol/L, **REDUCE** Etoposide to 75% dose.
3. If CrCl < 0.2mL/sec, **REDUCE** Etoposide to 50% dose.

**Hepatic Dysfunction**
1. If T.Bili = 25-51umol/L or AST = 60-180 IU/L, **REDUCE** Etoposide to 50% dose.
2. If T.Bili > 60umol/L, or AST > 180 IU/L, **REDUCE** Mitoxantrone to 50% dose.
3. If T.Bili = 52-85umol/L, **REDUCE** Etoposide to 25% dose.
4. If T.Bili > 85umol/L or AST > 180 IU/L, **OMIT** Etoposide dose.

**Pulmonary**
1. Clinical pulmonary exam, pulmonary toxicity rating.

**SUGGESTED ACTION**
- Clinical toxicity assessment (including stomatitis, gastrointestinal, pulmonary toxicity ). Baseline and regular liver function tests. Baseline and renal function tests and urinalysis.

**REFERENCES**
HEMAMID

PAMIDRONATE Therapy
Prevention of Skeletal Events (Pathologic Fractures), Bony Pain, and Radiotherapy to the Bones-Associated With Multiple Myeloma

PAMIDRONATE 90mg IV Day 1
FOR ALL DOSES:
- Admix 90mg into 250mL Normal Saline ambulatory pump (Intermate LV50) and infuse over 5 hours at home.
- All first dose patients are required to remain in the chemotherapy suite for 30 minutes after the start of the Pamatronate pump, in case of any potential reactions.
- Presently the Centre Pharmacy dispenses the premixed Pamidronate Intermates prepared by Baxter.

REPEAT EVERY 28 DAYS
- For myeloma patients in remission after 2 years of monthly Pamidronate treatment: physician may decrease frequency of treatment to every 3 months.

PAMIDRONATE 90mg IV Day 1
- Admix 90mg into 250mL Normal Saline ambulatory pump (Intermate LV50) and infuse over 5 hours at home.
- Presently the Centre Pharmacy dispenses the premixed Pamidronate Intermates prepared by Baxter.

REPEAT EVERY 90 DAYS

TESTS:
Baseline Tests: WBC HB PLT ANC Ca K Glucose Cr T.Bili ALT AlkPhosphatase Urate
Every 90 days: WBC HB PLT ANC Ca K Glucose Cr T.Bili Albumin ALT
Day 1: WBC HB PLT ANC Ca K Glucose Cr T.Bili Albumin ALT

Test Notes: Additional tests to include: SPEP, QI, UPEP(24h)

PATIENT VISITS and APPOINTMENT TYPE:
- First dose: 30min Type A
- Subsequent doses: 15min Type A

CLINICAL MONITORING:
- Creatinine should be monitored regularly.
- Consider a reduced initial dose or an infusion time of at least 4 hours in patients with pre-existing renal impairment (CrCl<30mL/min).
- Use is not recommended for the treatment of bone metastases in patients with severe renal impairment.
- In patients who develop renal deterioration during bisphosphonate therapy (>44umol/L in patients with normal baseline or >88umol/L in patients with abnormal baseline), consider holding dose. Resumption of therapy (at the same dose) may be considered when serum creatinine returns to within 10% of baseline.
- Monitor calcium.
- If corrected serum calcium < 2.10mmol/L, HOLD Pamidronate for 1 week, or until Serum Calcium levels are in normal range.

Hypocalcemia
0. Serum calcium > 2.10mmol/L
1. Serum calcium = 2.10-1.93mmol/L
2. Serum calcium = 1.92-1.74mmol/L
3. Serum calcium = 1.73-1.51mmol/L
4. Serum calcium <1.50mmol/L
- Rated on assessment of anti-hypercalcemia response and at periodic visits, or in response to patient complaint.

FORMULAE:
Corrected Serum Calcium (mmol/L) = Measured Serum Calcium + [(40 - serum albumin) x 0.02]
CrCl - Cockcroft & Gault (mL/sec) Male: [140-age(yrs)] x TBW(Kg) / [50 x SCr(umol/L)]
CrCl - Cockcroft & Gault (mL/sec) Female: [140-age(yrs)] x TBW(Kg) / [50 x SCr(umol/L)] x 0.85

OPIS CODES:
- PAMIDRONATE 30MG
- PAMIDRONATE 60MG
- PAMIDRONATE 90MG
- PAMID 30MG Q3M
- PAMID 60MG Q3M
- PAMID 90MG Q3M

CCO Eligibility Form Required ✔ Non-Formulary Form Required ❌ Date revised: 10/08/2008
RITUXIMAB (Henderson Outpatient Regimen)
Follicular Lymphoma, Mantle cell Lymphoma, Low grade lymphoma CD20-positive

RITUXIMAB
375 mg/m² IV Days 1,8,15,22
- Mix in Normal Saline or 5% Dextrose to a final concentration 1-4mg/mL.

First infusion
Start the initial infusion at 50mg/hr and, after 60 minutes increase rate by increments of 50mg/hr every 30 minutes, as tolerated, to a final rate of 400mg/hr.

Subsequent infusions
- Subsequent infusions may be initiated at 100mg/hr and increase by increments of 100mg/hr every 30 minutes to the maximum of 400mg/hr, as tolerated by patient.
- Take complete vital signs prior to and after treatment.
- Exercise caution when considering treatment of patients with bulky adenopathy (> 10cm) or circulating lymphoma cells (> 50).

WEEKLY
ACETAMINOPHEN 650 mg PO Pre-chemo
- Give 2 tablets of Acetaminophen (325mg) pre each infusion.

DIPHENHYDRAMINE 50 mg PO Pre-chemo
- Give 1 capsule (50mg) pre each infusion.

SALBUTAMOL INH 2 puffs INH Q2H prn
- If reaction occurs, give 2 puffs of Salbutamol Q2H pm.

TESTS:
Baseline Tests WBC HB PLT ANC Cr T.Bili ALT AlkPhosphatase
Test Notes
- Baseline CBC & diff., Cr, T.bili, ALT, alkaline phosphatase, LDH, HBsAg, HBCab (suggestion).
- Before treatment #1 & #4: CBC & diff.

TOXICITIES:
Hematologic
- Neutropenia- Exercise caution when considering treatment of patients with ANC < 1.5 x 10^9/L or PLT < 75 x 10^9/L.

CLINICAL MONITORING:
- Close observation for infusion related symptoms including: fever, chills, pain, asthenia and other flu-like symptoms. If treatment is well tolerated during loading dose and early maintenance doses, observation time may be reduced.
- Clinical cardiac monitoring for all patients with cardiac risk factors or previous cardiac conditions (eg. arrhythmia, angina CA, Observe for symptoms of hypersensitivity including; hypotension, bronchospasm and angioedema.
- Rituximab is contraindicated in patients with known anaphylactic reaction to murine protein.
- Fatal Cytokine Release Syndrome has been reported. It usually occurs within 1-2 hours of initiating the first infusion. Initially, it is characterized by severe dyspnea (often with bronchospasm and hypoxia) in addition to fever, chills, rigors, urticaria and angioedema. There may be features of tumor lysis syndrome and pulmonary infiltration. Aggressive symptomatic treatment is required.
- Rituximab is possibly associated with Hepatitis B reactivation. All patients should be tested for HBsAg and HBCab. If either test is positive, such patients should be treated with Lamivudine 100mg/day orally, for the entire duration of chemotherapy and for two months afterwards. Such patients should be monitored with frequent liver tests and hepatitis B virus DNA (at least every two months) up to one year following Rituximab therapy.

HYPERSENSITIVITY:
- Rituximab can cause allergic type reaction during infusion. If an allergic reaction occurs, stop infusion and the physician in charge should determine a safe time to resume infusion.
- After recovery of symptoms, restart Rituximab infusion one infusion rate below the rate at which the reaction occurred and continue with escalation of infusion rates on the appropriate schedule.

Allergic Reaction
1. Transient flushing or rash; drug fever < 38 degrees C
2. Rash; flushing; urticaria; dyspnea; drug fever > 38 degrees C
3. Symptomatic bronchospasm, with or without urticaria; parenteral medication(s) indicated; allergy-related edema/angioedema; hypotension 4. Anaphylaxis 5. Death

READED AT EACH CLINIC VISIT
Have available in treatment room:
1. epinephrine for injection 2. Diphenhydramine hydrochloride for injection

INTERNAL CODE:
RITUXIMAB MONOTHERAPY

REFERENCES:

Date revised: 10/08/2008
HE - RITUXAN

RITUXIMAB MONOTHERAPY (Inpatient Regimen)
Treatment of Relapsed or Refractory Low-Grade Lymphoma or Malignant Lymphoma or
Follicular B-cell Non Hodgkin’s Lymphoma which is CD 20 positive

RITUXIMAB
375mg/m² IV Days 1,8,15, & 22 Round to nearest 1mg
- Mix in Normal Saline or 5% Dextrose to a final concentration 1-4mg/mL.

First infusion
Start the initial infusion at 50mg/hr and, after 60 minutes increase rate by increments of 50mg/hr every 30 minutes, as tolerated, to a final rate 400mg/hr.

Subsequent infusions
Subsequent infusion may be initiated at rate 100mg/hr and increased by increments of 100mg/hr every 30 minutes to a maximum rate 400mg/hr, as tolerated by the patient.
- Take complete vital signs prior to and after treatment.
- Observe for 30-60 minutes after infusion. DO NOT ADMINISTER AS IV PUSH OR BOLUS
- Exercise caution when considering treatment of patients with bulky adenopathy (> 10cm) or circulating lymphoma cells (> 50).

ACETAMINOPHEN 650mg PO Pre-chemo
- Give 2 tablets of Acetaminophen (325mg) before each infusion.

DIPHENHYDRAMINE 50mg PO Pre-chemo
- Give 1 capsule (50mg) before each infusion.

SALBUTAMOL INH 2 puffs INH q2h prn
- If reaction occurs, give 2 puffs of Salbutamol q2h prn.

TESTS:
Baseline Tests
WBC  HB  PLT  ANC  Cr  T.Bili  ALT  AlkPhosphatase
Test Notes
- Baseline CBC & diff., Cr, T.bili, ALT, alkaline phosphatase, LDH, HBsAg, HBcAb (suggestion).
- Before treatment #1 and #4: CBC & diff.

TOXICITIES:
Hematologic
1. Neutropenia- Exercise caution when considering treatment of patients with ANC < 1.5 x 10⁹/L or PLT < 75 x 10⁹/L.

Hepatic Dysfunction
1. Risk of Hepatitis B reactivation.

CLINICAL MONITORING:
- Close observation for infusion related symptoms including: fever, chills, pain, asthenia and other flu-like symptoms.
- If treatment is well tolerated during loading dose and early maintenance doses, observation time may be reduced.
- Clinical cardiac monitoring for all patients with cardiac risk factors or previous cardiac conditions (eg. arrhythmia, angina). Observe for symptoms of hypersensitivity including: hypotension, bronchospasam and angioedema.
- Rituximab is contraindicated in patients with known anaphylactic reaction to murine protein.
- Fatal Cytokine Release Syndrome has been reported. It usually occurs within 1-2 hours of initiating the first infusion. Initially, it is characterized by severe dyspnea (often with bronchospasam and hypoxia) in addition to fever, chills, rigors, urticaria and angioedema. There may be features of tumor lysis syndrome and pulmonary infiltration. Aggressive symptomatic treatment is required.
- Rituximab is possibly associated with Hepatitis B reactivation. All patients should be tested for HBsAg and HbcAb. If either test is positive, such patients should be treated with Lamivudine 100mg/day orally, for the entire duration of chemotherapy and for two months afterwards. Such patients should be monitored with frequent liver tests and hepatitis B virus DNA (at least every two months) up to one year following Rituximab therapy.

HYPERSENSITIVITY:
- Rituximab can cause allergic type reaction during infusion. If an allergic reaction occurs, stop infusion and the physician in charge should determine a safe time and rate to resume infusion.
- After recovery of symptoms, restart Rituximab infusion one infusion rate below the rate at which the reaction occurred and continue with escalation of infusion rates on the appropriate schedule.

Allergic Reaction
1. Transient flushing or rash; drug fever < 38 degrees C
2. Rash; flushing; urticaria; dyspnea; drug fever > 38 degrees C
3. Symptomatic bronchospasam, with or without urticaria; parenteral medication(s) indicated; allergy-related edema/angioedema; hypotension
4. Anaphylaxis
5. Death

REARED AT EACH CLINIC VISIT
Have available in treatment room:
1. epinephrine for injection
2. Diphenhydramine hydrochloride for injection

INTERNAL CODE:
RITUXIMAB MONOTHERAPY

REFERENCES:

Date revised: 10/08/2008

Hematological
RITUXIMAB Maintenance Therapy

Non Hodgkin’s Lymphoma (Low Grade) for patients who have responded to induction treatment with combination chemotherapy and/or Rituximab.

**RITUXIMAB** 375 mg/m² IV Day 1

- Mix in **Normal Saline** or 5 % Dextrose to a final concentration 1-4 mg/mL (concentration used at JCC is 2mg/mL).
- Infusion may be initiated at 100mg/hr and increased by increments of 100mg/hr every 30 minutes to a maximum rate 400mg/hr, as tolerated by the patient.
- For eligible patients, *Rituximab may be given as a Rapid infusion*.
- Mix Rituximab in 250mL (or 500mL) Normal Saline; infuse 75mL (or 100mL of 500mL bag) over 30 minutes, then infuse the remaining volume over 60 minutes.
- Take complete vital signs prior to and after treatment.
- Observe for 30-60 minutes after infusion. **DO NOT ADMINISTER AS IV PUSH OR BOLUS**
- Caution using Rituximab with bulky disease (10cm diameter) or circulating lymphoma cells (> 50 x 10⁹/L).
- Eligible patients show no reaction with first infusion.

**EVERY 3 MONTHS** for duration treatment of maximum two years or until relapse

### ACETAMINOPHEN
- 650 mg PO Pre-chemo
- Give 2 tablets of Acetaminophen (325mg) pre each infusion.

### DIPHENHYDRAMINE
- 50 mg PO Pre-chemo
- Give 1 capsule (50mg) pre each infusion.

### HYDROCORTISONE
- 100 mg IV Pre-chemo
- Give 1 capsule (50mg) pre each infusion.

### SODIUM SUCCINATE
- 100 ml Normal Saline
- Admix in at least 100ml Normal Saline and infuse over 10 minutes.
- Protect from light

### TOXICITIES:

**Hematologic**
- Neutropenia- Exercise caution when considering treatment of patients with ANC < 1.5 x 10⁹/L or PLT < 75 x 10⁹/L.

**CLINICAL MONITORING:**
- Close observation for infusion related symptoms including: fever, chills, pain, asthenia and other flu-like symptoms. If treatment is well tolerated during loading dose and early maintenance doses, observation time may be reduced.
- Clinical cardiac monitoring for all patients with cardiac risk factors or previous cardiac conditions (e.g. arrhythmia, angina). Observe for symptoms of hypersensitivity including: hypotension, bronchospasm and angioedema.
- Rituximab is contraindicated in patients with known anaphylactic reaction to murine protein.
- Fatal Cytokine Release Syndrome has been reported. It usually occurs within 1-2 hours of initiating the first infusion. Initially, it is characterized by severe dyspnea (often with bronchospasm and hypoxia) in addition to fever, chills, rigors, urticaria and angioedema. There may be features of tumor lysis syndrome and pulmonary infiltration.
- Aggressive symptomatic treatment is required.
- Rituximab is possibly associated with Hepatitis B reactivation. All patients should be tested for HBsAg and HBCAb. If either test is positive, such patients should be treated with Lamivudine 100mg/day orally, for the entire duration of chemotherapy and for two months afterwards. Such patients should be monitored with frequent liver tests and hepatitis B virus DNA (at least every two months) up to one year following Rituximab therapy.

**HYPERSENSITIVITY:**
- Rituximab can cause allergic type reaction during infusion. If an allergic reaction occurs, stop infusion and the physician in charge should determine a safe time to resume infusion.
- After recovery of symptoms, restart Rituximab infusion one infusion rate below the rate at which the reaction occurred and continue with escalation of infusion rates on the appropriate schedule.

**Allergic Reaction**
1. Transient flushing or rash; drug fever < 38 degrees C
2. Rash; flushing; urticaria; dyspnea; drug fever ≥ 38 degrees C
3. Symptomatic bronchospasm, with or without urticaria; parenteral medication(s) indicated; allergy-related edema/angioedema; hypotension
4. Anaphylaxis
5. Death

**RETIRED AT EACH CLINIC VISIT**

### HAVE AVAILABLE IN TREATMENT ROOM:

1. epinephrine for injection 2. Diphenhydramine hydrochloride for injection

**REFERENCES:**


**Date revised:** 05/12/2009
MOBILIZATION OF PERIPHERAL BLOOD PROGENITOR CELLS (PBPCs)

Pre- Stem Cell Harvest Chemotherapy

**CYCLOPHOSPHAMIDE** 2500mg/m² IV Day 1 Round to nearest 10mg
- Mix in **400mL** bag Normal Saline, infuse over 2 hours

**MESNA** 500mg/m² IV q6h Round to nearest 10 mg
- Mix in 100ml bag Normal Saline. Give first dose 30 min prior Cyclophosphamide, second dose 6 hours after first dose.

**HYDRATION:**
- IV Normal Saline at 150mL/m²/h X 12 hours. Start hydration 4 hours prior Cyclophosphamide
- Add 10-20 mEq KCL to each liter of IV fluid if required
- Add Furosemide 10-20 mg if required

**TESTS:**
- **Baseline Tests**
  - WBC  HB  PLT  ANC  Ca  K  Na  Chloride  Cr  Urea  Albumin  AST  ALT
- **AlkPhosphatase**

**ANTIEMETIC PRE-CHEMO REGIMEN:**
- Level C
  - Day 1 Ondansetron 8 mg pre-chemo, may repeat once in 8 hours

**REFERENCES:**

**CCO Eligibility Form Required** [ ] **Non-Formulary Form Required** [ ]  
*Date revised: 06/25/2008*
THALIDOMIDE Therapy
Multiple Myeloma - Special Access Drug

THALIDOMIDE 200mg PO Daily at bedtime 50mg capsule
- Start at 50-100mg daily, and then increase as tolerated to 200mg.
- Administer at bedtime to minimize daytime somnolence.
- Continue treatment until disease progression or unacceptable toxicities.
- Outpatient prescription available as 50mg capsules.
- Special access drug.
- Trade name is Thalomid™

CONTINUOUS TREATMENT

TESTS:
Baseline Tests - WBC HB PLT ANC Ca K Glucose Cr Urea T.Bili Albumin ALT AlkPhosphatase
Test Notes - Baseline and regular CBC’s every month.
- Calcium and potassium levels.

ANCILLARY:
- Risk of thromboembolism, give low dose ASA.
- Women must use effective contraception for 1 month before, during and 1 month after thalidomide therapy.
- In women of childbearing potential, a pregnancy test must be done prior to therapy and monthly during therapy.
- Men must use an effective birth control method because thalidomide is present in semen and seminal fluid.

CLINICAL MONITORING:

Somniaone
1. Asymptomatic 2. Somnolence or sedation interfering with function, but not interfering with ADL 3.Otundation or stupor; difficult to arouse; interfering with ADL 4. Coma 5. Death
- May be dose related and may improve with continued use, or by dose reduction.
- Somnolence and fatigue may be dose related; may improve with continued use or by dose reduction.
- Schedule Thalidomide dose at bedtime.

Rash
1. Macular or papular eruption or erythema without associated symptoms 2. Macular or papular eruption or erythema with pruritus or other associated symptoms; localized desquamation or other lesions covering < 50% of body surface area (BSA) 3. Severe, generalized erythroderma or macular, papular or vesicular eruption; desquamation covering >=50% BSA 4. Generalized exfoliative, ulcerative, or bullous dermatitis 5. Death
- Rash on trunk, back and proximal extremities may appear 10-14 days after start of treatment.
- Resolution occurs within 24 hours of discontinuation, but patient may be rechallenged at a lower dose.

Sensory
1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function. 2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL. 3. Sensory alteration or paresthesia interfering with ADL. 4. Disabling. 5. Death
- Monitor for peripheral neuropathy (stocking glove distribution).
- Thalidomide should be discontinued in the early stages of sensory effects to prevent irreversible changes. Restart treatment when neuropathy returns to baseline levels. May require dose reduction.

Constipation
1. Occasional or intermittent symptoms; occasional use of stool softeners, laxatives, dietary modification, or enema 2. Persistent symptoms with regular use of laxatives or enemas indicated 3. Symptoms interfering with ADL, obstipation with manual evacuation indicated 4. Life-threatening consequences (e.g., obstruction, toxic megacolon) 5. Death
RATED AT EACH CLINIC VISIT
- Thalidomide is a human TERATOGEN and can cause life threatening birth defects or fetal death if taken during pregnancy.
- It is not known if thalidomide is present in breast milk, therefore discontinue nursing with maternal thalidomide usage.

REFERENCES:
- CCO Formulary, Thalidomide, 2006/2007
- Celgene. Thalidomide product monograph.2006

CCO Eligibility Form Required ☐ Non-Formulary Form Required ☐ Date revised: 01/16/2009
**HEMATOLOGICAL**

**VINCRISTINE- DOXORUBICIN- DEXAMETHASONE**

**Chemotherapy**

*Multiple Myeloma; Standard first-line therapy when autologous stem cell transplantation is planned. May be used as second-line therapy for patients previously treated with Melphalan and Prednisone.*

**VINCRISTINE**

- Admix Vinchristine & Doxorubicin together with Normal Saline to 192mL. Infuse over 96hrs via Infusor LV2 pump (2mL/hr).
- Infuse through a central venous catheter.

**DOXORUBICIN**

- Admix Vinchristine & Doxorubicin together with Normal Saline to 192mL. Infuse over 96hrs via Infusor LV2 pump (2mL/hr).
- Infuse through a central venous catheter.
- Cap BSA at 2.2m²

**DEXAMETHASONE**

- **BID for 4 days** (8 doses) starting Days 1 & 15.
- Outpatient prescription.

**REPEAT EVERY 21-28 DAYS for 6 cycles**

**TESTS:**

<table>
<thead>
<tr>
<th>Baseline Tests</th>
<th>WBC</th>
<th>HB</th>
<th>PLT</th>
<th>ANC</th>
<th>Ca</th>
<th>Glucose</th>
<th>Cr</th>
<th>AST</th>
<th>ALT</th>
<th>AlkPhosphatase</th>
<th>Urate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1</td>
<td>WBC</td>
<td>HB</td>
<td>PLT</td>
<td>ANC</td>
<td>Ca</td>
<td>CR</td>
<td>AST</td>
<td>ALT</td>
<td>AlkPhosphatase</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Day 15</td>
<td>WBC</td>
<td>HB</td>
<td>PLT</td>
<td>ANC</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

**Test Notes:**

- Additional baseline tests: Protein electrophoresis (SPEP), Quantitative immunoglobulins (QIs) and 24-hour urine for UPEP.
- Additional tests on therapy:
  - Day 1: Protein electrophoresis (SPEP)
  - Selected patients, especially those with IgA or IgD myeloma, may be better followed by specific measurement of relevant immunoglobulin level - in these cases repeating of SPEP is not necessary.
  - Routine duplication measurement of SPEP and QIs should be avoided.
  - 24-hour urine for UPEP should be repeated with every cycle if positive and every 3 cycles if negative.

**ANTIEMETIC PRE-CHEMO REGIMEN:**

**Level A**

- Prochlorperazine 10mg PO prn

**ANTIEMETIC TAKE-HOME REGIMEN:**

**Level A**

- Prochlorperazine 10mg PO q4-6h prn

**PATIENT VISITS and APPOINTMENT TYPE:**

- **Day 1** 15min Type A
- **Day 5** (Pump disconnect) 10min Type A

**TOXICITIES:**

**Hematologic**

**Day 1**

- If ANC < 1.0 x 10⁹/L, **DELAY** therapy 1 week.
- If PLT < 75 x 10⁹/L, **DELAY** therapy 1 week.

**Day 15**

- If ANC < 0.5 x 10⁹/L, **OMIT** Dexamethasone.
- Dose attenuations may be over-ridden if cytopenias presumed to be due to underlying disease.

**Hepatic Dysfunction**

- If T.Bili = 26-51umol/L, or AST = 60-180 IU/L, **REDUCE** Doxorubicin to 75% dose and Vinchristine to 50% dose.
- If T.Bili = 52-85umol/L, or AST > 180 IU/L, **REDUCE** Doxorubicin to 50% dose and Vinchristine to 25% dose.
- If T.Bili > 85umol/L, **OMIT** Doxorubicin & Vinchristine.

**Neurologic**

- If peripheral neuropathy >2, **OMIT** Vinchristine.

**SUGGESTED ACTION**

**CLINICAL MONITORING:**

- Clinical exam for symptoms of CHF.
- Clinical exam for proximal muscle myopathy.
- Neurologic toxicity ratings (Sensory, Constipation) at each visit.

**Sensory**

- Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function 2.
- Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL 3. Sensory alteration or paresthesia interfering with ADL 4. Disabling 5. Death

**Constipation**

- Occasional or intermittent symptoms; occasional use of stool softeners, laxatives, dietary modification, or enema
- Persistent symptoms with regular use of laxatives or enemas indicated
- Symptoms interfering with ADL: obstipation with manual evacuation indicated

**Rated at each Clinic Visit**

**Date revised:** 10/08/2008
Hematological

**VINCRISTINE- DOxorubicin- Dexamethasone**
Chemotherapy with PAMIDRONATE

*Multiple Myeloma; Standard first-line therapy when autologous stem cell transplantation is planned. May be used as second-line therapy for patients previously treated with Melphalan and Prednisone.*

**VINCRISTINE** 0.4mg/day IV Days 1-4 Round to nearest 0.1mg
- Admix Vincristine & Doxorubicin together with Normal Saline to 192mL; Infuse over 96hrs via Infusor LV2 pump (2mL/hr).
- Infuse through a central venous catheter.

**DOxorubicin** 9mg/m²/day IV Days 1-4 Round to nearest 1mg
- Admix Vincristine & Doxorubicin together with Normal Saline to 192mL; Infuse over 96hrs via Infusor LV2 pump (2mL/hr).
- Infuse through a central venous catheter.

**Dexamethasone** 40mg PO Days 1-4 & 15-19 4mg tablet
- Daily for 4 days starting Days 1 & 15.
- Outpatient prescription.

**PAMIDRONATE** 90mg IV Day 1
- Admix 90mg into 250mL Normal Saline ambulatory pump (Intermate LV50) and infuse over 5 hours at home.
- All first dose patients are required to remain in the chemotherapy suite for 30 minutes after the start of the Pamidronate pump, in case of any potential reactions.
- Presently the Centre Pharmacy dispenses the premixed Pamidronate Intermates prepared by Baxter.

**TESTS:**
- Baseline Tests WBC HB PLT ANC Ca K Na Chloride Phosphate Glucose Cr Urea T.Bili Albumin AST ALT AlkPhosphatase Urate
- Day 1 WBC HB PLT ANC Ca K Na Glucose Cr Urea T.Bili Albumin ALT AlkPhosphatase
- Test Notes - LVEF if clinically indicated.
- Protein electrophoresis (PEP) to be added to Baseline & Day 1 testing.

**ANTIEMETIC PRE-CHEMO REGIMEN:**
Level A Days 1-4 & 15-19 - Prochlorperazine 10mg PO pm

**ANTIEMETIC TAKE-HOME REGIMEN:**
Level A Days 1-4 & 15-19 - Prochlorperazine 10mg PO q4-6h pm

**PATIENT VISITS and APPOINTMENT TYPE:**
- Day 1: 30min Type B
- Day 5 (Pump disconnect) 10min Type A

**TOXICITIES:**

**Hematologic**
1. If ANC < 1.0 x 10⁹/L, or if PLT < 100 x 10⁹/L, HOLD chemotherapy for 1 week.
2. If Corrected Serum Calcium < 2.10mmol/L, HOLD Pamidronate for 1 week, or until serum calcium is within normal range.

**Hepatic Dysfunction**
1. If T.Bili = 26-51umol/L, or AST = 60-180 IU/L, REDUCE Doxorubicin to 75% dose and Vincriistine to 50% dose.
2. If T.Bili = 52-85umol/L, or AST > 180 IU/L, REDUCE Doxorubicin to 50% dose and Vincriistine to 25% dose.
3. If T.Bili > 85umol/L, OMIT Doxorubicin and Vincriistine.

**Neurologic**
1. If peripheral neuropathy > 2, OMIT Vincriistine.

**SUGGESTED ACTION**
Hematological

VINCRISTINE- DOXORUBICIN- DEXAMETHASONE
Chemotherapy with PAMIDRONATE

CLINICAL MONITORING:
- Clinical exam for symptoms of CHF.
- Periodic cardiac tests for all patients with cardiac risk factors and patients at or above the threshold dose levels (Doxorubicin 450mg/m²).
- Clinical exam for proximal muscle myopathy.
- Neurologic toxicity ratings (Sensory, Constipation) at each visit.

Sensory
1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function 2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL 3. Sensory alteration or paresthesia interfering with ADL 4. Disabling 5. Death

Constipation
1. Occasional or intermittent symptoms; occasional use of stool softeners, laxatives, dietary modification, or enema
2. Persistent symptoms with regular use of laxatives or enemas indicated
3. Symptoms interfering with ADL; obstruction with manual evacuation indicated
4. Life-threatening consequences (e.g., obstruction, toxic megacolon)
5. Death

- Creatinine should be monitored regularly.
- Consider a reduced initial dose or an infusion time of at least 4 hours in patients with pre-existing renal impairment (CrCl<30ml/min).
- Use is not recommended for the treatment of bone metastases in patients with severe renal impairment.
- In patients who develop renal deterioration during bisphosphonate therapy (>44umol/L in patients with normal baseline or >88umol/L in patients with abnormal baseline), consider holding dose. Resumption of therapy (at the same dose) may be considered when serum creatinine returns to within 10% of baseline.
- Monitor calcium.
- If corrected serum calcium < 2.10mmol/L, HOLD Pamidronate for 1 week, or until Serum Calcium levels are in normal range.

Hypocalcemia
0. Serum calcium > 2.10mmol/L
1. Serum calcium = 2.10-1.93mmol/L
2. Serum calcium = 1.92-1.74mmol/L
3. Serum calcium = 1.73-1.51mmol/L
4. Serum calcium <1.50mmol/L

- Rated on assessment of anti-hypercalcemia response and at periodic visits, or in response to patient complaint.

FORMULAE:
Corrected Serum Calcium (mmol/L) = Measured Serum Calcium + [(40 - serum albumin) x 0.02]

CrCl - Cockcroft & Gault (mL/sec)
Male: [(140-age(yrs)] x TBW(Kg) / [50 x SCr(umol/L)]
Female: [(140-age(yrs))] x TBW(Kg) / [50 x SCr(umol/L)] x 0.85

Date revised: 10/08/2008
VINBLASTINE Chemotherapy
Hodgkin’s Lymphoma - Standard therapy for recurrence after autologous stem cell transplantation

VINBLASTINE 6mg/m² IV Day 1 Round to nearest 0.1mg
- Slow push through sidearm of free flowing IV; inject over 1 minute.
- Cap BSA at 2.2m²

REPEAT EVERY 14-21 DAYS as long as effective and tolerated

TESTS:
Baseline Tests WBC HB PLT ANC Ca Glucose Cr T.Bili ALT AlkPhosphatase
With Each Treatment WBC HB PLT ANC
Every 2 Months WBC HB PLT ANC Ca Cr T.Bili Albumin ALT AlkPhosphatase
Test Notes - Protein electrophoresis to be added to Baseline testing.
- Every 2 months test for protein.

ANTIEMETIC PRE-CHEMO REGIMEN:
Level A Day 1 - Prochlorperazine 10mg PO prn

ANTIEMETIC TAKE-HOME REGIMEN:
Level A Day 1 - Prochlorperazine 10mg PO q4-6h prn

PATIENT VISITS and APPOINTMENT TYPE:
⇒ Day 1: 15min Type A

TOXICITIES:
Hematologic
1. If ANC < 1.0 x 10⁹/L, DELAY therapy 1 week.
2. If PLT < 75 x 10⁹/L, DELAY therapy 1 week.
- Dose attenuations may be over-ridden if cytopenias presumed to be due to underlying disease.

Hepatic Dysfunction
1. If T.Bili = 26-51umol/L, or AST = 60-180 IU/L, REDUCE Vinblastine to 50% dose.
2. If T.Bili = 52-85umol/L, or AST > 180 IU/L, REDUCE Vinblastine to 25% dose.
3. If T.Bili > 85umol/L, OMIT Vinblastine doses.

Neurologic
1. If peripheral neuropathy > 2, OMIT Vinblastine.

SUGGESTED ACTION

CLINICAL MONITORING:
- Neurologic toxicity ratings (Sensory, Constipation) at each visit.
  Sensory
  1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function 2.
  2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL 3. Sensory alteration or paresthesia interfering with ADL 4. Disabling 5. Death
  Constipation
  1. Occasional or intermittent symptoms; occasional use of stool softeners, laxatives, dietary modification, or enema
  2. Persistent symptoms with regular use of laxatives or enemas indicated
  3. Symptoms interfering with ADL; obstipation with manual evacuation indicated
  4. Life-threatening consequences (e.g., obstruction, toxic megacolon)
  5. Death
  RATED AT EACH CLINIC VISIT

INTERNAL CODE:
OPIS CODE: VINBLASTINE

REFERENCES:

CCO Eligibility Form Required [☐] Non-Formulary Form Required [☐] Date revised: 10/08/2008
CARBOPLATIN-ETOPOside Concurrent Chemotherapy

Non-Small Cell Lung Cancer - concurrent with radiotherapy

CARBOPLATIN
AUC = 5
- Admix in 250mL 5% Dextrose. Infuse over 30-60 minutes.

ETOPOSIDE
50mg/m²
- Admix in 500mL Normal Saline; connect piggyback to IV line. Infuse over 30-60 minutes.

RADIATION
1 or 2 phase plan Daily
Technique: 1 or 2 phase
Modality: 6-10 MV
Dose Specification: 100%
Total Dose: 6300 cGy
Pattern: Daily
If a 2 phase plan, options may include:
4200/20 + 2100/10 boost OR 4725/25 + 1680/10 boost

TESTS:
Baseline Tests
WBC HB PLT ANC Ca K Na Chloride Mg Glucose Cr Urea T.Bili Albumin AST ALT GGT AlkPhosphatase
Days 1 & 29
WBC HB PLT ANC K Na Chloride Mg Cr Urea
Test Notes - Additional Baseline tests: LDH & CO₂

ANTIEMETIC REGIMEN:

Level C
- Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
- Dexamethasone 20mg PO/IV

Level B
- Dexamethasone 8-10 mg PO/IV, may add Ondansetron 8mg PO /IV or Granisetron 1mg PO/IV
- May add or substitute Prochlorperazine 10mg PO/IV pm

PATIENT VISITS and APPOINTMENT TYPE:
 Days 1 & 29 2.5hrs Type C
 Days 2 to 5 & 30 to 33 1.5hrs Type C

ANCILLARY:
- Increase fluids if poor oral intake.
- Adjust Etoposide rate of infusion if blood pressure drops.

TOXICITIES:
Hematologic
1. If ANC < 1.5 x 10⁹/L, or PLT < 100 x 10⁹/L, HOLD chemotherapy.

Renal Failure
Carboplatin:
1. Adjust Carboplatin dose if estimated CrCl changes > 10%.

ETOPOside:
1. If CrCl = 0.5-1.0mL/sec, or SrCr = 136-185umol/L, REDUCE Etoposide to 75% dose.
2. If CrCl < 0.2mL/sec, REDUCE Etoposide to 50% dose.

Hepatic Dysfunction
1. If T.Bili = 26-51umol/L, or AST = 60-180 IU/L, REDUCE Etoposide to 50% dose.
2. If T.Bili > 85umol/L, REDUCE Etoposide to 25% dose.
3. If T.Bili > 85umol/L, or AST > 180 IU/L, OMIT Etoposide.

SUGGESTED ACTION

CLINICAL MONITORING:
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.

Hearing
1. Asymptomatic, detected on exam/testing only
2. Symptomatic, not interfering with ADL
3. Symptomatic, interfering with ADL
4. Life-threatening; disabling
5. Death

Sensory
1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function
2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL
3. Sensory alteration or paresthesia interfering with ADL 4. Disabling 5. Death

RATED AT EACH CLINIC VISIT

FORMULAE:
CrCl - Cockcroft & Gault (mL/sec)
CrCl - Cockcroft & Gault (mL/sec)
Creatinine Cl (mL/min)
Calvert Formula

INTERNAL CODE:
OPIS CODE: CARBO 5 ETOP 50
Lung

CARBOPLATIN-ETOPOSIDE Concurrent Chemotherapy

Calvert Formula

\[ \text{Dose (in mg)} = \text{target AUC} \times (\text{GFR} + 25) \]

**REFERENCES:**

- CCO Practice Guideline 7-13-3: The Role of Thoracic Radiotherapy as an Adjunct to Standard Chemotherapy in Limited-Stage Small Cell Lung Cancer.

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**Date revised:** 09/23/2008
CARBOPLATIN–ETOPOSIDE Chemotherapy
Small Cell Lung Cancer

CARBOPLATIN
AUC = 5
- Infuse over 30-60 minutes.

ETOPOSIDE
100mg/m²
- Infuse over 30-60 minutes.

REPEAT EVERY 21 DAYS

TESTS:
Baseline Tests: WBC HB PLT ANC Ca K Na Chloride Glucose Cr Urea T.Bili Albumin AST ALT GGT AlkPhosphatase
Day 1: WBC HB PLT ANC Ca K Na Chloride Cr Urea
Test Notes: Additional Baseline tests: LDH & CO₂
- Day 1: Additional tests may need to be repeated if baseline tests abnormal.

ANTIEMETIC PRE-CHEMO REGIMEN:
Level C
- Day 1: Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
- Dexamethasone 20mg PO/IV
- Modified (Level C)
- Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
- Dexamethasone 8mg PO/IV
- May add or substitute Prochlorperazine 10mg PO/IV pm

ANTIEMETIC TAKE-HOME REGIMEN:
Level A
- Day 3: Prochlorperazine 10mg PO q4-6h prn

PATIENT VISITS and APPOINTMENT TYPE:
- Day 1: 2-3hrs Type C
- Days 2 & 3: 1.5hrs Type C

ANCILLARY:
- Oral hydration is strongly encouraged; poorly hydrated patients may need more IV hydration (to prevent renal toxicity).

TOXICITIES:
Hematologic
1. If ANC < 1.5 x 10⁹/L, or PLT < 100 x 10⁹/L, HOLD chemotherapy.

Renal Failure
Carboplatin:
1. Adjust Carboplatin dose if estimated CrCl changes > 10%.

ETOPOSIDE:
1. If CrCl = 0.2-1.0ml/sec, or SrCr = 136-185umol/L, REDUCE Etoposide to 75% dose.
2. If CrCl < 0.2ml/sec, REDUCE Etoposide to 50% dose.

Hepatic Dysfunction
1. If T.Bili = 26-51umol/L, or AST = 60-180 IU/L, REDUCE Etoposide to 50% dose.
2. If T.Bili > 52umol/L, or AST >180 IU/L, OMIT Etoposide.

SUGGESTED ACTION:
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.
- Baseline & routine renal function tests, especially if there are other concurrent nephrotoxic drugs.

FORMULAE:
- CrCl - Cockcroft & Gault (mL/sec) Male: [140-age(ys)] x TBW(Kg) / [50 x SCr(umol/L)]
- CrCl - Cockcroft & Gault (mL/sec) Female: [140-age(ys)] x TBW(Kg) / [50 x SCr(umol/L)] x 0.85
- Creatinine Cl (mL/min)
- Calvert Formula
- Dose (in mg) = target AUC x (GFR + 25) GFR in mL/min

REFERENCES:

Date revised: 07/25/2008
CARBOPLATIN-GEMCITABINE Chemotherapy  
Non-Small Cell Lung Cancer

**CARBOPLATIN**  
AUC = 5  
IV Day 1  
Round to nearest 5mg  
- Administer in 250mL bag 5% Dextrose; Infuse over 30-60 minutes.

**GEMCITABINE**  
1250mg/m²  
IV Days 1 & 8  
Round to nearest 19mg  
- Administer in 250mL bag Normal Saline or 5% Dextrose; Infuse over 30 minutes.

**TESTS:**  
Baseline Tests: WBC Hb PLT ANC Ca K Na Chloride Glucose Cr Urea T.Bili Albumin AST ALT GGT AlkPhosphatase  
Day 8: WBC Hb PLT ANC  
Day 1: WBC Hb PLT ANC K Na Chloride Cr Urea

**ANTIEMETIC PRE-CHEMO REGIMEN:**  
- Level C: Day 1 - Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV  
- Dexamethasone 20mg PO/IV  
- Day 8 - Prochlorperazine 10mg PO/IV  
- May add or substitute Dexamethasone 8mg PO/IV

**ANTIEMETIC TAKE-HOME REGIMEN:**  
- Level B/C: Day 1 - Ondansetron 8mg PO BID for 2-3 days, or Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days  
- Dexamethasone 8mg PO BID for 2-3 days  
- Prochlorperazine 10mg PO q4-6h prn  
- Day 8 - Prochlorperazine 10mg PO q4-6h prn

**PATIENT VISITS and APPOINTMENT TYPE:**  
- Day 1: 2hrs Type C  
- Days 1 & 8: 45min Type B

**TOXICITIES:**  
Hematologic:  
Day 1:  
1. If ANC < 1.5 x 10⁹/L, or if PLT < 100 x 10⁹/L, HOLD chemotherapy.  
2. If ANC = 1.0-1.5 x 10⁹/L, GIVE 50% of dose.  
3. If ANC < 1.0 x 10⁹/L, OMIT Day 8.  
4. If PLT = 75-100 x 10⁹/L, GIVE 50% of dose.  
5. If PLT < 75 x 10⁹/L, OMIT Day 8.

Renal Failure:  
- Adjust Carboplatin dose if estimated CrCl changes > 10%.

**CLINICAL MONITORING:**  
- Baseline & routine renal function tests/especially if there are other concurrent nephrotoxic drugs.

**SENSORY**  
1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function 2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL 3. Sensory alteration or paresthesia interfering with ADL 4. Disabling 5. Death  
RATED AT EACH CLINIC VISIT

**FORMULAE:**  
- CrCl - Cockcroft & Gault (mL/sec)  
  Male: [140-age(yrs)] x TBW(Kg) / [50 x Scr(umol/L)]  
  Female: [140-age(yrs)] x TBW(Kg) / [50 x Scr(umol/L)] x 0.85  
  mL/min = 60 x CrCl mL/sec  
- Creatinine CI (mL/min)  
- Calvert Formula  
- Dose (in mg) = target AUC x (GFR + 25)  
- GFR in mL/min

**INTERNAL CODE:**  
OPIS CODE: CARB-GEM

**REFERENCES:**  
DOXORUBICIN-CYCLOPHOSPHAMIDE-CISPLATIN (CAP)
Chemotherapy
Treatment of Thymoma

CYCLOPHOSPHAMIDE 500mg/m² IV Day 1 Round to nearest 10mg
- Mix in 250mL bag Normal saline. Infuse over 10-20 minutes.

DOXORUBICIN 50mg/m² IV Day 1 Round to nearest 1mg
- Slow push through sidearm of free flowing IV. Give 2 to 4mg (1-2mL) per minute.

CISPLATIN 50mg/m² IV Day 1 Round to nearest 1mg
- Mix in 500mL bag Normal saline; Infuse over 60 minutes.

REPEAT EVERY 21 DAYS

HYDRATION:

Pre
- Infuse 1000mL Normal saline with 20mEq potassium chloride IV over 2 hours before Cisplatin.

Concurrent
- Give 250mL of 20% Mannitol solution (50G) IV; Infuse through sidearm concurrent with Cisplatin.

Post
- Infuse 1000mL Normal saline with 10mEq Potassium Chloride & 2G Magnesium Sulfate IV over 2 hours after Cisplatin.

TESTS:
Baseline Tests: WBC HB PLT ANC Ca K Na Chloride Mg Glucose Cr Urea T.Bili Albumin AST ALT GGT AlkPhosphatase

Day 1: WBC HB PLT ANC K Na Chloride Mg Cr Urea

Test Notes: Additional Baseline tests: LDH & CO₂

ANTIEMETIC PRE-CHEMO REGIMEN:
Level C Day 1 - Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
- Dexamethasone 20mg PO/IV

ANTIEMETIC TAKE-HOME REGIMEN:
Level B/C Day 1 - Ondansetron 8mg PO BID for 2-3 days, or
- Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days
- Dexamethasone 8mg PO BID for 2-3 days
- Prochlorperazine 10mg PO q4-6h prn

PATIENT VISITS and APPOINTMENT TYPE:
⇒ Day 1 6hrs Type D

ANCILLARY:
- Increase fluids if poor oral intake.

TOXICITIES:

Hematologic
1. If ANC < 1.5 x 10⁹/L, or if PLT < 100 x 10⁹/L, HOLD chemotherapy for 1 week.

Renal Failure
1. If CrCl = 0.5-1.0mL/sec, or SrCr = 136-185umol/L, REDUCE Cisplatin to 50% dose.
2. If CrCl < 0.5mL/sec, or SrCr > 185umol/L, OMIT Cisplatin dose.

Hepatic Dysfunction
1. If T.Bili = 26-51umol/L, or AST = 60-180 IU/L, give 75% Doxorubicin dose.
2. If T.Bili = 52-85umol/L, or AST > 180 IU/L, give 50% Doxorubicin dose.
3. If T.Bili > 85umol/L, OMIT Doxorubicin.

SUGGESTED ACTION

CLINICAL MONITORING:
- Baseline renal function tests (if failure suspected) and liver function tests (especially if poor Performance Status).
- Clinical exam for symptoms of CHF.
- Periodic cardiac tests for all patients with cardiac risk factors and patients at or above the threshold dose levels (Doxorubicin 450mg/m²).
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.

Sensory
1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function 2.
2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL 3.
3. Sensory alteration or paresthesia interfering with ADL  4. Disabling  5. Death

Hearing
1. Asymptomatic, detected on exam/testing only 2. Symptomatic, not interfering with ADL 3. Symptomatic, interfering with ADL  4. Life-threatening; disabling  5. Death

RATED AT EACH CLINIC VISIT

FORMULAE:
CrCl - Cockcroft & Gault (mL/sec) Male: [140-age(ys)] x TBW(Kg) / [50 x SCr(umol/L)]
CrCl - Cockcroft & Gault (mL/sec) Female: [140-age(ys)] x TBW(Kg) / [50 x SCr(umol/L)] x 0.85
DOXORUBICIN-CYCLOPHOSPHAMIDE-CISPLATIN (CAP) Chemotherapy

INTERNAL CODE: CDC LU

REFERENCES:

Date revised: 07/25/2008
CYCLOPHOSPHAMIDE-DOXORUBICIN-VINCRISTINE (CAV)
Chemotherapy
Small Cell Lung Cancer

CYCLOPHOSPHAMIDE  1000mg/m²  IV  Day 1  Round to nearest 10mg
   - Mix in 250-500mL bag Normal Saline; Infuse over 20-30 minutes

DOXORUBICIN  50mg/m²  IV  Day 1  Round to nearest 1mg
   - Slow push through sidearm of free flowing IV; Give 2 to 4mg (1-2mL) per minute.

VINCRISTINE  2mg  IV  Day 1  Round to nearest 0.1mg
   - Mix in 50mL bag Normal Saline; infuse over 10 minutes.

REPEAT EVERY 21 DAYS

TESTS:
Baseline Tests  WBC  HB  PLT  ANC  Ca  K  Na  Chloride  Glucose  Cr  Urea  T.Bili  Albumin  AST  ALT  GGT  AlkPhosphatase  LVEF
Day 1  WBC  HB  PLT  ANC

Test Notes  - Additional Baseline tests: LDH, CO₂ & LVEF (ordered only on specific patients)
   Day 1:
   - Chemistry repeated if baseline abnormal.
   - Consider monitoring LFT after 3 cycles.

ANTIEMETIC PRE-CHEMO REGIMEN:
Level C  Day 1  - Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
   - Dexamethasone 20mg PO/IV

ANTIEMETIC TAKE-HOME REGIMEN:
Level B/C  Day 1  - Ondansetron 8mg PO BID for 2-3 days, or Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days
   - Dexamethasone 8mg PO BID for 2-3 days
   - Prochlorperazine 10mg PO q4-6h prn

PATIENT VISITS and APPOINTMENT TYPE:
→ Day 1  90min  Type C

ANCILLARY:
- Oral hydration is strongly encouraged; poorly hydrated patients may need more IV hydration (to prevent renal toxicity).

TOXICITIES:
Hematologic
1. If ANC < 1.5 x 10⁹/L, or if PLT < 100 x 10⁹/L, HOLD dose for 1 week (Until AGC ≥ 1.5 x 10⁹/L).

Renal Failure
1. If SrCr > 265umol/L, REDUCE Doxorubicin to 50% dose.
2. If CrCl < 0.2mL/sec, OMIT Cyclophosphamide dose.

Hepatic Dysfunction
1. If T.Bili = 26-51umol/L, or AST = 60-180 IU/L, REDUCE Doxorubicin to 75% dose and Vincristine to 50% dose.
2. If T.Bili = 52-85umol/L, or AST > 180 IU/L, REDUCE Cyclophosphamide to 75% dose, Doxorubicin to 50% dose and Vincristine to 25% dose.
3. If T.Bili > 85umol/L, OMIT ALL drugs.

SUGGESTED ACTION
CLINICAL MONITORING:
- Urinalysis (RBCs) periodic and in response to patient complaint.
- Clinical exam for symptoms of CHF.
- Periodic cardiac tests for all patients with cardiac risk factors or patients at or above the threshold dose levels (Doxorubicin 450mg/m²).

Sensory
1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function
2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL
3. Sensory alteration or paresthesia interfering with ADL
4. Disabling
5. Death

Constipation
1. Occasional or intermittent symptoms; occasional use of stool softeners, laxatives, dietary modification, or enema
2. Persistent symptoms with regular use of laxatives or enemas indicated
3. Symptoms interfering with ADL

REFERENCES:

Date revised: 07/25/2008
CISPLATIN-ETOPOSIDE Concurrent Chemotherapy

Non-Small Cell Lung Cancer Stage III - Concurrent with Radiotherapy

CISPLATIN
50mg/m² IV Days 1, 8, 29 & 36 Round to nearest 1mg
- Admix in 500mL-1000mL bag Normal Saline; Infuse over 60 minutes.

ETOPOSIDE
50mg/m² IV Days 1-5 & 29-33 Round to nearest 10mg
- Admix in 500mL bag of Normal Saline; connect piggyback to IV line; Infuse over 30-60 minutes.
- Adjust rate if blood pressure drops.
- Use Non-PVC equipment and filter.
- Give Etoposide BEFORE Cisplatin, to hydrate patient.

RADIATION
1 or 2 Phase Daily
Technique: 1 or 2 phase
Modality: 6-10 MV
Dose Specification: 100%
Total Dose: 6300 cGy
Fraction Dose: 210 cGy per day
Pattern: Daily
If a 2 phase plan, options may include:
4200/20 + 2100/10 boost OR 4725/25 + 1680/10 boost

HYDRATION:
Pre
- Infun 1000mL Normal Saline with 20mEq Potassium Chloride IV over 2 hours before Cisplatin.

Concurrent
- Give 250mL of 20% Mannitol solution (50G) IV; Infuse through sidearm concurrent with Cisplatin.

Post
- Infuse 500mL Normal Saline with 10mEq Potassium Chloride & 2G Magnesium Sulfate IV over 1 hour after Cisplatin.

TESTS:
Baseline Tests: WBC HB PLT ANC Ca K Na Chloride Mg Glucose Cr Urea T.Bili Albumin AST ALT GGT AlkPhosphatase
Days 1,8,29 & 36 WBC HB PLT ANC K Na Chloride Mg Cr Urea Test Notes: - Additional baseline tests: LDH & CO2

ANTIEMETIC PRE-CHEMO REGIMEN:
Level C Days 1,8,29 & 36 - Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
- Dexamethasone 20mg PO/IV
- May add or substitute Prochlorperazine 10mg PO/IV pm

Level B Days 2-5, & 30-33 Modified (Level B)
- Dexamethasone 8-10 mg PO/IV, may add Ondansetron 8mg PO /IV or Granisetron 1mg PO/IV
- May add or substitute Prochlorperazine 10mg PO/IV pm

ANTIEMETIC TAKE-HOME REGIMEN:
Level B/C Days 1,8,29 & 36 - Ondansetron 8mg PO BID for 2-3 days, or Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days
- Dexamethasone 8mg PO BID for 2-3 days
- Prochlorperazine 10mg PO q4-6h pm

Level A Days 2-5 & 30-33
- Prochlorperazine 10mg PO q4-6h pm

PATIENT VISITS and APPOINTMENT TYPE:
- Days 1, 8, 29 & 36 6hrs Type E
- Days 2-5 & 28-33 1.5hrs Type C
- Days 1-36 Radiation 30min

ANCILLARY:
- Increase fluids if poor oral intake.

TOXICITIES:
Hematologic
1. If ANC < 1.5 x 10⁹/L, or PLT < 100 x 10⁹/L, HOLD dose.

Renal Failure
1. If CrCl = 0.5-1.0mL/sec, or SrCr = 136-185umol/L, REDUCE Cisplatin to 50% dose, and Etoposide to 75% dose.
2. If CrCl < 0.5mL/sec, or SrCr > 185umol/L, OMIT Cisplatin dose.
3. If CrCl < 0.2mL/sec, REDUCE Etoposide to 50% dose.

Hepatic Dysfunction
1. If T.Bili = 26-51umol/L, or AST = 60-180 IUL, REDUCE Etoposide to 50% dose.
2. If T.Bili = 52-85umol/L, REDUCE Etoposide to 25% dose.
3. If T.Bili > 85umol/L, or AST > 190 IU/L, OMIT Etoposide.

SUGGESTED ACTION
CISPLATIN-ETOPOSIDE Concurrent Chemotherapy

**CLINICAL MONITORING:**
- Clinical assessment of stomatitis; oral examination upon patient complaint of sore mouth.

**Sensory**
1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function 2.
2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL 3.
3. Sensory alteration or paresthesia interfering with ADL 4. Disabling 5. Death

**Hearing**
1. Asymptomatic, detected on exam/testing only 2. Symptomatic, not interfering with ADL 3.
4. Symptomatic, interfering with ADL 5. Death

**RATED AT EACH CLINIC VISIT**

**FORMULAE:**
- Cockcroft & Gault: 
  
  Male: \[\frac{140-\text{age (yrs)}}{\text{TBW (Kg)}} \times \frac{\text{SCr (umol/L)}}{50}\]

  Female: \[\frac{140-\text{age (yrs)}}{\text{TBW (Kg)}} \times \frac{\text{SCr (umol/L)}}{50} \times 0.85\]

**REFERENCES:**

**Date revised:** 09/23/2008
CISPLATIN-ETOPOSIDE Chemotherapy
Small Cell Lung Cancer; Non Small Cell Lung Cancer -Adjuvant Therapy

CISPLATIN
25mg/m² IV Days 1-3 Round to nearest 1mg
- Admix in 250mL bag Normal Saline; Infuse over 30-60 minutes.
- May also admix 10G Mannitol (50mL of 20% solution or 100mL of 10% solution) with Cisplatin.

ETOPOSIDE
100mg/m² IV Days 1-3 Round to nearest 10mg
- Dose < 200mg, mix in 500mL Normal Saline; Infuse over 30-60 minutes.
- Dose > 200mg, mix in 1000mL Normal Saline; Infuse over 2 hours.
- Use Non-PVC equipment and filter.
- Adjust rate if blood pressure drops.
- Give Etoposide AFTER Cisplatin.

REPEAT EVERY 21 DAYS

HYDRATION:
- Pre - Infuse 500mL Normal Saline IV over 1 hour.

TESTS:
Baseline Tests WBC HB PLT ANC Ca K Na Chloride Mg Glucose Cr Urea T.Bili Albumin
AST ALT GGT AlkPhosphatase
Day 1 WBC HB PLT ANC K Na Chloride Mg Cr Urea

ANTIEMETIC PRE-CHEMO REGIMEN:
Level C Days 1 - 3 - Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
- Dexamethasone 20mg PO/IV

PATIENT VISITS and APPOINTMENT TYPE:
Days 1-3 3hrs Type C

ANCILLARY:
- Adjust Etoposide rate of infusion if blood pressure drops.

TOXICITIES:
Hematologic
1. If ANC < 1.5 x 10⁹/L, or PLT < 100 x 10⁹/L, HOLD dose.
Renal Failure
1. If CrCl = 0.5-1.0mL/sec, or SrCr = 136-185umol/L, REDUCE Cisplatin to 50% dose and Etoposide to 75% dose.
2. If CrCl < 0.5mL/sec, or SrCr > 185umol/L, OMIT Cisplatin dose.
3. If CrCl < 0.2mL/sec, REDUCE Etoposide to 50% dose.

Hepatic Dysfunction
1. If T.Bili = 26-51umol/L, or AST = 60-180 IU/L, REDUCE Etoposide to 50% dose.
2. If T.Bili = 52-85umol/L, REDUCE Etoposide to 25% dose.
3. If T.Bili > 85umol/L, or AST > 180 IU/L, OMIT Etoposide.

SUGGESTED ACTION:
- Baseline & periodic liver function tests (esp. if poor Performance Status).

FORMULAE:
CrCl - Cockcroft & Gault (mL/sec)
Male: \[(140-\text{age(yrs)}) \times \text{TBW(Kg)} / (50 \times \text{SCr(umol/L)})\]
CrCl - Cockcroft & Gault (mL/sec)
Female: \[(140-\text{age(yrs)}) \times \text{TBW(Kg)} / (50 \times \text{SCr(umol/L)}) \times 0.85\]

REFERENCES:
CISPLATIN-GEMCITABINE Chemotherapy
Non-Small Cell Lung Cancer

CISPLATIN  75mg/m²  IV  Day 1  Round to nearest 1mg
- Admix in 500mL bag Normal Saline; Infuse over 60 minutes.

GEMCITABINE  1250mg/m²  IV  Days 1 & 8  Round to nearest 19mg
- Admix in 250mL bag Normal Saline, Infuse over 30 minutes through free-flowing IV.

REPEAT EVERY 21 DAYS

HYDRATION:
Pre
- Infuse 1000mL Normal Saline with 20mEq Potassium Chloride IV over 2 hours before Cisplatin.

Concurrent
- Give 250mL of 20% Mannitol solution (50G) IV; Infuse through side arm concurrent with Cisplatin.

Post
- Infuse 1000mL Normal Saline with 10mEq Potassium Chloride + 2G Magnesium Sulfate IV over 2 hours after Cisplatin.

TESTS:
Baseline Tests  WBC  HB  PLT  ANC  Ca  K  Na  Chloride  Mg  Glucose  Cr  Urea  T.Bili  Albumin  AST  ALT  GGT  AlkPhosphatase
Day 8  WBC  HB  PLT  ANC
Day 1  WBC  HB  PLT  ANC  K  Na  Chloride  Mg  Cr  Urea
Test Notes - Additional Baseline tests: LDH & CO₂

ANTIEMETIC PRE-CHEMO REGIMEN:
Level C  Day 1
- Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
- Dexamethasone 20mg PO/IV
- May add Aprepitant 125mg PO before chemo (reduce PO Dexamethasone by 50%)

Level B  Day 8
- Prochlorperazine 10mg PO/IV pm
- May add or substitute Dexamethasone 8mg PO/IV

ANTIEMETIC TAKE-HOME REGIMEN:
Level B/C  Day 1
- Ondansetron 8mg PO BID for 2-3 days, or Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days
- Dexamethasone 8mg PO BID for 2-3 days
- May add Aprepitant 80mg PO on Days 2&3 (reduce PO Dexamethasone by 50%)
- Prochlorperazine 10mg PO q4-6h pm
- Prochlorperazine 10mg PO q4-6h pm

Level A  Day 8

PATIENT VISITS and APPOINTMENT TYPE:
- Day 1  6hrs  Type D
- Day 8:  45min  Type B

ANCILLARY:
- Oral hydration is strongly encouraged; poorly hydrated patients may need more IV hydration (to prevent renal toxicity).

TOXICITIES:
Hematologic
Day 1:
1. If ANC < 1.5 x 10⁹/L, or If PLT < 100 x 10⁹/L, HOLD chemotherapy.
Day 8:
1. If ANC = 1.0-1.5 x 10⁹/L, GIVE 50% of dose.
2. If ANC < 1.0 x 10⁹/L, OMIT Day 8.
3. If PLT = 75-100 x 10⁹/L, GIVE 50% of dose.
4. If PLT < 75 x 10⁹/L, OMIT Day 8.

Renal Failure
1. If CrCl = 0.5-1.0mL/sec, or SrCr = 136-185umol/L, REDUCE Cisplatin to 50% dose.
2. If CrCl < 0.5mL/sec, or SrCr > 185umol/L, OMIT Cisplatin dose.

Gastrointestinal
1. If Mucositis or Diarrhea > Grade 3 in previous course, REDUCE to 2/3 dose.

SUGGESTED ACTION
CISPLATIN-GEMCITABINE Chemotherapy

CLINICAL MONITORING:

- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.

Hearing

1. Asymptomatic, detected on exam/testing only 2. Symptomatic, not interfering with ADL
3. Symptomatic, interfering with ADL 4. Life-threatening; disabling 5. Death

Sensory

1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function 2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL 3. Sensory alteration or paresthesia interfering with ADL 4. Disabling 5. Death

Diarhoea

1. Increase of < 4 stools per day over baseline; mild increase in ostomy output compared to baseline
2. Increase of 4 - 6 stools per day over baseline; IV fluids indicated < 24 hrs; moderate increase in ostomy output compared to baseline; not interfering with ADL 3. Increase of >7 stools per day over baseline; incontinence; IV fluids >24 hrs; hospitalization; severe increase in ostomy output compared to baseline; interfering with ADL 4. Life-threatening consequences (e.g., hemodynamic collapse)
5. Death

Mucositis

1. Erythema of the mucosa 2. Patchy ulcerations or pseudomembranes 3. Confluent ulcerations or pseudomembranes; bleeding with minor trauma 4. Tissue necrosis; significant spontaneous bleeding; life-threatening consequences 5. Death

RATED AT EACH CLINIC VISIT

Edema limb

1. 5 - 10% inter-limb discrepancy in volume or circumference at point of greatest visible difference; swelling or obscuration of anatomic architecture on close inspection; pitting edema
2. >10 - 30% inter-limb discrepancy in volume or circumference at point of greatest visible difference; readily apparent obscuration of anatomic architecture; obliteration of skin folds; readily apparent deviation from normal anatomic contour
3. >30% inter-limb discrepancy in volume; lymphorrhea; gross deviation from normal anatomic contour; interfering with ADL
4. Progression to malignancy (i.e., lymphangiosarcoma); amputation indicated; disabling 5. Death

RATED IF EDEMA NOTED ON ROUTINE VISITS

FORMULAE:

CrCl - Cockcroft & Gault (mL/sec) Male: \[\frac{140 - \text{age}(\text{yrs}) \times \text{TBW(Kg)}}{50 \times \text{SCr(umol/L)}}\]
CrCl - Cockcroft & Gault (mL/sec) Female: \[\frac{140 - \text{age}(\text{yrs}) \times \text{TBW(Kg)}}{50 \times \text{SCr(umol/L)}} \times 0.85\]

REFERENCES:


CCO Eligibility Form Required ✔ Non-Formulary Form Required ☐ Date revised: 07/25/2008
Lung

CISPLATIN-VINORELBINE Chemotherapy
Non-Small Cell Lung Cancer

CISPLATIN 75mg/m² IV Day 1 Round to nearest 1mg
- Mix in 500mL bag Normal Saline; Infuse over 60 minutes.

VINORELBINE 25-30mg/m² IV Days 1 & 8 Round to nearest 1mg
- Mix in 50mL Normal Saline minibag; to a final concentration < 3mg/mL.
- Infuse over 6-10 minutes into the sidearm of a free-flowing IV line.
- Flush IV line with at least 100mL Normal Saline or 5% Dextrose.
- Hydrocortisone 100mg IV may be given if patient experiences pain on administration.
- Acute pain syndrome at the tumour site can be managed with nonsteroidal anti-inflammatory drugs or corticosteroids.
- If extravasation occurs during administration, discontinue immediately and infuse the remaining dose through another IV site.

REPEAT EVERY 21 DAYS

HYDRATION:
Pre - Infuse 1000mL Normal Saline with 20mEq Potassium Chloride IV over 2 hours before Cisplatin.
Concurrent - Over 250mL of 20% Mannitol solution (50G) IV; Infuse through side arm concurrent with Cisplatin.
Post - Infuse 1000mL Normal Saline with 10mEq Potassium Chloride & 2G Magnesium Sulfate IV over 2 hours after Cisplatin.

TESTS:
Baseline Tests: WBC HB PLT ANC Ca K Na Chloride Mg Glucose Cr Urea T.Bili Albumin AST ALT GGT AlkPhosphatase
Day 1 WBC HB PLT ANC Ca K Na Chloride Mg Cr Urea
Day 8 WBC HB PLT ANC
Test Notes: Additional Baseline tests: LDH & CO₂

ANTIEMETIC PRE-CHEMO REGIMEN:
Level C Day 1 - Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
- Dexamethasone 20mg PO/IV
- May add Aprepitant 125mg PO before chemo (reduce PO Dexamethasone by 50%)
Level A Day 8 - Prochlorperazine 10mg PO pm

ANTIEMETIC TAKE-HOME REGIMEN:
Level B/C Day 1 - Ondansetron 8mg PO BID for 2-3 days, or Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days
- Dexamethasone 8mg PO BID for 2-3 days
- May add Aprepitant 80mg PO on Days 2&3 (reduce PO Dexamethasone by 50%)
- Prochlorperazine 10mg PO q4-6h pm
- Prochlorperazine 10mg PO q4-6h pm
Level A Day 8 - Prochlorperazine 10mg PO q4-6h pm

PATIENT VISITS and APPOINTMENT TYPE:
- Day 1 5hrs Type D
- Day 8 30min Type B

ANCILLARY:
- Increase fluids if poor oral intake.

TOXICITIES:
Hematologic
1. If ANC < 1.5 x 10⁹/L, or if PLT < 100 x 10⁹/L, HOLD chemotherapy for 1 week.
Renal Failure
1. If CrCl = 0.5-1.0mL/sec, or SrCr = 136-185umol/L, REDUCE Cisplatin to 50% dose.
2. If CrCl < 0.5mL/sec, or SrCr > 185umol/L, OMIT Cisplatin dose.

SUGGESTED ACTION

CLINICAL MONITORING:
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.
Hearing
1. Asymptomatic, detected on exam/testing only 2. Symptomatic, not interfering with ADL
3. Symptomatic, interfering with ADL 4. Life-threatening; disabling 5. Death
Sensory
1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function 2.
Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL 3. Sensory alteration or paresthesia interfering with ADL 4. Disabling 5. Death
RATED AT EACH CLINIC VISIT

FORMULAE:
CrCl - Cockcroft & Gault (mL/sec) Male: [140-age(ylrs)] x TBW(Kg) / [50 x SCr(umol/L)]
CrCl - Cockcroft & Gault (mL/sec) Female: [140-age(ylrs)] x TBW(Kg) / [50 x SCr(umol/L)] x 0.85

Lung
CISPLATIN-VINORELBINE Chemotherapy

REFERENCES:

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Date revised: 09/24/2008
CISPLATIN-VINORELBINE Chemotherapy
Non-Small Cell Lung Cancer- Adjuvant Treatment

**CISPLATIN**
50mg/m² IV Days 1 & 8 Round to nearest 1mg
- Adminix in 500mL bag Normal Saline; Infuse over 60 minutes.

**VINORELBINE**
25mg/m² IV Days 1,8,15 & 22 Round to nearest 1mg
- Mix in 50mL Normal Saline minibag; to a final concentration of less than 3mg/mL.
- Infuse over 6-10 minutes into the sidearm of a free-flowing IV line.
- Flush IV line with at least 100mL Normal Saline or 5% Dextrose.
- Hydrocortisone 100mg IV may be given if patient experiences pain on administration.
- Acute pain syndrome at the tumour site can be managed with nonsteroidal anti-inflammatory drugs or corticosteroids.
- If extravasation occurs during administration, discontinue immediately and infuse the remaining dose through another IV site.

**REPEAT EVERY 28 DAYS for a total of 4 cycles**

**HYDRATION:**

**Pre**
- Infuse 1000mL Normal Saline with 20mEq Potassium Chloride IV over 2 hours before Cisplatin.

**Concurrent**
- Give 250mL of 20% Mannitol solution (50G) IV; Infuse through sidearm concurrent with Cisplatin.

**Post**
- Infuse 1000mL Normal Saline with 10mEq Potassium Chloride & 2G Magnesium Sulfate IV over 2 hours after Cisplatin.

**TESTS:**

**Baseline Tests**
- WBC HB PLT ANC Ca K Na Chloride Mg Glucose Cr Urea T.Bili Albumin
- AST ALT GGT AlkPhosphatase

**Days 15 & 22**
- WBC HB PLT ANC

**Days 1 & 8**
- WBC HB PLT ANC K Na Chloride Mg Cr Urea

**Test Notes**
- Additional Baseline tests: LDH & CO₂

**ANTIEMETIC PRE-CHEMO REGIMEN:**

**Level C**
- Days 1 & 8
  - Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
  - Dexamethasone 20mg PO/IV

**Level A**
- Days 15 & 22
  - Prochlorperazine 10mg PO pm

**ANTIEMETIC TAKE-HOME REGIMEN:**

**Level B/C**
- Days 1 & 8
  - Ondansetron 8mg PO BID for 2-3 days, or Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days
  - Dexamethasone 8mg PO BID for 2-3 days
  - Prochlorperazine 10mg PO q4-6h pm
  - Prochlorperazine 10mg PO q4-6h pm

**Level A**
- Days 15 & 22
  - Prochlorperazine 10mg PO q4-6h pm

**PATIENT VISITS and APPOINTMENT TYPE:**

- Days 1 & 8 5hrs **Type D**
- Days 15 & 22 30min **Type B**

**TOXICITIES:**

**Hematologic**
1. If ANC < 1.5 x 10⁹/L, or PLT < 100 x 10⁹/L, HOLD chemotherapy for 1 week.

**Renal Failure**
1. If CrCl = 0.5-1.0mL/sec, or SrCr = 136-185umol/L, REDUCE Cisplatin to 50% dose.
2. If CrCl < 0.5mL/sec, or SrCr > 185umol/L, OMIT Cisplatin dose.

**Clinical Monitoring:**
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.
- **Hearing**
  1. Asymptomatic, detected on exam/testing only
  2. Symptomatic, not interfering with ADL
  3. Symptomatic, interfering with ADL
  4. Life-threatening; disabling
  5. Death
- **Sensory**
  1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function 2.
  2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL 3.
  3. Sensory alteration or paresthesia interfering with ADL 4. Disabling 5. Death

**RATED AT EACH CLINIC VISIT**

**FORMULAE:**
- CrCl - Cockcroft & Gault (ml/sec) Male: [(140-age(yrs)) x TBW(Kg)] / [50 x SCr(umol/L)]
- CrCl - Cockcroft & Gault (ml/sec) Female: [(140-age(yrs)) x TBW(Kg)] / [50 x SCr(umol/L)] x 0.85

**REFERENCES:**
CISPLATIN-VINORELBINE Chemotherapy concurrent with radiation
Locally Advanced Stage IIIa or IIIb Non-Small Cell Lung Cancer

Order Group 1
- Cycle 1 & 4
CISPLATIN 80mg/m² IV Days 1 Round to nearest 1mg
  - Admix in 500mL bag Normal Saline; infuse over 60 minutes.
VINORELBINE 25mg/m² IV Days 1, 8 & 15 Round to nearest 1mg
  - Mix in 50mL Normal Saline minibag; to a final concentration of less than 3mg/mL.
  - Infuse over 6-10 minutes into the sidearm of a free-flowing IV line.
  - Flush IV line with at least 100mL Normal Saline or 5% Dextrose.
  - Hydrocortisone 100mg IV may be given if patient experiences pain on administration.
  - Acute pain syndrome at the tumor site can be managed with nonsteroidal anti-inflammatory drugs or corticosteroids.
  - If extravasation occurs during administration, discontinue immediately and infuse the remaining dose through another IV site.

Order Group 2
- Cycle 2 & 3 while on radiation
CISPLATIN 80mg/m² IV Day 1 Round to nearest 1mg
  - Admix in 500mL bag Normal Saline; infuse over 60 minutes.
VINORELBINE 12.5mg/m² IV Days 1, 8 & 15 Round to nearest 1mg
  - Mix in 50mL Normal Saline minibag; to a final concentration of less than 3mg/mL.
  - Infuse over 6-10 minutes into the sidearm of a free-flowing IV line.
  - Flush IV line with at least 100mL Normal Saline or 5% Dextrose.
  - Hydrocortisone 100mg IV may be given if patient experiences pain on administration.
  - Acute pain syndrome at the tumor site can be managed with nonsteroidal anti-inflammatory drugs or corticosteroids.
  - If extravasation occurs during administration, discontinue immediately and infuse the remaining dose through another IV site.

RADIATION Daily
- 60cGy/30 fraction (5 fraction per week) over a 6 week period starting on Day 4 of Cycle 2.
- Radiation to be given PRIOR to chemotherapy on Day 8 & 15 of Cycle 2 and PRIOR to chemotherapy on Days 1, 8 and 15 of Cycle 3.

REPEAT EVERY 28 DAYS for a total of 4 cycles
HYDRATION:
Pre
  - Infuse 1000mL Normal Saline with 20mEq Potassium Chloride IV over 2 hours before Cisplatin.
Concurrent
  - Give 250mL of 20% Mannitol solution (50G) IV; Infuse through sidearm concurrent with Cisplatin.
Post
  - Infuse 1000mL Normal Saline with 10mEq Potassium Chloride & 2G Magnesium Sulfate IV over 2 hours after Cisplatin.

TESTS:
Baseline Tests
  WBC HB PLT ANC Ca K Na Chloride Mg Glucose Cr Urea T.Bili Albumin
  AST ALT GGT AlkPhosphatase
Days 1 & 8
  WBC HB PLT ANC Ca K Na Chloride Mg Glucose Cr Urea

Test Notes
  Additional Baseline tests: LDH & CO2

ANTIEMETIC PRE-CHEMO REGIMEN:
Level C Day 1
  - Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
  - Dexamethasone 20mg PO/IV
  - May add Aprepitant 125mg PO before chemo (reduce PO Dexamethasone by 50%)

Level A Days 8 & 15
  - Prochlorperazine 10mg PO pm

ANTIEMETIC TAKE-HOME REGIMEN:
Level B/C Day 1
  - Ondansetron 8mg PO BID for 2-3 days, or Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days
  - Dexamethasone 8mg PO BID for 2-3 days
  - May add Aprepitant 80mg PO on Days 2&3 (reduce PO Dexamethasone by 50%)
  - Prochlorperazine 10mg PO q4-6h pm
CISPLATIN-VINORELBINE Chemotherapy concurrent with radiation

**Level A**

Days 8 & 15 - Prochlorperazine 10mg PO q4-6h prn

**PATIENT VISITS and APPOINTMENT TYPE:**

- Day 1 5hrs Type D
- Days 8 & 15 30min Type B

**ANCILLARY:**

- Increase fluids if poor oral intake.

**TOXICITIES:**

**Hematologic**

1. If ANC < 1.5 x 10^9/L, or PLT < 100 x 10^9/L, HOLD chemotherapy for 1 week.

**Renal Failure**

1. If CrCl = 0.5-1.0mL/sec, or SrCr = 136-185umol/L, REDUCE Cisplatin to 50% dose.
2. If CrCl < 0.5mL/sec, or SrCr > 185umol/L, OMIT Cisplatin dose.

**SUGGESTED ACTION**

**CLINICAL MONITORING:**

- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.

**Hearing**

1. Asymptomatic, detected on exam/testing only 2. Symptomatic, not interfering with ADL
3. Symptomatic, interfering with ADL  4. Life-threatening; disabling  5. Death

**Sensory**

1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function 2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL 3. Sensory alteration or paresthesia interfering with ADL 4. Disabling 5. Death

**RATED AT EACH CLINIC VISIT**

**FORMULAE:**

- CrCl - Cockcroft & Gault (mL/sec)
  Male: [140-age(yrs)] x TBW(Kg) / [50 x SCr(umol/L)]

- CrCl - Cockcroft & Gault (mL/sec)
  Female: [140-age(yrs)] x TBW(Kg) / [50 x SCr(umol/L)] x 0.85

**REFERENCES:**


**Date revised:** 09/24/2008
DOCETAXEL Chemotherapy (weekly)
Non-Small Cell Lung Cancer- 2nd Line Treatment for Platinum-Resistant Tumours

DOCETAXEL 25mg/m² IV Day 1 Round to nearest 5mg
- Mix in 100mL bag 5% Dextrose or Normal Saline to a maximum concentration at or below 0.9mg/mL.
- Range: (0.3 to 0.9mg/mL); Use non-PVC equipment without a filter.
- Elasto-gel™ gloves should be placed on both hands and treatment should begin 15 minutes before the infusion starts and conclude 15 minutes after the infusion is done.
- Gloves should be changed after 45 minutes to sustain the cold temperature.
- Infuse through main IV line.
First and Second Dose:
- Infuse at a slower rate and then increase incrementally.
- Infuse at 30mL/hr for 5 minutes, then at 60mL/hr for 5 minutes, then at 125mL/hr for 5 minutes, then finally at 200mL/hr until infusion complete.
Subsequent doses:
- Infuse over 30 minutes.

DEXAMETHASONE 8mg PO Day 0 4mg tablet
- BID For 3 doses, starting the night before chemotherapy.

DIPHENHYDRAMINE 50mg IV Day 1
- If previous hypersensitivity reaction.
- May be mixed in 50mL minibag Normal Saline (or 5% Dextrose); Give over 10-15 minutes.

TESTS:
Baseline Tests
  WBC HB PLT ANC Ca K Na Chloride Glucose Cr Urea T.Bili Albumin AST ALT GGT AlkPhosphatase
Day 1
  WBC HB PLT ANC
Test Notes - Additional Baseline tests: LDH & CO₂
- LFTs to be done monthly.

ANTIEMETIC PRE-CHEMO REGIMEN:
Level B Day 1 - Dexamethasone 4-8mg PO/IV (if patient has not taken PO dexamethasone at home).
- May add Prochlorperazine 10mg PO/IV if needed.

ANTIEMETIC TAKE-HOME REGIMEN:
Level A Day 1 - Prochlorperazine 10mg PO q4-6h prn

PATIENT VISITS and APPOINTMENT TYPE:
Day 1 (first 2 doses) 60min Type C
Day 1 DOCE (subsequent) 60min Type B

TOXICITIES:
Hematologic
1. If ANC < 1.5 x 10⁹/L, or if PLT < 100 x 10⁹/L, HOLD dose for 1 week.

Hepatic Dysfunction
1. DECREASE dose if LFTs > 1.5 x normal.
2. If AST or ALT > 53 IU/L, or if Alk Phos > 180 IU/L, REDUCE dose by 50%.

CLINICAL MONITORING:
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.
- Watch for symptoms of fever and infection.
- Skin assessment at each visit, including nails.

Skin Toxicity
Fluid Retention
0. None 1. Mild peripheral edema 2. Pleural effusion, outpatient management 3. Pleural effusion, inpatient management 4. Intubation required
Nail Changes
1. Discoloration; ridging (koilonychias); pitting 2. Partial or complete loss of nail(s); pain in nailbed(s) 3. Interfering with ADL

RATED AT EACH CLINIC VISIT
DOCETAXEL Chemotherapy (weekly)

HYPERSENSITIVITY:
Docetaxel Hypersensitivity Procedures:
- If hypersensitivity reaction during administration:
  1. Discontinue Docetaxel immediately if there are signs or symptoms of moderate or severe hypersensitivity. (Mild symptoms may resolve with a decrease in the rate of infusion).
  2. Rapid IV administration of Diphenhydramine 50mg and Hydrocortisone 100mg.
  3. Re-initiate infusion after 30 minutes, or when signs of reaction are resolved. Resume infusion at a slower rate, then increase incrementally to the initial planned rate, eg. infuse at 30mL/hr (a 3.3-hour rate) for 5 minutes, then at 60mL/hr (a 1.6-hour rate) for 5 minutes, then at 125mL/hr (a 0.8-hour rate) for 5 minutes, then finally, resume at 200mL/hr (0.5-hour infusion rate).
  4. Depending on the intensity of the reaction, additional oral or IV pre-medication with an antihistamine should also be given for the next cycle of treatment and the rate of infusion should be decreased initially and then increased back to the recommended 1-hour infusion.

INTERNAL CODE:
OPIS CODE: DOCE WEEKLY-LU

REFERENCES:

CCO Eligibility Form Required ☑ Non-Formulary Form Required ☐ Date revised: 07/25/2008
DOCETAXEL Chemotherapy
Non-Small Cell Lung Cancer—Second Line Treatment for Platinum-Resistant Tumours

DOCETAXEL 75mg/m² IV Day 1 Round to nearest 5mg
- Mix in 250mL bag 5% Dextrose or Normal Saline to a maximum concentration of 0.3 - 0.9 mg/mL.
- Use non-PVC equipment without a filter; Infuse through main IV line.
- Elasto-gel™ gloves should be placed on both hands and treatment should begin 15 minutes before the infusion starts and conclude 15 minutes after the infusion is done.
- Gloves should be changed after 45 minutes to sustain the cold temperature.

First and Second Dose:
- Infuse at a slower rate and then increase incrementally.
- Infuse at 30mL/hr for 5 minutes, then at 60mL/hr for 5 minutes, then at 125mL/hr for 5 minutes, then finally at 250mL/hr until infusion complete.

Subsequent doses:
- Infuse over 1 hour.

DEXAMETHASONE 8mg PO Day 0 4mg tablet
- BID for 3 days, starting evening before chemotherapy.

DIPHENHYDRAMINE 50mg IV Day 1
- If previous hypersensitivity reaction.
- May be mixed in 50mL minibag (Normal Saline or 5% Dextrose); Give over 10-15 minutes.
- Wait 30 minutes before Docetaxel infusion started.

TESTS:
Baseline Tests WBC HB PLT ANC Ca K Na Chloride Mg Glucose Cr Urea T.Bili Albumin AST ALT GGT AlkPhosphatase
Day 1 WBC HB PLT ANC K Na Chloride Cr Urea T.Bili Albumin AST ALT GGT AlkPhosphatase

Test Notes - Additional Baseline tests: LDH & CO₂

ANTIEMETIC PRE-CHEMO REGIMEN:
Level B Day 1 - Dexamethasone 8mg PO/IV (if patient has not taken PO dexamethasone at home)
- May add or substitute Prochlorperazine 10mg PO/IV pm

ANTIEMETIC TAKE-HOME REGIMEN:
Level A Day 1 - Prochlorperazine 10mg PO q4-6h pm

PATIENT VISITS and APPOINTMENT TYPE:
⇒ Day 1 DOCE (first 2 doses) 2hrs Type D
⇒ Day 1 DOCE (subsequent) 2hrs Type C

TOXICITIES:
Hematologic
1. If ANC < 1.5 x 10⁹/L, or if PLT < 100 x 10⁹/L, HOLD dose for 1 week.

Hepatic Dysfunction
1. DECREASE dose if LFTs > 1.5 x normal.
2. If AST or ALT > 53 IU/L, or if Alk Phos > 180 IU/L, REDUCE dose by 50%.

SUGGESTED ACTION

CLINICAL MONITORING:
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.
- Watch for symptoms of fever and infection.
- Skin assessment at each visit, including nails.

Skin Toxicity

Fluid Retention
0. None 1. Mild peripheral edema 2. Pleural effusion, outpatient management 3. Pleural effusion, inpatient management 4. Intubation required

Nail Changes
1. Discoloration; ridging (koilonychias); pitting 2. Partial or complete loss of nail(s); pain in nailbed(s) 3. Interfering with ADL

RATED AT EACH CLINIC VISIT
DOCETAXEL Chemotherapy

HYPERSENSITIVITY:

Docetaxel Hypersensitivity Procedures:
- If hypersensitivity reaction during administration:
1. Discontinue Docetaxel immediately if there are signs or symptoms of moderate or severe hypersensitivity. (Mild symptoms may resolve with a decrease in the rate of infusion.)
2. Rapid IV administration of Diphenhydramine 50mg and Hydrocortisone 100mg.
3. Re-initiate infusion after 30 minutes, or when signs of reaction are resolved. Resume infusion at a slower rate, then increase incrementally to the initial planned rate, eg. infuse at 30mL/hr (an 8-hour rate) for 5 minutes, then at 60mL/hr (a 4-hour rate) for 5 minutes, then at 125mL/hr (a 2-hour rate) for 5 minutes, then finally, resume at 250mL/hr (1-hour infusion rate).
4. Depending on the intensity of the reaction, additional oral or IV pre-medication with an antihistamine should also be given for the next cycle of treatment and the rate of infusion should be decreased initially and then increased back to the recommended 1-hour infusion.

INTERNAL CODE:
OPIS CODE: DOCETAX-LU

REFERENCES:

CCO Eligibility Form Required ☑ Non-Formulary Form Required ☐ Date revised: 07/25/2008
**Oral ERLOTINIB Chemotherapy**

**Advanced Non-Small Cell Lung Cancer**

**ERLOTINIB** 150mg PO Daily 25mg

- 150mg **once daily** on an empty stomach (one-hour before or two hours after a meal).
- Second or Third Line treatment of Advanced Non Small Cell Lung Cancer.
- Outpatient prescription available in 25mg, 100mg, and 150mg tablets.
- Trade Name: Tarceva™

**Continuous Treatment Until Disease Progression or Unacceptable Toxicities**

**TESTS:**

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<tr>
<th>Baseline Tests</th>
<th>WBC HB PLT ANC Ca T.Bili Albumin AST ALT GGT AlkPhosphatase</th>
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<tr>
<td>Each Visit</td>
<td>WBC HB PLT ANC Ca T.Bili Albumin AST ALT GGT AlkPhosphatase</td>
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<td>Test Notes</td>
<td>- Liver function tests, chest X-ray and scans as required to monitor lesions and to rule out development of interstitial pneumonitis in presence of dyspnea.</td>
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**TOXICITIES:**

**Cutaneous**

- Rash:
  - Usually will improve with time but early intervention with steroid cream and antibiotic cream (clindamycin) is recommended.
  - If severe rash, may consider oral antibiotics such as minocycline or doxycycline. If severe rash despite appropriate management, may require treatment interruption and/or dose modification.

**Hepatic Dysfunction**

- Elevated liver enzymes:
  1. > ULN-2.5 xULN
  2. >2.5-5 xULN
  3. >5-20xULN
  4. >20xULN
  - If Grade 3 elevation of transaminases, hold treatment and restart at a lower dose once LFTs improve.

**Pulmonary**

- Pulmonary Symptoms:
  - Acute onset of new and/or progressive unexplained pulmonary symptoms, such as dyspnea, cough and fever, therapy should be interrupted pending diagnostic evaluation. If interstitial lung disease (ILD) is diagnosed, treatment should be discontinued.

**Gastrointestinal**

- Gastrointestinal Bleed:
  - Treatment should be discontinued.

- Diarrhea:
  - Optimal use of antidiarrheal medications such as Loperamide or Diphenoxylate/Atropine. If severe, may require treatment interruption and/or dose modification.
  - When dose reduction is necessary, it is recommended to reduce in 50 mg steps.

**SUGGESTED ACTION**

**CLINICAL MONITORING:**

- Close monitoring of INR in patients on Warfarin especially initially, or when dose held, modified or discontinued.
- Erlotinib is metabolized via CYP3A4.
- CYP3A4 inducers (e.g. Phenobarbital, Carbazepine, Rifampin etc.) will reduce erlotinib plasma concentration and CYP3A4 inhibitors (e.g. azole antifungals, calcium channel blockers, macrolide antibiotics, grapefruit juice etc.) will increase erlotinib plasma concentrations.

**Diarrhea:**

1. Increase of <4 stools per day over baseline; mild increase in ostomy output compared to baseline
2. Increase of 4-6 stools per day over baseline; IV fluids indicated <24hrs; moderate increase in ostomy output compared to baseline; not interfering with ADL 3. Increase of >=7 stools per day over baseline; incontinence; IV fluids >24 hours; hospitalization; severe increase in ostomy output compared to baseline; interfering with ADL 4. Life-threatening consequences (e.g., hemodynamic collapse) 5. Death

**Rash:**

1. Macular or papular eruption or erythema without associated symptoms 2. Macular or papular eruption or erythema with pruritus or other associated symptoms; localized desquamation or other lesions covering <50% of body surface area (BSA) 3. Severe, generalized erythroderma or macular, papular or vesicular eruption; desquamation covering >=50% BSA 4. Generalized exfoliative, ulcerative, or bullous dermatitis 5. Death

**Liver Function Tests:**

1. > ULN-2.5 xULN
2. >2.5-5 xULN
3. >5-20xULN
4. >20xULN

Reduced Erlotinib doses should be considered for subjects with moderate hepatic impairment. Hepatic function should be closely monitored in patients with pre-existing liver disease or concomitant hepatotoxic medications. Erlotinib dosing should be interrupted if significant changes in liver function tests are observed.

**Pneumonitis:**

1. Asymptomatic, radiographic findings only 2. Symptomatic, not interfering with ADL 3. Symptomatic, interfering with ADL; O2 indicated 4. Life-threatening; ventilatory support indicated 5. Death

**Ocular surface disease:**

1. Asymptomatic or minimally symptomatic but not interfering with function 2. Symptomatic, interfering with function but not interfering with ADL; topical antibiotics or other topical intervention indicated 3. Symptomatic, interfering with ADL; operative intervention indicated.

**RATED AT EACH CLINIC VISIT**
Oral ERLOTINIB Chemotherapy

INTERNAL CODE:
OPIS CODE: ERLOT*PO LU

REFERENCES:

Date revised: 07/10/2008
**Oral ETOPOSIDE Chemotherapy**

**Small Cell Lung Cancer**

**ETOPOSIDE**
- 50-100mg PO Daily 50mg capsule
- Daily for 14 days.
- Outpatient prescription available as 50mg capsules.
- Trade name: Vepesid™

**REPEAT EVERY 21 DAYS**

**TESTS:**
- Baseline Tests: WBC HB PLT ANC Ca K Na Chloride Glucose Cr Urea T.Bili Albumin AST ALT GGT AlkPhosphatase
- Day 1: WBC HB PLT ANC K Na Chloride Cr Urea T.Bili Albumin AST ALT GGT AlkPhosphatase

**Test Notes:** Additional Baseline tests: LDH & CO₂

**ANTIEMETIC TAKE-HOME REGIMEN:**
- Prochlorperazine 10mg PO q4-6h prn

**TOLERANCES:**

**Hematologic**
1. If ANC < 1.5 x 10⁹/L, or PLT < 100 x 10⁹/L, HOLD dose.

**Hepatic Dysfunction**
1. If T.Bili = 26-51umol/L, or AST = 60-180 IU/L, REDUCE Etoposide to 50% dose.
2. If T.Bili = 52-85umol/L, REDUCE Etoposide to 25% dose.
3. If T.Bili > 85umol/L, or AST > 180 IU/L, OMIT Etoposide.

**SUGGESTED ACTION**

**CLINICAL MONITORING:**
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.

**INTERNAL CODE:**
- OPIS CODE: ETOP*PO LU

**REFERENCES:**

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**CCO Eligibility Form Required**
**Non-Formulary Form Required**
**Date revised:** 09/23/2008
GEMCITABINE Chemotherapy  
Non-Small Cell Lung Cancer

**GEMCITABINE**  
1000mg/m² IV Days 1 & 8  
Round to nearest 19mg

- Mix in **250mL** bag **Normal Saline**.  
- Infuse over **30 minutes** through free-flowing IV.

**REPEAT EVERY 21 DAYS**

**TESTS:**
- **Baseline Tests**  
  - WBC  
  - HB  
  - PLT  
  - ANC  
  - Ca  
  - K  
  - Na  
  - Chloride  
  - Mg  
  - Glucose  
  - Cr  
  - Urea  
  - T.Bili  
  - Albumin  
  - AST  
  - ALT  
  - GGT  
  - AlkPhosphatase

- **Days 1 & 8**  
  - Additional Baseline tests: LDH & CO₂

**Antiemetic Pre-Chemo Regimen:**
- **Level B**  
  - Days 1 & 8: Dexamethasone 8mg PO/IV  
  - May add or substitute Prochlorperazine 10mg PO/IV pm

**Antiemetic Take-Home Regimen:**
- **Level A**  
  - Days 1 & 8: Prochlorperazine 10mg PO q4-6h pm

**Patient Visits and Appointment Type:**
- **Days 1 & 8:** 45min Type B

**Toxicities:**

**Hematologic**
1. If ANC = 1.0-1.5 x 10⁹/L, or if PLT < 100 x 10⁹/L, REDUCE to **50%**.
2. If ANC < 1.0 x 10⁹/L, or if PLT < 75 x 10⁹/L, **OMIT** dose.

**Gastrointestinal**
1. If Mucositis or Diarrhea > Grade 3 in previous course, REDUCE to **2/3 dose**.

**Suggested Action**

**Clinical Monitoring:**

**Diarrhea**
1. Increase of < 4 stools per day over baseline; mild increase in ostomy output compared to baseline
2. Increase of 4 - 6 stools per day over baseline; IV fluids indicated < 24hrs; moderate increase in ostomy output compared to baseline; not interfering with ADL 3. Increase of ≥7 stools per day over baseline; incontinence; IV fluids ≥24 hrs; hospitalization; severe increase in ostomy output compared to baseline; interfering with ADL 4. Life-threatening consequences (e.g., hemodynamic collapse)
5. Death

**Mucositis**
1. Erythema of the mucosa  
2. Patchy ulcerations or pseudomembranes  
3. Confluent ulcerations or pseudomembranes; bleeding with minor trauma  
4. Tissue necrosis; significant spontaneous bleeding; life-threatening consequences
5. Death

**Rated at Each Clinical Visit**

**Edema Limb**
1. 5 - 10% inter-limb discrepancy in volume or circumference at point of greatest visible difference; swelling or obscuration of anatomic architecture on close inspection; pitting edema  
2. >10 - 30% inter-limb discrepancy in volume or circumference at point of greatest visible difference; readily apparent obscuration of anatomic architecture; obliteration of skin folds; readily apparent deviation from normal anatomic contour  
3. >30% inter-limb discrepancy in volume; lymphorrhea; gross deviation from normal anatomic contour; interfering with ADL  
4. Progression to malignancy (i.e., lymphangiosarcoma); amputation indicated; disabling
5. Death

**Rated if Edema on Routine Visits**

**Internal Code:**

**OPI/S Code: GEMCIT-LU**

**References:**

**CCO Eligibility Form Required**  
**Non-Formulary Form Required**

**Date Revised:** 07/25/2008
PACLITAXEL-CARBOPLATIN Chemotherapy
Non-Small Cell Lung Cancer

**PACLITAXEL**
200mg/m² IV Day 1 Round to nearest 3mg
- Mix in **500mL** bag **Normal Saline** (dilution concentration 0.3-1.2 mg/mL).
- Use non-PVC equipment, including 0.22 micron in-line filter.
- Infuse over **3 hours**, before Carboplatin.

**DEXAMETHASONE**
20mg PO Day 1 4mg tablet
- To be administered at home 12 and 6 hours before Paclitaxel (if not taken at home, Dexamethasone 20mg IV 30 minutes before Paclitaxel).

**DIPHENHYDRAMINE**
50mg IV Day 1
- Admix in **50-100mL** minibag 5% Dextrose or **Normal Saline**.
- Give over **10-15 minutes** (may be admixed with Ranitidine).
- Administer 30 minutes before Paclitaxel.

**RANITIDINE**
50mg IV Day 1
- Admix in **50-100mL** minibag 5% Dextrose or **Normal Saline**.
- Give over **10-15 minutes** (may be admixed with Diphenhydramine).
- Administer 30 minutes before Paclitaxel.

**CARBOPLATIN**
AUC = 5-6 IV Day 1 Round to nearest 5mg
- Mix in **250mL 5% Dextrose**.
- Infuse over **30-60 minutes**, after Paclitaxel.

**CARBOPLATIN**
AUC = 5-6 IV Day 1 Round to nearest 5mg
- Mix in **250mL 5% Dextrose**.
- Infuse over **30-60 minutes**, after Paclitaxel.

**REPEAT EVERY 21 DAYS**

**TESTS:**
Baseline Tests: WBC HB PLT ANC Ca K Na Chloride Mg Glucose Cr Urea T.Bili Albumin AST ALT GGT AlkPhosphatase
Day 1: WBC HB PLT ANC Ca K Na Chloride Mg Glucose Cr Urea T.Bili Albumin AST ALT GGT AlkPhosphatase
Test Notes: - Additional Baseline tests: LDH & CO₂

**ANTIEMETIC PRE-CHEMO REGIMEN:**
Level C: Day 1
- Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
- Dexamethasone 20mg PO/IV (if patient has not taken PO dexamethasone at home)

**ANTIEMETIC TAKE-HOME REGIMEN:**
Level B/C: Day 1
- Ondansetron 8mg PO BID for 2-3 days, or Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days
- Dexamethasone 8mg PO BID for 2-3 days
- Prochlorperazine 10mg PO q4-6h prn

**PATIENT VISITS and APPOINTMENT TYPE:**
- Day 1 6hrs Type D

**ANCILLARY:**
- Take a baseline blood pressure measurement, if prior hypotension.

**TOXICITIES:**

**Hematologic**
1. If ANC < 1.5 x 10^9/L, or if PLT < 100 x 10^9/L, **HOLD** dose for 1 week.

**Hepatic Dysfunction**
1. If T.Bili < 25umol/L, GIVE Paclitaxel maximum dose of 135mg/m².
2. If T.Bili = 26-51umol/L, or AST = 60-180 IU/L, GIVE Paclitaxel maximum dose of 75mg/m².
3. If T.Bili = 52-85umol/L, GIVE Paclitaxel maximum dose of 50mg/m².

**Renal Failure**
1. Adjust Carboplatin dose if estimated CrCl changes > 10%.

**SUGGESTED ACTION**
PACLITAXEL-CARBOPLATIN Chemotherapy

**CLINICAL MONITORING:**
- Watch for symptoms of fever and infection.
- Blood pressure and pulse rate monitoring during drug administration & for the following hour.

**Sensory**
1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function.
2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL.
3. Sensory alteration or paresthesia interfering with ADL.
4. Disabling
5. Death

**Flu-like Symptoms**
1. Symptoms present but not interfering with function
2. Moderate or causing difficulty performing some ADL
3. Severe symptoms interfering with ADL
4. Disabling
5. Death

**Allergic Reaction**
1. Transient flushing or rash; drug fever < 38 degrees C
2. Rash; flushing; urticaria; dyspnea; drug fever ≥ 38 degrees C
3. Symptomatic bronchospasm, with or without urticaria; parenteral medication(s) indicated; allergy-related edema/angioedema; hypotension
4. Anaphylaxis
5. Death

**HYPERSENSITIVITY:**

**Retreatment for Paclitaxel Hypersensitivity Reaction:**
If Paclitaxel hypersensitivity reaction occurs during administration:
1. Discontinue Paclitaxel immediately if there are signs or symptoms of hypersensitivity.
2. Rapid IV administration of Diphenhydramine 50mg direct IV push over 1 minute and Hydrocortisone 100mg in 100ml Normal Saline over 5-10 minutes.
3. Reinitiate Paclitaxel infusion after 30 minutes, or when signs of reaction are resolved. Resume Paclitaxel infusion at 17mL/hr (10% of original rate) for 15 minutes, then at 42mL/hr (25% of original rate) for 15 minutes. If no further symptoms develop, continue at original rate until infusion complete.
4. If reaction recurs, STOP Paclitaxel for this dose and treat patient symptoms.

**Desensitization for Paclitaxel Hypersensitivity Reactions:**
If Paclitaxel hypersensitivity recurs during previous administration despite retreatment plan:
1. Dexamethasone 20mg PO 36 hours and 12 hours before chemotherapy, and 20mg PO morning of chemotherapy.
2. Dexamethasone 20mg IV, Diphenhydramine 50mg IV & Ranitidine 50mg IV about 30min before infusion.
3. Paclitaxel Infusion: 2mg in 100mL Normal Saline over 30min; if no reaction, 10mg in 100mL Normal Saline over 30min; if no reaction, remainder of dose in 500mL Normal Saline over 3 hours.
4. If reaction occurs, discontinue infusion; Diphenhydramine 50mg direct IV push over 1 minute and Hydrocortisone 100mg in 100ml Normal Saline over 5-10 minutes.
5. Restart Paclitaxel infusion after 30 minutes.

**FORMULAE:**

**CrCl - Cockcroft & Gault (mL/sec)**

- Male: \[140 - \text{age(yrs)} \times \text{TBW(Kg)} / [50 \times \text{SCr(umol/L)}] \]
- Female: \[140 - \text{age(yrs)} \times \text{TBW(Kg)} / [50 \times \text{SCr(umol/L)}] \times 0.85 \]

**Creatinine CI (mL/min)**

Calvert Formula

**FORMULAE:**

**INTERNAL CODE:**

- OPIS CODE:
  - PACLI-CARB 5
  - PACLI-CARB 6

**REFERENCES:**
- CCO Practice Guideline 7-7-1: The Role of Taxanes in First-line Therapy for Advanced Non-Small Cell Lung Cancer.

**Date revised:** 07/25/2008

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**Date revised:** 07/25/2008
PEMETREXED Chemotherapy
Non Small Cell Lung Cancer - Second line

PEMETREXED 500mg/m² IV Day 1 Round to nearest 25mg
- Admix in 100 mL Normal Saline; infuse over 8-15 minutes.
- Trade name Alimta™

CYANOCOBALAMIN 1000mcg IM Day -14
- Inject IM every 9 weeks beginning 1-2 weeks prior to first dose.
- Outpatient prescription.

FOLIC ACID 0.4mg PO Day -14
- Daily beginning 1-2 weeks prior to first dose.
- Outpatient prescription.

DEXAMETHASONE 4mg PO Days 0, 1 & 2 4mg tablet
- Q12H on the day before, the day of and the day after Pemetrexed.
- Outpatient prescription.

TESTS:
Baseline Tests WBC HB PLT ANC Ca K Na Chloride Cr Urea AST ALT
Day 1 WBC HB PLT ANC Cr Urea AST ALT

ANTIEMETIC PRE-CHEMO REGIMEN:
Level C Day 1 - Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV

ANTIEMETIC TAKE-HOME REGIMEN:
Level A Day 1 - Prochlorperazine 10mg PO q4-6h prn

PATIENT VISITS and APPOINTMENT TYPE:
Day 1 30min Type B

TOXICITIES:
Hematologic
1. If ANC < 1.5 x 10⁹/L, or if PLT < 100 x 10⁹/L, HOLD dose for 1 week.

Renal Failure
1. If CrCl < 0.75mL/sec, HOLD Pemetrexed.

Hepatic Dysfunction
Pemetrexed:
1. If T.Bili > 1.5 times upper limit of normal (ULN), HOLD Pemetrexed.
2. If AP, AST & ALT > 3 times ULN (unless liver involvement, then > 5 times ULN), HOLD Pemetrexed.

SUGGESTED ACTION

CLINICAL MONITORING:
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.
- Baseline & routine renal function tests especially if there are other concurrent nephrotoxic drugs.
- Concurrent NSAID treatment:
  - Ibuprofen 400mg QID can be administered with Pemetrexed in patients with normal renal function (CrCl>80mL/min). Patients with mild to moderate renal insufficiency (45-90mL/min) should avoid taking NSAIDs with short elimination half lives at least 2 days prior to, the day of and at least 2 days after Pemetrexed. Studies have shown a decrease clearance of Pemetrexed following co-administration.
  - All patients taking NSAIDs with short elimination half lives should interrupt treatment at least 5 days prior, the day of, and at least 2 days after Pemetrexed. If concommitant administration is necessary, the patient should be monitored for myelosuppression, renal and gastrointestinal toxicity.

RATED AT EACH CLINIC VISIT

FORMULAE:
CrCl - Cockcroft & Gault (mL/sec)
Male: [140-age(yrs)] x TBW(Kg) / [50 x SCr(umol/L)]
CrCl - Cockcroft & Gault (mL/sec)
Female: [140-age(yrs)] x TBW(Kg) / [50 x SCr(umol/L)] x 0.85

REFERENCES:
- CCO Practice Guidelines: Second Line or Subsequent Systemic Therapy for Recurrent or Progressive Non-Small Cell Lung Cancer.

Date revised: 09/23/2008

Lung
PEMETREXED-CISPLATIN Chemotherapy
Malignant Pleural Mesothelioma

PEMETREXED
500mg/m² IV Day 1 Round to nearest 25mg
- Admix in 100 mL Normal Saline; Infuse over 8-15 minutes.
- Administer Pemetrexed approximately 30 minutes before Cisplatin.
- Trade name Alimta™

CISPLATIN
75mg/m² IV Day 1 Round to nearest 1mg
- Admix in 500mL bag Normal Saline; Infuse over 60 minutes.

CYANOCOBALAMIN
1000mcg IM Day -14
- Inject IM every 8 weeks beginning 1-2 weeks prior to first dose.
- Outpatient prescription.

FOLIC ACID
0.4mg PO Day -14
- Daily beginning 1-2 weeks prior to first dose.
- Outpatient prescription.

DEXAMETHASONE
4mg PO Days 0 4mg tablet
- 4mg Q12H the day before Pemetrexed.

HYDRATION:
- Infuse 1000mL Normal Saline with 20mEq Potassium Chloride IV over 2 hours.

TESTS:
Baseline Tests: WBC HB PLT ANC Ca K Na Chloride Mg Glucose Cr Urea T.Bili Albumin
AST ALT GGT AlkPhosphatase

Day 1 WBC HB PLT ANC K Na Chloride Mg Glucose Cr Urea

ANTIEMETIC PRE-CHEMO REGIMEN:
Level C Day 1
- Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
- Dexamethasone 20mg PO/IV
- May add Aprepitant 125mg PO before chemo (reduce PO Dexamethasone by 50%)

ANTIEMETIC TAKE-HOME REGIMEN:
Level B/C Day 1
- Ondansetron 8mg PO BID for 2-3 days, or Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days
- Dexamethasone 8mg PO BID for 2-3 days
- May add Aprepitant 80mg PO on Days 2&3 (reduce PO Dexamethasone by 50%)
- Prochlorperazine 10mg PO q4-6h prn

PATIENT VISITS and APPOINTMENT TYPE:
⇒ Day 1 6hrs Type D

ANCILLARY:
- Oral hydration is strongly encouraged; poorly hydrated patients may need more IV hydration to prevent renal toxicity.

TOXICITIES:
Hematologic
1. If ANC < 1.5 x 10^9/L, or if PLT < 100 x 10^9/L, HOLD dose for 1 week.

Renal Failure
1. If CrCl = 0.5-1.0mL/sec, or SrCr = 136mmol/L, REDUCE Cisplatin to 50% dose.
2. If CrCl < 0.5mL/sec, or SrCr > 185mmol/L, OMIT Cisplatin dose.
3. If CrCl < 0.75mL/sec, HOLD Pemetrexed.

Hepatic Dysfunction
Pemetrexed:
1. T.Bili < 1.5 times upper limit of normal (ULN).
2. AP, AST & ALT < 3 times ULN (unless liver involvement, then < 5 times ULN).

SUGGESTED ACTION
PEMETREXED-CISPLATIN Chemotherapy

**CLINICAL MONITORING:**
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.
- Baseline & routine renal function tests especially if there are other concurrent nephrotoxic drugs.

**Hearing**
1. Asymptomatic, detected on exam/testing only  
2. Symptomatic, not interfering with ADL  
3. Symptomatic, interfering with ADL  
4. Life-threatening; disabling  
5. Death

**Sensory**
1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function  
2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL  
3. Sensory alteration or paresthesia interfering with ADL  
4. Disabling  
5. Death

RATED AT EACH CLINIC VISIT

**FORMULAE:**
- CrCl - Cockcroft & Gault (mL/sec)  
  Male: \[\frac{[140-\text{age(yrs)}] \times \text{TBW(Kg)}}{[50 \times \text{SCr(umol/L)}]}\]  
- CrCl - Cockcroft & Gault (mL/sec)  
  Female: \[\frac{[140-\text{age(yrs)}] \times \text{TBW(Kg)}}{[50 \times \text{SCr(umol/L)}] \times 0.85}\]  
- Creatinine Cl (mL/min)  
  \[\text{mL/min} = 60 \times \text{CrCl mL/sec}\]

**REFERENCES:**
- CCO Practice Guideline 7-14-1 ES: The Use of Chemotherapy in Patients with Advanced Malignant Pleural Mesothelioma.
Porfimer for Photodynamic Therapy

Treatment of patients with advanced non-small cell lung cancer who have symptomatic bronchial obstruction

**PORFIMER**

2mg/kg IV Day 1 Round to nearest 1mg

- Reconstitute dry powder vial with **D5W only**.
- Reconstitution with normal saline solutions will precipitate.
- Avoid contact with the eyes and skin during preparation and/or administration.
- Administer as a single slow intravenous injection over 3 to 5 minutes.
- Followed by illumination with appropriate laser light approximately 40-50 hours after porfimer injection.
- Depending on the indication a second laser light application approximately 96-120 hours after drug administration may be given.
- Trade name Photofrin™

Repeat every 30 days if needed, to a maximum of 3 cycles.

**PATIENT VISITS and APPOINTMENT TYPE:**

- **Day 1** 30 min Type A

**ANCILLARY:**

- Use of other photosensitizing drugs may increase photosensitivity ex. Phenothiazines, thiazide diuretics, tetracyclines, fluoroquinolones, sulfonamide antibiotics, sulfonurea hypoglycemiants.
- Use with DMSO may reduce efficacy.

**CLINICAL MONITORING:**

- Care should be taken to prevent extravasation at the injection site.
- If extravasation occurs, the area should be protected from light for a minimum of 30 days.
- Photosensitivity may last at least 4-6 weeks.

**Photosensitivity:**

1. Painless erythema 2. Painful erythema 3. Erythema with desquamation 4. Life-Threatening; disabling

RATED AT EACH CLINIC VISIT

CCO Eligibility Form Required ✔ Non-Formulary Form Required □ Date revised: 09/23/2008
LUNG — RALTI-CIS

**RALTITREXED-CISPLATIN Chemotherapy**

**Malignant Pleural Mesothelioma**

**RALTITREXED**

3mg/m² IV Day 1 Round to nearest 0.1mg
- Mix in **100mL** minibag Normal Saline or 5% Dextrose; Infuse over **15 minutes**. Administer before Cisplatin.
- Trade name Tomudex™

**CISPLATIN**

80mg/m² IV Day 1 Round to nearest 1mg
- Admix in **500mL** bag Normal Saline; Infuse over **60 minutes**.

**REPEAT EVERY 21 DAYS** until disease progression

**HYDRATION:**

**Pre**
- Infuse **1000mL Normal Saline** with **20mEq Potassium Chloride** IV over **2 hours**.

**Concurrent**
- Give **250mL of 20% Mannitol solution (50G)** IV; Infuse through sidearm **concurrent** with Cisplatin.

**Post**
- Infuse **1000mL Normal Saline** with **10mEq Potassium Chloride & 2G Magnesium Sulfate** IV over **2 hours**.

**TESTS:**

**Baseline Tests**
- WBC HB PLT ANC Ca K Na Chloride Mg Glucose Cr Urea T.Bili Albumin AST ALT GGT AlkPhosphatase

**Day 1**
- WBC HB PLT ANC K Na Chloride Mg Glucose Cr Urea

**ANTIEMETIC PRE-CHEMO REGIMEN:**

**Level C**
- Day 1
  - Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
  - Dexamethasone 20mg PO/IV
  - May add Aprepitant 125mg PO before chemo (reduce PO Dexamethasone by 50%)

**ANTIEMETIC TAKE-HOME REGIMEN:**

**Level B/C**
- Day 1
  - Ondansetron 8mg PO BID for 2-3 days, or Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days
  - Dexamethasone 8mg PO BID for 2-3 days
  - May add Aprepitant 80mg PO on Days 2&3 (reduce PO Dexamethasone by 50%)
  - Prochlorperazine 10mg PO q4-6h prn

**PATIENT VISITS and APPOINTMENT TYPE:**

→ Day 1 5.5hrs Type D

**ANCILLARY:**
- Oral hydration is strongly encouraged; poorly hydrated patients may need more IV hydration to prevent renal toxicity.

**TOXICITIES:**

**Hematologic**

1. If ANC < 1.5 x 10⁹/L, or if PLT < 100 x 10⁹/L, **HOLD** chemotherapy for 1 week.
   Dose adjustments for Raltitrexed for next treatment cycles:
2. If ANC = 0.5-1.0 x 10⁹/L, or if PLT = 25-50 x 10⁹/L, **DECREASE** Raltitrexed to 2.25mg/m², or if in conjunction with Grade 3 diarrhea, **DISCONTINUE** Raltitrexed.
3. If ANC < 0.5 x 10⁹/L, or if PLT < 25 x 10⁹/L, **DECREASE** Raltitrexed to 1.5mg/m².

**Renal Failure**

**Cisplatin:**
1. If CrCl = 0.5-1.0mL/sec, or SrCr = 136mmol/L, **REDUCE** Cisplatin to 50% dose.
2. If CrCl < 0.5mL/sec, or SrCr > 185mmol/L, **OMIT** Cisplatin dose.

**Raltitrexed:**
1. If CrCl < 65mL/min(1.1mL/sec), **REDUCE** to 75% dose every 4 weeks.
2. If CrCl <55mL/min(0.9mL/sec), use % dose equivalent to mL/min every 4 weeks (eg. 30mL/mL=30% dose).
3. If CrCl <25mL/min(0.4mL/sec), **NO** treatment.

**Gastrointestinal**

1. If Diarrhea = Grade 2, **REDUCE** Raltitrexed to 2.25mg/m².
2. If Diarrhea = Grade 3, **REDUCE** Raltitrexed to 1.5mg/m².
3. If Diarrhea = Grade 4, **STOP** Raltitrexed.

**SUGGESTED ACTION**
RALTITREXED-CISPLATIN Chemotherapy

**CLINICAL MONITORING:**
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.
- Baseline & routine renal function tests/ especially if there are other concurrent nephrotoxic drugs.

**Sensory**
1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function
2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL
3. Sensory alteration or paresthesia interfering with ADL
4. Disabling
5. Death

**Hearing**
1. Asymptomatic, detected on exam/testing only
2. Symptomatic, not interfering with ADL
3. Symptomatic, interfering with ADL
4. Life-threatening; disabling
5. Death

**Diarrhea**
1. Increase of < 4 stools per day over baseline; mild increase in ostomy output compared to baseline
2. Increase of 4 - 6 stools per day over baseline; IV fluids indicated < 24hrs; moderate increase in ostomy output compared to baseline; not interfering with ADL
3. Increase of ≥ 7 stools per day over baseline; incontinence; IV fluids ≥ 24 hrs; hospitalization; severe increase in ostomy output compared to baseline; interfering with ADL
4. Life-threatening consequences (e.g., hemodynamic collapse)
5. Death

**RATED AT EACH CLINIC VISIT**

**FORMULAE:**
- **CrCl - Cockcroft & Gault (mL/sec)**
  - Male: \[140 - \text{age(yrs)} \times \text{TBW(Kg)} / (50 \times \text{SCr(umol/L)})\]
  - Female: \[140 - \text{age(yrs)} \times \text{TBW(Kg)} / (50 \times \text{SCr(umol/L)}) \times 0.85\]
- **Creatinine Cl (mL/min)**
  - \(\text{mL/min} = 60 \times \text{CrCl mL/sec}\)

**REFERENCES:**
- CCO Practice Guideline 7-14-1 ES: The Use of Chemotherapy in Patients with Advanced Malignant Pleural Mesothelioma.
VINORELBINE Chemotherapy
Non-Small Cell Lung Cancer

VINORELBINE 30mg/m² IV Days 1 & 8 Round to nearest 1mg

- Add to 50mL Normal Saline minibag; Infuse over 6-10 minutes into the side-arm of a free-flowing IV line.
- Flush IV line with at least 100mL Normal Saline or 5% Dextrose.
- Hydrocortisone 100mg IV may be given if patient experiences pain on administration.
- If extravasation occurs during administration, discontinue immediately and infuse the remaining dose through another IV site (into another vein).

Test Results:

Baseline Tests: WBC HB PLT ANC Ca K Na Chloride Mg Glucose Cr Urea T.Bili Albumin AST ALT GGT AlkPhosphatase

Day 1 WBC HB PLT ANC
Test Notes: Additional Baseline tests: LDH & CO₂
- Consider checking LFTs every 2 or 3 cycles.

ANTIEMETIC PRE-CHEMO REGIMEN:
Level A Days 1 & 8
- Prochlorperazine 10mg PO pm

ANTIEMETIC TAKE-HOME REGIMEN:
Level A Days 1 & 8
- Prochlorperazine 10mg PO q4-6h pm

PATIENT VISITS and APPOINTMENT TYPE:
→ Days 1 & 8: 30min Type B

TOXICITIES:

Hematologic
1. If ANC < 1.5 x 10⁹/L, or PLT < 100 x 10⁹/L, HOLD dose.

SUGGESTED ACTION

CLINICAL MONITORING:
- Watch for symptoms of fever and infection.
- Sensory
  1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function 2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL 3. Sensory alteration or paresthesia interfering with ADL 4. Disabling 5. Death
- Constipation
  1. Occasional or intermittent symptoms; occasional use of stool softeners, laxatives, dietary modification, or enema 2. Persistent symptoms with regular use of laxatives or enemas indicated 3. Symptoms interfering with ADL; obstipation with manual evacuation indicated 4. Life-threatening consequences (e.g., obstruction, toxic megacolon) 5. Death

RATED AT EACH CLINIC VISIT

REFERENCES:

Date revised: 09/24/2008

CCO Eligibility Form Required ☑ Non-Formulary Form Required ☐
CARMUSTINE-CISPLATIN-DACARBAZINE Chemotherapy
Malignant Melanoma

CARMUSTINE 150mg/m^2 IV Day 1
- Reduce to 75mg/m^2 IV cycle 1 ONLY.
- Mix in 250-500mL fluid in polyolefin bag Normal Saline (or 5% Dextrose). Use non-PVC equipment without filter. Protect from light.
- Infuse over 60 minutes or longer (faster infusion, if tolerated).
- Cumulative lifetime dose limit for Carmustine = 1400mg/m^2.

CISPLATIN 25mg/m^2 IV Days 1-3 & 22-24
- Mix in 250mL bag Normal Saline; Infuse over 30-60 minutes.

DACARBAZINE 220mg/m^2 IV Days 1-3 & 22-24
- Mix in 250-500mL bag Normal Saline; Infuse through main IV line, with an additional 500mL Normal Saline run at same time by piggyback, to reduce vein irritation.
- Infuse over 30-120 minutes; If vein irritation, infuse slowly.
- Protect from light.

REPEAT EVERY 42 DAYS

TESTS:
Baseline Tests
Day 1 & 22
ANTIEMETIC PRE-CHEMO REGIMEN:
Level C
- Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
- Dexamethasone 20mg PO/IV

ANTIEMETIC TAKE-HOME REGIMEN:
Level B/C
- Ondansetron 8mg PO BID for 2-3 days, or
  - Granisetron 1mg PO 12 hours posts chemotherapy, then 2mg PO OD for 2-3 days
  - Dexamethasone 8mg PO BID for 2-3 days
  - Prochlorperazine 10mg PO q4-6h prn

PATIENT VISITS and APPOINTMENT TYPE:
⇒ Day 1 3hrs Type D
⇒ Days 2-3 & Days 22-24 1.5hrs Type C

TOXICITIES:
Hematologic
1. If ANC < 1.5 x 10^9/L, or if PLT < 100 x 10^9/L on Days 1 or 22, HOLD dose 1 week.

Renal Failure
1. If CrCl = 0.5-1.0mL/sec, or SrCr = 136-185umol/L, REDUCE Cisplatin to 50% dose.
2. If CrCl < 0.5mL/sec, or SrCr > 185umol/L, OMIT dose of Cisplatin.
3. If CrCl < 1.0mL/sec, REDUCE dose of Carmustine & Dacarbazine by 25-50%.

SUGGESTED ACTION
CLINICAL MONITORING:
- Baseline & routine renal function tests, especially if there are other concurrent nephrotoxic drugs.
- Clinical pulmonary exam, including auscultation, pulmonary toxicity ratings (Cough, SOB).

Sensory
1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function
2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL
3. Sensory alteration or paresthesia interfering with ADL
4. Disabling
5. Death

Hearing
1. Asymptomatic, detected on exam/testing only
2. Symptomatic, not interfering with ADL
3. Symptomatic, interfering with ADL
4. Life-threatening; disabling
5. Death

Dyspnea
1. Dyspnea on exertion, but can walk 1 flight of stairs without stopping
2. Dyspnea on exertion but unable to walk 1 flight of stairs or 1 city block (0.1km) without stopping
3. Dyspnea with ADL
4. Dyspnea at rest; intubation/ventilator indicated
5. Death

Cough
1. Symptomatic, non-narcotic medication only indicated
2. Symptomatic and narcotic medication indicated
3. Symptomatic and significantly interfering with sleep or ADL

RATED AT EACH CLINIC VISIT

FORMULAE:
CrCl = Cockcroft & Gault (mL/sec)
- Male: \[ \frac{[140-(\text{age}) \times \text{TBW}(\text{Kg})]}{[50 \times \text{SCr(umol/L})]} \]
- Female: \[ \frac{[140-(\text{age}) \times \text{TBW}(\text{Kg})]}{[50 \times \text{SCr(umol/L}) \times 0.85] \]

REFERENCES:

CCO Eligibility Form Required ☐ Non-Formulary Form Required ☐ Date revised: 09/03/2008
DACARBABINE Chemotherapy  
Malignant Melanoma

**DACARBABINE**  
1000mg/m²  
IV  Day 1  
Round to nearest 10mg

- Mix in 250-500mL bag Normal Saline.
- Infuse through main IV line with an additional 500mL Normal Saline run at same time by piggyback to reduce vein irritation (more IV fluid if ordered).
- Infuse over **120 minutes**: If vein irritation, infuse slowly.
- Protect from light.

**REPEAT EVERY 21 DAYS**

**TESTS:**
Baseline Tests  
WBC  HB  PLT  ANC  Cr  Urea  T.Bili  AST  ALT  GGT  AlkPhosphatase

**ANTIEMETIC PRE-CHEMO REGIMEN:**
Level C  
Day 1  
- Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
- Dexamethasone 20mg PO/IV

**ANTIEMETIC TAKE-HOME REGIMEN:**
Level B/C  
Day 1  
- Ondansetron 8mg PO BID for 2-3 days, or Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days
- Dexamethasone 8mg PO BID for 2-3 days
- Prochlorperazine 10mg PO q4-6h prn

**PATIENT VISITS and APPOINTMENT TYPE:**
- Day 1  
2.5hrs  
Type C

**TOXICITIES:**

**Hematologic**
1. If ANC < 1.5 x 10⁹/L, or if PLT < 100 x 10⁹/L on Day 1, **HOLD** dose for 1 week.

**Renal Failure**
1. If CrCL < 1.0mL/sec, **REDUCE** dose of Dacarbazine by 25-50%.

**SUGGESTED ACTION**

**REFERENCES:**

**Date revised:** 03/07/2005
INTERFERON INDUCTION Therapy
High Risk Malignant Melanoma

INTERFERON
20MU/m² IV Days 1-5 Round to nearest 1MU
- Mix in 50mL Normal Saline minibag; Infuse over 20 minutes.

ACETAMINOPHEN
650mg PO Days 1-5 325mg tablet
- Administer before each dose of Interferon.

REPEAT DAILY for 4 WEEKS

HYDRATION:
- Infuse 500mL Normal Saline over 30 minutes concurrent with each Interferon dose.

TESTS:
Baseline Tests WBC HB PLT ANC Glucose Cr T.Bili Albumin AST ALT AlkPhosphatase
Monday and WBC HB PLT ANC Glucose T.Bili AST ALT AlkPhosphatase
Thursday each week
Test Notes - Blood work done twice weekly (Monday and Thursday).

ANTIEMETIC PRE-CHEMO REGIMEN:
Level A Days 1-5 each week
- Prochlorperazine 10mg PO pm

ANTIEMETIC TAKE-HOME REGIMEN:
Level A Days 1-5 each week
- Prochlorperazine 10mg PO q4-6h pm

PATIENT VISITS and APPOINTMENT TYPE:
Days 1-5 each week 45min Type A

CLINICAL MONITORING:
Fatigue
1. Mild fatigue over baseline
2. Moderate or causing difficulty performing some ADL
3. Severe fatigue interfering with ADL
4. Disabling

Flu-like syndrome
1. Symptoms present but not interfering with function
2. Moderate or causing difficulty performing some ADL
3. Severe symptoms interfering with ADL
4. Disabling
5. Death
RATED AT EACH CLINIC VISIT

HEMATOLOGIC
Level I Toxicity:
1. ANC = 0.25 to < 0.5 x 10⁹/L
2. PLT = 50-50 x 10⁹/L
- HOLD Interferon until toxicity less than Level I severity, then resume at 50% full dose.

Level II Toxicity:
1. ANC < 0.25 x 10⁹/L
2. PLT < 25 x 10⁹/L
- DISCONTINUE Interferon.

HEPATIC DYSFUNCTION
Level I Toxicity:
1. AST > 5-10 times Normal (> 175-350 IU/L)
2. T.Bili 1.5-2 times Normal (> 27-36 umol/L)
- HOLD Interferon until toxicity less than Level I severity, then resume at 50% full dose.

Level II Toxicity:
1. AST > 10 times Normal (> 350 IU/L)
2. T.Bili > 2.1 times Normal (> 37 umol/L)
- DISCONTINUE Interferon.

REFERENCES:

Date revised: 09/03/2008
**INTERFERON Maintenance**

**Malignant Melanoma**

**INTERFERON**

- **10MU/m²**
- **SC**
- **Three times weekly**

- Administer (at home) subcutaneously on Monday, Wednesday and Friday for 48 weeks.
- Outpatient prescription.

**INTRONTM PENS:**

- **18 MU:** Doses available: 1.5 MU, 3.0 MU, 4.5 MU, 6.0 MU
- **30 MU:** Doses available: 2.5 MU, 5.0 MU, 7.5 MU, 10.0 MU
- **60 MU:** Doses available: 5.0 MU, 10.0 MU, 15.0 MU, 20.0 MU

**INTRONTM SOLUTION:**

- **10MU/mL:** - 10MU and 25MU vials
  - **6MU/mL:** - 18MU vial

**ACETAMINOPHEN**

- **650mg PO**
- **Three times weekly**
- **325mg tablet**

- Administer on Monday, Wednesday & Friday before Interferon dose.

**A USUAL TOTAL OF 48 WEEKS**

**TESTS:**

**Baseline Tests**

- WBC
- HB
- PLT
- ANC
- Glucose
- Cr
- Urea
- T.Bili
- Albumin
- AST
- ALT
- AlkPhosphatase

**Every 4 weeks**

- WBC
- HB
- PLT
- ANC
- Glucose
- T.Bili
- AST
- ALT
- AlkPhosphatase

**Test Notes**

- Baseline tests done with Interferon IV induction.
- Tests done every 4 weeks at physician appointment.

**TOXICITIES:**

**Hematologic**

**Level I Toxicity:**

1. ANC = 0.25 to < 0.5 x 10^9/L
2. PLT = 25-50 x 10^9/L
- **HOLD** Interferon until toxicity less than Level I severity, then resume at **50%** full dose.

**Level II Toxicity:**

1. ANC < 0.25 x 10^9/L
2. PLT < 25 x 10^9/L
- **DISCONTINUE** Interferon.

**Hepatic Dysfunction**

**Level I Toxicity:**

1. AST > 5-10 times Normal (> 175-350 IU/L)
2. T.Bili 1.5-2 times Normal (> 27-36umol/L)
- **HOLD** Interferon until toxicity less than Level I severity, then resume at **50%** full dose.

**Level II Toxicity:**

1. AST > 10 times Normal (> 350 IU/L)
2. T.Bili > 2.1 times Normal (> 37umol/L)
- **DISCONTINUE** Interferon.

**CLINICAL MONITORING:**

**Fatigue**

1. Mild fatigue over baseline
2. Moderate or causing difficulty performing some ADL
3. Severe fatigue interfering with ADL
4. Disabling

**Flu-like syndrome**

1. Symptoms present but not interfering with function
2. Moderate or causing difficulty performing some ADL
3. Severe symptoms interfering with ADL
4. Disabling
5. Death

**RATED AT EACH CLINIC VISIT**

**REFERENCES:**


CCO Eligibility Form Required [☐] Non-Formulary Form Required [☐] Date revised: 09/03/2008
**IPILIMUMAB Induction Therapy-SPECIAL ACCESS DRUG**

*High Risk Malignant Melanoma*

### ACETAMINOPHEN

<table>
<thead>
<tr>
<th>Dose</th>
<th>Route</th>
<th>Day</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>650mg</td>
<td>PO</td>
<td>Day 1</td>
<td>325mg</td>
</tr>
</tbody>
</table>

- Give 2 tablets of Acetaminophen (325mg) 30 minutes prior to Ipilimumab infusion.

### IPILIMUMAB

<table>
<thead>
<tr>
<th>Dose</th>
<th>Route</th>
<th>Day</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>10mg/kg</td>
<td>IV</td>
<td>Day 1</td>
<td>2.5mg</td>
</tr>
</tbody>
</table>

- Transfer to an empty DEHP-free IV bag and infuse undiluted over **90 minutes**, Ipilimumab must be administered through DEHP-free and latex-free IV set with a 1.2 micron in-line filter. Keep refrigerated until chemo nurse ready to administer.
- Use 10ml Normal Saline flush at the completion of the infusion.
- If dose is less than 450mg (90ml of solution) then the total dose needed should be diluted with **Normal Saline** to a total volume of 90ml, to a concentration not lower than 0.25mg/ml.
- Ipilimumab may be stored undiluted (5mg/ml) or following dilution in Normal Saline, in infusion bags for up to 3 hours at room temperature/under room light or refrigerated (2-8°C) for up to 24 hours.
- Observe patients for 1 hour for infusion reactions after completion of the infusion.

**DO NOT ADMINISTER AS IV PUSH OR BOLUS.**

### DIPHENHYDRAMINE

<table>
<thead>
<tr>
<th>Dose</th>
<th>Route</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>50mg FLAT</td>
<td>IV</td>
<td>Prn</td>
</tr>
</tbody>
</table>

- Admix in **50-100mL minibag 5% Dextrose or Normal Saline**.
- Administer IV over **15-30 minutes**, as needed for pruritus, flushing, rash, dyspnea due to Ipilimumab.

### MEPERIDINE

<table>
<thead>
<tr>
<th>Dose</th>
<th>Route</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>25mg FLAT</td>
<td>IV</td>
<td>Prn</td>
</tr>
</tbody>
</table>

- Admix in **50-100mL minibag 5% Dextrose or Normal Saline**.
- Administer IV over **15-30 minutes**, as needed for rigors/chills due to Ipilimumab.

**REPEAT EVERY 21 DAYS FOR 4 CYCLES**

### TESTS:

**Baseline Tests**

<table>
<thead>
<tr>
<th>Test</th>
<th>WBC</th>
<th>HB</th>
<th>PLT</th>
<th>ANC</th>
<th>Ca</th>
<th>K</th>
<th>Na</th>
<th>Chloride</th>
<th>Phosphate</th>
<th>Mg</th>
<th>Glucose</th>
<th>Urea</th>
<th>T.Bili</th>
<th>Albumin</th>
<th>AST</th>
<th>ALT</th>
<th>AlkPhosphatase</th>
</tr>
</thead>
</table>

**Day 1**

<table>
<thead>
<tr>
<th>Test</th>
<th>WBC</th>
<th>HB</th>
<th>PLT</th>
<th>ANC</th>
<th>Ca</th>
<th>K</th>
<th>Na</th>
<th>Chloride</th>
<th>Phosphate</th>
<th>Mg</th>
<th>Glucose</th>
<th>Urea</th>
<th>T.Bili</th>
<th>Albumin</th>
<th>AST</th>
<th>ALT</th>
<th>AlkPhosphatase</th>
</tr>
</thead>
</table>

**Test Notes**

- Check TSH levels every 3 weeks.
- LDH, lipase and total protein to be done before each clinic visit.
- Monitor blood pressure.
- ACTH and cortisol levels to be done at the discretion of the physician.
- Urinalysis
- Tumour assessment to be done at week 12, if there is a clinical response then move to maintenance phase starting at week 24.

### PATIENT VISITS and APPOINTMENT TYPE:

<table>
<thead>
<tr>
<th>Type</th>
<th>Frequency</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>E</td>
<td>3hrs</td>
<td></td>
</tr>
</tbody>
</table>

**ANCILLARY:**

Monitor vital signs (pulse, blood pressure, temperature) pre-infusion, then every 30 minutes for the duration of the ipilimumab infusion and 1 hour following the completion of the infusion.

### TOXICITIES:

#### Hematologic

1. If ANC < 1.0 x 10^9/L, or if PLT < 100 x 10^9/L, **HOLD** Ipilimumab dose.

#### Hepatic Dysfunction

1. If AST/ALT > 60 IU/L, **HOLD** Ipilimumab dose.
2. If ALP > 160 IU/L, **HOLD** Ipilimumab dose.
3. If total bilirubin > 5xULN then **DISCONTINUE** Ipilimumab therapy.

**SUGGESTED ACTION**

---

**Melanoma**
**CLINICAL MONITORING:**

**Diarrhea**
1. Increase of < 4 stools per day over baseline; mild increase in ostomy output compared to baseline
2. Increase of 4 - 6 stools per day over baseline; IV fluids indicated < 24hrs; moderate increase in ostomy output compared to baseline; not interfering with ADL
3. Increase of ≥ 7 stools per day over baseline; incontinence; IV fluids ≥ 24 hrs; hospitalization; severe increase in ostomy output compared to baseline; interfering with ADL
4. Life-threatening consequences (e.g., hemodynamic collapse).
5. Death

**PATIENT SHOULD CONTACT PHYSICIAN IMMEDIATELY IF CHANGE IN BOWEL HABITS.**

**Colitis**
1. Asymptomatic, pathologic or radiographic findings only
2. Abdominal pain; mucus or blood in stool
3. Abdominal pain, fever, change in bowel habits with ileus; peritoneal signs
4. Life-threatening consequences (e.g. perforation, bleeding, ischemia, necrosis, toxic megacolon)
5. Death

**Rash**
1. Macular or papular eruption or erythema without associated symptoms
2. Macular or papular eruption or erythema with pruritus or other associated symptoms; localized desquamation or other lesions covering < 50% of body surface area (BSA)
3. Severe, generalized erythroderma or macular, papular or vesicular eruption; desquamation covering ≥ 50% BSA
4. Generalized exfoliative, ulcerative, or bullous dermatitis
5. Death

**Hypothyroidism**
1. Asymptomatic, intervention not indicated
2. Symptomatic, not interfering with ADL; thyroid replacement indicated
3. Symptoms interfering with ADL; hospitalization indicated
4. Life-threatening; disabling
5. Death

**RATED AT EACH CLINIC VISIT**

**HYPERSENSITIVITY:**

**Ipilimumab Infusion Reactions:**
- For mild symptoms (localized cutaneous reactions such as mild pruritus, flushing, rash): Decrease the rate of infusion until recovery from symptoms, remain at bedside and monitor patient; complete Ipilimumab infusion at the initial planned rate. Diphenhydramine 50mg may be administered at the discretion of the treating physician. Patients may receive additional doses with close monitoring; premedication prior to future doses may be given at the discretion of the physician.
- For moderate symptoms (any symptom not listed above [mild symptoms] or below [severe symptoms] such as generalized pruritus, flushing, rash, dyspnea, hypotension with systolic BP > 80 mmHg): Interrupt Ipilimumab, administer Diphenhydramine 50 mg IV, remain at bedside and monitor patient until resolution of symptoms. Corticosteroids may abrogate any beneficial immunologic effect, but may be administered at the discretion of the treating physician. Resume Ipilimumab infusion after recovery of symptoms. At the discretion of the treating physician, Ipilimumab infusion may be resumed at one half the initial infusion rate, then increased incrementally to the initial infusion rate. If symptoms develop after resumption of the infusion, the infusion should be discontinued and no additional Ipilimumab should be administered that day. The next dose of Ipilimumab will be administered at its next scheduled time and may be given with pre-medication (Diphenhydramine and Acetaminophen) and careful monitoring, following the same treatment guidelines outlined above. At the discretion of the treating physician additional oral or IV antihistamine may be administered.
- For severe symptoms (any reaction such as bronchospasm, generalized urticaria, systolic blood pressure < 80 mm Hg, or angioedema): Immediately discontinue infusion of Ipilimumab, and disconnect infusion tubing from the patient. Consider bronchodilators, Epinephrine 1 mg IV or subcutaneously, and/or Diphenhydramine 50 mg IV, with Solumedrol 100 mg IV, as needed. Patients should be monitored until the physician is comfortable that the symptoms will not recur. No further Ipilimumab will be administered.
- In case of late-occurring hypersensitivity symptoms (e.g., appearance within one week after treatment of a localized or generalized pruritus), symptomatic treatment may be given (e.g., oral antihistamine, or corticosteroids).

**FORMULAE:**

\[
\text{CrCl} = \frac{140 - \text{age}(\text{yrs}) \times \text{TBW}(\text{Kg})}{50 \times \text{SCr}(\text{umol/L})}
\]

\[
\text{CrCl} = \frac{140 - \text{age}(\text{yrs}) \times \text{TBW}(\text{Kg})}{50 \times \text{SCr}(\text{umol/L})} \times 0.85
\]

**REFERENCES:**
- Guideline for Compassionate Use of Ipilimumab in Patients with Advanced Melanoma. 10/15/2007.
- Investigator Brochure, Ipilimumab BMS-734016/MDX-010.
- University Health Network: Princess Margaret Hospital; Pharmacy Department, Investigational Drug Data Sheet MDX-010.

**Date revised:** 03/28/2008
**IPILIMUMAB Maintenance Therapy-SPECIAL ACCESS**

**DRUG**

**Melanoma**

**ACETAMINOPHEN**

<table>
<thead>
<tr>
<th>Dosage</th>
<th>Route</th>
<th>Start</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>650mg</td>
<td>PO</td>
<td>Day 1</td>
<td>325mg</td>
</tr>
</tbody>
</table>

- Give 2 tablets of Acetaminophen (325mg) 30 minutes prior to Ipilimumab infusion.

**IPILIMUMAB**

<table>
<thead>
<tr>
<th>Dosage</th>
<th>Route</th>
<th>Start</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>10mg/kg</td>
<td>IV</td>
<td>Day 1</td>
<td>every 12 weeks</td>
</tr>
</tbody>
</table>

- Transfer to an empty DEHP-free IV bag and infuse undiluted over 90 minutes. Ipilimumab must be administered through DEHP-free and latex-free IV set with a 1.2 micron in-line filter. Keep refrigerated until chemo nurse ready to administer.
- Use 10ml Normal Saline flush at the completion of the infusion.
- If dose is less than 450mg (90ml of solution) then the total dose needed should be diluted with **Normal Saline** to a total volume of 90ml, to a concentration not lower than 0.25mg/ml.
- Ipilimumab may be stored undiluted (5mg/ml) or following dilution in Normal Saline, in infusion bags for up to 3 hours at room temperature/under room light or refrigerated (2-8°C) for up to 24 hours.
- Observe patients for 1 hour for infusion reactions after completion of the infusion.

DO NOT ADMINISTER AS IV PUSH OR BOLUS.

**DIPHENHYDRAMINE**

<table>
<thead>
<tr>
<th>Dosage</th>
<th>Route</th>
<th>Start</th>
</tr>
</thead>
<tbody>
<tr>
<td>50mg</td>
<td>FLAT</td>
<td>IV</td>
</tr>
</tbody>
</table>
- Admix in 50-100mL minibag 5% Dextrose or **Normal Saline**.
- Administer IV over **15-30 minutes**, as needed for pruritis, flushing, rash, dyspnea due to Ipilimumab.

**MEPERIDINE**

<table>
<thead>
<tr>
<th>Dosage</th>
<th>Route</th>
<th>Start</th>
</tr>
</thead>
<tbody>
<tr>
<td>25mg</td>
<td>FLAT</td>
<td>IV</td>
</tr>
</tbody>
</table>
- Admix in 50-100mL minibag 5% Dextrose or **Normal Saline**.
- Administer IV over **15-30 minutes**, as needed for rigors/chills due to Ipilimumab.

**EVERY 12 WEEKS STARTING FROM WEEK 24 UNTIL DISEASE PROGRESSION**

**TESTS:**

- WBC  HB  PLT  ANC  Ca  K  Na  Chloride  Phosphate  Mg  Glucose  Cr  Urea  T.Bili  Albumin  AST  ALT  AlkPhosphatase

**Test Notes**

- Check TSH levels.
- LDH, lipase and total protein to be done before each clinic visit.
- Monitor blood pressure.
- Urinalysis.
- ACTH and cortisol levels to be done at the discretion of the physician.

**PATIENT VISITS and APPOINTMENT TYPE:**

- **Type E**

**ANCILLARY:**

- Monitor vital signs (pulse, blood pressure, temperature) pre-infusion, then every 30 minutes for the duration of the ipilimumab infusion and 1 hour following the completion of the infusion.

**TOXICITIES:**

**Hematologic**

1. If ANC < 1 x 10⁹/L, or if PLT < 100 x 10⁹/L, **HOLD** Ipilimumab dose.

**Hepatic Dysfunction**

1. If AST/ALT > 60 IU/L, **HOLD** Ipilimumab dose.
2. If ALP > 160 IU/L, **HOLD** Ipilimumab dose.
3. If total bilirubin > 5xULN then **DISCONTINUE** Ipilimumab therapy.

**SUGGESTED ACTION**
**IPILUMIMAB Maintenance Therapy-SPECIAL ACCESS DRUG**

**CLINICAL MONITORING:**

**Diarrhea**
1. Increase of < 4 stools per day over baseline; mild increase in ostomy output compared to baseline
2. Increase of 4 - 6 stools per day over baseline; IV fluids indicated < 24hrs; moderate increase in ostomy output compared to baseline; not interfering with ADL
3. Increase of > 7 stools per day over baseline; hospitalization; severe increase in ostomy output compared to baseline; interfering with ADL
4. Life-threatening consequences (e.g., hemodynamic collapse)
5. Death

**PATIENT SHOULD CONTACT PHYSICIAN IMMEDIATELY IF CHANGE IN BOWEL HABITS.**

**Colitis**
1. Asymptomatic, pathologic or radiographic findings only
2. Abdominal pain; mucus or blood in stool
3. Abdominal pain, fever, change in bowel habits with ileus; peritoneal signs
4. Life-threatening consequences (e.g., perforation, bleeding, ischemia, necrosis, toxic megacolon)
5. Death

**Rash**
1. Macular or papular eruption or erythema without associated symptoms
2. Macular or papular eruption or erythema with pruritus or other associated symptoms; localized desquamation or other lesions covering < 50% of body surface area (BSA)
3. Severe, generalized erythroderma or macular, papular or vesicular eruption; desquamation covering > 50% BSA
4. Generalized exfoliative, ulcerative, or bullous dermatitis
5. Death

**Hypothyroidism**
1. Asymptomatic, intervention not indicated
2. Symptomatic, not interfering with ADL; thyroid replacement indicated
3. Symptoms interfering with ADL; hospitalization indicated
4. Life-threatening; disabling
5. Death

**Rated at each clinic visit**

**HYPERSENSITIVITY:**

**Ipilimumab Infusion Reactions:**
- For mild symptoms (localized cutaneous reactions such as mild pruritus, flushing, rash): Decrease the rate of infusion until recovery from symptoms, remain at bedside and monitor patient; complete Ipilimumab infusion at the initial planned rate. Diphenhydramine 50mg may be administered at the discretion of the treating physician. Patients may receive additional doses with close monitoring; premedication prior to future doses may be given at the discretion of the physician.
- For moderate symptoms (any symptom not listed above [mild symptoms] or below [severe symptoms] such as generalized pruritus, flushing, rash, dyspnea, hypotension with systolic BP > 80 mmHg): Interrupt Ipilimumab, administer Diphenhydramine 50 mg IV, remain at bedside and monitor patient until resolution of symptoms. Corticosteroids may abrogate any beneficial immunologic effect, but may be administered at the discretion of the treating physician. Resume Ipilimumab infusion after recovery of symptoms. At the discretion of the treating physician, Ipilimumab infusion may be resumed at one half the initial infusion rate, then increased incrementally to the initial infusion rate. If symptoms develop after resumption of the infusion, the infusion should be discontinued and no additional Ipilimumab should be administered that day. The next dose of Ipilimumab will be administered at its next scheduled time and may be given with pre-medication (Diphenhydramine and Acetaminophen) and careful monitoring, following the same treatment guidelines outline above. At the discretion of the treating physician additional oral or IV antihistamine may be administered.
- For severe symptoms (any reaction such as bronchospasm, generalized urticaria, systolic blood pressure < 80 mm Hg, or angioedema): Immediately discontinue infusion of Ipilimumab, and disconnect infusion tubing from the patient. Consider bronchodilators, Epinephrine 1 mg IV or subcutaneously, and/or Diphenhydramine 50 mg IV, Solumedrol 100 mg IV, as needed. Patients should be monitored until the physician is comfortable that the symptoms will not recur. No further Ipilimumab will be administered.
- In case of late-occurring hypersensitivity symptoms (e.g., appearance within one week after treatment of a localized or generalized pruritus), symptomatic treatment may be given (e.g., oral antihistamine, or corticosteroids).

**FORMULAE:**

\[
\text{CrCl} - \text{Cockcroft & Gault (mL/sec)} = \begin{cases} 
\text{Male: } & \left(\frac{140-\text{age(yrs)}}{\text{TBW(Kg)}}\right) \\
\text{Female: } & \left(\frac{140-\text{age(yrs)}}{\text{TBW(Kg)}}\times 0.85\right) 
\end{cases} \\
\text{CRCl - Cockcroft & Gault (mL/sec)} = \left(\frac{\text{[140-age(yrs)] x TBW(Kg)}}{\text{[50 x SCR(umol/L)]}}\right)
\]

**REFERENCES:**

- Guideline for Compassionate Use of Ipilimumab in Patients with Advanced Melanoma. 10/15/2007.
- Investigator Brochure, Ipilimumab BMS-734016/MDX-010.
- University Health Network: Princess Margaret Hospital. Pharmacy Department, Investigational Drug Data Sheet MDX-010.

**Date revised:** 03/31/2008

**Melanoma**
**PACLITAXEL-CARBOPLATIN Chemotherapy**

**Second Line Therapy for Metastatic Melanoma**

- **PACLITAXEL**
  - 100mg/m² IV Day 1, 8 & 15 Round to nearest 3mg
  - Mix in **500mL** bag **Normal Saline** (dilution concentration 0.3-1.2 mg/mL).
  - Use non-PVC equipment, including 0.22 micron in-line filter.
  - Infuse over **3 hours**, before Carboplatin.

- **DEXAMETHASONE**
  - 20mg PO Day 1, 8 & 15 4mg tablet
  - To be administered at home 12 and 6 hours before Paclitaxel (if not taken at home, Dexamethasone 20mg IV 30 minutes before Paclitaxel).

- **DIPHENHYDRAMINE**
  - 50mg PO Day 1, 8 & 15
  - Administer 30 minutes before Paclitaxel.

- **RANITIDINE**
  - 150mg PO Day 1, 8 & 15
  - Administer 30 minutes before Paclitaxel.

- **CARBOPLATIN**
  - AUC = 2 IV Day 1, 8 & 15 Round to nearest 5mg
  - Mix in **250mL 5% Dextrose**.
  - Infuse over **30-60 minutes**, after Paclitaxel.

**REPEAT EVERY 28 DAYS**

<table>
<thead>
<tr>
<th>TESTS:</th>
<th></th>
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</thead>
<tbody>
<tr>
<td><strong>Baseline</strong>: WBC HB PLT ANC Ca K Na Chloride Mg Glucose Cr Urea T.Bili Albumin AST ALT GGT AlkPhosphatase</td>
<td></td>
</tr>
<tr>
<td><strong>Day 8 &amp; 15</strong>: WBC HB PLT ANC Cr Urea</td>
<td></td>
</tr>
<tr>
<td><strong>Day 1</strong>: WBC HB PLT ANC K Na Chloride Mg Glucose Cr Urea T.Bili Albumin AST ALT GGT AlkPhosphatase</td>
<td></td>
</tr>
</tbody>
</table>

- **Test Notes**: Additional Baseline tests: LDH & CO₂

<table>
<thead>
<tr>
<th>ANTIEMETIC PRE-CHEMO REGIMEN:</th>
<th></th>
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</thead>
<tbody>
<tr>
<td><strong>Level C</strong> Day 1,8&amp;15</td>
<td></td>
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<tr>
<td>- Granisetron 1mg PO 30 minutes before chemo.</td>
<td></td>
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<tr>
<td>- Dexamethasone 20mg PO (IV if patient has not taken PO dexamethasone at home) 12 and 6 hours before Paclitaxel.</td>
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<tr>
<th>ANTIEMETIC TAKE-HOME REGIMEN:</th>
<th></th>
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</thead>
<tbody>
<tr>
<td><strong>Level B/C</strong> Day 1,8&amp;15</td>
<td></td>
</tr>
<tr>
<td>- Granisetron 1mg PO 12 hours post chemotherapy, then 1mg PO BID for 2 days.</td>
<td></td>
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<tr>
<td>- Dexamethasone 8mg PO BID for 2 days.</td>
<td></td>
</tr>
<tr>
<td>- Prochlorperazine 10mg PO q4-6h prn.</td>
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</tr>
</tbody>
</table>

- **PATIENT VISITS and APPOINTMENT TYPE**: Day 1,8&15 4hrs Type C

- **ANCILLARY**: Take a baseline blood pressure measurement, if prior hypotension.

- **TOXICITIES**: Hematologic
  1. If ANC < 1.5 x 10⁹/L, or if PLT < 100 x 10⁹/L, **HOLD** dose for 1 week.

- **Hepatic Dysfunction**
  1. If T.Bili = 25-50umol/L, **GIVE** Paclitaxel maximum dose of **75mg/m²**.
  2. If T.Bili > 50umol/L, **GIVE** Paclitaxel maximum dose of **50mg/m²**.

- **Renal Failure**
  1. Adjust Carboplatin dose if estimated CrCl changes > 10%.

- **SUGGESTED ACTION**

- **CLINICAL MONITORING**:
  - Watch for symptoms of fever and infection.
  - Blood pressure and pulse rate monitoring during drug administration & for the following hour.
  - **Sensory**
    1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function.
    2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL.
    3. Sensory alteration or paresthesia interfering with ADL.
    4. Disabling.
    5. Death
  - **Flu-like Symptoms**
    1. Symptoms present but not interfering with function.
    2. Moderate or causing difficulty performing some ADL.
    3. Severe symptoms interfering with ADL.
    4. Disabling.
    5. Death
  - **Allergic Reaction**
    1. Transient flushing or rash; drug fever < 38 degrees C.
    2. Rash; flushing; urticaria; dyspnea; drug fever ≥ 38 degrees C.
    3. Symptomatic bronchospasms, with or without urticaria; parenteral medication(s) indicated; allergy-related edema/angioedema; hypotension.
    4. Anaphylaxis.
    5. Death

**RATED AT EACH CLINIC VISIT**

Melanoma
PACLITAXEL-CARBOPLATIN Chemotherapy

HYPERSENSITIVITY:

Paclitaxel Procedures

Retreatment for Paclitaxel Hypersensitivity Reaction:

If Paclitaxel hypersensitivity reaction occurs during administration:

1. Discontinue Paclitaxel immediately if there are signs or symptoms of hypersensitivity.
2. Rapid IV administration of Diphenhydramine 50mg direct IV push over 1 minute and Hydrocortisone 100mg in 100ml Normal Saline over 5-10 minutes.
3. Reinitiate Paclitaxel infusion after 30 minutes, or when signs of reaction are resolved. Resume Paclitaxel infusion at 17mL/hr (10% of original rate) for 15 minutes, then at 42mL/hr (25% of original rate) for 15 minutes. If no further symptoms develop, continue at original rate until infusion complete.
4. If reaction recurs, STOP Paclitaxel for this dose and treat patient symptoms.

Desensitization for Paclitaxel Hypersensitivity Reactions:

If Paclitaxel hypersensitivity recurs during previous administration despite retreatment plan:

1. Dexamethasone 20mg PO 36 hours and 12 hours before chemotherapy, and 20mg PO morning of chemotherapy.
2. Dexamethasone 20mg IV, Diphenhydramine 50mg IV & Ranitidine 50mg IV about 30min before infusion.
3. Paclitaxel Infusion: 2mg in 100mL Normal Saline over 30min; if no reaction, 10mg in 100mL Normal Saline over 30min; if no reaction, remainder of dose in 500mL Normal Saline over 3 hours.
4. If reaction occurs, discontinue infusion; Diphenhydramine 50mg direct IV push over 1 minute and Hydrocortisone 100mg in 100ml Normal Saline over 5-10 minutes.
5. Restart Paclitaxel infusion after 30 minutes.

FORMULAE:

CrCl - Cockcroft & Gault (mL/sec)

Male: \[
\frac{140 - \text{age (yrs)}}{\text{TBW (Kg)}} \times \frac{1}{50 \times \text{SCr (umol/L)}}
\]

CrCl - Cockcroft & Gault (mL/sec)

Female: \[
\frac{140 - \text{age (yrs)}}{\text{TBW (Kg)}} \times \frac{0.85}{50 \times \text{SCr (umol/L)}}
\]

Creatinine Cl (mL/min)

\[
\text{mL/min} = 60 \times \text{CrCl mL/sec}
\]

Calvert Formula

Dose (in mg) = target AUC \times (\text{GFR} + 25) \quad \text{GFR} \text{ in mL/min}

INTERNAL CODE:

- PACLI-CARB 2

REFERENCES:


Date revised: 06/08/2009

Melanoma
TEMOZOLOMIDE Chemotherapy
Malignant Melanoma

TEMOZOLOMIDE 200mg/m² PO Days 1-5 5mg, 20mg, 100mg & 250mg capsules

- Days 1 to 5.
- Outpatient prescription available as 5mg, 20mg, 100mg & 250mg capsules.
- Trade name = Temodal™

REPEAT EVERY 28 DAYS

TESTS:
Baseline Tests WBC HB PLT ANC Cr Urea T.Bili AST ALT GGT AlkPhosphatase
Day 1 WBC HB PLT ANC Cr

ANTIEMETIC PRE-CHEMO REGIMEN:
Level C Days 1-5 - Ondansetron 8mg or Granisetron 2mg PO daily before each oral chemotherapy dose and 24 hours after last dose.

TOXICITIES:
Hematologic
1. If ANC < 1.5 x 10⁹/L, or if PLT < 100 x 10⁹/L on Day 1, HOLD dose for 5-7 days.
2. If ANC < 0.5 x 10⁹/L, or if PLT < 75 x 10⁹/L at Day 22, HOLD dose for 1 week and continue at 150mg/m² or lower dose.

Renal Failure
1. If CrCl < 1.0mL/sec, REDUCE dose by 25-50%.
SUGGESTED ACTION

INTERNAL CODE:
OPIS CODE: TEMOZOL ME

REFERENCES:
- Agarwala SS, Kirkwood IM. Temozolomide, a novel alkylating agent with activity in the central nervous system, may improve the treatment of advanced metastatic melanoma. The Oncologist, April 2000; 5(2): 144-151.

CCO Eligibility Form Required ☐ Non-Formulary Form Required ☐ Date revised: 09/03/2008
DOXORUBICIN-BLEOMYCIN-VINBLASTINE Chemotherapy
Kaposi’s Sarcoma - Palliative Intent

DOXORUBICIN
40mg/m² IV Day 1 Round to nearest 1mg
- Slow push through sidearm of free flowing IV; Give 2 to 4mg (1-2mL) per minute.
- Alternate dosing: 20mg/m² Days 1 & 15.

BLEOMYCIN
10-15units IV Days 1 & 15 Round to nearest 1unit
- Slow push through sidearm of free flowing IV over 10 minutes.
- May be given by direct IV push, followed by a Normal Saline flush.

VINBLASTINE
6mg/m² IV Day 1 Round to nearest 0.1mg
- Slow push through sidearm of free flowing IV; Inject over 1 minute.

REPEAT EVERY 28 DAYS

TESTS:
Baseline Tests WBC HB PLT ANC Cr Urea T.Bili AST ALT AlkPhosphatase
Day 15 WBC HB PLT ANC
Day 1 WBC HB PLT ANC
Test Notes - Cr, BUN & LFTs prn

ANTIEMETIC PRE-CHEMO REGIMEN:
Level C Day 1
- Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
- Dexamethasone 20mg PO/IV

Level A Day 15
- Prochlorperazine 10mg PO prn

ANTIEMETIC TAKE-HOME REGIMEN:
Level B/C Day 1
- Ondansetron 8mg PO BID for 2-3 days, or Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days
- Dexamethasone 8mg PO BID for 2-3 days
- Prochlorperazine 10mg PO q4-6h prn
- Prochlorperazine 10mg PO q4-6h prn

Level A Day 15

PATIENT VISITS and APPOINTMENT TYPE:
⇒ Day 1 1hr Type C
⇒ Day 15: 15min Type A

ANCILLARY:
- Oral hydration is strongly encouraged; poorly hydrated patients may need more IV hydration.

TOXICITIES:
Hematologic
1. If ANC < 1.6 x 10⁹/L, or if PLT < 125 x 10⁹/L, GIVE 50% dose of Doxorubicin & Vinblastine.
2. If ANC < 0.8 x 10⁹/L, or if PLT < 75 x 10⁹/L, HOLD dose for 1 week.

Renal Failure
1. If CrCl = 0.2-1.0mL/sec, REDUCE Bleomycin to 75% dose.
2. If CrCl < 0.2mL/sec, REDUCE Bleomycin to 50% dose.
3. If SrCr > 2.65umol/L, REDUCE Doxorubicin to 50% dose.

Hepatic Dysfunction
1. If T.Bili = 26-51umol/L, or AST = 60-180 IU/L, REDUCE Doxorubicin to 75% dose & Vinblastine to 50% dose.
2. If T.Bili > 52-85umol/L, or AST >180 IU/L, REDUCE Doxorubicin to 50% dose & Vinblastine to 25% dose.
3. If T.Bili > 85umol/L, OMIT Doxorubicin & Vinblastine doses.

SUGGESTED ACTION

CLINICAL MONITORING:
- Clinical pulmonary exam, including auscultation, pulmonary toxicity ratings (Cough, SOB).
- Clinical exam for symptoms of CHF.
- Periodic cardiac tests for all patients with cardiac risk factors or patients at or above the threshold dose levels (Doxorubicin 450mg/m²).
- Neurologic toxicity ratings (Sensory, Constipation) at each visit.

Sensory
1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function
2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL
3. Sensory alteration or paresthesia interfering with ADL
4. Disabling
5. Death

Constipation
1. Occasional or intermittent symptoms; occasional use of stool softeners, laxatives, dietary modification, or enema
2. Persistent symptoms with regular use of laxatives or enemas indicated
3. Symptoms interfering with ADL; obstipation with manual evacuation indicated
4. Life-threatening consequences (e.g., obstruction, toxic megacolon)
5. Death

Dyspnea
1. Dyspnea on exertion, but can walk 1 flight of stairs without stopping
2. Dyspnea on exertion but unable to walk 1 flight of stairs or 1 city block (0.1km) without stopping
3. Dyspnea with ADL
4. Dyspnea at rest; intubation/ventilator indicated
5. Death

Cough
1. Symptomatic, non-narcotic medication only indicated
2. Symptomatic and narcotic medication indicated
3. Symptomatic and significantly interfering with sleep or ADL

RATED AT EACH CLINIC VISIT

REFERENCES:

Date revised: 08/29/2008
Sarcoma

CISPLATIN-DOXORUBICIN (modified) Chemotherapy

Osteosarcoma

DOXORUBICIN 75mg/m² Day 1 Round to nearest 1mg
- Slow push through sidearm of free flowing IV
- Give 2 to 4mg (1-2mL) per minute.
- May be given during prehydration.

CISPLATIN 100mg/m² IV Day 1 Round to nearest 1mg
- Mix in 500mL Normal Saline; Infuse over 60 minutes.

REPEAT EVERY 21 DAYS

HYDRATION:
Pre
- Infuse 1000mL Normal Saline with 20mEq Potassium Chloride IV over 2 hours before Cisplatin.
Concurrent
- May give 250mL of 20% Mannitol solution (50G) IV; Infuse through sidearm concurrent with Cisplatin.
Post
- Infuse 500mL Normal Saline with 10mEq Potassium Chloride IV over 1 hour after Cisplatin.

TESTS:
Baseline Tests WBC HB PLT ANC Mg Cr Urea T.Bili AST ALT AlkPhosphatase
Day 1 WBC HB PLT ANC Mg Cr Urea
Test Notes - Baseline & routine renal function tests, especially if there are other concurrent nephrotoxic drugs.

ANTIEMETIC PRE-CHEMO REGIMEN:
Level C Day 1
- Granisetron 1mg IV
- Dexamethasone 20mg PO/IV
- May add Aprepitant 125mg po 1 hour before chemo (reduce PO Dexamethasone by 50%)

ANTIEMETIC TAKE-HOME REGIMEN:
Level B/C Day 1
- Granisetron 1mg PO Q12H on Days 2&3
- Dexamethasone 8mg PO BID on Days 2&3
- May add Aprepitant 80mg PO on Days 2&3 (reduce PO Dexamethasone by 50%)
- Prochlorperazine 10mg PO q4-6h prn

PATIENT VISITS and APPOINTMENT TYPE:
- Day 1 4-6hrs Type D

ANCILLARY:
- Increase fluids if poor oral intake.

TOXICITIES:
Hematologic
1. If ANC < 1.5 x 10⁹/L, or if PLT < 100 x 10⁹/L, HOLD dose for 1 week.

Renal Failure
1. If CrCl = 0.5-1.0mL/sec, or SrCr = 136-185umol/L, REDUCE Cisplatin to 50% dose.
2. If CrCl < 0.5mL/sec, or SrCr > 185umol/L, OMIT Cisplatin dose
3. If SrCr > 265umol/L, REDUCE Doxorubicin dose to 50%.

Hepatic Dysfunction
1. If T.Bili = 26-51umol/L, or AST = 60-180 IU/L, REDUCE Doxorubicin to 25% dose.
2. If T.Bili = 52-85umol/L, or AST > 180 IU/L, REDUCE Doxorubicin to 50% dose.
3. If T.Bili > 85umol/L, OMIT Doxorubicin.

SUGGESTED ACTION
Sarcoma

CISPLATIN-DOXORUBICIN (modified) Chemotherapy

CLINICAL MONITORING:
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.
- Skin assessment, especially extremities.

Sensory
1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function
2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL
3. Sensory alteration or paresthesia interfering with ADL
4. Disabling
5. Death

Hearing
1. Asymptomatic, detected on exam/testing only
2. Symptomatic, not interfering with ADL
3. Symptomatic, interfering with ADL
4. Life-threatening; disabling
5. Death

Mucositis
1. Erythema of the mucosa
2. Patchy ulcerations or pseudomembranes
3. Confluent ulcerations or pseudomembranes; bleeding with minor trauma
4. Tissue necrosis; significant spontaneous bleeding; life-threatening consequences
5. Death

- Clinical exam for symptoms of CHF.
- Periodic cardiac tests for all patients with cardiac risk factors at or above the threshold dose levels.

LV Systolic Dysfunction
1. Asymptomatic, resting ejection fraction (EF) < 60 - 50%; shortening fraction (SF) < 30 - 24%
2. Asymptomatic, resting EF < 50 - 40%; SF < 24 - 15%
3. Symptomatic CHF responsive to intervention; EF < 40 - 20%; SF < 15%
4. Refractory CHF or poorly controlled; EF < 20%; intervention such as ventricular assist device, ventricular reduction surgery, or heart transplant indicated
5. Death

- For Cardiac Toxicity Ratings: First rating at the cumulative dose threshold of 450mg/m², and repeat ratings at each cumulative dose increment of 100mg/m² above threshold. (Cumulative dose sooner for high risk patients, eg. pre-existing cardiac disease, prior chest irradiation).
- Note: Threshold Cumulative dose reduced proportionately if other anthracycline or anthracenedione drugs have been given; cardiotoxicity is additive.

RATED AT EACH CLINIC VISIT

FORMULAE:
CrCl - Cockcroft & Gault (mL/sec)

Male: \[
\frac{140 - \text{age (yrs)}}{\text{TBW (Kg)}} \times \frac{\text{SCr (umol/L)}}{50}
\]

CrCl - Cockcroft & Gault (mL/sec) Female: \[
\frac{140 - \text{age (yrs)}}{\text{TBW (Kg)}} \times \frac{\text{SCr (umol/L)}}{50} \times 0.85
\]

INTERNAL CODE:
OPIS CODE: CISP-DOXO (MOD)

REFERENCES:
-BCCA Protocol Summary for Adjuvant Therapy for osteosarcoma using Doxorubicin and Cisplatin.

Date revised: 02/05/2008
Sarcoma CYCLOPHOSPHAMIDE-TOPOTECAN Chemotherapy-weekly  
Ewing's Sarcoma/Rhabdomyosarcoma

**CYCLOPHOSPHAMIDE**  250mg/m²  IV  Days 1-5  Round to nearest 10mg
- Mix in 250mL bag Normal Saline.
- Infuse over 20 minutes.

**TOPOTECAN**  0.75 mg/m²  IV  Days 1-5  Round to nearest 0.1mg
- Admix in 50mL bag Normal Saline.
- Infuse over 30 minutes after Cyclophosphamide.

**FILGRASTIM**  5mcg/kg  SC  Days 6-14  300mcg & 480mcg vials
- Starting dose is 5mcg/kg/day.
- Doses may be increased in increments of 5mcg/kg/day for each chemotherapy cycle, according to duration and severity of AGC nadir.
- May give Acetaminophen 325mg, 1-2 tablets for temporary bone pain at initiation.
- Outpatient prescription (Keep refrigerated).
- Vial sizes available: 300mcg and 480mcg.
- Trade name Neupogen™

**HYDRATION:**
Pre
- Infuse 500ml Normal Saline at 250mL/hr for 2 hours I.V. before Cyclophosphamide
Post
- Oral hydration is strongly encouraged; for I.V. Cyclophosphamide 2-3L of fluid/day.

**TESTS:**
Baseline Tests  WBC HB PLT ANC Ca Phosphate Mg Cr Urea T.Bili AST ALT
Day 1  WBC HB PLT ANC Ca Phosphate Mg Cr Urea T.Bili AST ALT

**ANTIEMETIC PRE-CHEMO REGIMEN:**
Level C  Days 1-5
- Granisetron 1mg PO/IV and Dexamethasone 20mg PO/IV
- May add or substitute Prochlorperazine 10mg PO/IV pm

**ANTIEMETIC TAKE-HOME REGIMEN:**
Level B/C  Day 5
- Ondansetron 8mg PO BID for 2-3 days, or
- Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days
- Dexamethasone 8mg PO BID for 2-3 days
- Prochlorperazine 10mg PO q4-6h pm

**PATIENT VISITS and APPOINTMENT TYPE:**
⇒ Days 1-5  3 hours  Type D

**TOXICITIES:**

**Hematologic**
1. If ANC < 1.5 x 10⁹/L, or if PLT <100 x 10⁹/L, **HOLD** dose for 1 week.

**Renal Failure**
1. If CrCl 0.6-1.0mL/sec, **REDUCE** to 50% dose of Topotecan.
2. If CrCl 0.3-0.6mL/sec, **REDUCE** to 75% dose of Topotecan.
3. If CrCl <0.3mL/sec, **OMIT** dose of Topotecan.

**SUGGESTED ACTION**

**CLINICAL MONITORING:**
- Baseline renal function tests (esp. if failure suspected).
- Pulmonary toxicity ratings at each visits (SOB).
- Watch for symptoms of fever and infection.
- Urinalysis (RBCs) periodic and in response to patient complaint.

**Dyspnea** (shortness of breath)
1. Dyspnea on exertion, but can walk 1 flight of stairs without stopping  2. Dyspnea on exertion but unable to walk 1 flight of stairs or 1 city block (0.1km) without stopping 3. Dyspnea with ADL  4. Dyspnea at rest; intubation/ventilator indicated  5. Death

**Fever**
1. 138.0 - 39.0°C (100.4 - 102.2°F)  2. >39.0 - 40.0°C (102.3 - 104.0°F)  3. >40.0°C (>104.0°F) for <24 hrs  4. > 40.0° C (>104.0°F) for >24 hrs  5. Death

RATED AT EACH CLINIC VISIT
SA  CYCLO-TOPO

Sarcoma  CYCLOPHOSPHAMIDE-TOPOTECAN Chemotherapy-weekly

REFERENCES:

Data revised: 12/07/2007

CCO Eligibility Form Required  [ ]  Non-Formulary Form Required  [ ]
DACARBAZINE Chemotherapy
Metastatic Soft Tissue Sarcoma

DACARBAZINE 1200mg/m² IV Day 1 Round to nearest 10mg
- Mix in 250-500mL bag Normal Saline.
- Infuse through main IV line with an additional 500mL Normal Saline run at same time by piggyback to reduce vein irritation (more IV fluid if ordered).
- Infuse over 30-120 minutes; If vein irritation, infuse slowly.
- Protect from light.

REPEAT EVERY 21 DAYS

TESTS:
Baseline Tests WBC HB PLT ANC Cr Urea T.Bili AST ALT GGT AlkPhosphatase
Day 1 WBC HB PLT ANC Cr

ANTIEMETIC PRE-CHEMO REGIMEN:
Level C Day 1 - Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
- Dexamethasone 20mg PO/IV

ANTIEMETIC TAKE-HOME REGIMEN:
Level B/C Day 1 - Ondansetron 8mg PO BID for 2-3 days. or
Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days
- Dexamethasone 8mg PO BID for 2-3 days
- Prochlorperazine 10mg PO q4-6h prn

PATIENT VISITS and APPOINTMENT TYPE:
 Day 1 2.5hrs Type C

TOXICITIES:
Hematologic
1. If ANC < 1.5 x 10⁹/L, or if PLT < 100 x 10⁹/L on Day 1, HOLD dose for 1 week.

Renal Failure
1. If CrCl < 1.0mL/sec, REDUCE dose of Dacarbazine by 25-50%.

SUGGESTED ACTION

INTERNAL CODE:
OPIS CODE: DACARB-SA

REFERENCES:

Date revised: 03/07/2005
LIPOSOMAL DAUNORUBICIN Chemotherapy - SPECIAL ACCESS DRUG

DAUNORUBICIN 40mg/m² IV Day 1 Round to nearest 1mg

LIPOSOMAL
- Dilute in 50-100mL bag 5% Dextrose ONLY
- Infuse over 60 minutes through the side arm of a free-flowing IV.
- Do NOT use an in-line Filter.
- Special access drug.

REPEAT EVERY 14-21 DAYS

TESTS:
Baseline Tests: WBC HB PLT ANC K Na Chloride Cr Urea T.Bili Albumin AST ALT GGT AlkPhosphatase
Day 1: WBC HB PLT ANC K Na Chloride Cr Urea T.Bili Albumin AST ALT GGT AlkPhosphatase

Test Notes - LVEF if cardiac risk factors present.

ANTIEMETIC PRE-CHEMO REGIMEN:
Level B Day 1 - Dexamethasone 8mg PO/IV
- May add/substitute Prochlorperazine 10mg PO/IV prn

ANTIEMETIC TAKE-HOME REGIMEN:
Level A Day 1 - Prochlorperazine 10mg PO q4-6h pm

PATIENT VISITS and APPOINTMENT TYPE:
→ Day 1: 60min Type B

TOXICITIES:
Hematologic
1. If ANC < 1.5 x 10⁹/L, or if PLT < 100 x 10⁹/L, HOLD dose for 1 week.

Renal Failure
1. If SrCr >265umol/L, reduce dose to 50%.

Hepatic Dysfunction
1. If T.Bili = 26-51umol/L, or AST = 60-180 IU/L, give 75% dose.
2. If T.Bili = 52-85umol/L, or AST > 180 IU/L, give 50% dose.
3. If T.Bili > 85umol/L, OMIT dose.

SUGGESTED ACTION

CLINICAL MONITORING:
- Baseline liver function tests (esp if poor performance status).
- Observation for infusion reaction (back pain, flushing, chest tightness) during and for 30 minutes after first injection (emergency treatment available - ie. Antihistamine injection).

REFERENCES:

CCO Eligibility Form Required ✔ Non-Formulary Form Required □ Date revised: 03/07/2005
**DOCETAXEL-GEMCITABINE Chemotherapy**

**Leiomyosarcoma**

### GEMCITABINE
- **Dosage:** 900mg/m²
- **Route:** IV
- **Day:** 1 & 8
- **Preparation:** Administer in 250mL bag 5% Dextrose or Normal Saline; Infuse over 30 minutes.
- **Timing:** Give before Docetaxel.

### DOCETAXEL
- **Dosage:** 100mg/m²
- **Route:** IV
- **Day:** 8
- **Preparation:** Mix in 250mL bag 5% Dextrose or Normal Saline to a maximum concentration of 0.3 - 0.9 mg/mL.
- **Administration:** Use non-PVC equipment without a filter; Infuse through main IV line.
- **Precautions:** Elasto-gel™ gloves should be placed on both hands and treatment should begin 15 minutes before the infusion starts and conclude 15 minutes after the infusion is done. Gloves should be changed after 45 minutes to sustain the cold temperature.

#### First and Second Dose:
- Infuse at a slower rate and then increase incrementally.
- Infuse at 30mL/hr for 5 minutes, then at 60mL/hr for 5 minutes, then at 125mL/hr for 5 minutes, then finally at 250mL/hr until infusion complete.

#### Subsequent doses:
- Infuse over 1 hour.

### REPEAT EVERY 21 DAYS

#### DEXAMETHASONE
- **Dosage:** 8mg
- **Route:** PO
- **Day:** 7
- **Preparation:** Take 8mg Q12H for 3 days starting one day before Docetaxel chemotherapy.

#### DIPHENHYDRAMINE
- **Dosage:** 50mg
- **Route:** IV
- **Day:** 8
- **Preparation:** May be mixed in 50mL minibag 5% Dextrose, Normal Saline; Give over 10-15 minutes. Wait 30 minutes before Docetaxel started.

#### TESTS:
- **Baseline Tests:** WBC, HB, PLT, ANC, Ca, K, Na, Chloride, Glucose, T.Bili, Albumin, AST, ALT, GGT, AlkPhosphatase
- **Day 1 & 8:** WBC, HB, PLT, ANC, Cr, Urea, T.Bili
- **Test Notes:** Repeat lytes, urea, Cr, LFTs every 3 cycles or prn

#### ANTIEMETIC PRE-CHEMO REGIMEN:
- **Level A**
  - Day 1: Dexamethasone 8mg PO/IV
  - May add or substitute Prochlorperazine 10mg PO/IV prn
- **Level B**
  - Day 8: Dexamethasone 8mg PO/IV (if not taken at home prior to treatment)
  - May add Prochlorperazine 10mg po/iv if needed

#### ANTIEMETIC TAKE-HOME REGIMEN:
- **Level A**
  - Day 1 & 8: Prochlorperazine 10mg PO q4-6h pm

#### PATIENT VISITS and APPOINTMENT TYPE:
- **Day 1:** 45min Type A
- **Day 8:** 2hrs Type C

#### ANCILLARY:
- Take a baseline blood pressure measurement, if prior hypotension.

#### TOXICITIES:
**Hematologic**
1. If AGC < 1.5 x 10⁹/L, or if PLT < 100 x 10⁹/L, **HOLD** Docetaxel dose for 1 week.
2. If AGC < 1.5 x 10⁹/L, or if PLT 75-100 x 10⁹/L, **REDUCE** Gemcitabine dose by 50%
3. If AGC < 1.0 x 10⁹/L, or if PLT < 75x 10⁹/L, **HOLD** Gemcitabine dose

**Hepatic Dysfunction**
1. **DECREASE** Docetaxel dose if LFTs > 1.5 x normal.
2. If AST or ALT > 1.5 ULN or > 53 IU/L, or if Alk Phos > 2.5ULN or > 180 IU/L, **REDUCE** Docetaxel dose to 60mg/m² or by 50%.

**SUGGESTED ACTION**
**SA DOCE-GEM**

**Sarcoma**

**DOCETAXEL-GEMCITABINE Chemotherapy**

**CLINICAL MONITORING:**
- Watch for symptoms of fever or infection.
- Blood pressure and pulse rate monitoring during drug administration and for the following hour.
- Skin assessment at each visit, including nails.

**Sensory**
1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function 2.
   Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL 3. Sensory alteration or paresthesia interfering with ADL 4. Disabling 5. Death

**Allergic Reaction**
1. Transient flushing or rash; drug fever < 38 degrees C 2. Rash; flushing; urticaria; dyspnea; drug fever ≥ 38 degrees C 3. Symptomatic bronchospasm, with or without urticaria; parenteral medication(s) indicated; allergy-related edema/angioedema; hypotension 4. Anaphylaxis 5. Death

**Skin Toxicity**

**Fluid retention/ Pleural effusion:**
1. Asymptomatic 2. Symptomatic, intervention such as diuretics or up to 2 therapeutic thoracenteses indicated 3. Symptomatic and supplemental oxygen, >2 therapeutic thoracenteses, tube drainage, or pleurodesis indicated 4. Life-threatening (e.g., causing hemodynamic instability or ventilatory support indicated) 5. Death

**Nail Changes**
1. Discoloration; ridging (koilonychias); pitting 2. Partial or complete loss of nail(s); pain in nailbed(s) 3. Interfering with ADL

**HYPERSENSITIVITY:**

**Docetaxel Hypersensitivity Procedures:**
- If hypersensitivity reaction during administration:
  1. Discontinue Docetaxel immediately if there are signs or symptoms of moderate or severe hypersensitivity. (Mild symptoms may resolve with a decrease in the rate of infusion.)
  2. Rapid IV administration of Diphenhydramine 50mg and Hydrocortisone 100mg.
  3. Re-initiate infusion after 30 minutes, or when signs of reaction are resolved. Resume infusion at a slower rate, then increase incrementally to the initial planned rate. eg. infuse at 30mL/hr (an 8-hour rate) for 5 minutes, then at 60mL/hr (a 4-hour rate) for 5 minutes, then at 125mL/hr (a 2-hour rate) for 5 minutes, then finally, resume at 250mL/hr (1-hour infusion rate).
  4. Depending on the intensity of the reaction, additional oral or IV pre-medication with an antihistamine should also be given for the next cycle of treatment and the rate of infusion should be decreased initially and then increased back to the recommended 1-hour infusion.

**INTERNAL CODE:**

**OPIS CODE: DOCE-GEM**

**REFERENCES:**
- CCO Practice Guideline 4-1-2: First-line chemotherapy for postoperative patients with stage II, III or IV Epithelial Ovarian Cancer, Fallopian Tube Cancer, or Primary Peritoneal.

**Date revised: 05/19/2009**

Sarcoma
**DOXORUBICIN Chemotherapy**

**Soft Tissue Sarcoma: Adjuvant & Palliative Treatment**

**DOXORUBICIN**

<table>
<thead>
<tr>
<th>60-75mg/m²</th>
<th>IV</th>
<th>Day 1</th>
<th>Round to nearest 1mg</th>
</tr>
</thead>
</table>

*Slow push through sidearm of free flowing IV.* Give 2 to 4mg (1-2mL) per minute.

**TESTS:**

<table>
<thead>
<tr>
<th>Baseline Tests</th>
<th>WBC</th>
<th>HB</th>
<th>PLT</th>
<th>ANC</th>
<th>T.Bili</th>
<th>AST</th>
<th>ALT</th>
<th>AlkPhosphatase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1 Baseline Test</td>
<td>WBC</td>
<td>HB</td>
<td>PLT</td>
<td>ANC</td>
<td>T.Bili</td>
<td>AST</td>
<td>ALT</td>
<td>AlkPhosphatase</td>
</tr>
</tbody>
</table>

**Test Notes:**

- LVEF if clinically indicated.

**ANTIEMETIC PRE-CHEMO REGIMEN:**

**Level C**

- Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
- Dexamethasone 20mg PO/IV

**ANTIEMETIC TAKE-HOME REGIMEN:**

**Level B/C**

- Ondansetron 8mg PO BID for 2-3 days, or
- Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days
- Dexamethasone 8mg PO BID for 2-3 days
- Prochlorperazine 10mg PO q4-6h prn

**PATIENT VISITS and APPOINTMENT TYPE:**

- Day 1 60min Type C

**TOXICITIES:**

**Hematologic**

1. If ANC < 1.5 x 10⁹/L, or if PLT < 100 x 10⁹/L, **HOLD** dose for 1 week.

**Renal Failure**

1. If SrCr > 265µmol/L, reduce Doxorubicin to **50%** dose.

**Hepatic Dysfunction**

1. If T.Bili = 26-51µmol/L, or AST = 60-180 IU/L, reduce Doxorubicin to **75%** dose.
2. If T.Bili = 52-85µmol/L, or AST > 180 IU/L, reduce Doxorubicin to **50%** dose.
3. If T.Bili > 85µmol/L, **OMIT** Doxorubicin dose.

**SUGGESTED ACTION**

**CLINICAL MONITORING:**

- Clinical exam for symptoms of CHF.
- Periodic cardiac tests for all patients with cardiac risk factors or patients at or above the threshold dose levels.

**Cardiac**

0. None
1. None
2. Asymptomatic, resting ejection fraction decline by >10% baseline; or abnormal cardiac function tests (LVEF >50) with no baseline for comparison
3. Mild Congestive Heart Failure, responds to therapy
4. Severe/ refractory Congestive Heart Failure

**At cumulative dose threshold and subsequent intervals**

For Cardiac Toxicity Rating:

- First rating at the cumulative dose **threshold** of 450mg/m², and repeat rating at each cumulative dose increment of 100mg/m² above threshold. (Cumulative dose sooner for high risk patients, eg. pre-existing cardiac disease, prior chest irradiation.)
- Note: Threshold Cumulative dose reduced proportionately if other anthracycline or anthraacenedione drugs have been given; cardiotoxicity is additive.

RATED AT EACH CLINIC VISIT

**REFERENCES:**


**CCO Eligibility Form Required**

**Non-Formulary Form Required**

**Date revised:** 03/07/2005
**SA-DOXORUBICIN LIPO**

**Sarcoma**

**PEGYLATED-LIPOSOMAL DOXORUBICIN Chemotherapy**

**Kaposi’s Sarcoma**

**DOXORUBICIN**

**LIPOSOMAL**

- If dose < 90mg, admix in **250mL Dextrose 5%** or if dose > 90mg, admix in **500mL Dextrose 5%**.

For the INITIAL Dose of Doxorubicin Liposomal:

- Test dose: 20mg admix into 100mL D5W and infuse over 1 hour.

- If no reaction occurs, admix the remaining dose into a 250mL D5W and infuse at 150mL/hr for 10 minutes then 200mL/hr for 10 minutes then if tolerated, full rate.

For the subsequent infusions:

- Infuse the **250mL** over **1 hour**.

- **DO NOT USE** an in-line filter.

- Trade name Caelyx™

**DIPHENHYDRAMINE**

- 50mg **IV** Day 1

- Before first dose of Doxorubicin Liposomal and prn for subsequent doses.

- Admix in **50-100mL minibag** 5% Dextrose or **Normal Saline**.

- Give over **10-15 minutes**.

**TESTS:**

<table>
<thead>
<tr>
<th>Baseline Tests</th>
<th>WBC HB PLT ANC T.Bili Albumin AST ALT GGT AlkPhosphatase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1</td>
<td>WBC HB PLT ANC</td>
</tr>
</tbody>
</table>

- LVEF if cardiac risk factors present.

**ANTIEMETIC PRE-CHEMO REGIMEN:**

**Level B**

- Day 1 - Dexamethasone 8mg PO/IV

- May add or substitute Prochlorperazine 10mg PO/IV prn

**ANTIEMETIC TAKE-HOME REGIMEN:**

**Level A**

- Day 1 - Prochlorperazine 10mg PO q4-6h pm

**PATIENT VISITS and APPOINTMENT TYPE:**

- Type B

**1.5hrs**

**TOXICITIES:**

**Hematologic**

1. If ANC < 1.5 x 10^9/L, or if PLT< 100 x 10^9/L, HOLD dose for 1 week.

**Renal Failure**

1. If SrCr > 265umol/L, REDUCE dose to 50%.

**Hepatic Dysfunction**

1. If T.Bili = 26-51umol/L, or AST = 60-80 IU/L, GIVE 75% dose.

2. If T.Bili = 52-85umol/L, or AST > 180 IU/L, GIVE 50% dose.

3. If T.Bili > 85umol/L, OMIT dose.

**SUGGESTED ACTION**

**CLINICAL MONITORING:**

- Observation for infusion reaction (back pain, flushing, chest tightness) during and for 30 minutes after first injection (emergency treatment available- ie. Antihistamine injection).

**Hand-Foot Skin Reaction:**

1. Minimal skin changes or dermatitis (e.g., erythema) without pain

2. Skin changes (e.g., peeling, blisters, bleeding, edema) or pain, not interfering with function

3. Ulcerative dermatitis or skin changes with pain interfering with function

**RATED AT EACH CLINIC VISIT**

**HYPERSONSITIVITY:**

Management of Hypersensitivity Reactions during Doxorubicin Liposomal (CAELYX™) Infusion:

- **Mild** (mild flushing, rash, pruritis)

  - Complete infusion. Supervise at bedside. No treatment required.

- **Moderate** (moderate rash, flushing, chest discomfort, mild hypotension, back pain)

  - Stop infusion. Give IV Diphenhydramine 25-50mg and IV Dexamethasone 10mg.

  - After recovery of symptoms, resume infusion at a rate of 50% of the initial rate of infusion.

- **Severe** (one or more of respiratory distress requiring treatment, generalized urticaria, angioedema, hypotension requiring therapy)

  - Stop infusion.

  - Give IV antihistamine and steroid as above, add Epinephrine or bronchodilators if indicated.

**INTERNAL CODE:**

OPIS CODE: DOXORUBICIN LIPOSOMAL

**REFERENCES:**


DOXORUBICIN-DACARBAZINE Chemotherapy

**Soft Tissue Sarcoma - Palliative**

**DOXORUBICIN**

- **60mg/m²**
- **IV**
- **Day 1**
- Round to nearest 1mg

- **Slow push through sidearm of free flowing IV**
- **Give 2 to 4mg (1-2mL) per minute.**

**DACARBAZINE**

- **850mg/m²**
- **IV**
- **Day 1**
- Round to nearest 5mg

- **Mix in 250-500mL bag Dextrose 5% or Normal Saline.**
- **Infuse over 30-120 minutes**: If vein irritation, infuse slowly; protect from light.
- **REPEAT EVERY 21 DAYS for a Usual Total of 6 Cycles**

**TESTS:**

Baseline Tests: WBC HB PLT ANC Cr Urea T.Bili AST ALT AlkPhosphatase

Day 1: WBC HB PLT ANC Cr Urea T.Bili ALT ALkPhosphatase

**Test Notes**: LVEF if clinically indicated.

**ANTIEMETIC PRE-CHEMO REGIMEN:**

- **Level C**
  - **Day 1**
    - Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
    - Dexamethasone 20mg PO/IV

**ANTIEMETIC TAKE-HOME REGIMEN:**

- **Level B/C**
  - **Day 1**
    - Ondansetron 8mg PO BID for 2-3 days, or Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days
    - Dexamethasone 8mg PO BID for 2-3 days
    - Prochlorperazine 10mg PO q4-6h prn

**PATIENT VISITS and APPOINTMENT TYPE:**

- **Day 1**
  - **2.5hrs**
  - **Type D**

**TOXICITIES:**

- **Hematologic**
  1. If ANC < 1.5 x 10⁹/L, or if PLT < 75 x 10⁹/L, **HOLD** dose for 1 week.

- **Renal Failure**
  1. If SrCr > 265umol/L, reduce Doxorubicin to **50%** dose.

- **Hepatic Dysfunction**
  1. If T.Bili = 26-51umol/L, or AST = 60-180 IU/L, **REDUCE** Doxorubicin to **75%** dose.
  2. If T.Bili = 52-85umol/L, or AST > 180 IU/L, **REDUCE** Doxorubicin to **50%** dose.
  3. If T.Bili > 85umol/L, **OMIT** Doxorubicin dose.

**SUGGESTED ACTION**

**CLINICAL MONITORING:**

- Clinical exam for symptoms of CHF.
- Periodic cardiac tests for all patients with cardiac risk factors or patients at or above the threshold dose levels.

**Cardiac**

- **0. None**
- **1. None**
- **2. Asymptomatic, resting ejection fraction decline by >10% baseline; or abnormal cardiac function tests (LVEF >50) with no baseline for comparison**
- **3. Mild Congestive Heart Failure, responds to therapy**
- **4. Severe/ refractory Congestive Heart Failure**

At cumulative dose threshold and subsequent intervals

For Cardiac Toxicity Rating:

- First rating at the cumulative dose **threshold of 450mg/m²**, and repeat rating at each cumulative dose increment of 100mg/m² above threshold. (Cumulative dose sooner for high risk patients, eg. pre-existing cardiac disease, prior chest irradiation.)
- **Note**: Threshold Cumulative dose reduced proportionately if other anthracycline or anthracenedione drugs have been given; cardiotoxicity is additive.

RATED AT EACH CLINIC VISIT

**REFERENCES:**

- CCO Practice Guideline 11-1: Doxorubicin-based Chemotherapy for the Palliative Treatment of Adult Patients with Locally Advanced or Metastatic Soft Tissue Sarcoma.

[CCO Eligibility Form Required] [Non-Formulary Form Required] Date revised: 08/29/2008
INTERFERON Chemotherapy

Kaposi’s Sarcoma - Indolent Disease - Palliative Intent

INTERFERON

<table>
<thead>
<tr>
<th>Dose</th>
<th>Route</th>
<th>Duration</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>3MU</td>
<td>SC</td>
<td>Daily x 4 weeks, then 3 times/week x 4 weeks</td>
<td>See Administration for Intron™ Pen doses</td>
</tr>
</tbody>
</table>

Administration:
- Starting dose: 3MU SC daily for 4 weeks, then three times weekly for 4 weeks.
- If no response: 9MU SC or IM daily for 2 weeks.
- If 9MU is the maximum tolerated dose, treat at 9MU for up to 1 year.
- If higher doses are tolerated, continue escalating dose:
  18MU SC or IM Daily for 2 weeks
  36MU SC or IM Daily for 2 weeks
  36MU SC or IM three times weekly

INTRONTM A PENS:
18 MU: Doses available: 1.5 MU, 3.0 MU, 4.5 MU, 6.0 MU
30 MU: Doses available: 2.5 MU, 5.0 MU, 7.5 MU, 10.0 MU
60 MU: Doses available: 5.0 MU, 10.0 MU, 15.0 MU, 20.0 MU

INTRONTM SOLUTION: 10MU/mL - 10MU and 25MU vials
6MU/mL - 18MU vial

CONTINUOUS TREATMENT until disease progression

Premed
ACETAMINOPHEN 325-650mg PO Daily x 4 weeks, then 3 times/week x 4 weeks
325mg tablet
- Administer before each Interferon dose for routine prophylaxis of flu-like symptoms (especially if this adverse effect occurs with early doses).

TESTS:
Baseline Tests WBC HB PLT ANC Glucose Cr Urea T.Bili AST ALT AlkPhosphatase LVEF
Test Notes - Laboratory tests to be done every 4 weeks.

ANCILLARY:
- May treat with HART concurrently (for AIDS therapy).

TOXICITIES:

Hematologic
Level I Toxicity:
1. ANC = 0.25 to < 0.5 x 10^9/L
2. PLT = 25-50 x 10^9/L
- HOLD Interferon until toxicity less than Level I severity, then resume at 50% full dose.

Level II Toxicity:
1. ANC < 0.25 x 10^9/L
2. PLT < 25 x 10^9/L
- DISCONTINUE Interferon.

Hepatic Dysfunction
Level I Toxicity:
1. AST > 5-10 times Normal (> 175-350 IU/L)
2. T.Bili 1.5-2 times Normal (> 27-36umol/L)
- HOLD Interferon until toxicity less than Level I severity, then resume at 50% full dose.

Level II Toxicity:
1. AST > 10 times Normal (> 350 IU/L)
2. T.Bili > 2.1 times Normal (> 37umol/L)
- DISCONTINUE Interferon.

CLINICAL MONITORING:
- Routine toxicity ratings of Flu-like Symptoms and Fatigue, at follow-up visits.

Fatigue
1. Mild fatigue over baseline 2. Moderate or causing difficulty performing some ADL 3. Severe fatigue interfering with ADL 4. Disabling

Flu-like Symptoms
RATED AT EACH CLINIC VISIT

REFERENCES:

Date revised: 08/29/2008
IFOSFAMIDE-DOXORUBICIN Chemotherapy

**DOXORUBICIN**
- 25mg/m² IV Days 1-3
  - Slow push through sidearm of free flowing IV. Give 2-4mg (1-2mL) per minute.
  - May be given during prehydration.

**MESNA**
- 1500mg/m² IV Days 1-3
  - Admix in 100mL **Normal Saline** and infuse over **15 minutes** prior to Ifosfamide.

**IFOSFAMIDE**
- 1500mg/m² IV Days 1-3
  - Admix in **500mL Normal Saline** and infuse over **1 hour**.

**MESNA (ORAL)**
- 500mg FLAT PO Days 1-3
  - Give 6-8 hours after Ifosfamide infusion.
  - IV Mesna may be taken ORALLY, diluted in juice, milk or carbonated beverage (Dispense in glass amber jars for oral use; stability of 8 days at room temperature).
  - Drink the Mesna dose by itself (preferable cold to minimize unpleasant taste) or dissolved with 15mL of desired liquid listed above, follow IMMEDIATELY by a glassful of the desired liquid.
  - May take Prochlorperazine 10mg tablet 30 minutes before oral Mesna dose to prevent nausea and vomiting.
  - If patient vomits within 1 hour of a dose of oral Mesna, repeat dose (emergency dose).
  - If patient vomits emergency dose of oral Mesna, drink 1.5 litre (6 cups) of water or beverage of choice over 2 hours.

**FILGRASTIM**
- 5-10mcg/kg SC Day 5
  - If previous episodes of febrile neutropenia, give G-CSF 5-10mcg/kg sc daily for 10 days
  - Give 48 hours **AFTER** combination chemotherapy.

**HYDRATION:**
- Infuse **500mL Normal Saline** IV over **1 hour** prior to Ifosfamide.
  - Infuse **1000ml Normal Saline** IV over **2 hours** post Ifosfamide.

**TESTS:**
- **Baseline Tests**
  - WBC, HB, PLT, ANC, Ca, K, Na, Chloride, Phosphate, Mg, Cr, T.Bili, Albumin, ALT
- **Day 1 Tests**
  - WBC, HB, PLT, ANC, Ca, K, Na, Chloride, Phosphate, Mg, Cr, Urea, T.Bili, Albumin, ALT, AlkPhosphatase

**ANTIEMETIC PRE-CHEMO REGIMEN:**
- **Level C**
  - Granisetron 1mg IV Days 1-3
  - Dexamethasone 20mg IV

**ANTIEMETIC TAKE-HOME REGIMEN:**
- **Level C**
  - Granisetron 1mg PO the evening of each chemo (Day 1-3) and Q12H for 3 days after chemotherapy.
  - Dexamethasone 8mg PO BID for 3 days after chemotherapy.
  - Prochlorperazine 10mg PO q4-6h prn and 30 minutes prior to oral Mesna dose.

**PATIENT VISITS and APPOINTMENT TYPE:**
- Days 1-3 4.5 hours Type D

**ANCILLARY:**
- PORT or PICC line is recommended.
- Oral hydration is strongly encouraged; poorly hydrated patients may need more IV hydration (to prevent renal toxicity).

**TOXICITIES:**

**Hematologic**
- If ANC < 1.5 x 10⁹/L, and PLT < 100 x 10⁹/L, **HOLD** for 1 week.

**Hepatic Dysfunction**
- If T.Bili ≥ 26-51umol/L or AST = 60-180 IU/L, **REDUCE** Ifosfamide to 50% dose
- If T.Bili ≥ 26-51umol/L, or AST = 60-180 IU/L, **REDUCE** Doxorubicin to 75% dose.
- If T.Bili = 52-85umol/L, or AST > 180 IU/L, **REDUCE** Doxorubicin to 90% dose.
- If T.Bili > 85umol/L, **OMIT** Doxorubicin dose.

**Renal Failure**
- If SrCr > 200umol/L, **REDUCE** Ifosfamide to 75%.
- If SrCr > 300umo/L, **REDUCE** Ifosfamide to 67%.
- If SrCr > 265umol/L, **REDUCE** Doxorubicin to 50% dose.

**SUGGESTED ACTION**

**Sarcoma**
**IFOSFAMIDE-DOXORUBICIN Chemotherapy**

**CLINICAL MONITORING:**
- Urinalysis (RBCs) periodic and in response to patient complaint.

**Cystitis**
1. Asymptomatic
2. Frequency with dysuria; macroscopic hematuria
3. Transfusion; IV pain medications; bladder irrigation indicated
4. Catastrophic bleeding; major non-elective intervention indicated
5. Death

**Encephalopathy**
1. Asymptomatic
2. Mild signs or symptoms; not interfering with ADL
3. Signs or symptoms interfering with ADL; hospitalization indicated
4. Life-threatening; disabling
5. Death

- Chemo RN to monitor for signs of sleepiness during infusion of drug, confusion or loss of consciousness.
- For Ifosfamide-induced encephalopathy, may give Methylene Blue 10% 50mg by slow IV push over 5 minutes or admix in 50ml NSaline and infuse over 5 minutes. Methylene Blue can be given as a single dose or every 4-8 hours until symptoms resolve.
- Clinical exam for symptoms of CHF.
- Periodic cardiac tests for all patients with cardiac risk factors or patients at or above the threshold dose levels.

**Cardiac**
0. None
1. None
2. Asymptomatic, resting ejection fraction decline by >10% baseline; or abnormal cardiac function tests (LVEF >50) with no baseline for comparison
3. Mild Congestive Heart Failure, responds to therapy
4. Severe/ refractory Congestive Heart Failure

**At cumulative dose threshold and subsequent intervals**
- First rating at the cumulative dose threshold of 450mg/m², and repeat rating at each cumulative dose increment of 100mg/m² above threshold. (Cumulative dose sooner for high risk patients, eg. pre-existing cardiac disease, prior chest irradiation.)
- Note: Threshold Cumulative dose reduced proportionately if other anthracycline or anthracenedione drugs have been given; cardiotoxicity is additive.

**RATED AT EACH CLINIC VISIT**

**FORMULAE:**

- **CrCl - Cockcroft & Gault (mL/sec)**
  - Male: \[\frac{[140-\text{age(yrs)}] \times \text{TBW(Kg)}}{[50 \times \text{SCr(umol/L)}]}\]
  - Female: \[\frac{[140-\text{age(yrs)}] \times \text{TBW(Kg)}}{[50 \times \text{SCr(umol/L)}]} \times 0.85\]

**INTERNAL CODE:**
- OPIS CODE: IFOS-DOXO

**REFERENCES:**
- CCO Practice Guidelines: Ifosfamide-based Combination Chemotherapy in Advanced Soft Tissue Sarcoma.
- Fredrick B. Hagemeister, Jr, MD, The University of Texas, MD Anderson Cancer Center, Protocol for Outpatient Administration of MINE=Mesna, Ifosfamide, Mitoxantrone, Etoposide.
- Kingston Regional Cancer Centre outpatient regimen Ifosfamide/ Doxorubicin/ Mesna
- Toronto Sunnybrook Regional Cancer Centre outpatient regimen Doxorubicin/ Ifosfamide/ Mesna

**Date revised:** 04/30/2008

Sarcoma
IFOSFAMIDE-ETOPOSIDE Chemotherapy
Adjuvant-Ewing’s Sarcoma/PNET/small round blue cell tumour; palliative-Osteogenic Sarcoma/Advance Soft Tissue Sarcoma

ETOPOSIDE
100mg/m² IV Days 1 to 5 Round to nearest 10mg
- Dose ≤ 200mg, mix in 500mL Normal Saline; Infuse over 30-60 minutes.
- Dose > 200mg, mix in 1000mL Normal Saline; Infuse over 1 to 2 hours.
- Use Non-PVC equipment and filter.
- Adjust rate if blood pressure drops.
- Give Etoposide before Ifosfamide to hydrate patient.
- Administer daily for 5 days.

MESNA
360mg/m² IV Days 1 to 5
- Admix in 100mL bag Normal Saline, infuse over 15 minutes prior to Ifosfamide.

IFOSFAMIDE
1800mg/m² IV Days 1 to 5 Round to nearest 100mg
- Admix in 500mL bag of Normal Saline, infuse over 1 hour.

MESNA (ORAL)
720mg/m² PO Days 1 to 5
- Give at 5hr and 9hr post Ifosfamide daily with 0hr being the start of Ifosfamide infusion.
- IV Mesna may be taken ORALLY, diluted in juice, milk or carbonated beverage (Dispense in glass amber jars for oral use; stability of 8 days at room temperature).
- Drink the Mesna dose by itself (preferable cold to minimize unpleasant taste) or dissolved with 15mL of desired liquid listed above, follow IMMEDIATELY by a glassful of the desired liquid.
- May take Prochlorperazine 10mg tablet 30 minutes before oral Mesna dose to prevent nausea and vomiting.
- If patient vomits within 1 hour of a dose of oral Mesna, repeat the dose (emergency dose).
- If patient vomits emergency Mesna dose, drink 1.5 litre (6 cups) of water or beverage of choice over 2 hours.

HYDRATION:
Post
- Infuse 1000mL Normal Saline IV over 2 hours post Ifosfamide.

TESTS:
Baseline Tests WBC HB PLT ANC Ca K Na Chloride Phosphate Mg Cr Urea Albumin
Day 1 WBC HB PLT ANC Ca K Na Chloride Mg Cr Urea T.Bili Albumin ALT AlkPhosphatase

Test Notes - Baseline: CBC, BUN, Cr, electrolytes, calcium, albumin, magnesium and LFTs

ANTIEMETIC PRE-CHEMO REGIMEN:
Level C Days 1-5
- Granisetron 1mg IV
- Dexamethasone 20mg IV

ANTIEMETIC TAKE-HOME REGIMEN:
Level C Day 1
- Granisetron 1mg PO the evening of each chemo (Day 1-5) and Q12H for 3 days after chemotherapy.
- Dexamethasone 8mg PO BID for 3 days after chemotherapy.
- Prochlorperazine 10mg PO q4-6h pm and 30 minutes prior to oral Mesna dose.

PATIENT VISITS and APPOINTMENT TYPE:
⇒ Days 1-5 4.5 hrs Type D

ANCILLARY:
- PORT or PICC line is recommended.
- Oral hydration is strongly encouraged; poorly hydrated patients may need more IV hydration (to prevent renal toxicity).

TOXICITIES:
Hematologic
1. If ANC < 1.5 x 10⁹/L or PLT < 100 x 10⁹/L, HOLD dose for 1 week.
Renal Failure
2. If CrCl < 0.2-0.8mL/sec, or SrCr > 130umol/L, REDUCE Etoposide to 75% dose.
3. If CrCl < 0.2mL/sec, REDUCE Etoposide to 50% dose.
4. If SrCr > 200umol/L, REDUCE Ifosfamide to 75% dose.
5. If SrCr > 300umol/L, REDUCE Ifosfamide to 67% dose.

Hepatic Dysfunction
1. If T.Bili = 26-51umol/L, or AST = 60-180 IU/L, REDUCE Etoposide, Ifosfamide to 50% dose
2. If T.Bili = 52-85umol/L, or AST > 180 IU/L, REDUCE Etoposide to 25% dose
3. If T.Bili > 85umol/L, OMIT Etoposide dose

SUGGESTED ACTION
**SARCOMA**

**IFOSFAMIDE-ETOPOSIDE Chemotherapy**

**CLINICAL MONITORING:**
- Baseline blood pressure at each treatment, monitor for hypotension.
- Urinalysis (RBCs) periodic and in response to patient complaint. Baseline and periodic liver and renal function test.

**Cystitis**
1. Asymptomatic
2. Frequency with dysuria; macroscopic hematuria
3. Transfusion; IV pain medications; bladder irrigation indicated
4. Catastrophic bleeding; major non-elective intervention indicated
5. Death

**Encephalopathy**
1. Asymptomatic
2. Mild signs or symptoms; not interfering with ADL
3. Signs or symptoms interfering with ADL; hospitalization indicated
4. Life-threatening; disabling
5. Death

- Chemo RN to monitor for signs of sleepiness during infusion of drug, confusion or loss of consciousness.
- For Ifosfamide-induced encephalopathy, may give Methylene Blue 10% 50mg by slow IV push over 5 minutes or admix in 50ml N.Saline and infuse over 5 minutes. Methylene Blue can be given as a single dose or every 4-8 hours until symptoms resolve.

**RATED AT EACH CLINIC VISIT**

**FORMULAE:**

\[
\text{CrCl - Cockcroft & Gault (mL/sec)} = \frac{[140-\text{age(yrs)}] \times \text{TBW(Kg)}}{[50 \times \text{SCr(umol/L)}]}
\]

\[
\text{CrCl - Cockcroft & Gault (mL/sec)} = \frac{[140-\text{age(yrs)}] \times \text{TBW(Kg)}}{[50 \times \text{SCr(umol/L)}] \times 0.85}
\]

**REFERENCES:**
- CCO Formulary guidelines
- BC Cancer Agency Protocol Summary for Etoposide, Ifosfamide-Mesna for patients with newly diagnosed Ewing’s Sarcoma/Peripheral Neuroectodermal Tumours (PNET) or Rhabdomyosarcoma or advanced soft tissue or bony sarcomas

**Date revised: 04/30/2008**
SA IMATINIB

Sarcoma

IMATINIB Therapy
Gastrointestinal Stromal Cell Tumours

IMATINIB 400-800mg PO Daily 100mg capsule
- Once daily with food and a large glass of water (until evidence of disease progression).
- Outpatient prescription available in 100mg and 400mg tablets.
- Trade name Gleevec™

CONTINUOUS TREATMENT until disease progression

TESTS:
Baseline Tests: WBC HB PLT ANC Cr Urea T.Bili Albumin AST ALT AlkPhosphatase
Every 3 months: WBC HB PLT ANC Cr Urea T.Bili Albumin AST ALT AlkPhosphatase

ANTIEMETIC PRE-CHEMO REGIMEN:
Level A Daily
- Prochlorperazine 10mg PO pm

ANTIEMETIC TAKE-HOME REGIMEN:
Level A Daily
- Prochlorperazine 10mg PO q4-6h pm

TOXICITIES:
Hematologic
1. If ANC < 1.0 x 10⁹/L and/or PLT < 50 x 10⁹/L, STOP Imatinib until ANC > 1.5 x 10⁹/L and PLT > 75 x 10⁹/L.
2. Resume treatment with Imatinib at 400mg dose.
3. If recurrence of ANC < 1.0 x 10⁹/L and/or PLT < 50 x 10⁹/L, repeat step 1 and resume Imatinib at a reduced dose of 300mg.
Hepatic Dysfunction
1. If T.Bili is > 3 x ULN or liver transaminases are > 5 x ULN, HOLD Imatinib until T.Bili has returned to < 1.5 x ULN or liver transaminase levels to < 2.5 x ULN.
2. Continue treatment at a reduced daily dose (eg. 300mg if treated at 400mg or 400mg if treated at 600mg).

CLINICAL MONITORING:
- Monitor patients for edema and fluid retention (may be dose related).
- Imatinib is metabolized by CYP3A4 and has many drug interactions (eg. Warfarin).

INTERNAL CODE:
OPIS CODE: IMATINIB-SA

REFERENCES:

Date revised: 08/29/2008

Sarcoma
SA-PACLI

Green STR

Sarcoma

PACLITAXEL Chemotherapy

Kaposi’s Sarcoma- Third Line Treatment

PACLITAXEL 175mg/m² IV Day 1 Round to nearest 3mg
- Mix in 500mL bag Normal Saline (dilution concentration 0.3-1.2 mg/mL).
- Use non-PVC equipment, including 0.22 micron in-line filter.
- Infuse over 3 hours.

Dexamethasone 20mg PO Day 1 4mg tablet
- 12 and 6 hours before Paclitaxel administration (if not taken at home, give 20mg Dexamethasone IV 30-60 minutes before Paclitaxel).

DIPHENHYDRAMINE 50mg IV Day 1
- Admix in 50-100mL minibag 5% Dextrose or Normal Saline.
- Give over 10-15 minutes (May be admixed with Ranitidine).
- Administer 30 minutes before Paclitaxel.

RANITIDINE 50mg IV Day 1
- Admix in 50-100mL minibag 5% Dextrose or Normal Saline.
- Give over 10-15 minutes (May be admixed with Diphenhydramine).
- Administer 30 minutes before Paclitaxel.

REPEAT EVERY 21 DAYS

TESTS:
Baseline Tests WBC HB PLT ANC T.Bili AST ALT AlkPhosphatase
Day 1 WBC HB PLT ANC T.Bili AST ALT AlkPhosphatase
Test Notes - LFTs only if clinically indicated.

ANTIEMETIC PRE-CHEMO REGIMEN:
Level B Day 1 - Dexamethasone -see regimen information for pre-medications.
- May add Prochlorperazine 10mg PO/IV pm

ANTIEMETIC TAKE-HOME REGIMEN:
Level A Day 1 - Prochlorperazine 10mg PO q4-6h prn

PATIENT VISITS and APPOINTMENT TYPE:
→ Day 1 5hrs Type D

TOXICITIES:

Hematologic
1. If ANC < 1.5 x 10⁹/L, or if PLT < 100 x 10⁹/L, HOLD dose for 1 week.

Hepatic Dysfunction
1. If AST > 70 IU/L, or T.Bili < 25umol/L, give maximum Paclitaxel dose of 135mg/m².
2. If T.Bili = 25-50umol/L, give maximum Paclitaxel dose of 75mg/m².
3. If T.Bili > 50umol/L, give maximum Paclitaxel dose of 50mg/m².

SUGGESTED ACTION

CLINICAL MONITORING:
- Take a baseline blood pressure measurement, if prior hypotension.
- Observe patient for the first 5 minutes of the Paclitaxel infusion, then periodically for the remainder of the infusion.
- Watch for symptoms of fever and infection.
- Blood pressure and pulse rate monitoring during drug administration & for the following hour.

Sensory
1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function
2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL
3. Sensory alteration or paresthesia interfering with ADL
4. Disabling
5. Death

Flu-like Syndrome:
1. Symptoms present but not interfering with function
2. Moderate or causing difficulty performing some ADL
3. Severe symptoms interfering with ADL
4. Disabling
5. Death

Allergic Reaction:
1. Transient flushing or rash; drug fever < 38°C
2. Rash; flushing; urticaria; dyspnea; drug fever ≥ 38°C
3. Symptomatic bronchospasm, with or without urticaria; parenteral medication(s) indicated; allergy-related edema/angioidema; hypotension
4. Anaphylaxis
5. Death

RATED AT EACH CLINIC VISIT

Sarcoma
HYPERSENSITIVITY:

Paclitaxel Procedures

Retreatment for Paclitaxel Hypersensitivity Reaction:

1. If Paclitaxel hypersensitivity reaction occurs during administration:
   1. Discontinue Paclitaxel immediately if there are signs or symptoms of hypersensitivity.
   2. Rapid IV administration of Diphenhydramine 50mg direct IV push over 1 minute and Hydrocortisone 100mg in
      100ml Normal Saline over 5-10 minutes.
   3. Reinitiate Paclitaxel infusion after 30 minutes, or when signs of reaction are resolved. Resume Paclitaxel infusion
      at 17mL/hr (10% of original rate) for 15 minutes, then at 42mL/hr (25% of original rate) for 15 minutes. If no further
      symptoms develop, continue at original rate until infusion complete.
   4. If reaction recurs, STOP Paclitaxel for this dose and treat patient symptoms.

Desensitization for Paclitaxel Hypersensitivity Reactions:

1. If Paclitaxel hypersensitivity recurs during previous administration despite retreatment plan:
   1. Dexamethasone 20mg PO 36 hours and 12 hours before chemotherapy, and 20mg PO morning of chemotherapy.
   2. Dexamethasone 20mg IV, Diphenhydramine 50mg IV & Ranitidine 50mg IV about 30min before infusion.
   3. Paclitaxel Infusion: 2mg in 100mL Normal Saline over 30min; if no reaction, 10mg in 100mL Normal Saline over
      30min; if no reaction, remainder of dose in 500mL Normal Saline over 3 hours.
   4. If reaction occurs, discontinue infusion; Diphenhydramine 50mg direct IV push over 1 minute and Hydrocortisone
      100mg in 100ml Normal Saline over 5-10 minutes.
   5. Restart Paclitaxel infusion after 30 minutes.

INTERNAL CODE:
OPIS CODE: PACLI SA

REFERENCES:

Date revised: 08/29/2008
**PACLITAXEL** Chemotherapy (weekly)

**Kaposi’s Sarcoma - Third Line Treatment**

**PACLITAXEL** 58mg/m² IV Day 1 Round to nearest 3mg

- Mix in **250mL** bag **Normal Saline** (dilution concentration 0.3-1.2 mg/mL).
- Use non-PVC equipment, including 0.22 micron in-line filter.
- Infuse over **1 hour**.

**DEXAMETHASON**E 8mg PO Day 1 4mg tablet

- 12 and 6 hours before Paclitaxel (if not taken at home, 8mg IV 30 minutes pre Paclitaxel).

**DIPHENHYDRAMINE** 50mg IV Day 1

- Admix in **50-100mL** minibag **5% Dextrose or Normal Saline**.
- Give over **10-15 minutes**, (May be admixed with Ranitidine).
- Administer 30 minutes before Paclitaxel.

**RANITIDINE** 50mg IV Day 1

- Admix in **50-100mL** minibag **5% Dextrose or Normal Saline**.
- Give over **10-15 minutes**, (May be admixed with Diphenhydramine).
- Administer 30 minutes before Paclitaxel.

**REPEAT EVERY 7 DAYS**

**TESTS:**

<table>
<thead>
<tr>
<th>Baseline Tests</th>
<th>WBC  HB  PLT  ANC  T.Bili  AST  ALT  AlkPhosphatase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1</td>
<td>WBC  HB  PLT  ANC</td>
</tr>
</tbody>
</table>

**Test Notes** - LFTs only if clinically indicated on Day 1.

**ANTIEMETIC PRE-CHEMO REGIMEN:**

**Level A**

- Day 1 - Prochlorperazine 10mg PO/IV pm

**ANTIEMETIC TAKE-HOME REGIMEN:**

**Level A**

- Day 1 - Prochlorperazine 10mg PO q4-6h pm

**PATIENT VISITS and APPOINTMENT TYPE:**

- Day 1 90min Type D

**TOXICITIES:**

**Hematologic**

1. If ANC < 1.5 x 10^9/L, or if PLT < 100 x 10^9/L, **HOLD** dose for 1 week.

**Hepatic Dysfunction**

1. If AST > 70 IU/L, or T.Bili < 25umol/L, **GIVE** Maximum dose of **45mg/m²**.
2. If T.Bili = 25-50umol/L, **GIVE** Maximum dose of **25mg/m²**.
3. If T.Bili > 50umol/L, **GIVE** Maximum dose of **16mg/m²**.

**SUGGESTED ACTION**

**CLINICAL MONITORING:**

- Take a baseline blood pressure measurement, if prior hypotension.
- Observe patient for the first 5 minutes of the Paclitaxel infusion, then periodically for the remainder of the infusion.
- Watch for symptoms of fever and infection.
- Blood pressure and pulse rate monitoring during drug administration and for the following hour.

**Sensory:**

1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function.  
2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL.  
3. Sensory alteration or paresthesia interfering with ADL.  
4. Disabling  
5. Death

**Flu-like Syndrome:**

1. Symptoms present but not interfering with function  
2. Moderate or causing difficulty performing some ADL  
3. Severe symptoms interfering with ADL  
4. Disabling  
5. Death

**Allergic Reaction:**

1. Transient flushing or rash; drug fever < 38°C  
2. Rash; flushing; urticaria; dyspnea; drug fever > 38°C  
3. Symptomatic bronchospasm, with or without urticaria; parenteral medication(s) indicated; allergy-related edema/angioedema; hypotension  
4. Anaphylaxis  
5. Death

**RATED AT EACH CLINIC VISIT**

Sarcoma
PACLITAXEL Chemotherapy (weekly)

**HYPERSENSITIVITY:**

### Paclitaxel Procedures

**Retreatment for Paclitaxel Hypersensitivity Reaction:**

1. Discontinue Paclitaxel immediately if there are signs or symptoms of hypersensitivity.
2. Rapid IV administration of Diphenhydramine 50mg direct IV push over 1 minute and Hydrocortisone 100mg in 100ml Normal Saline over 5-10 minutes.
3. Reinitiate Paclitaxel infusion after 30 minutes, or when signs of reaction are resolved. Resume Paclitaxel infusion at 17mL/hr (10% of original rate) for 15 minutes, then at 42mL/hr (25% of original rate) for 15 minutes. If no further symptoms develop, continue at original rate until infusion complete.
4. If reaction recurs, STOP Paclitaxel for this dose and treat patient symptoms.

**Desensitization for Paclitaxel Hypersensitivity Reactions:**

1. Dexamethasone 20mg PO 36 hours and 12 hours before chemotherapy, and 20mg PO morning of chemotherapy.
2. Dexamethasone 20mg IV, Diphenhydramine 50mg IV & Ranitidine 50mg IV about 30min before infusion.
3. Paclitaxel Infusion: 2mg in 100mL Normal Saline over 30min; if no reaction, 10mg in 100mL Normal Saline over 30min; if no reaction, remainder of dose in 500mL Normal Saline over 3 hours.
4. If reaction occurs, discontinue infusion; Diphenhydramine 50mg direct IV push over 1 minute and Hydrocortisone 100mg in 100ml Normal Saline over 5-10 minutes.
5. Restart Paclitaxel infusion after 30 minutes.

**INTERNAL CODE:**

OPIS CODE: PACLI *W SA 58MG/M2

**REFERENCES:**


CCO Eligibility Form Required ☐ Non-Formulary Form Required ☑ Date revised: 08/29/2008

Sarcoma
SA-SARCMOD1

Sarcoma

SARCOMA MODULE 1: IFOSFAMIDE 24 HR
Soft Tissue Sarcoma - adjuvant therapy

DOXORUBICIN
60-75mg/m² IV Day 1
- Slow push through sidearm of free flowing IV. Give 2-4mg (1-2mL) per minute.
- May be mixed in 50mL minibag 5% Dextrose for doses < 100mg, doses > 100mg may be mixed in 100mL minibag
  5% Dextrose; Infuse through central venous catheter over 15-30 minutes.
- Protect from light.

MESNA
1250mg/m² IV Day 1
- Mix in 1000mL bag Normal Saline, infuse over 15 minutes prior to Ifosfamide.

IFOSFAMIDE
5000mg/m² IV Day 1
- May mix in 1000mL bag 2/3 and 1/3 IV solution, infuse over 24 hours.

MESNA
2500mg/m² IV Day 1
- Mix in 2000mL 2/3 and 1/3 IV solution (dispensed as 1250mg/m² in 1000mL x 2 bags); infuse IV through a Y-
tubing connection with Ifosfamide over 24 hours.

MESNA
1250mg/m² IV Day 2
- Mix in 1000mL 2/3 and 1/3 IV solution, infuse IV over 12 hours with 1000mL 2/3 and 1/3 IV solution
  through Y-tubing connection. If nausea and/or vomiting persists, continue IV infusion with 2/3 and 1/3 solution at
  150mL/hr after chemotherapy completed.

REPEAT CYCLE EVERY 21 DAYS

LORAZEPAM
1mg PO tid prn

HYDRATION:
- 2/3 and 1/3 IV solution TKVO prior to chemotherapy.

TESTS:
Baseline Tests WBC HB PLT ANC Ca K Na Chloride Phosphate Mg Cr T.Bili Albumin ALT
Test Notes Baseline CBC, BUN, Cr, electrolytes, calcium, magnesium, albumin, LFTs
- Daily: CBC, BUN, Cr, electrolytes, calcium, magnesium and albumin

ANTIEMETIC PRE-CHEMO REGIMEN:
Level B/C Days 1-3
- Ondansetron 8mg PO/IV pre-chemo, then q12h x 3 days
- Dexamethasone 8mg PO/IV pre-chemo, then q12h x 3 days
- Prochlorperazine 10mg PO/IV q4h pm

INPATIENT ANTIEMETICS:
- Give Ondansetron and Dexamethasone pre-chemo, then q12h x 3 days
- Ondansetron 8mg PO/IV q12h can be substituted with Granisetron 1-2mg PO/IV daily

TOXICITIES:
Hematologic
1. If ANC < 1.5 X 10³/L, and PLT < 100 x 10⁹/L, HOLD for 1 week.

Hepatic Dysfunction
1. If T.Bili = 26-51umol/L, or AST = 60-180 IU/L, REDUCE Ifosfamide to 50% dose
2. If T.Bili = 26-51umol/L, or AST = 60-180 IU/L, REDUCE Doxorubicin to 75% dose.
3. If T.Bili = 52-85umol/L, or AST > 180 IU/L, REDUCE Doxorubicin to 50% dose.
4. If T.Bili > 85umol/L, OMIT Doxorubicin dose.

Renal Failure
1. If SrCr > 200umol/L, REDUCE Ifosfamide to 75%.
2. If SrCr > 300umol/L, REDUCE Ifosfamide to 67%.
3. If SrCr > 265umol/L, REDUCE Doxorubicin to 50% dose.

CLINICAL MONITORING:
Cystitis
0. None 1. Mild symptoms 2. Symptoms relieved with therapy 3. Symptoms not relieved
4. Life-threatening
Cardiac
- Baseline cardiogram to be done prior treatment.
0. None 1. None 2. Asymptomatic, resting ejection fraction decline by > 10% baseline; or abnormal cardiac
  function test (LVEF > 50) with no baseline for comparison 3. Mild Congestive Heart Failure, responds to therapy
4. Severe/ refractory Congestive Heart Failure

At cumulative dose threshold and subsequent intervals
For Cardiac Toxicity Rating :
- First rating at the cumulative dose threshold of 450mg/m², and repeat rating at each cumulative dose increment of
  100mg/m² above threshold.

FORMULAE:
CrCl - Cockcroft & Gault (mL/sec)
Male: \[\frac{[140 \text{ age (yrs)}] \times \text{TBW (Kg)}}{[50 \times \text{SCr (umol/L)}]}\]
CrCl - Cockcroft & Gault (mL/sec)
Female: \[\frac{[140 \text{ age (yrs)}] \times \text{TBW (Kg)}}{[50 \times \text{SCr (umol/L)}]} \times 0.85\]

INTERNAL CODE:
CCO Eligibility Form Required [ ] Non-Formulary Form Required [ ] Date revised: 03/07/2005
SARCOMA MODULE 3: ETOPOSIDE-IFOSFAMIDE-MESNA
(Inpatient regimen)

Ewing’s Sarcoma/Osteogenic Sarcoma - Palliative Intent Advance Soft Tissue Sarcoma

**ETOPOSIDE**
100mg/m²  IV  Day 1 to 5  Hour 0 to 1  Round to nearest 10mg
- Premixed in **500mL** bag of 2/3 and 1/3 IV solution, infuse IV over 1 hour.
- Administer daily for 5 days.

**IFOSFAMIDE**
1800mg/m²  IV  Day 1 to 5  Hour 1 to 2  Round to nearest 100mg
- Premixed Ifosfamide in **250mL** bag of 2/3 and 1/3 IV solution, infuse over 1 hour together with Mesna through a Y-tubing connection.

**MESNA**
360mg/m²  IV  Day 1 to 5  Hour 1 to 2
- Premixed in **100mL** bag of Normal Saline; infuse IV over 1 hour through Y-connection tubing together with Ifosfamide.

**MESNA**
360mg/m²  IV  Day 1 to 5  Hour 1 to 2
- Premixed Mesna in **1000mL** bag of 2/3 and 1/3 IV solution, infuse IV over 3 hours.

**MESNA**
360mg/m²  IV  Day 1 to 5  Hour 5, 8 and 11
- Premixed Mesna in **100mL** bag Normal Saline, infuse IV over 15 minutes.

**2/31/3 IV SOLUTION**
- Infuse 2/3 and 1/3 IV solution at 150mL/hr.

**LORAZEPAM**
1 mg  PO  tid pm

**HYDRATION:**
- 2/3 and 1/3 IV solution TKVO prior to chemotherapy.

**TESTS:**
Baseline Tests: WBC, HB, PLT, ANC, Ca, K, Na, Chloride, Phosphate, Mg, Cr, Urea, Albumin
- Daily: CBC, BUN, Cr, electrolytes, calcium, albumin, magnesium and LFTs
- Baseline: CBC, BUN, Cr, electrolytes, calcium, albumin, magnesium and albumin

**ANTIEMETIC PRE-CHEMO REGIMEN:**
- Ondansetron 8mg PO/IV pre-chemo then q12h x 5 days
- Dexamethasone 8mg PO/IV pre-chemo then q12h x 5 days
- Prochlorperazine 10mg PO/IV q4h prn

**INPATIENT ANTIEMETICS:**
- Ondansetron 8mg PO/IV can be substituted with Granisetron 1-2mg PO/IV daily.

**TOXICITIES:**

**Hematologic**
1. IfANC < 1.5 x 10⁹/L or PLT < 100 x 10⁹/L, HOLD dose for 1 week.

**Renal Failure**
1. If CrCl = 0.2-0.8mL/sec, or SrCr > 30umol/L, REDUCE Etoposide to 75% dose.
2. If CrCl < 0.2mL/sec, REDUCE Etoposide to 50% dose.
3. If SrCr > 200umol/L, REDUCE Ifosfamide to 75% dose.
4. If SrCr > 300umol/L, REDUCE Ifosfamide to 67% dose.

**Hepatic Dysfunction**
1. If T.Bili = 25-51umol/L, or AST = 60-180 IU/L, REDUCE Etoposide, Ifosfamide to 50% dose
2. If T.Bili = 52-85umol/L, or AST > 180 IU/L, REDUCE Etoposide to 25% dose
3. If T.Bili > 85umol/L, OMIT Etoposide dose

**CLINICAL MONITORING:**
- Baseline blood pressure at each treatment, monitor for hypotension.
- Urinalysis - for RBCs. Baseline and periodic liver and renal function test.

**CYSTIS**

**FORMULAE:**
- CrCl - Cockcroft & Gault (mL/sec)
  - Male: [140-age(yrs)] x TBW(Kg) / [50 x SCR(umol/L)]
  - Female: [140-age(yrs)] x TBW(Kg) / [50 x SCR(umol/L)] x 0.85

**REFERENCES:**

**CCO Eligibility Form Required**  [ ]  **Non-Formulary Form Required**  [ ]  **Date revised:** 03/07/2005

Sarcoma
Sarcoma  CYCLOPHOSPHAMIDE-DOXORUBICIN-VINCRISTINE  
Chemotherapy  
-Newly diagnosed patients with Ewing sarcoma, who have good performance status.  
Localized disease  

<table>
<thead>
<tr>
<th>VINCRIINE</th>
<th>1mg/m²</th>
<th>IV</th>
<th>Day 1 Hour 0</th>
<th>Round to nearest 0.1mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Push through sidearm of free flowing IV. Inject over at least 1 minute. Max dose = 2mg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MESNA</td>
<td>480mg/m²</td>
<td>IV</td>
<td>Day 1 and 2 Hour 0 to 1</td>
<td></td>
</tr>
<tr>
<td>- Mix in 100mL bag Normal Saline. Infuse over 1 hour through a Y- tubing connection with Cyclophosphamide.</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>CYCLOPHOSPHAMIDE</td>
<td>2100mg/m²</td>
<td>IV</td>
<td>Day 1 and 2 Hour 0 to 1</td>
<td>Round to nearest 10mg</td>
</tr>
<tr>
<td>- Mix in 500mL bag Normal Saline. Infuse over 60 minutes through a Y- tubing connection with Mesna.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MESNA</td>
<td>480mg/m²</td>
<td>IV</td>
<td>Day 1 and 2 Hour 1 to 4</td>
<td></td>
</tr>
<tr>
<td>- Mix in 1000mL bag 2/3 and 1/3 IV solution. Infuse over 3 hours.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MESNA</td>
<td>480mg/m²</td>
<td>IV</td>
<td>Day 1 and 2 Hour 4 to 4.5</td>
<td></td>
</tr>
<tr>
<td>- Mix in 250mL bag 2/3 and 1/3 IV solution, infuse over 30 minutes, then 2/3 and 1/3 IV solution TKVO till after Hour - 10 Mesna, then lock off.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DOXORUBICIN</td>
<td>75mg/m²</td>
<td>IV</td>
<td>Day 1 and 2 Hour 4.5 to 52.5</td>
<td></td>
</tr>
<tr>
<td>- Mix in 2000mL bag 2/3 and 1/3 IV solution (dispensed as 37.5mg/m² in 1000mL x 2 bags). Infuse over 48 hours, through a Y-tubing connection with 2/3 and 1/3 IV solution at rate 125mL/hr for 48 hours.</td>
<td></td>
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</tr>
<tr>
<td>- Infuse through central venous catheter. Protect from light.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MESNA</td>
<td>480mg/m²</td>
<td>IV</td>
<td>Day 1 &amp; 2 Hour 7 &amp; 10</td>
<td></td>
</tr>
<tr>
<td>- Mix in 100mL bag Normal Saline, infuse over 15 minutes.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**HYDRATION:**  
Pre  
- 2/3 and 1/3 IV solution TKVO pre-chemo.  
Post  
- If nausea persists, continue IV infusion with 2/3 and 1/3 IV solution at rate 150mL/hr following chemotherapy.  

**TESTS:**  
Baseline Tests  
- WBC, HB, PLT, ANC, Ca, K, Na, Chloride, Phosphate, Mg, Cr, Urea, T.Bili, Albumin, AST, ALT, LVEF  
Test Notes  
- Baseline CBC, BUN, Cr, electrolytes, calcium, albumin, magnesium, LFTs, baseline ECG before first treatment.  
- Daily: CBC, BUN, Cr, electrolytes, calcium, magnesium and albumin.  

**ANTIEMETIC PRE-CHEMO REGIMEN:**  
Level B/C  
- Ondansetron 8mg PO/IV pre-chemo, then q12h or Granisetron 1-2mg PO/IV daily.  
- Dexamethasone 8mg pre-chemo, then q12h x 3 days  
- Prochlorperazine 10mg PO/IV q4h pm.  

**INPATIENT ANTIEMETICS:**  
- Give Ondansetron and Dexamethasone pre-chemo, then q12h x 3 days.  
- Ondansetron can be substituted with Granisetron 1-2mg PO/IV daily.  

**TOXICITIES:**  

**Hematologic:**  
1. If ANC < 1.5 x 10⁹/L, or if PLT < 100 x 10⁹/L, HOLD dose for 1 week.  

**Hepatic Dysfunction:**  
1. If T.Bili = 26-51umol/L, or AST = 60-180 IU/L, REDUCE Vincristine to 50% dose and Doxorubicin to 75% dose.  
2. If T.Bili = 52-85umol/L, or AST > 180 IU/L, REDUCE Vincristine to 25% dose, Doxorubicin to 50% dose and Cyclophosphamide to 75% dose.  
3. If T.Bili > 85umol/L, OMIT all drugs.  

**Renal Failure:**  
1. If SrCr > 265umol/L, REDUCE Doxorubicin to 50% dose and OMIT Cyclophosphamide.  

**SUGGESTED ACTION**  

**CLINICAL MONITORING:**  
- Baseline liver function tests.  
- Clinical exam for symptoms of CHF.  
- Baseline and periodic cardiac test for all patients with cardiac risk factors or patients at or above the threshold dose levels.  

**Cardiac:**  
- None  
- 2. Asymptomatic, resting ejection fraction decline by >10% baseline or abnormal cardiac function test (LVEF > 50 ) with no baseline for comparison  
- 3. Mild Congestive Heart Failure, responds to therapy  
- 4. Severe/Refractory Congestive Heart Failure  

At cumulative dose threshold and subsequent intervals  

**For Cardiac Toxicity Ratings:**  
First rating at the cumulative dose threshold of 450mg/m² and repeat ratings at each cumulative dose increment of 100mg/m² above threshold.
SA-SARCOMAMOD2

B

Sarcoma

CYCLOPHOSPHAMIDE-DOXORUBICIN-VINCRISTINE

Chemotherapy

Newly diagnosed patients with Ewing sarcoma, who have good performance status.

Localized disease

VINCRISTINE

1mg/m² (max 2mg) IV Day 1 Hour 0 Round to nearest 0.1mg

- Push through sidearm of free flowing IV. Inject over at least 1 minute.

CYCLOPHOSPHAMIDE

1200mg/m² IV Day 1 Hour 0-1 Round to nearest 10 mg

- Mix in 500mL bag Normal Saline. Infuse over 1 hour, through a Y-tubing connection with Mesna.

MESNA

360mg/m² IV Day 1 Hour 0 to 1

- Mix in 100mL bag Normal Saline, infuse over 1 hour through a Y-tubing connection with Cyclophosphamide.

MESNA

360mg/m² IV Day 1 Hour 1 to 4

- Mix in 1000mL bag 2/3 and 1/3 IV solution, infuse over 3 hours.

MESNA

360mg/m² IV Day 1 Hour 4 to 4.5

- Mix in 250mL bag 2/3 and 1/3 IV solution. Infuse over 30 minutes; then 2/3 and 1/3 IV solution TKVO till after Hour 10 Mesna, then lock off.

DOXORUBICIN

75mg/m² IV Day 1 Hour 4.5 to 52.5 Round to nearest 1mg

- Mix in 2000mL bag 2/3 and 1/3 IV solution (dispensed as 37.5mg/m² in 1000mL x 2 bags) infuse over 48 hours, through a Y-tubing connection with 2/3 and 1/3 IV solution at rate 125mL/hr. Infuse through central venous catheter. Protect from light.

MESNA

360mg/m² IV Day 1 Hours 7-10

- Mix in 100mL Normal Saline, infuse over 15 minutes.

REPEAT CYCLE ON WEEK 12, 21, 27

LORAZEPAM

1mg PO tid pm

HYDRATION:

Pre

- 2/3 and 1/3 IV solution TKVO prior to chemotherapy.

Post

- If nausea and/or vomiting persists, continue IV infusion with 2/3 and 1/3 solution at rate 150mL/hr following chemotherapy.

TESTS:

Baseline Tests

- WBC HB PLT ANC Ca K Na Chloride Phosphate Mg Cr Urea T.Bili AST LVEF

Test Notes

- Baseline CBC, BUN, Cr, electrolytes, calcium, albumin, magnesium, LFTs, baseline ECG before first treatment.
- Daily : CBC, BUN, Cr, electrolytes, calcium, magnesium, albumin

ANTIEMETIC PRE-CHEMO REGIMEN:

Level B/C

Days 1-3 - Ondansetron 8mg PO/IV pre-chemo, then q12h x 3 days

- Dexamethasone 8mg pre-chemo, then q12h x 3 days

- Prochlorperazine 10mg PO/IV q4h prn.

INPATIENT ANTIEMETICS:

- Give Ondansetron & Dexamethasone pre-chemo & q12h x 3 days.
- Ondansetron can be substituted with Granisetron 1-2mg PO/IV daily.

TOXICITIES:

Hematologic

1. If ANC < 1.5 x 10⁹/L , or PLT< 100 x 10⁹/L, HOLD dose for 1 week.

SUGGESTED ACTION

Hepatic Dysfunction

1. If T.Bili = 26-51umol/L, or AST = 60-180 IU/L, REDUCE Vincristine to 50% dose and Doxorubicin to 75% dose.
2. If T.Bili = 52-85umol/L, or AST > 180 IU/L, REDUCE Vincristine to 25% dose, Doxorubicin to 50% dose and Cyclophosphamide to 75% dose.
3. If T.Bili > 85 umol/L, OMIT all drugs.

SUGGESTED ACTION

Renal Failure

1. If SrCr > 265umol/L, REDUCE Doxorubicin to 50% dose and OMIT Cyclophosphamide.

SUGGESTED ACTION

CLINICAL MONITORING:

- Baseline liver function tests.
- Clinical exam for symptoms of CHF.
- Baseline and periodic cardiac test for all patients with cardiac risk factors or patients at or above the threshold dose levels.

Cardiac

0. None 1. None 2. Asymptomatic, resting ejection fraction decline by 10% baseline; or abnormal cardiac function test (LVEF > 50 ) with no baseline for comparison

3. Mild Congestive Heart Failure, responds to therapy
4. Severe/Refractory Congestive Heart Failure

At cumulative dose threshold and subsequent intervals

For Cardiac Toxicity Ratings:

First rating at the cumulative dose threshold of 450mg/m², and repeat ratings at each cumulative dose increment of 100mg/m² above threshold.

CCO Eligibility Form Required ☐ Non-Formulary Form Required ☐ Date revised: 03/07/2005
**CISPLATIN- DOXORUBICIN Chemotherapy**

**Osteogenic Sarcoma, Non metastatic**

**DOXORUBICIN**
25mg/m² IV Days 1, 2 & 3 Round to nearest 1mg
- Slow push through sidearm of free flowing IV. Give 2-4mg (1-2mL) per minute. First dose may be given during prehydration.
- Give second dose of Doxorubicin after Cisplatin completed.
- Give third dose of Doxorubicin when post hydration completed.

**CISPLATIN**
100mg/m² IV Day 1 24hr infusion Round to nearest 1mg
- Mix in 1000mL bag Normal Saline, infuse over 24 hours and through a Y-tubing connection, infuse IV solution (see concurrent hydration).

**LORAZEPAM**
1mg SL tid prn
- Give 1 tablet SL tid prn.

**HYDRATION:**

**Pre**
- Infuse 2/3 and 1/3 IV solution at rate 400mL/hr for 4 hours prior chemotherapy.

**Concurrent**
- Infuse Normal Saline 2000mL with KCL 20-40mEq/L and Mannitol 16G/L (dispensed in 2 x 1000mL bags) over 24 hours through a Y-tubing connection with Cisplatin.

**Post**
- Day 2: After Cisplatin and Doxorubicin (second dose) completed, administer the following IV solutions:
  - Bag #1 Dextrose 5% IV solution with KCL 20mEq/L and Mannitol 16G/L at rate 200mL/hr for 5 hours.
  - Bag #2 Normal Saline IV solution with KCL 20mEq/L with MgSO4 2mmol/L and Calcium Gluconate 0.6mmol/L at 200mL/hr for 5 hours.
  - Bag #3 Dextrose 5% IV solution with KCL 20mEq/L and Mannitol 16G/L at rate 100mL/hr for 11 hours.
  - Day 3: If nausea and/or vomiting persists, continue IV infusion with 2/3 and 1/3 IV at rate 150mL/hr.

**TESTS:**

**Baseline Tests**
WBC HB PLT ANC Ca K Na Chloride Phosphate Mg Cr Urea T.Bili Albumin AST Urate LVEF

**Test Notes**
Baseline CBC,BUN, Cr, electrolytes, calcium, albumin, magnesium, LFTs, baseline ECG before first treatment

**Strick input and output every 6 hours**

**ANTIEMETIC PRE-CHEMO REGIMEN:**

**Level B/C**
Day 1-3
- Ondansetron 8mg PO/IV pre-chemo then q12h x 3 days
- Dexamethasone 8 mg PO/IV pre -chemo then q12h x 3 days
- Prochlorperazine 10 mg PO/IV q4h pm

**INPATIENT ANTIEMETICS:**
- Give Ondansetron and Dexamethasone pre chemo and then 8mg q12h x 3 days.

**TOXICITIES:**

**Hematologic**
1. If ANC < 1.5 x10⁹/L, or PLT < 100 x10⁹/L, HOLD dose for 1 week.

**SUGGESTED ACTION**

**Hepatic Dysfunction**
1. If T.Bili = 26-51umol/L, or AST = 60-180 IU/L, REDUCE Cisplatin to 50% dose and Doxorubicin to 75% dose.
2. If T.Bili = 52-85umol/L, or AST = >180 IU/L, REDUCE Cisplatin to 25% dose and Doxorubicin to 50% dose.
3. If T.Bili > 85umol/L, OMIT all drugs.

**Renal Failure**
1. If CrCl = 0.5-1.0mL/sec, or SrCr = 136-185umol/L, REDUCE Cisplatin to 50% dose.
2. If CrCl < 0.5mL/sec, or SrCr > 185umol/L, OMIT Cisplatin dose.

**CLINICAL MONITORING:**

- Baseline liver function tests. Clinical exam for symptoms of CHF.
- Baseline and periodic cardiac test for all patients with cardiac risk factors or patients at or above the threshold dose levels.
- Cardiac:
  0. None
  1. None
  2. Asymptomatic, resting ejection fraction decline by > 10% baseline; or abnormal cardiac function test ( LVEF > 50 ) with no baseline for comparison
  3. Mild Congestive Heart Failure, responds to therapy
  4. Severe/ refractory Congestive Heart Failure

**At cumulative dose threshold and subsequent intervals**
For Cardiac Toxicity Rating :
- First rating at the cumulative dose threshold of 450mg/m², and repeat rating at each cumulative dose increment of 100mg/m² above threshold.

**FORMULAE:**

CrCl - Cockcroft & Gault (mL/sec)
- Male: [140-age(yrs)] x TBW(Kg) / [50 x SCR(umol/L)]
- Female: [140-age(yrs)] x TBW(Kg) / [50 x SCR(umol/L)] x 0.85

**Date revised:** 02/14/2005
## HIGH DOSE METHOTREXATE Chemotherapy

**Osteogenic Sarcoma, Advanced - Palliative Intent**

### METHOTREXATE
- **Dosage:** 8-12G/m² IV Day 1
- **Admix:** Methotrexate in **1000mL 5% Dextrose** with Sodium Bicarbonate 1 amp (50mEq).
  - **Infuse:** over 4 hours.

### LEUCOVORIN
- **Dosage:** 20 mg IV q6h
- **Leucovorin (Folinic Acid):** q6h exactly 24 hours after Methotrexate commenced and continue until Methotrexate level < 0.05umol/L. (May require up to 72 hours.)

### LORAZEPAM
- **Dosage:** 1mg SL tid prn

### HYDRATION:
- **Pre:**
  - IV fluid 2/3 and 1/3 with 100mEq Sodium Bicarbonate per litre at rate 250mL/hr, starting 4-6 hours prior to Methotrexate.
  - Check urine pH q3h after first litre IV through. Give Methotrexate when urine pH > 7.4. Measure in and out Q4H.
- **Post:**
  - After completion of Methotrexate, continue alkalinizing regimen with IV 2/3 and 1/3 solution and Sodium Bicarbonate 100mEq per litre at rate 250mL/hr for 4 hours, then change rate to 150mL/hr.
  - Maintain urine output at 120mL/hr; if urine output < 120mL/hr, increase IV rate to 200mL/hr.

### TESTS:
**Baseline Tests**
- WBC HB PLT ANC Ca K Na Chloride Phosphate Mg Cr Albumin AST
**Test Notes**
- Baseline and pretreatment: CBC & diff, BUN, PLT, Cr, electrolytes, albumin, AST, T.Bili, urine pH.
- Daily: CBC, BUN, Cr, electrolytes, calcium, magnesium, albumin.
- Methotrexate level with daily blood work beginning 24, 48 & 72 hours after medication commenced.

### ANTIEMETIC PRE-CHEMO REGIMEN:
- **Level A**
  - Start day 1 Prochlorperazine 10mg PO/IV q4h prn

### INPATIENT ANTIEMETICS:
- Give Prochlorperazine 10mg PO/IV q4h prn

### ANCILLARY:
- Observe skin colour and condition, especially around pressure points, for 5 days after each dose.

### TOXICITIES:
**Hematologic**
1. If ANC < 1.5 x 10⁹/L, or PLT< 100 x 10⁹/L, HOLD dose for 1 week.

**Hepatic Dysfunction**
1. If T.Bili = 52-85umol/L, or AST > 180 IU/L, REDUCE Methotrexate to 75% dose.

**Renal Failure**
1. If CrCl = 0.2-0.8mL/sec, or SrCr = 100-180umol/L, GIVE 50% of Methotrexate dose.

**Pulmonary**
1. Pulmonary toxicity - pneumonitis, pulmonary infiltrates.

### CLINICAL MONITORING:
- Monitor renal & hepatic function test and serum electrolytes before and during treatment.
- Monitor input and output of fluids and urine. Daily auscultation of the chest for 1-2 days after each dose; chest X-ray if necessary to rule out effusion.

### FORMULAE:
- **CrCl - Cockcroft & Gault (mL/sec)**
  - Male: \([140\text{-age(yrs)}] \times \text{TBW(Kg)} / [50 \times \text{SCr(umol/L)}]\)
  - Female: \([140\text{-age(yrs)}] \times \text{TBW(Kg)} / [50 \times \text{SCr(umol/L)} \times 0.85]\)

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**CCO Eligibility Form Required** ☐ **Non-Formulary Form Required** ☐

**Date revised:** 03/07/2005
**SUNITINAB Therapy**

*Gastrointestinal Stromal Tumour (GIST) after failure of Imatinib (Gleevec) treatment due to resistance or intolerance.*

**SUNITINIB**

<table>
<thead>
<tr>
<th>50mg</th>
<th>PO</th>
<th>Day 1</th>
<th>12.5mg</th>
</tr>
</thead>
</table>

- Sunitinib is taken orally 50mg **once daily** for 4 weeks followed by 2 weeks rest.
- May be given with or without food but should not be given with grapefruits or grapefruit juice.

**Alternate Dosing:**

- If patient shows rapid progression during the 2 week break then Sunitinib may be given as 37.5mg once daily continuously.
- Outpatient prescription available as 12.5mg, 25mg, and 50mg capsules.
- Trade name is Sutent™

**CONTINUOUS TREATMENT** until disease progression

**TESTS:**

- **Baseline Tests:** WBC HB PLT ANC Ca K Na Chloride Phosphate Mg Cr Urea T.Bili Albumin AST ALT GGT AlkPhosphatase Urate LVEF

- **Day 1 Tests:** WBC HB PLT ANC Cr Urea T.Bili ALT

**Test Notes:**

- Blood pressure monitoring every 2 weeks for first several cycles.
- MUGA scan or echocardiogram if clinically indicated or if history of cardiac problems.
- Thyroid function test if patients develop symptoms suggestive of hypothyroidism.
- Clinical toxicity assessments (including bleeding, congestive heart failure, adrenal insufficiency and pancreatitis).
- Sunitinib has not been studied in patient with hepatic or renal impairment.

**TOXICITIES:**

**Hematologic**

1. If ANC < 1.0 x 10^9/L, or if PLT < 75 x 10^9/L, **HOLD** Sunitinib dose for 1 week.

**SUGGESTED ACTION**

**CLINICAL MONITORING:**

**Hand-Foot Skin Reaction**

1. Minimal skin changes or dermatitis (e.g., erythema) without pain. 2. Skin changes (e.g., peeling, blisters, bleeding, edema) or pain, not interfering with function. 3. Ulcerative dermatitis or skin changes with pain interfering with function.

**RATED AT EACH CLINIC VISIT**

**INTERNAL CODE:**

OPIS CODES:

- SUNIT

**REFERENCES:**

- Sunitinib™ current product monograph, Pfizer Canada Inc.

**CCO Eligibility Form Required**

**Non-Formulary Form Required**

**Date revised:** 05/28/2008

*SA- SUNIT*  
*Sarcoma*  
*Ivory STR*
VINCRISEINE-DACTINOMYCIN-CYCLOPHOSPHAMIDE
Chemotherapy
Rhabdomyosarcoma

DACTINOMYCIN 0.4mg/m² IV Weekly x 6 Round to nearest 0.1mg
- Slow push through sidearm of free flowing IV

VINCRISTINE 1.5mg/m² IV Weekly x 6, then every 2 weeks x 3 Round to nearest 0.1mg
- Mix in 50mL bag Normal Saline; infuse over 10 minutes.
- Maximum dose = 2mg

CYCLOPHOSPHAMIDE 300mg/m² IV Weekly x 6, then every 2 weeks x 3 Round to nearest 10mg
- Mix in 250mL bag Normal Saline; infuse over 20 minutes
- Maximum dose = 2mg

TESTS:
Baseline Tests WBC HB PLT ANC Cr Urea 24Hr CrCl T.Bili Albumin AST ALT AlkPhosphatase
Every 6 weeks WBC HB PLT ANC Cr Urea 24Hr CrCl T.Bili Albumin AST ALT AlkPhosphatase
Weekly WBC HB PLT ANC

ANTIEMETIC PRE-CHEMO REGIMEN:
Level C Day 1 (each week) - Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
- Dexamethasone 20mg PO/IV

ANTIEMETIC TAKE-HOME REGIMEN:
Level B/C Day 1 (each week) - Ondansetron 8mg PO BID for 2-3 days, or
- Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days
- Dexamethasone 8mg PO BID for 2-3 days
- Prochlorperazine 10mg PO q4-6h prn

PATIENT VISITS and APPOINTMENT TYPE:
 Day 1 (Weekly): 45min Type B

ANCILLARY:
- Oral hydration is strongly encouraged; poorly hydrated patients may need more IV hydration to prevent renal toxicity.

TOXICITIES:
Hematologic
1. If ANC < 1.5 x 10⁹/L, or if PLT < 100 x 10⁹/L, HOLD dose for 1 week.

Hepatic Dysfunction
1. If T.Bili = 25-50umol/L, or AST = 60-180 IU/L, REDUCE Vincristine to 50% dose.
2. If T.Bili = 51-85umol/L, or AST > 180 IU/L, REDUCE Cyclophosphamide to 75% dose and Vincristine to 25% dose.
3. If T.Bili > 85umol/L, OMIT all drugs.

Neurologic
1. If Neurotoxicity > Grade 2, HOLD Vincristine dose for 1 week or until resolved.
2. If severe paresthesia or foot drop, REDUCE Vincristine to 50% dose.

CLINICAL MONITORING:
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.
- Urinalysis (RBCs) & cystitis toxicity ratings- ONLY in response to patient complaint.

Sensory
1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function 2.
2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL 3.
3. Sensory alteration or paresthesia interfering with ADL 4.
4. Sensory alteration or paresthesia interfering with ADL 5. Death

Constipation
1. Occasional or intermittent symptoms; occasional use of stool softeners, laxatives, dietary modification, or enema
2. Persistent symptoms with regular use of laxatives or enemas indicated 3. Symptoms interfering with ADL
3. Obstipation with manual evacuation indicated 4. Life-threatening consequences (e.g., obstruction, toxic megacolon)
4. Death

RATED AT EACH VISIT

INTERNAL CODE:
- VAC WEEKS 1-6
- VAC WEEKS 8,10 + 12

REFERENCES:
### Sarcoma: Vincristine-Dactinomycin-Cyclophosphamide Chemotherapy-high dose

**SA-VAC-HIGH DOSE**  
**Green STR**

#### High Dose

**VINCRISTINE**  
1.5mg/m² IV Day 1  
- Mix in 50mL bag Normal Saline; infuse over 10 minutes.  
- Maximum dose = 2mg

**DACTINOMYCIN**  
0.045mg/kg (max 2.5mg) IV Day 1  
- Maximum dose = 2.5mg  
- Admix in 50mL Normal Saline and infuse over 10-15 minutes.  
- UV protective bag required.

**CYCLOPHOSPHAMIDE**  
1100mg/m² IV Days 1 & 2  
- Admix along with Mesna 360mg/m² in 500mL bag 5% Dextrose, and infuse over 1 hour.

**MESNA**  
360mg/m² IV Days 1 & 2  
- Admix along with Cyclophosphamide 1100mg/m² in 500mL bag 5% Dextrose and infuse over 1 hour.

**MESNA (ORAL)**  
500mg/m² PO Days 1 & 2  
- Give at 2hr and 6hr after Cyclophosphamide infusion daily.  
- IV Mesna may be taken ORALLY, diluted in juice, milk or carbonated beverage (Dispense in glass amber jars for oral use; stability of 8 days at room temperature).  
- Drink the Mesna dose by itself (preferable cold to minimize unpleasant taste) or dissolved with 15mL of desired liquid listed above, follow IMMEDIATELY by a glassful of the desired liquid.  
- May take Prochlorperazine 10mg tablet 30 minutes before oral Mesna dose to prevent nausea and vomiting.

#### Tests:

**Baseline Tests**  
- WBC  
- HB  
- PLT  
- ANC  
- Ca  
- K  
- Na  
- Chloride  
- Phosphate  
- Mg  
- Cr  
- Urea  
- T.Bili  
- Albumin  
- AST  
- ALT  
- AlkPhosphatase

**Day 1**  
- WBC  
- HB  
- PLT  
- ANC  
- Ca  
- K  
- Na  
- Chloride  
- Phosphate  
- Cr  
- Urea

**Test Notes**  
- Baseline CBC, BUN, Cr, electrolytes, calcium, magnesium, albumin, LFTs.

#### Antiemetic Pre-Chemo Regimen:

**Level C**  
- Day 1 & 2  
  - Granisetron 1mg IV  
  - Dexamethasone 20mg IV

#### Antiemetic Take-home Regimen:

**Level B/C**  
- Day 1  
  - Granisetron 1mg PO the evening of chemo (Day 1-2) and Q12H for 3 days after chemotherapy.  
  - Dexamethasone 8mg PO BID for 3 days after chemotherapy.  
  - Prochlorperazine 10mg PO q4-6h pm and 30 minutes prior to oral Mesna dose.

#### PATIENT VISITS and APPOINTMENT TYPE:

- Day 1  
  1 hour and 45 min  
  Type C

- Day 2  
  1 hour and 15 min  
  Type B

#### Ancillary:

- PORT or PICC line is recommended.
- Oral hydration is strongly encouraged; poorly hydrated patients may need more IV hydration to prevent renal toxicity.

#### Toxicities:

**Hematologic**
1. If ANC < 1.5 x 10^9/L, or if PLT < 100 x 10^9/L, HOLD dose for 1 week.

**Hepatic Dysfunction**
1. If T.Bili = 25-50umol/L, or AST = 60-180 IU/L, REDUCE Vincristine to 50% dose.  
2. If T.Bili = 51-85umol/L, or AST > 180 IU/L, REDUCE Cyclophosphamide to 75% dose and Vincristine to 25% dose.  
3. If T.Bili > 85umol/L, OMIT all drugs.

**Neurologic**
1. If Neurotoxicity > Grade 2, HOLD Vincristine dose for 1 week or until resolved.  
2. If severe paresthesia or foot drop, REDUCE Vincristine to 50% dose.

**Renal Failure**
1. If CrCl < 0.2mL/sec, OMIT Cyclophosphamide dose.

#### Suggested Action

RePEAT CYCLE EVERY 21 DAYS
SA - VAC-HIGH DOSE

Sarcoma

VINCRISTINE-DACTINOMYCIN-CYCLOPHOSPHAMIDE
Chemotherapy-high dose

CLINICAL MONITORING:
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.
- Urinalysis (RBCs) & cystitis toxicity ratings - ONLY in response to patient complaint.

Mucositis
1. Erythema of the mucosa
2. Patchy ulcerations or pseudomembranes
3. Confluent ulcerations or pseudomembranes; bleeding with minor trauma
4. Tissue necrosis; significant spontaneous bleeding; life-threatening consequences
5. Death

Cystitis
1. Asymptomatic
2. Frequency with dysuria; macroscopic hematuria
3. Transfusion; IV pain medications; bladder irritation indicated
4. Catastrophic bleeding; major non-elective intervention indicated
5. Death

Sensory
1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function
2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL
3. Sensory alteration or paresthesia interfering with ADL
4. Disabling
5. Death

Constipation
1. Occasional or intermittent symptoms; occasional use of stool softeners, laxatives, dietary modification, or enema
2. Persistent symptoms with regular use of laxatives or enemas indicated
3. Symptoms interfering with ADL; obstipation with manual evacuation indicated
4. Life-threatening consequences (e.g., obstruction, toxic megacolon)
5. Death

RATED AT EACH CLINIC VISIT

FORMULAE:

\[
\text{CrCl} = \frac{(140 - \text{age (yrs)}) \times \text{TBW (Kg)}}{50 \times \text{SCr (umol/L)}}
\]

Male: \[\frac{(140 - \text{age (yrs)}) \times \text{TBW (Kg)}}{50 \times \text{SCr (umol/L)}}\]

Female: \[\frac{(140 - \text{age (yrs)}) \times \text{TBW (Kg)}}{50 \times \text{SCr (umol/L)}} \times 0.85\]

INTERNAL CODE:
OPIS CODE: VAC-HIGH DOSE

REFERENCES:

Date revised: 04/30/2008

CCO Eligibility Form Required □ Non-Formulary Form Required □
SA  VDC

Sarcoma

VINCRISTINE-DOxorubicin-CYCLOPHosphamide

Chemotherapy

Ewing’s Sarcoma / Peripheral Neuroectodermal Tumour (PNET) / Small Round Blue Cell Tumour - adjuvant/palliative

VINCRISTINE 1.5mg/m² IV Day 1 Round to nearest 0.1mg
- Mix in 50mL bag Normal Saline; infuse over 10 minutes.
- Maximum dose = 2mg

DOxorubicin 75mg/m² IV Day 1 Round to nearest 1mg
- Slow push through sidearm of free flowing IV. Give 2 to 4mg (1-2mL) per minute.

CYCLOPHosphamide 1200mg/m² IV Day 1 Round to nearest 10 mg
- Mix in 500mL bag Normal Saline. Infuse over 1 hour.

REPEAT CYCLE EVERY 21 DAYS

HYDRATION:
Pre
- Infuse 500mL Normal Saline IV over 1 hour.

TESTS:
Baseline Tests: WBC HB PLT ANC Ca K Na Chloride Glucose Cr Urea T.Bili Albumin AST ALT GGT AlkPhosphatase LVEF
Day 1 WBC HB PLT ANC
Test Notes - Additional Baseline tests: LDH, CO₂ & LVEF (ordered only on specific patients).
- Chemistry repeated if baseline abnormal.
- Consider monitoring LFT after 3 cycles.

ANTIEMETIC PRE-CHEMO REGIMEN:
Level C Days 1
- Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
- Dexamethasone 20mg PO/IV

ANTIEMETIC TAKE-HOME REGIMEN:
Level B/C Day 1
- Ondansetron 8mg PO BID for 2-3 days, or
- Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days
- Dexamethasone 8mg PO BID for 2-3 days
- Prochlorperazine 10mg PO q4-6h pm

PATIENT VISITS and APPOINTMENT TYPE:
Day 1 3 hours Type D

ANCILLARY:
- Oral hydration is strongly encouraged; poorly hydrated patients may need more IV hydration (to prevent renal toxicity).

TOXICITIES:

Hematologic
1. If ANC < 1.5 x 10⁹/L, or PLT < 100 x 10⁹/L, HOLD dose for 1 week (Until AGC > 1.5 x 10⁹/L).

Hepatic Dysfunction
1. If T.Bili = 26-51umol/L, or AST = 60-180 IU/L, REDUCE Vincristine to 50% dose and Doxorubicin to 75% dose.
2. If T.Bili = 52-85umol/L, or AST > 180 IU/L, REDUCE Vincristine to 25% dose, Doxorubicin to 50% dose and Cyclophosphamide to 75% dose.
3. If T.Bili > 85 umol/L, OMIT all drugs.

Renal Failure
1. If SrCr > 265umol/L, REDUCE Doxorubicin to 50% dose.
2. If CrCl < 0.2mL/sec, OMIT Cyclophosphamide dose.

Neurologic
1. If Neurotoxicity > Grade 2, HOLD Vincristine dose for 1 week or until resolved.
2. If severe paresthesia or foot drop, REDUCE Vincristine to 50% dose.

SUGGESTED ACTION
VINCRISTINE-DOXORUBICIN-CYCLOPHOSPHAMIDE
Chemotherapy

CLINICAL MONITORING:
- Urinalysis (RBCs) periodic and in response to patient complaint.
- Clinical exam for symptoms of CHF.
- Periodic cardiac tests for all patients with cardiac risk factors or patients at or above the threshold dose levels (Doxorubicin 450mg/m²).

Cardiac
0. None
1. None
2. Asymptomatic, resting ejection fraction decline by >10% baseline; or abnormal cardiac function test (LVEF > 50) with no baseline for comparison
3. Mild Congestive Heart Failure, responds to therapy
4. Severe/Refractory Congestive Heart Failure

At cumulative dose threshold and subsequent intervals
For Cardiac Toxicity Ratings:
First rating at the cumulative dose threshold of 450mg/m², and repeat ratings at each cumulative dose increment of 100mg/m² above threshold. (Cumulative dose sooner for high risk patients, eg. pre-existing cardiac disease, prior chest irradiation).
- Note: Threshold Cumulative dose reduced proportionately if other anthracycline or anthracenedione drugs have been given; cardiotoxicity is additive.

Sensory
1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function
2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL
3. Sensory alteration or paresthesia interfering with ADL
4. Disabling
5. Death

Constipation
1. Occasional or intermittent symptoms; occasional use of stool softeners, laxatives, dietary modification, or enema
2. Persistent symptoms with regular use of laxatives or enemas indicated
3. Symptoms interfering with ADL; obstipation with manual evacuation indicated
4. Life-threatening consequences (e.g., obstruction, toxic megacolon)
5. Death

RATED AT EACH CLINIC VISIT

INTERNAL CODE:
OPIS CODE: VDC

REFERENCES:
- BCCA Protocol Summary for Vincristine, Doxorubicin and Cyclophosphamide combination for patients with newly diagnosed Ewing’s sarcoma/ peripheral neuroectodermal tumour (PNET) and rhabdomyosarcoma with pelvic primaries or chemotherapy induced hematuria

Date revised: 08/29/2008
SA-VINBLAST

VINBLASTINE Chemotherapy
Kaposi’s Sarcoma - Palliative Intent

VINBLASTINE 5mg/m² IV Day 1 Round to nearest 0.1mg
- Quick push through sidearm of free flowing IV (5% Dextrose, Normal Saline); Inject over 1 minute.

REPEAT EVERY 7 (OR 14) DAYS

TESTS:
Baseline Tests WBC HB PLT ANC T.Bili Albumin AST ALT AlkPhosphatase
Day 1 WBC HB PLT ANC T.Bili Albumin AST ALT AlkPhosphatase
Test Notes Day 1 chemistry only if clinically indicated.

ANTIEMETIC PRE-CHEMO REGIMEN:
Level A Day 1 - Prochlorperazine 10mg PO pm

ANTIEMETIC TAKE-HOME REGIMEN:
Level A Day 1 - Prochlorperazine 10mg PO q4-6h pm

PATIENT VISITS and APPOINTMENT TYPE:
→ Day 1 15min Type A

TOXICITIES:
Hematologic
1. If ANC < 1.6 x 10⁹/L, or if PLT < 125 x 10⁹/L, give 50% dose of Vinblastine.
2. If ANC < 0.8 x 10⁹/L, or if PLT < 75 x 10⁹/L, HOLD dose for 1 week.

Hepatic Dysfunction
1. If T.Bili = 25-50umol/L, or AST = 60-180 IU/L, REDUCE to 50% dose.
2. If AST > 180 IU/L, REDUCE to 25% dose.

Neurologic
1. If Neurotoxicity > Grade 2, HOLD dose for 1 week or until resolved.
2. If severe paresthesia or foot drop, REDUCE to 50% dose.

CLINICAL MONITORING:
Sensory
1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function 2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL 3. Sensory alteration or paresthesia interfering with ADL 4. Disabling 5. Death
RATED AT EACH CLINIC VISIT

REFERENCES:

CCO Eligibility Form Required ☐ Non-Formulary Form Required ☐ Date revised: 03/07/2005
**SA-VINB-MTX**

**Green STR**

**Sarcoma**

**VINBLASTINE-METHOTREXATE Chemotherapy**

*Aggressive Fibromatosis (Desmoid Tumours)*

**METHOTREXATE**

30mg/m² IV Day 1 Round to nearest 5mg

- Maximum dose of 50mg
- **Inject by direct IV push**, followed by a Normal Saline flush (if no IV line has been set up).
- May give by slow push through sidearm of free flowing IV (D5W, Normal Saline).
- Rate of administration < 10mg per minute.
- Doses > 100mg, mix in 50-100mL Normal Saline and infuse over 30-60 minutes.

**VINBLASTINE**

6mg/m² IV Day 1 Round to nearest 0.1mg

- Maximum dose of 10mg
- **Slow push through sidearm of free flowing IV**: Inject over 1 minute.

**TESTS:**

<table>
<thead>
<tr>
<th>Baseline Tests</th>
<th>WBC HB PLT ANC Cr Urea T.Bili AST ALT GGT AlkPhosphatase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Test Notes</td>
<td>- Cr, BUN &amp; LFTs pm</td>
</tr>
</tbody>
</table>

**ANTIEMETIC PRE-CHEMO REGIMEN:**

**Level A**  
Day 1 - Prochlorperazine 10mg PO pm

**ANTIEMETIC TAKE-HOME REGIMEN:**

**Level A**  
Day 1 - Prochlorperazine 10mg PO q4-6h pm

**PATIENT VISITS and APPOINTMENT TYPE:**

› Day 1: 30min Type B

**TOXICITIES:**

**Hematologic**

1. If ANC < 1.5 x 10⁹/L, or if PLT < 100 x 10⁹/L, **HOLD** dose for 1 week.

**Renal Failure**

1. If CrCl = 0.2-0.8mL/sec, or SrCr = 100-180umol/L, **GIVE 50%** of Methotrexate dose.
2. If CrCl < 0.2mL/sec, or SrCr > 180umol/L, **OMIT** Methotrexate dose.

**Hepatic Dysfunction**

1. If T.Bili = 26-51umol/L, or AST = 60-180 IU/L, **REDUCE** Vinblastine to 50% dose.
2. If T.Bili = 52-85umol/L, or AST > 180 IU/L, **REDUCE** Methotrexate to 75% dose and Vinblastine to 25% dose.
3. If T.Bili > 85umol/L, **OMIT** Methotrexate and Vinblastine doses.

**SUGGESTED ACTION**

**CLINICAL MONITORING:**

- Neurologic toxicity ratings (Sensory, Constipation) at each visit.

**Sensory**

1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function 2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL 3. Sensory alteration or paresthesia interfering with ADL 4. **Disabling** 5. Death

**Constipation**

1. Occasionally or intermittent symptoms; occasional use of stool softeners, laxatives, dietary modification, or enema 2. Persistent symptoms with regular use of laxatives or enemas indicated 3. Symptoms interfering with ADL; obstipation with manual evacuation indicated 4. **Life-threatening consequences** (e.g., obstruction, toxic megacolon) 5. Death

**RATED AT EACH CLINIC VISIT**

**INTERNAL CODE:**

OPIS CODE: VINB-MTX SA

**REFERENCES:**


**CCO Eligibility Form Required**

**Non-Formulary Form Required**

**Date revised:** 03/07/2005

*SA*
SA-VINOR-METH

Sarcoma

VINORELBINE-METHOTREXATE Chemotherapy
Agressive Fibromatosis (Desmoid Tumours)

**METHOTREXATE**
20-25mg/m² IV Day 1,8 &15 Round to nearest 5mg
- Maximum dose of 50mg
- **Inject by direct IV push**, followed by a Normal Saline flush (if no IV line has been set up).
- May give by slow push through sidearm of free flowing IV (D5W, Normal Saline).
- Rate of administration < 10mg per minute.
- Doses > 100mg, mix in 50-100mL Normal Saline and infuse over 30-60 minutes.

**VINORELBINE**
20-25mg/m² IV Day 1,8 &15 Round to nearest 1mg
- Add to 50mL Normal Saline minibag.
- Infuse over **6-10 minutes** into the sidearm of a free-flowing IV line.
- Flush IV line with at least 100mL Normal Saline or 5% Dextrose.
- Hydrocortisone 100mg IV may be given if patient experiences pain on administration.
- Acute pain syndrome at the tumour site can be managed with nonsteroidal anti-inflammatory drugs or corticosteroids.
- If extravasation occurs during administration, discontinue immediately and infuse the remaining dose through another IV site (into another vein).

**REPEAT EVERY 28 DAYS**

**TESTS:**
Baseline Tests  WBC  HB  PLT  ANC  Cr  Urea  T.Bili  AST  ALT  GGT  AlkPhosphatase
Day 1  WBC  HB  PLT  ANC  Cr  Urea
Test Notes  - Cr, BUN & LFTs prn

**ANTIEMETIC PRE-CHEMO REGIMEN:**
Level A  Day 1,8 &15 - Prochlorperazine 10mg PO pm

**ANTIEMETIC TAKE-HOME REGIMEN:**
Level A  Day 1,8 & 15 - Prochlorperazine 10mg PO q4-6h pm

**PATIENT VISITS and APPOINTMENT TYPE:**
- Day 1,8 & 15  30min  Type B

**TOXICITIES:**
Hematologic
1. If ANC < 1.5 x 10⁹/L, or if PLT< 100 x 10⁹/L, HOLD dose for 1 week.

Renal Failure
1. If CrCl = 0.2-0.8mL/sec, or SrCr = 100-180umol/L, GIVE 50% of Methotrexate dose.
2. If CrCl < 0.2mL/sec, or SrCr > 180umol/L, OMIT Methotrexate dose.

Hepatic Dysfunction
1. If T.Bili 1-2xULN, REDUCE Vinorelbine to 75% dose.
2. If T.Bili 2-3xULN, REDUCE Methotrexate to 50% dose.
3. If T.Bili >3xULN, OMIT Methotrexate.
4. If T.Bili >4xULN, OMIT Vinorelbine.

**SUGGESTED ACTION**

**CLINICAL MONITORING:**
- Neurologic toxicity ratings (Sensory, Constipation) at each visit.
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.

Sensory
1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function
2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL
3. Sensory alteration or paresthesia interfering with ADL
4. Disabling
5. Death

Constipation
1. Occasional or intermittent symptoms; occasional use of stool softeners, laxatives, dietary modification, or enema
2. Persistent symptoms with regular use of laxatives or enemas indicated
3. Symptoms interfering with ADL; obstipation with manual evacuation indicated
4. Life-threatening consequences (e.g., obstruction, toxic megacolon)
5. Death

Mucositis
1. Erythema of the mucosa
2. Patchy ulcerations or pseudomembranes
3. Confluent ulcerations or pseudomembranes; bleeding with minor trauma
4. Tissue necrosis; significant spontaneous bleeding; life-threatening consequences
5. Death

**RATED AT EACH CLINIC VISIT**

**INTERNAL CODE:**
OPIS CODE: VINOR-METH SA

**REFERENCES:**

CCO Eligibility Form Required  [ ]  Non-Formulary Form Required  [x]  Date revised: 01/12/2009

Sarcoma
Zoledronic Acid Therapy

Giant Cell Tumour

Zoledronic Acid 3-4mg IV Day 1
- Mix in 100mL bag 5% Dextrose or Normal Saline.
- Infuse over a minimum of 15 minutes.
- Serum creatinine should be measured before each dose.

Dosing for mild to moderate renal impairment:
1. If baseline CrCl > 60mL/min, give 4mg dose.
2. If baseline CrCl 50-60mL/min, give 3.5mg dose.
3. If baseline CrCl 40-49mL/min, give 3.3mg dose.
4. If baseline CrCl 30-39mL/min, give 3mg dose.
- Do not mix with Calcium-containing infusion solutions eg. Lactated Ringer’s solution.

REPEAT EVERY 21-28 DAYS for 3 doses after surgery
(May have 2 doses before surgery)

Tests:
Baseline Tests WBC HB PLT ANC Ca K Na Chloride Cr Urea Albumin
Day 1 WBC HB PLT ANC Ca K Na Chloride Cr Urea Albumin

Patient Visits and Appointment Type:
Day 1: 15min Type A

Toxicities:
Renal Failure
- During treatment, serum creatinine should be measured before each dose and treatment should be withheld for renal deterioration.

In the clinical studies, renal deterioration was defined as follows:
- For patients with normal baseline creatinine (< 123umol/L), an increase of 44umol/L.
- For patients with abnormal baseline creatinine (> 123umol/L), an increase of 88umol/L.
- In the clinical studies, treatment was resumed at the same dose when the creatinine level returned to within 10% of the baseline value.

Suggested Action

Formulæ:

CrCl - Cockcroft & Gault (mL/sec)
Male: \[140 - \text{age(yrs)}\] x TBW(Kg) / [50 x SCr(umol/L)]
CrCl - Cockcroft & Gault (mL/sec)
Female: \[140 - \text{age(yrs)}\] x TBW(Kg) / [50 x SCr(umol/L)] \times 0.85
Creatinine CI (mL/min)
\[\text{mL/min} = 60 \times \text{CrCl mL/sec}\]
Corrected Serum Calcium (mmol/L)
\[
\text{Measured Serum Calcium} + \left(\frac{40 - \text{serum albumin}}{x} \times 0.02\right)
\]

Internal Code:
OPIS Code: Zoled Acid

References:

CCO Eligibility Form Required [ ] Non-Formulary Form Required [x] Date revised: 03/30/2009
CISPLATIN-ETOPOSIDE-BLEOMYCIN (PEB) Chemotherapy
Cancer of Unknown Origin- Suspect Germ Cell

**CISPLATIN**
20mg/m² IV Days 1-5 Round to nearest 1mg
- Admix in 250mL bag Normal Saline; Infuse over 30-60 minutes.

**ETOPOSIDE**
100mg/m² IV Days 1-5 Round to nearest 10mg
- Dose ≤ 200mg, mix in 500mL Normal Saline; Infuse over 30-60 minutes.
- Dose > 200mg, mix in 1000mL Normal Saline; Infuse over 1 to 2 hours.
- Use Non-PVC equipment and filter.
- Adjust rate if blood pressure drops.
- Give Etoposide BEFORE Cisplatin, to hydrate patient.

**BLEOMYCIN**
30units IV Days 1, 8 & 15 Round to nearest 1 unit
- Slow push through sidearm of free flowing IV over 10 minutes.
- May be given by direct IV push, followed by a Normal Saline flush.

**ACETAMINOPHEN**
650mg IV Days 1, 8 & 15 325mg tablet
- Administer before Bleomycin dose.

**HYDRATION:**
- Pre Infuse 1000mL Normal Saline with 20mEq Potassium Chloride IV over 1 hour on Days 1-5.
- Post Infuse 1000mL Normal Saline IV over 1-2 hours on Days 1-5.

**TESTS:**
Baseline Tests
WBC HB PLT ANC K Na Chloride Cr Urea

**ANTIEMETIC PRE-CHEMO REGIMEN:**
- Level C
  Days 1-5
  - Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
  - Dexamethasone 20mg PO/IV
- Level A
  Days 8 & 15
  - Prochlorperazine 10mg PO pm

**ANTIEMETIC TAKE-HOME REGIMEN:**
- Level B/C
  Day 5
  - Ondansetron 8mg PO BID for 2-3 days, or
  Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days
  - Dexamethasone 8mg PO BID for 2-3 days
  - Prochlorperazine 10mg PO q4-6h pm
  - Prochlorperazine 10mg PO q4-6h pm
- Level A
  Days 8 & 15
  - Prochlorperazine 10mg PO q4-6h pm

**PATIENT VISITS and APPOINTMENT TYPE:**
- Days 1-5 3hrs Type C
- Days 8 & 15: 30min Type A

**ANCILLARY:**
- Increase fluids if poor oral intake.
- Adjust rate of Etoposide infusion if blood pressure drops

**TOXICITIES:**
**Hematologic**
1. If ANC < 1.5 x 10⁹/L, or if PLT < 75 x 10⁹/L, HOLD dose for 1 week.

**Renal Failure**
1. If CrCl = 0.5-1.0mL/sec, or SrCr = 136-185umol/L, REDUCE Cisplatin to 50% dose and Bleomycin and Etoposide to 75% dose.
2. If CrCl < 0.5mL/sec, or SrCr > 185umol/L, OMIT Cisplatin dose.
3. If CrCl < 0.2mL/sec, REDUCE Bleomycin and Etoposide to 50% dose.

**Hepatic Dysfunction**
1. If T.Bili = 26-51umol/L, or AST = 60-180 IU/L, REDUCE Etoposide 25%.
2. If T.Bili > 52-85umol/L, REDUCE Etoposide to 50% dose.
3. If T.Bili > 85umol/L, or AST > 180 IU/L, OMIT Etoposide dose.

**SUGGESTED ACTION**
CLINICAL MONITORING:
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.
- Baseline & routine renal function tests, especially if there are other concurrent nephrotoxic drugs.
- Clinical pulmonary exam, including auscultation, pulmonary toxicity ratings (Cough, SOB).

Sensory
1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function 2.
2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL 3. Sensory alteration or paresthesia interfering with ADL 4. Disabling 5. Death

Hearing
1. Asymptomatic, detected on exam/testing only 2. Symptomatic, not interfering with ADL
3. Symptomatic, interfering with ADL 4. Life-threatening; disabling 5. Death

Dyspnea
1. Dyspnea on exertion, but can walk 1 flight of stairs without stopping 2. Dyspnea on exertion but unable to walk 1 flight of stairs or 1 city block (0.1km) without stopping 3. Dyspnea with ADL 4. Dyspnea at rest; intubation/ventilator indicated 5. Death

Cough
1. Symptomatic, non-narcotic medication only indicated 2. Symptomatic and narcotic medication indicated 3. Symptomatic and significantly interfering with sleep or ADL

RATED AT EACH CLINIC VISIT

FORMULAE:
- CrCl - Cockcroft & Gault (mL/sec) Male: \(\frac{140-\text{age(yrs)}}{\text{TBW(Kg)}} \times \frac{50}{\text{SCr(umol/L)}}\)
- CrCl - Cockcroft & Gault (mL/sec) Female: \(\frac{140-\text{age(yrs)}}{\text{TBW(Kg)}} \times \frac{50}{\text{SCr(umol/L)}} \times 0.85\)

INTERNAL CODE:
- OPIS CODE: CEB (UNKNOWN)

| CCO Eligibility Form Required | Non-Formulary Form Required | Date revised: 06/04/2008 |
CISPLATIN-ETOPOSIDE Chemotherapy

**Cancer of Unknown Origin**

### CISPLATIN

- **25mg/m² IV Days 1-3**
- Round to nearest 1mg
- Admix in **250mL bag Normal Saline**.
- Infuse over **30-60 minutes**.
- May also admix 10G Mannitol (50mL of 20% solution or 100mL of 10% solution) with Cisplatin.

### ETOPOSIDE

- **100mg/m² IV Days 1-3**
- Round to nearest 10mg
- Dose ≤ 200mg, mix in **500mL Normal Saline**; Infuse over **30-60 minutes**.
- Dose > 200mg, mix in **1000mL Normal Saline**; Infuse over **1 to 2 hours**.
- Use Non-PVC equipment and filter.
- Adjust rate if blood pressure drops.
- Give Etoposide BEFORE Cisplatin, to hydrate patient.

**REPEAT EVERY 21 DAYS**

### TESTS:

<table>
<thead>
<tr>
<th>Baseline Tests</th>
<th>WBC HB PLT ANC K Na Chloride Cr Urea 24Hr CrCl T.Bili AST ALT GGT AlkPhosphatase</th>
</tr>
</thead>
</table>

**Day 1**

<table>
<thead>
<tr>
<th>Test Notes</th>
<th>WBC HB PLT ANC K Na Chloride Cr Urea</th>
</tr>
</thead>
</table>

**ANTIEMETIC PRE-CHEMO REGIMEN:**

- **Level C** Days 1-3
  - Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
  - Dexamethasone 20mg PO/IV

**ANTIEMETIC TAKE-HOME REGIMEN:**

- **Level B/C** Day 3
  - Ondansetron 8mg PO BID for 2-3 days, or Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days
  - Dexamethasone 8mg PO BID for 2-3 days
  - Prochlorperazine 10mg PO q4-6h prn

### PATIENT VISITS and APPOINTMENT TYPE:

- **Days 1-3 2hrs Type C**

### ANCILLARY:

- Oral hydration strongly encouraged; poorly hydrated patients may need more IV hydration (to prevent renal toxicity).
- Adjust Etoposide infusion rate if blood pressure drops.

### TOXICITIES:

#### Hematologic

1. If ANC < 1.5 x 10⁹/L, or if PLT < 100 x 10⁹/L, **HOLD** dose for 1 week.

2. If CrCl < 0.5-1.0mL/sec, or SrCr = 136-185umol/L, **REDUCE 50%** dose.

#### Renal Failure

1. If CrCl > 185umol/L, **OMIT** dose.

#### Hepatic Dysfunction

1. If T.Bili = 26-51umol/L, or AST = 60-180 IU/L, **REDUCE 50%** dose.

2. If T.Bili = 52-85umol/L, **REDUCE 25%** dose.

3. If T.Bili > 85umol/L, or AST > 180 IU/L, **OMIT** dose.

**SUGGESTED ACTION**

#### CLINICAL MONITORING:

- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.

#### Sensory

1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function
2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL
3. Sensory alteration or paresthesia interfering with ADL
4. Disabling
5. Death

#### Hearing

1. Asymptomatic, detected on exam/testing only
2. Symptomatic, not interfering with ADL
3. Symptomatic, interfering with ADL
4. Life-threatening; disabling
5. Death

**RATED AT EACH CLINIC VISIT**

**FORMULAE:**

- CrCl - Cockcroft & Gault (mL/sec) Male: [140-age(yrs)] x TBW(Kg) / [50 x SCr(umol/L)]
- CrCl - Cockcroft & Gault (mL/sec) Female: [140-age(yrs)] x TBW(Kg) / [50 x SCr(umol/L)] x 0.85

**INTERNAL CODE:**

- OPIS CODE: CISP-ETOP (UNKNOWN)

**CCO Eligibility Form Required** [ ] Non-Formulary Form Required [ ] Date revised: 06/04/2008
Low Dose 5-FLUOROURACIL-LEUCOVORIN
Cancer of Unknown Origin

**5-FLUOROURACIL**
400mg/m² IV Days 1-4 Round to nearest 25mg
- **Inject by direct IV push over 1-3 minutes**, followed by a Normal Saline flush.
- Patients are recommended to suck on ice chips about 5 minutes before treatment begins until 30 minutes after treatment is completed to reduce the incidence and severity of stomatitis.

**LEUCOVORIN**
20mg/m² IV Days 1-4 Round to nearest 1mg
- **Inject by direct IV push**, followed by a Normal Saline flush (if no IV line has been set up).
- May give by slow push through sidearm of free flowing IV (D5W, Normal Saline).
- Do not exceed 160mg/min.

**Tests:**
- Baseline Tests: WBC HB PLT ANC K Na Chloride Cr T.Bili AST ALT GGT AlkPhosphatase
- Day 1: WBC HB PLT ANC

**Antiemetic Pre-Chemo Regimen:**
- Level B: Days 1-4 - Dexamethasone 8mg PO/IV
  - May add/substitute Prochlorperazine 10mg PO/IV prn

**Antiemetic Take-Home Regimen:**
- Level A: Days 1-4 - Prochlorperazine 10mg PO q4-6h prn

**Patient Visits and Appointment Type:**
- Days 1-4: 15min Type A

**Ancillary:**
- Sucking ice chips during 5-Fluorouracil treatment is recommended to reduce mucositis following chemotherapy.

**Toxicities:**

**Hematologic**
1. If ANC < 1.5 x 10⁹/L, or if PLT < 100 x 10⁹/L, REDUCE to 50% dose.
2. If ANC < 1.0 x 10⁹/L, or if PLT < 75 x 10⁹/L, HOLD dose for 1 week.

**Hepatic Dysfunction**
1. If T.Bili > 85umol/L (marked hepatic dysfunction), OMIT dose.

**Gastrointestinal**
1. If Mucositis or diarrhea > Grade 3 in previous course, REDUCE to 2/3 dose.

**Suggested Action**

**Clinical Monitoring:**
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth.

**Diarrhea**
1. Increase of < 4 stools per day over baseline; mild increase in ostomy output compared to baseline
2. Increase of 4 - 6 stools per day over baseline; IV fluids indicated < 24hrs; moderate increase in ostomy output compared to baseline; not interfering with ADL
3. Increase of ≥ 7 stools per day over baseline; incontinence; IV fluids > 24 hrs; hospitalization; severe increase in ostomy output compared to baseline; interfering with ADL
4. Life-threatening consequences (e.g., hemodynamic collapse)
5. Death

**Mucositis**
1. Erythema of the mucosa
2. Patchy ulcerations or pseudomembranes
3. Confluent ulcerations or pseudomembranes; bleeding with minor trauma
4. Tissue necrosis; significant spontaneous bleeding; life-threatening consequences
5. Death

**Rated at Each Clinical Visit**

**CCO Eligibility Form Required** ☐ **Non-Formulary Form Required** ☐
**Date revised:** 06/04/2008
PACLITAXEL-CARBOPLATIN Chemotherapy
Primary Peritoneal/Ovarian Cancer

PACLITAXEL 175mg/m² IV Day 1 Round to nearest 3mg
- Mix in 500mL bag Normal Saline (dilution concentration 0.3-1.2 mg/mL).
- Use non-PVC equipment, including 0.22 micron in-line filter.
- Infuse over 3 hours, before Carboplatin.

DEXAMETHASONE 20mg PO Day 1 4mg tablet
- To be administered at home 12 and 6 hours before Paclitaxel (if not taken at home, Dexamethasone 20mg IV 30-60 minutes pre Paclitaxel).

DIPHENHYDRAMINE 50mg IV Day 1
- Admix in 50-100mL minibag 5% Dextrose or Normal Saline.
- Give over 10-15 minutes. (May be admixed with Ranitidine).
- Administer 30-60 minutes before Paclitaxel.

RANITIDINE 50mg IV Day 1
- Admix in 50-100mL minibag, 5% Dextrose or Normal Saline.
- Give over 10-15 minutes, (May be admixed with Diphenhydramine).
- Administer 30-60 minutes before Paclitaxel.

CARBOPLATIN AUC = 5 to 7.5 IV Day 1 Round to nearest 5mg
- Mix in 250mL 5% Dextrose.
- Infuse over 30 to 60 minutes, after Paclitaxel.

REPEAT EVERY 21 DAYS

TESTS:
Baseline Tests
Day 1
- WBC HB PLT ANC 24Hr CrCl T.Bili Albumin AST ALT GGT AlkPhosphatase
- Urea

Test Notes
- Additional Baseline tests: LDH & CO2

ANTIEMETIC PRE-CHEMO REGIMEN:
Level C
Day 1
- Ondansetron 8mg PO/IV or Granisetron 1mg PO/IV
- Dexamethasone 20mg PO/IV (if patient has not taken PO dexamethasone at home)

ANTIEMETIC TAKE-HOME REGIMEN:
Level B/C
Day 1
- Ondansetron 8mg PO BID for 2-3 days, or Granisetron 1mg PO 12 hours post chemotherapy, then 2mg PO OD for 2-3 days
- Dexamethasone 8mg PO BID for 2-3 days
- Prochlorperazine 10mg PO q4-6h prn

PATIENT VISITS and APPOINTMENT TYPE:
Day 1 6hrs Type D

ANCILLARY:
- Take a baseline blood pressure measurement, if prior hypotension.

TOXICITIES:
Hematologic
1. If ANC < 1.5 x 10⁹/L, or if PLT < 100 x 10⁹/L, HOLD dose for 1 week.

Hepatic Dysfunction
1. If T.Bili ≤ 25umol/L, GIVE Paclitaxel dose of 135mg/m².
2. If T.Bili = 26-51umol/L, or AST = 60-180 IU/L, GIVE Paclitaxel maximum dose of 75mg/m².
3. If T.Bili = 52-85umol/L, GIVE Paclitaxel maximum dose of 50mg/m².

Renal Failure
1. Adjust Carboplatin dose if estimated CrCl changes > 10%.

SUGGESTED ACTION

CLINICAL MONITORING:
- Watch for symptoms of fever and infection.
- Blood pressure and pulse rate monitoring during drug administration & for the following hour.

Sensory
1. Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function.
2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL.
3. Sensory alteration or paresthesia interfering with ADL.
4. Disabling.
5. Death

Flu-like Symptoms
1. Symptoms present but not interfering with function.
2. Moderate or causing difficulty performing some ADL.
3. Severe symptoms interfering with ADL.
4. Disabling.
5. Death

Hypersensitivity/Allergy
1. Transient flushing or rash; drug fever < 38°C 2. Rash; flushing; urticaria; drug fever ≥ 38°C
2. Symptomatic bronchospasm, with or without urticaria; parenteral medication(s) indicated; allergy-related edema/angioedema; hypotension
3. Anaphylaxis
5. Death

RATED AT EACH CLINIC VISIT

Unknown
PACLITAXEL-CARBOPLATIN Chemotherapy

HYPERSENSITIVITY:

Retreatment for Paclitaxel Hypersensitivity Reaction:

1. Discontinue Paclitaxel immediately if there are signs or symptoms of hypersensitivity.
2. Rapid IV administration of Diphenhydramine 50mg direct IV push over 1 minute and Hydrocortisone 100mg in 100ml Normal Saline over 5-10 minutes.
3. Reinitiate Paclitaxel infusion after 30 minutes, or when signs of reaction are resolved. Resume Paclitaxel infusion at 17mL/hr (10% of original rate) for 15 minutes, then at 42mL/hr (25% of original rate) for 15 minutes. If no further symptoms develop, continue at original rate until infusion complete.
4. If reaction recurs, STOP Paclitaxel for this dose and treat patient symptoms.

Desensitization for Paclitaxel Hypersensitivity Reactions:

If Paclitaxel hypersensitivity recurs during previous administration despite retreatment plan:

1. Dexamethasone 20mg PO 36 hours and 12 hours before chemotherapy, and 20mg PO morning of chemotherapy.
2. Dexamethasone 20mg IV, Diphenhydramine 50mg IV & Ranitidine 50mg IV about 30min before infusion.
3. Paclitaxel Infusion: 2mg in 100mL Normal Saline over 30min; if no reaction, 10mg in 100mL Normal Saline over 30min; if no reaction, remainder of dose in 500mL Normal Saline over 3 hours. 4. If reaction occurs, discontinue infusion; Diphenhydramine 50mg direct IV push over 1 minute and Hydrocortisone 100mg in 100ml Normal Saline over 5-10 minutes. 5. Restart Paclitaxel infusion after 30 minutes.

FORMULAE:

- **CrCl - Cockcroft & Gault (mL/sec)**
  - Male: \([140\text{-age(yrs)}] \times \text{TBW(Kg)} / [50 \times \text{SCr(umol/L)}]\)
  - Female: \([140\text{-age(yrs)}] \times \text{TBW(Kg)} / [50 \times \text{SCr(umol/L)}] \times 0.85\)

- **Creatinine Cl (mL/min)**
  \(\text{mL/min} = 60 \times \text{CrCl mL/sec}\)

- **Calvert Formula**
  \[\text{Dose (in mg)} = \text{target AUC} \times (\text{GFR} + 25) \quad \text{GFR in mL/min}\]

**INTERNAL CODE:**

- **OPIS CODE: PACLI-CARB 5 (UNK)**

**REFERENCES:**


**Date revised:** 06/04/2008
Selective Serotonin Reuptake Inhibitors- SSRI
SSRI PO Daily
- First choice antidepressant because of greater tolerability of all antidepressants and ease of dosing. Time to onset is 2 to 4 weeks. Upon discontinuation, SSRIs should be tapered down slowly over 4 to 6 weeks.
Citalopram
- Starting dose is 10-20mg/day, usual dose is 20-40mg/day and high dose is 60mg/day.
- Out-patient prescription available as 10, 20 and 40mg tablets.
- Trade name is Celexa™ and generics.
Escitalopram
- Starting dose is 10mg/day, usual dose is 20mg/day and dosing in elderly is 10mg/day.
- Out-patient prescription available as 10 and 20mg tablet.
- Trade name is Cipralex™
Fluoxetine
- Starting dose is 10-20mg/day, usual dose is 20-40mg/day and high dose is 60-80mg/day.
- Out-patient prescription available as 10 and 20mg capsules. Oral solution available in a 20mg/5ml strength.
- Trade name is Prozac™ and generics.
Fluvoxamine
- Starting dose is 50-100mg/day, usual dose is 150-200mg/day and high dose is 400mg/day.
- Out-patient prescription available in 50 & 100mg tablets.
- Trade name is Luvox™ and generics.
Paroxetine
- Starting dose is 10-20mg/day, usual dose is 20-40mg/day and high dose is 60mg/day.
- Out-patient prescription available in 10, 20 & 30mg tablets. Controlled-release tablets available in 12.5mg & 25mg tablets.
- Trade name is Paxil™ and generics, Paxil™ CR
Sertraline
- Starting dose is 25-50mg/day, usual dose is 50-100mg/day and high dose is 150-200mg/day.
- Out-patient prescription available in 25, 50 and 100mg capsules.
- Trade name is Zoloft™ and generics.

Dual Action Antidepressants

DUAL ACTION PO Daily
- Time to onset is 2-4 weeks. Upon discontinuation, it is suggested to taper down slowly over 4 to 6 weeks.
Bupropion
- Starting dose is 100-150mg/day, usual dose is 150-300mg/day, and high dose is 375-450mg/day.
- First-line agent for major depression and indicated for smoking cessation as Zyban™
- Out-patient prescription available as Wellbutrin™SR 100mg and 150mg slow-release tablets and Wellbutrin™XL 150 and 300mg extended-release tablets.
Duloxetine
- Dosage is 40-60mg/day, starting dose in elderly is 20-40mg/day, usual dose in elderly is 40-60mg/day.
- Out-patient prescription is available as delayed release capsule of 30 and 60mg.
- Trade name is Cymbalta™
Mirtazapine
- Starting dose is 7.5-15mg/day, usual dose is 300-400mg/day, and high dose is 600mg/day.
- Out-patient prescription available as regular tablet 15, 30, and 45mg and rapid dissolving tablets of 15, 30, 45mg.
- Trade name is Remeron™
Trazodone
- Use of Trazodone as an antidepressant is often limited by excessive sedation at therapeutic dose; it is often prescribed as a hypnotic in combination with other antidepressants at lower doses of 50-100mg at bedtime.
- Starting dose is 150-200mg/day, usual dose is 300-400mg/day and high dose is 600mg/day.
- Out-patient prescription available as 50, 75, 100mg and dividose tablets of 150mg.
- Trade name is Desyrel™ and generics.
Venlafaxine
- Higher rate of response and remission have been reported with Venlafaxine compared to SSRIs.
- Starting dose is 37.5-75mg/day, usual dose is 112.5-225mg/day and high dose of 300-375mg/day.
- Out-patient prescription available as 37.5, 75, and 150mg capsule.
- Trade name is Effexor™XR.
ANTIDEPRESSANTS - Supportive Therapy

Tricyclic Antidepressants - TCA

TRICYCLICS
- Tricyclic antidepressants (TCA) are used as third-line agents when SSRIs or dual action antidepressants have been ineffective.
- For many TCAs, the average dose can be approximated by calculating 3mg/kg of body weight. In elderly, cachexic or medically ill patients, lower starting doses of 10-25mg are more appropriate and can be gradually increased to 1.5mg/kg of body weight.
- TCAs are lethal in overdose and are poorly adhered to because of unfavourable side effect profile. Time to onset is 2 to 4 weeks. Upon discontinuation, it is suggested to taper down slowly.

Amitriptyline
- Starting dose is 25-50mg/day, usual dose is 75-200mg/day and high dose is 250-300mg/day.
- Out-patient prescription available as 10, 25, 50 and 75mg tablets.
- Trade Name is Elavil™ (discontinued), generics only.

Clomipramine
- Starting dose is 50-75mg/day, usual dose is 100-250mg/day and high dose is 300-450mg/day.
- Out-patient prescription available as 10, 25, and 50mg tablets.
- Trade name is Anafranil™ and generics.

Doxepin
- Starting dose is 10-25mg/day, usual dose 25-150mg/day and high dose is 200-300mg/day.
- Out-patient prescription available in 10, 25, 50, 75 and 100mg capsules.
- Trade name is Sinequan™ and generics.

Nortriptyline
- Starting dose is 25-50mg/day, usual dose is 75-150mg/day and high dose is 200mg/day.
- Out-patient prescription available in 10 and 25mg capsules.
- Trade name is Aventyl™ and generics.

Tetracyclic Antidepressants

TETRACYCLICS
- Tetracyclic antidepressants are used in treatment of depressive affective disorders (mood disorders), dysthymic disorder, major depression and anxiety related to depression.

Maprotiline
- Starting dose is 75mg/day, usual dose in 75-150mg/day and maximum dose is 150-200mg/day.
- Out-patient prescription available in 25, 50 & 75mg tablets.
- Trade name is Ludometone™ (discontinued) and generic Novo-maprotiline™

Reversible Monoamine Oxidase Inhibitor MAOI-a

MONOAMINE OXIDASE INHIBITORS

Moclobemide
- Starting dose is 200-300mg/day, usual dose is 450mg/day and high dose is 600mg/day.
- Out-patient prescription available in 100, 150, and 300mg tablets.
- Trade name is Manerix™ and generics.

Irreversible & Non-Selective Monoamine Oxidase Inhibitor MAOI

IRREVERSIBLE MAOI
- Reserved for the treatment of resistant depression.

Phenelzine
- Starting dose is 15-30mg, usual dose is 30-75mg/day and high dose is 90-120mg/day.
- Out-patient prescription available in 15mg tablets.
- Trade name is Nardil™

Tranylcypromine
- Starting dose is 10-20mg/day, usual dose is 20-60mg/day and high dose is 60-80mg/day.
- Out-patient prescription available in 10mg tablets.
- Trade name is Parnate™
Selective Serotonin Reuptake Inhibitors - SSRI

Citalopram - nausea, dry mouth, somnolence, sexual dysfunction. Citalopram is a major substrate of CYP3A4 and CYP2C19 and drugs that inhibit CYP2C19 (ex. Bortezomib) and CYP3A4 (Imatinib) may in theory increase the levels/effects of Citalopram. Procarbazine may enhance the serotoninergic effect of Citalopram and may result in serotonin syndrome; use with or within 14 days is contraindicated.

Escitalopram - nausea, headache, sexual dysfunction. Escitalopram is a major substrate of CYP3A4 and CYP2C19 and drugs that inhibit CYP2C19 (ex. Bortezomib) and CYP3A4 (Imatinib) may in theory increase the levels/effects of escitalopram. Procarbazine may enhance the serotoninergic effect of Escitalopram and may result in serotonin syndrome; use with or within 14 days is contraindicated.

Fluoxetine - nausea, drowsiness, anorexia, insomnia, sexual dysfunction. Fluoxetine is a major substrate of CYP2C9 and CYP2D6 and levels/effects of Fluoxetine may in theory be increased by Imatinib (moderate inhibitor of CYP2D6). Fluoxetine is a moderate inhibitor of CYP1A2 and CYP2C19 may in theory increase levels/effects of drug metabolized via CYP1A2 (ex. Dacarbazine & Flutamide) and via CYP2C19 (ex. Bortezomib). Fluoxetine is a strong inhibitor of CYP2D6 and may in theory increase levels/effects of Duloxetine and Tamoxifen. Procarbazine may enhance the serotoninergic effect of Fluoxetine and may result in serotonin syndrome; use with or within 5 weeks is contraindicated.

Fluvoxamine - nausea, drowsiness, anorexia, sexual dysfunction. Fluvoxamine is a major substrate of CYP1A2 and CYP2D6 and levels/effects of Fluvoxamine may be increased by drugs that inhibit CYP1A2 and CYP2D6 (ex. Imatinib). Fluvoxamine is a strong inhibitor of CYP1A2 and may increase the levels/effects of Dacarbazine and Flutamide. Fluvoxamine is also a strong inhibitor of CYP2C19 and may increase levels/effects of Bortezomib. Procarbazine may enhance the serotoninergic effect of Fluvoxamine and may result in serotonin syndrome; use with or within 14 days is contraindicated.

Paroxetine - nausea, drowsiness, dizziness, sexual dysfunction. Paroxetine is a major substrate of CYP2D6 and drugs that inhibit CYP2D6 (ex. Imatinib) may increase levels/effects of Paroxetine. Paroxetine is a strong inhibitor of CYP2C19 and may in theory increase levels/effects of Duloxetine. Procarbazine is a strong inhibitor of CYP2D6 and may in theory increase levels/effects of acrolein (active metabolite of Cyclophosphamide). Procarbazine may enhance the serotoninergic effect of Paroxetine; may cause serotonin syndrome; use with or within 14 days is contraindicated.

Sertraline - nausea, tremors, diarrhea, dry mouth, sexual dysfunction. Sertraline is a major substrate of CYP2C19 and CYP2D6 and drugs that inhibit CYP2C19 (ex. Bortezomib) and CYP2D6 (ex. Imatinib) may increase levels/effects of Sertraline. Sertraline is a moderate inhibitor of CYP2B6, CYP2D6, CYP2C19 & CYP3A4 and therefore may in theory increase levels/effects of drugs metabolized via these pathways ex. Bortezomib (CYP2C19), Doxorubicin and Tamoxifen (CYP2D6), Etoposide, Cyclophosphamide, Ifosfamide, Bortezomib, Paclitaxel, Doxorubicin, Irinotecan, vinca alkaloids, tyrosine kinase inhibitor, Tensirolimus, Tamoxifen, Exemestane and Flutamide (CYP3A4). Sertraline is a moderate inhibitor of CYP2D6 and may decrease levels/effects of acrolein (active metabolite of Cyclophosphamide). Procarbazine may enhance the serotonergic effect of Sertraline and may result in serotonin syndrome, use with or within 14 days is contraindicated.

- SSRIs should not be used with Non Selective Monoamine Oxidase Inhibitor or other drugs with MAO inhibition such as Linezolide. Fatal reactions have been reported. Wait 2 weeks after stopping an MAO inhibitor before starting an SSRI. Wait 5 weeks after stopping Fluoxetine (longest half-life of all SSRIs) to start a non selective MAO inhibitor.
- Concurrent Selegiline use has been associated with mania, hypertension or serotonin syndrome but less than with Non Selective MAO inhibitors. Theoretic risk of serotonin syndrome when combined with triptans for migraine.

Dual Action Antidepressants

Bupropion - agitation, insomnia, dizziness, anorexia, tachycardia. Contraindicated in patients with bulimia or anorexia nervosa, head injury or seizure disorder because of an increased seizure risk. The risk of seizures is dose-dependent. Do not use an MAO inhibitor within 14 days.

- Bupropion is a major substrate of CYP2B6 and weak CYP2B6 inducer (ex. Cyclophosphamide) may in theory decrease serum concentration of Bupropion. Moderate CYP2B6 inhibitors (ex. Doxorubicin) may increase levels/effects of Bupropion. Procarbazine may enhance the neurototoxic (central) effect of Bupropion, use with or within 14 days is contraindicated.

Duloxetine - nausea, dry mouth, dizziness, headache.

- Duloxetine is a major substrate of CYP1A2 and 2D6. Imatinib is a moderate inhibitor of CYP2D6 and may in theory increase Duloxetine levels/effects. Duloxetine is a moderate CYP2D6 inhibitor and may increase levels/effects of Doxorubicin and Tamoxifen. Procarbazine may enhance the serotonergic effect of Duloxetine; may cause serotonin syndrome; use with or within 14 days is contraindicated.

Mirtazapine - sedation, weight gain, increased appetite, dry mouth, constipation.

- Mirtazapine is a major substrate of CYP1A2, 2D6 and 3A4. Imatinib may in theory increase levels/effects. Sedative effects may be potentiated by alcohol, Diazepam and other CNS depressants. Procarbazine may enhance the neurotoxic (central) effect of Mirtazapine; use with or within 14 days is contraindicated.

Trazodone - drowsiness, nausea, headache, dry mouth, priapism.

- May potentiate effects of other CNS depressants. Trazodone is a major substrate of CYP3A4 and CYP3A4 inhibitors (ex. Imatinib) may increase levels/effects of trazodone. CYP3A4 inducers may decrease levels/effects of Trazodone. Trazodone may decrease the levels/effects of CYP2D6 prodrug substrates ex. Codeine, Hydrocodone, Oxycodone and Tramadol. Trazodone may also in theory increase effects/levels of Doxorubicin and Tamoxifen by moderately inhibiting CYP2D6. Procarbazine may enhance the serotonergic effect of Trazodone; may cause serotonin syndrome; use with or within 14 days is contraindicated.

Venlafaxine - nausea, drowsiness, nervousness, dizziness, dry mouth, may increase blood pressure if dose>300mg/day.

- CYP2D6 inhibitors (Imatinib) and CYP3A4 inhibitors (Imatinib) may increase levels/effects of Venlafaxine. CYP2D6 and CYP3A4 inducers may decrease levels/effects of Venlafaxine. Procarbazine may enhance the serotoninergic

REFERENCES:


Date revised: 12/29/2008

Non-Formulary Form Required

**SC ANTIEMETICS**

**Supportive Care**

**Antiemetics - Supportive Therapy**

*For Chemotherapy Induced Nausea & Vomiting (CINV)*

**NEUROKININ 1 RECEPTOR ANTAGONISTS**

**Aprepitant**
- Prevention of acute and delayed nausea and vomiting associated with highly emetogenic chemotherapy (cisplatin ≥ 70mg/m²) in combination with a corticosteroid and 5-HT3 receptor antagonist and for patients who demonstrated delayed emesis with moderately to highly emetogenic chemotherapy.
- Dose is 125mg PO 30-90 minutes pre-chemotherapy on Day 1 and 80mg PO once daily on Days 2 & 3.
- Outpatient prescription available as 80mg and 125mg capsules.
- Trade Name: Emend™

**5-HT3 ANTAGONIST**

**Ondansetron**
- Prevention of nausea and vomiting associated with moderately to highly emetogenic chemotherapy.
- Highly effective in acute vomiting, less effective for delayed vomiting, also useful in radiation-related nausea & vomiting.
- 8mg PO/IV starting 30 minutes prior to chemotherapy, followed by 8mg PO q12h for 2-3 days post chemotherapy.
- Outpatient prescription available as 4mg and 8mg tablets, 4mg and 8mg oral disintegrating tablets (ODT), 4mg/5ml oral solution and 2mg/ml injection.
- Trade Name: Zofran™

**Granisetron**
- Prevention of nausea and vomiting associated with moderately to highly emetogenic chemotherapy.
- Highly effective in acute vomiting, less effective for delayed vomiting, also useful in radiation-related nausea & vomiting.
- 1mg IV 30 minutes prior to chemotherapy then 2mg PO once daily or 1mg PO bid for 2-3 days post chemotherapy.
- Outpatient prescription available as 1mg tablets or 1mg/ml injection.
- Trade Name: Kytril™

**CORTICOSTEROIDS**

**Dexamethasone**
- Prevention of delayed nausea and vomiting associated with moderately and highly emetogenic chemotherapy.
- 20 mg PO/IV prior to *highly* emetogenic chemotherapy followed by dexamethasone 4-8 mg PO bid for 2-4 days.
- 8 mg PO/10 mg IV prior to *moderately* emetogenic chemotherapy followed by dexamethasone 4-8 mg PO bid for 2-4 days.
- Outpatient prescription available as 0.5mg, 0.75mg, 2mg, 4mg tablets, 0.5mg/5ml oral solution, 10mg/ml and 4mg/ml injection.
- Trade Name: Decadron™

**DOPAMINE ANTAGONISTS**

**Prochlorperazine**
- Management of breakthrough nausea and vomiting, prevention of nausea & vomiting with mildly emetogenic chemotherapy and prevention of delayed NV in combination with other agents.
- 10 mg PO/IV pre-chemotherapy followed by 10 mg PO/PR q4-6h as needed.
- Outpatient prescription available as 5mg and 10mg tablets, 10mg suppositories and 5mg/ml injection.
- Trade Name: Stemetil™

**Haloperidol**
- Management of breakthrough nausea and vomiting, prevention of nausea & vomiting with mildly emetogenic chemotherapy and prevention of delayed NV in combination with other agents.
- 0.5-2 mg PO/IV/SC q8-12h pm for refractory nausea and vomiting.
- Outpatient prescription available as 0.5mg, 1mg, 2mg, 5mg, 10mg and 20mg tablets, 2mg/ml oral solution and 5mg/ml injection.
- Trade Name: Haldol™

**Metoclopramide**
- Management of breakthrough nausea and vomiting, prevention of nausea & vomiting with mildly emetogenic chemotherapy and prevention of delayed NV in combination with other agents.
- 10-20 mg PO q4-6h pm.
- Outpatient prescription available as 5mg and 10mg tablets, 5mg/ml injection.
- Trade Name: Maxeran™, Reglan™

**Domperidone**
- Management of breakthrough nausea and vomiting, prevention of nausea & vomiting with mildly emetogenic chemotherapy and prevention of delayed NV in combination with other agents.
- 10-20 mg PO q4-6h pm.
- Outpatient prescription available as 10mg tablets.
- Trade Name: Motilium™

**BENZODIAZEPINE**

**Lorazepam**
- Treatment and prevention of anticipatory emesis and treatment of breakthrough emesis.
- 0.5 to 2 mg PO/SL prior to chemotherapy followed by q4-6h pm.
- Outpatient prescription available as 0.5mg, 1mg, and 2mg tablets, 0.5mg, 1mg, 2mg sublingual tablets and 4mg/ml injection.
- Trade Name: Ativan™

Supportive Care
Supportive Care

Antiemetics - Supportive Therapy

CANNABINOIDS

Nabilone
- Management of refractory nausea and vomiting associated with chemotherapy.
- 1-2 mg PO bid prn up to 6mg/day.
- Outpatient prescription available as 0.25mg, 0.5mg and 1mg capsule.
- Trade Name: Cesamet™

Dronabinol
- Management of refractory nausea and vomiting associated with chemotherapy.
- 5-10 mg PO q4-6h prn.
- Outpatient prescription available as 0.25mg, 0.5mg and 1mg capsule.
- Trade Name: Marinol™

CLINICAL MONITORING:

Precautions:
Aprepitant:
- Contraindicated with pimozide and cisapride.
- Aprepitant is metabolized via CYP3A4. CYP3A4 inhibitors may increase serum concentration of aprepitant and CYP3A4 inducers may reduce serum concentration of aprepitant. Aprepitant has many drug interactions, refer to drug monograph.
- Aprepitant is a CYP3A4 inhibitor and its effect on orally administered substrate is greater than those administered intravenously. Dexamethasone PO dose must be reduced by 50% when combined with Aprepitant.
- Aprepitant induces CYP2C9, so metabolism of warfarin and phenytoin may be induced. INR should be monitored closely in the 2-week period, particularly at 7 to 10 days, following initiation of the 3-day regimen.
- Monitor for fatigue/asthenia, hiccups.

Ondansetron/Granisetron:
- Headache, constipation, transient increase in LFTs.

Dexamethasone:
- Hyperglycemia, psychosis/euphoria, insomnia, dyspepsia.
- Sedation, hypotension, extrapyramidal symptoms (tremor, restlessness, dystonia), reduce seizure threshold (haloperidol & prochlorperazine), prolong QT interval (haloperidol & domperidone).

Lorazepam:
- Sedation, dizziness, confusion, ataxia.

Nabilone/Dronabinol:
- Sedation, euphoria/dysphoria, reduce cognitive function, hallucinations, dizziness.

REFERENCES:

- Emend Product Monograph, Merck Frosst Canada.

Date revised: 07/08/2008
CALCITONIN Supportive Therapy
Hypercalcemia (Cancer or Therapy-related)

CALCITONIN

4 IU/kg
IM
Day 1

- May give IM or SC q12h.
- May increase to 8 IU/Kg q12h to a maximum dose of 8 IU/Kg q6h if serum calcium uncontrolled.
- May be self-administered by subcutaneous injection into a single site; if dose is greater than 2mL, intramuscular injection may be preferable.
- Outpatient prescription.

TREAT DAILY UNTIL NORMALIZATION OF SERUM CALCIUM LEVELS

TESTS:
Baseline Tests
Ca Albumin

CLINICAL MONITORING:
Recommended Clinical Monitoring:
- Serum electrolytes, including calcium.

Hypocalcemia
0. Serum Calcium > 2.10 mmol/L
1. Serum Calcium = 2.10 to 1.93 mmol/L
2. Serum Calcium = 1.92 to 1.74 mmol/L
3. Serum Calcium = 1.73 to 1.51 mmol/L
4. Serum Calcium < 1.50 mmol/L

Rated on assessment of anti-hypercalcemia response and at periodic visits or in response to patient complaint.

Expected Protocol Outcomes:
Hypercalcemia - Response Criteria
0. Serum Calcium < 2.64 mmol/L
1. Serum Calcium = 2.64 to 2.88 mmol/L
2. Serum Calcium = 2.89 to 3.12 mmol/L
3. Serum Calcium = 3.13 to 3.37 mmol/L
4. Serum Calcium > 3.37 mmol/L

Rated on assessment of anti-hypercalcemia response and at periodic visits or in response to patient complaint.

FORMULAE:
Corrected Serum Calcium (mmol/L) Measured Serum Calcium + [(40 - serum albumin) x 0.02]

Date revised: 03/07/2005

Supportive Care
Supportive Care

Constipation - Supportive Care

STIMULANT AGENTS

Sennoside
- 8.6mg/tablet PO BID and titrate up to 4 tablets PO BID (onset 6 to 12 hours).
- Over-the-counter product available as 8.6mg tablets and 1.7mg/ml syrup.
- Trade name: Senekot™

Bisacodyl
- 5-10mg PO TID prn (onset 6 to 12 hours)
- 10mg PR TID prn (15 to 60 minutes)
- Over-the-counter product of 5mg tablets and 5mg or 10mg suppository.
- Trade name: Dulcolax™

STOOL SOFTENER

Docusate Sodium
- 100mg PO BID and titrate up to 300mg PO TID (onset 12 to 72 hours).
- Over-the-counter product available as 100mg capsule, 10mg/ml drops and 20mg/5ml syrup.
- Trade name: Colace™

Docusate Calcium
- 240mg PO BID (onset 12 to 72 hours).
- Over-the-counter product available as 240mg capsule.
- Trade name: Surfak™

HYPEROSMOTIC AGENTS

Lactulose
- 15ml PO BID up to 30 ml PO TID (onset 24-48 hours).
- Over-the-counter product available as a 667mg/ml syrup.
- Trade name: Lactulose™

Glycerin
- 2.6gm PR prn (onset 15min-60min).
- Over-the-counter product available as a 2.6gm and 1.8gm suppository.
- Trade name: Glycerin™ Suppositories.

LAVAGE SOLUTIONS

Peglyte, Golytely, Colyte, Klean-Prep
- 125-250ml PO once daily (laxative), 1000-4000ml PO once daily (purgative).
- Available over-the-counter.

BULK-FORMING AGENTS

Psyllium Hydrophillic Mucilloid
- One rounded teaspoon (5.4gm) in 240ml of liquid TID.
- Used in combination with a stimulant but not on its own.
- May cause bowel obstruction if taken with insufficient liquid. Must drink plenty of fluids.
- Onset 12 to 72 hours.
- Over-the-counter products available in many different preparations.
- Trade Name: Metamucil™, Prodiem™

OSMOTIC/SALINE AGENTS

Magnesium Citrate
- 250ml PO PRN (onset 30 minutes to 6 hours)
- Trade name: CitroMag™

Magnesium Hydroxide
- 30 to 60ml daily (onset 30 minutes to 6 hours)
- Trade name: Milk of Magnesia™

Sodium Phosphate Enema
- 130ml PR PRN (onset 2-15 minutes)
- Trade name: Fleet™ Enema

Sodium Phosphate Oral
- 20ml PO (laxative dose), 45ml PO (purging dose) (onset 30 minutes to 6 hours)
- Trade name: Fleet™ Phospho-Soda
- Caution in renal failure, hypermagnesemia and hyperphosphatemia.

LUBRICANTS

Mineral Oil
- 15-45ml PO (onset 6 to 8 hours), 120ml PR (onset 2-15 minutes)
- Use with extreme caution because of risk of aspiration pneumonia.
- Should not be used with stool softener because of increase absorption of mineral oil.
- Mineral oil may decrease the absorption of fat-soluble vitamins.
- Trade name: Fleet™ Mineral Oil enema, Mineral Oil™ Heavy, Lansoyl™

REFERENCES:

- Relistor Drug Monograph.
DEFEROXAMINE Therapy
Chronic Iron Overload

DEFEROXAMINE 1000mg SC or IV Day 1 Test Dose

SC Administration:
- Admix a syringe containing 1000mg in 10mL sterile water. Inject subcutaneously in the anterior abdominal wall at a maximum rate of 1mL/min. A syringe pump may be used.

IV Administration:
- Admix in 250mL Normal Saline, and infuse at a maximum rate of 15mg/kg/hr.
- NO PROCHLORPERAZINE to be used concurrently with Deferoxamine.

PATIENT VISITS and APPOINTMENT TYPE:
- Day 1 SC 30min Type A
- Day 1 IV 1-2hrs Type B

ANCILLARY:
- Maximum of 200mg concurrent Vitamin C administration in adults. Vitamin C should not be used in patients with cardiac failure.

CLINICAL MONITORING:
- If disturbances of vision and/or hearing occur, treatment should be discontinued. Visual disturbances have been reported after a single dose. Low dose therapy reduces this risk.
- Following rapid IV administration: flushing of the skin, urticaria, hypotension and shock have occurred. IV rate should not exceed 15mg/kg/hr.

HYPERSENSITIVITY:
Frequent:
- Pain, swelling, induration, erythema, burning, pruritus, wheals and rash at the infusion or injection site, occasionally accompanied by fever, chills and malaise.
- When signs of local irritation occur, a lower concentration is recommended.

Rare:
- Anaphylactic reactions with or without shock, angioedema.

Date revised: 02/02/2006
DEXRAZOXANE Supportive Therapy
Protection Against Doxorubicin - Related Cardiotoxicity

DEXRAZOXANE  500mg/m²  IV  Before Doxo dose  Round to nearest 5mg
- 500mg/m² or dose may be calculated at a 10:1 ratio with the Doxorubicin dose.
- **Slow push over 15 minutes.**
- May be given undiluted as an IV bolus or as a rapid IV drip infusion (from an empty Viaflex bag) or may be given diluted in 50-100ml NS or D5W, infused over 15 minutes.
- Start dose **30 minutes BEFORE** planned start time for Doxorubicin.
- Dexrazoxane should only be initiated when patients have received > 300mg/m² of Doxorubicin.

**TESTS:**
Baseline Tests  WBC  HB  PLT  ANC  Cr  Urea  T.Bili  AST  ALT  AlkPhosphatase
Test Notes  - Monitor renal and hepatic dysfunction on a regular basis.
- Dexrazoxane may add to the myelosuppressive effects of doxorubicin.
- If hepatic dysfunction refer to doxorubicin guidelines for dose reduction and maintain ratio of 10:1 of dexrazoxane vs doxorubicin.

**ANTIEMETIC PRE-CHEMO REGIMEN:**
No Level  Doxorubicin days - As required for Chemotherapy regimen.

**PATIENT VISITS and APPOINTMENT TYPE:**
Doxorubicin Days - additional 30 minutes

**TOXICITIES:**
Renal Failure
1. If CrCl < 40 ml/min, reduce dexrazoxane dose by 50% so the calculated ratio becomes 5:1 with the doxorubicin dose.

**REFERENCES:**
- Zinecard Drug Monograph, Pfizer 2005.
- CCO Practice Guidelines: Use of Dexrazoxane as a cardioprotectant in patients receiving doxorubicin or epirubicin chemotherapy for the treatment of cancer.

CCO Eligibility Form Required  ☐  Non-Formulary Form Required  ☐  Date revised: 09/09/2008
Erythropoiesis-Stimulating Agents (ESAs)

**EPOETIN ALFA**

**Dosage Schedule:**
- 40,000 IU once weekly.
- Assess treatment at 4 weeks, if no response increase dose to 60,000 IU weekly for 4 weeks.
- If no response after 6-8 weeks (<10-20g/L Hb increase), consider discontinuing Epoetin or assess for causes of non-response (iron assessment).
- The target hemoglobin should be at or near a concentration of 120g/L.
- If hemoglobin increases by more than 10g/L in a 2 week period or if the hemoglobin exceeds 120g/L, the dose should be reduced by approximately 25%.
- If hemoglobin exceeds 130g/L, hold Epoetin until hemoglobin drops to <120g/L. May then reinstitute Epoetin at 75% of previous dose.
- Epoetin is restricted to patients with anemia who are receiving chemotherapy and should be discontinued when chemotherapy is completed or continued for the equivalent of 1-2 cycles or 6-8 weeks.

**Supplied:**
- Prefilled syringe (single dose) of 1000 IU/0.5 mL, 2000 IU/0.5 mL, 3000 IU/0.3 mL, 4000 IU/0.4 mL, 5000 IU/0.5 mL, 6000 IU/0.6 mL, 8000 IU/0.8 mL, 10 000 IU/mL, 20 000 IU/0.5 mL, 30 000 IU/0.75 mL, 40 000 IU/mL
- Vial: 20,000 IU multidose vial
- Outpatient prescription (Keep refrigerated).
- Trade name Eprex™

**DARBEPETOIN ALFA**

**Dosage Schedule:**
- 2.25ug/kg once weekly subcutaneously (dose should be rounded upward to the next available syringe strength) or 500ug every 3 weeks subcutaneously.
- Assess treatment at 6 weeks, if no response, weekly dose may be increased to 4.5ug/kg weekly. Dose escalation is not recommended for the every-3-weeks dosing schedule because of an absence of additional efficacy benefit at higher dose levels.
- If no response after 6-8 weeks (<10-20g/L Hb increase), consider discontinuing Darbepoetin or search for cause of non-response (iron assessment).
- The target hemoglobin concentration should be at or near a concentration of 120g/L.

**Weekly Schedule:**
- If the rate of hemoglobin increase is >10g/L in a 2-week period or when the hemoglobin is >120g/L, the dose should be reduced by 25%.
- If Hb >130g/L, dosing should be withheld temporarily until Hb drops to 120g/L. At that time therapy should be reintiated at a dose of 25% below the previous dose.

**Every 3-Weeks Schedule:**
- If the rate of Hb increase is >15g/L per 3-week period or when Hb >120g/L, the dose should be reduced by 40% of the previous dose.
- If Hb >130g/L, dosing should be withheld temporarily; once Hb drops to 120g/L, therapy should be reinitiated at a dose 40% below the previous dose.
- Darbepoetin is restricted to patients with anemia who are receiving chemotherapy and should be discontinued when chemotherapy is completed or continued for the equivalent of 1-2 cycles or 6-8 weeks.

**Supplied:**
- Prefilled syringes of 10, 15, 20, 30 40, 50, 60, 80, 100, 130, 150, 200, 250, 300, 400, and 500 mcg.
- Single-dose vials available in 15, 25, 40, 60, 100, 200, 325 and 500 mcg.
- Outpatient prescription (Keep refrigerated).
- Trade name Aranesp™

**TESTS:**

Baseline Tests: WBC HB PLT ANC

Test Notes: Monthly HB is recommended while on maintenance therapy.
Erythropoiesis-Stimulating Agents (ESAs)

**CLINICAL MONITORING:**
- Hemoglobin levels, blood pressure, signs of stroke, heart attack, pulmonary embolism, deep vein thrombosis, presence of premonitory neurologic symptoms (seizure), sudden loss of response to ESAs (pure red cell aplasia).

**WARNINGS AND PRECAUTION (EPOETIN)**
- ESAs shortened the time to tumor progression in patients with advanced head and neck cancer receiving radiation therapy when administered to target a hemoglobin greater than 120g/L.
- ESAs shortened overall survival and increased deaths attributed to disease progression at 4 months in patients with metastatic breast cancer receiving chemotherapy, when administered to target a hemoglobin of greater than 120 g/L.
- ESAs increased the risk of death when administered to target a hemoglobin of 120 g/L in patients with active malignant diseases receiving neither chemotherapy nor radiation therapy. ESAs are not indicated for this population.

**WARNINGS: INCREASED MORTALITY, SERIOUS CARDIOVASCULAR and THROMBOEMBOLIC EVENTS, and TUMOR PROGRESSION (DARBEPOETIN)**
- ESAs shortened overall survival and/or time-to-tumor progression in clinical studies in patients with breast, non-small cell lung, head and neck, lymphoid, and cervical cancers when dosed to target a hemoglobin of ≥120g/L.
- The risks of shortened survival and tumor progression have not been excluded when ESAs are dosed to target a hemoglobin of <120g/L.
- To minimize these risks, as well as the risks of serious cardio- and thrombovascular events, use the lowest dose needed to avoid red blood cell transfusions.
- Use only for treatment of anemia due to concomitant myelosuppressive chemotherapy.
- Discontinue following the completion of a chemotherapy course.
- ESAs are NOT intended for use in patients receiving myelosuppressive therapy when the expected outcome is cure.

**INTERNAL CODE:**
- EPOETIN
- DARBEPOETIN

**REFERENCES:**
- Mikhael et al; Canadian supportive care recommendations for the management of anemia in patients with cancer; Current Oncology, Volume 14, number 5, pp 209-217.

**Date revised:** 11/25/2008
Granulocyte Colony Stimulating Factor (G-CSF) Supportive Therapy

**FILGRASTIM**

5-10mcg/kg/day SC Daily (10-14 days of treatment) 300mcg & 480mcg vials

- Recommended when febrile neutropenia (FN) risk >20%, dose-dense chemotherapy regimen, or previous neutropenic complication.
- To be considered with standard dose chemotherapy with an intermediate risk of FN between 10-20% when intent is curative or (neo) adjuvant, dose delay >1 week, previous febrile neutropenia event or patient has one or more risk factors for febrile neutropenia.
- Not routinely recommended for chemotherapy associated with low risk <10% of febrile neutropenia.
- Starting dose is 5mcg/kg/day.
- Doses may be increased in increments of 5mcg/kg/day for each chemotherapy cycle, according to duration and severity of AGC nadir.
- 1-2 days after initiation of therapy, there is a transient increase in neutrophil counts. For a sustained therapeutic response, filgrastim therapy should be continued for 10-14 days following chemotherapy.
- Start treatment 24 hours AFTER last myelosuppressive chemotherapy dose given (NB. Includes oral chemotherapy doses).
- Stop treatment 24 hours BEFORE administration of next chemotherapy cycle.
- Outpatient prescription (Keep refrigerated).
- Vial sizes available: 300mcg and 480mcg.
- Trade name Neupogen™

**PEGFILGRASTIM**

6mg SC Once per chemotherapy cycle

- Start treatment 24-48 hours after myelosuppressive chemotherapy as a single dose. Not to be given the same day as chemo or with radiation.
- Not recommended for use with chemotherapy regimens that are <2 weeks apart.
- Recommended when febrile neutropenia (FN) risk >20%, dose-dense chemotherapy regimen, or previous neutropenic complication.
- To be considered with standard dose chemotherapy with an intermediate risk of FN between 10-20% when intent is curative or (neo) adjuvant, dose delay >1 week, previous febrile neutropenia event or patient has one or more risk factors for febrile neutropenia.
- Not routinely recommended for chemotherapy associated with low risk <10% of febrile neutropenia.
- May give analgesics at physician discretion for temporary bone pain at initiation.
- Outpatient prescription (Keep refrigerated).
- Supplied as a prefilled syringe of 6mg/ 0.6ml
- Trade name Neulasta™

**TESTS:**

Baseline Tests: WBC HB PLT ANC Chloride

Test Notes: CBC at start of cycle.

- Product monograph suggests: CBC before treatment and twice weekly during treatment. Therapy should be discontinued if AGC > 10 x 10^9/L after the AGC nadir has occurred.

**INTERNAL CODE:**

- FILGRAS
- PEGFILGRAS

Date revised: 07/03/2008
**MESNA Supportive Therapy**

**Prophylaxis and reduction of hemorrhagic cystitis associated with Ifosfamide and Cyclophosphamide**

**MESNA**

**PO/IV Day 1**

**Mesna**
- Different dosing schedule exist and depends on the concomitant treatment, disease and response.
- The dose is usually a percentage (60-100%) of the oxazaphosphorines (Ifosfamide&Cyclophosphamide) used and hour 0 refers to the start of the oxazaphosphorines infusion.
  - IV Bolus 20% at 0 hour, 4 hours and 8 hours post
  - IV Bolus 10-12mg/kg at 0 hour, 4 hours and 8 hours post
  - IV & Oral 20% IV at 0 hour, followed by 40% PO at 4 hours and 8 hours post
  - Oral 40% PO at 0 hour, 4 hours and 8 hours post
- Different administration schedule exist depending on the treatment.
  - Admix in 50-100 ml of Normal Saline and infuse over 15 minutes prior to Ifosfamide or Cyclophosphamide
  - Admix in a larger volume and infuse continuously over 6-24 hours; may use a CADD ambulatory pump and infuse over longer period of time
- May be given as IV push through side arm of a free-flowing IV line
- May be admixed directly in a bag with Cyclophosphamide or Ifosfamide
- May be infused concurrently with Cyclophosphamide or Ifosfamide
- Mesna does not have any antitumor activity but blocks major bladder damage from the urotoxic metabolites generated by Ifosfamide and Cyclophosphamide.
- IV Mesna may be taken orally, diluted in 15 ml of juice, milk or carbonated beverage to improve the taste, followed by a glassful of the desired liquid. Vomiting within 1 hour of taking oral Mesna should be reported to the physician, so that IV Mesna can be given. If IV Mesna is not available patient must repeat the dose by taking emergency dose provided. If patient vomits emergency dose, must drink 1.5L (6 cups) of water or beverage of choice over 2 hours.

**CLINICAL MONITORING:**
- Because Mesna is usually given with chemotherapy, it is often difficult to distinguish the side effects that may be due to the Mesna itself, from the side effects that may be due to the chemotherapy. Side effects from Mesna are rare but may be: nausea and vomiting, altered taste, headache, diarrhea, hypersensitivity and rash.
- Mesna treatment may cause false positive reactions in tests for ketone bodies in the urine. The color reaction is reddish purple rather than purple. (Chemstrip™)

**REFERENCES:**
- Cancer Cancer Ontario
- BC Cancer Agency
Treatment of neuropathic pain and more effective when pain is described in terms of constant and burning pain, superior for dysesthetic pain.

ANTIDEPRESSANTS

Daily

Tricyclic Antidepressants
- 10-25mg PO HS up to 200mg/day.
- Amitriptyline is the first choice because abundance of literature supporting its use, but all tricyclic antidepressants has analgesic properties. If patients are unable to tolerate Amitriptyline, Desipramine, Doxepine, Imipramine or Nortriptyline may be tried and better tolerated.
- Outpatient prescription: Elavil®, Norpramin®, Sinequan®, Tofranil® and Aventyl®

Paroxetine
- 10-20mg PO once daily up to 40mg/day.
- Outpatient prescription: Paxil®

Venlafaxine
- 37.5mg PO daily up to 350mg/day.
- Outpatient prescription. - Trade name: Effexor® XR

Treatment of neuropathic pain and more effective with shooting and paroxysmal neuropathic pain, superior for lancinating pain.

ANTICONVULSANTS

Daily

Gabapentin
- 100mg PO TID up to 3600mg/day
- Outpatient prescription Neurontin®

Pregabalin
- 75mg PO BID up to 600mg/day.
- Outpatient prescription: Lyrica®

Other anticonvulsants may be used; carbamazepine, lamotrigine, phenytoin, topiramate and valproic acid but gabapentin and pregabalin are the most commonly used.

Treatment of neuropathic pain when TCA’s, anticonvulsants and other alternatives are ineffective.

ANTIARRHYTHMICS

Daily

Flecainide, Tambocor®TM
- 50mg PO daily up to 300mg/day
- Outpatient prescription available as 50 & 100mg tablets

Mexiletine
- 100mg PO once to twice daily up to 200-300mg PO TID
- Outpatient prescription Mexitil® available as 100 & 200mg capsules.

CLINICAL MONITORING:

Antidepressants:
Tricyclic Antidepressants
- Dry mouth, drowsiness, constipation, orthostatic hypotension, tachycardia and arrhythmias.
Paroxetine
- Nausea and vomiting, headaches, insomnia, drowsiness and dry mouth.
- May have some analgesic properties, better tolerated than tricyclic antidepressants.
Venlafaxine
- Nausea and vomiting, asthena, anorexia and vertigo.
- May have some analgesic properties, better tolerated than tricyclic antidepressants.

Anticonvulsants:
Gabapentin
- Drowsiness, dizziness, fatigue and edema.
Pregabalin
- Sedation, peripheral edema.
- Requires adjustment in renal failure.

Antiarrhythmics:
- Dizziness, arrhythmias, LFT, CBC for blood dyscrasias
- Contraindicated with high degree (2nd & 3rd) AV Block in the absence of a pacemaker.

REFERENCES:
- Therapeutics Choice, Fourth Edition, Canadian Pharmacists Association
- Lyrica Drug Monograph
- CPS online version

CCO Eligibility Form Required □ Non-Formulary Form Required □ Date revised: 12/09/2008
**OCTREOTIDE Supportive Therapy**

**Bowel Obstruction Management - Palliative Intent**

**OCTREOTIDE**

50-1500mcg/day  SC  Continuous Treatment

**SC treatment:**
- Dose range = 50mcg-1500mcg/day in 2 to 4 divided doses (experience with doses above 750mcg/day is limited).
- Supplied as: 100mcg/1mL or 500mcg/1mL ampoules and 200mcg/mL 5mL vial

**IM treatment (Long Acting Injection):**
- Inject every 4 weeks for the first 3 months, then adjusted as per symptoms.
- Supplied as: 20mg/vial or 30mg/vial.
- Outpatient prescription.

**CONTINUOUS TREATMENT**

**CLINICAL MONITORING:**
- Ultrasonograph of the gall bladder, to assess the presence of gallstones (during long-term therapy).

| CCO Eligibility Form Required | Non-Formulary Form Required | Date revised: 03/07/2005 |
PAIN MANAGEMENT - Supportive Therapy

Treatment of pain - mild, moderate and severe

For treatment of mild to moderate pain

**CODEINE**
- 15-30mg PO Daily
- 15-30mg q4-6h pm up to 300mg of Codeine base q12h (dose-dependent analgesic ceiling), beyond that dose it is better to change for a strong opioid such as morphine or other.
- Immediate-release given q4-6h.
- Long-acting form usually given q12h sometimes q8h.
- Codeine is about 10 times weaker than oral morphine.
- Start low and titrate upward slowly.
- Titration of controlled-release form every 48-72 hours.
- Outpatient prescription available as: oral syrup 5mg/ml, immediate-release tablets of 15 & 30mg, controlled-release form (Codeine Contin™) of 50, 100, 150 & 200mg tablets which may be split in half except the 50 mg tablets.
- Many name brand and generic products of Codeine are also available as a combination with Acetaminophen. Some of these products are known as Tylenol #1, #2,#3 & #4, Atasol-8, 15 & 30, Lenoltec #1, #2, #3 & #4, Emtecm-30, and Tylenol elixir with Codeine. These products make titration difficult due to the maximum daily dose of Acetaminophen.
- Codeine injectable available as a 30 mg/ml ampoule.

**MORPHINE**
- Initial dose of 5-10 mg PO q4-6h pm in patients who have not previously received opioids.
- Immediate-release given q4-6h, long-acting form usually given q12h sometimes q8h except for Kadian™ which is given q24h.
- Start low and titrate upward slowly, no ceiling effect.
- Titration of controlled-release form every 48-72 hours.
- Outpatient prescription available as oral syrup of 1mg/ml and 5mg/ml, 10mg/ml & 20mg/ml
- Oral concentrate of 20mg/ml & 50mg/ml
- Immediate-release tablets of 5, 10, 20 & 30mg
- 12-hour Sustained-release tablet (MS Contin™) of 15, 30, 60, 100 & 200mg
- 24-hour Sustained-release capsule (Kadian™) of 10, 20, 50 & 100mg
- Injectable: 15mg/ml & 50mg/ml ampoule
- MS Contin™ cannot be split or chewed, except for the 200mg strength which can be split in half.
- M-Eslon™ and Kadian™ capsules may be opened and beads sprinkled over cold soft food such as apple sauce.

**OXYCODONE**
- Initial dose of 5-10 mg PO q4-6h pm in patients who have not previously received opioids.
- Oxycodone is about 2 times stronger than oral morphine.
- Start low and titrate upward slowly, no ceiling effect.
- Titration of controlled release form every 24 hours.
- Outpatient prescriptions available as:
  - Immediate release tablet of 5, 10 & 20 mg
  - Immediate release suppository of 10 & 20 mg
  - Controlled-release form of 5, 10, 20, 40 & 80 mg.
- No injectable form available in Canada.
- Also available in combination with acetaminophen as Oxycocet, Endocet, Percocet & Percocet-demi but dosing titration is difficult due to the maximum daily dose of Acetaminophen.
- Also available in combination with ASA as Oxycodan, Percodan & Endodan.

**NABILONE**
- In Marijuana naive patients, initiate at 0.25-0.5mg PO hs for 4-7 days and increase by adding 0.25-0.5mg daily in the morning for 4-7 days up to a maximum of 6 mg per day.
- Outpatient prescription available as 0.25, 0.5, and 1mg capsules.
- Trade Name: Cesamet™
For treatment of moderate to severe pain

METHADONE  
- Physician must obtain license from regulating agency in order to prescribe for pain management.
- Chronic pain in opioid-tolerant patient (conversion from oral Morphine to oral Methadone)
  - Daily oral Morphine dose <100mg, then estimated daily oral Methadone dose is 20% to 30% of total daily Morphine dose.
  - Daily oral Morphine dose of 100-300mg, then estimated daily oral Methadone dose is 10% to 20% of total daily Morphine dose.
  - Daily oral Morphine dose of 300-600mg, then estimated daily oral Methadone dose is 8% to 12% of total daily Morphine dose.
  - Daily oral Morphine dose of 600-1000mg, then estimated daily oral Methadone dose is 5% to 10% of total daily Morphine dose.
  - Daily oral Morphine dose >1000 mg, then estimated daily oral Methadone dose is < 5% of total daily Morphine dose.

Note: The total daily Methadone dose should then be divided to reflect the intended dosing schedule.

- Methadone accumulates with repeated doses and dosage reduction may be needed after 3-5 days to prevent CNS depressant effects.
- Most patients will be well-controlled on 8-12 hour dosing interval for chronic pain management. Some patients may require dosing interval of 4-8 hours to maintain analgesic effects.
- Doses should be titrated to appropriate effects.
- Outpatient prescription available as 1, 5, 10 and 25mg tablets. Also available as a 1mg/ml and 10mg/ml oral solution.
- Trade Name: Metadol™

For treatment of severe pain

HYDROMORPHONE 1-2mg PO Daily
- Initial dose of 1-2mg PO q4-6h prn in patients who have not previously received opioids.
- Hydromorphone is approximately 5 times stronger than oral morphine.
- Start low and titrate upward slowly, no ceiling effect.
- Titration of controlled release form every 48-72 hours
- Outpatient prescription available as a 1mg/ml oral syrup
- Immediate release tablets of 1, 2, 4 & 8 mg.
- 12-hour Controlled-release capsule in 3, 6, 12, 18, 24 & 30 mg (Hydromorph Contin™). Capsule may be opened and beads sprinkled over cold soft food such as apple sauce.
- Injectable: 2mg/ml ampoule, 10mg/ml, 20mg/ml, 50mg/ml vials.

For persistent moderate to severe chronic pain that requires around-the-clock pain analgesia for an extended period of time.

FENTANYL  
- Not for opioid naive patients.
- For patients already receiving at least the equivalent of 60 mg of oral Morphine per 24 hours.
- Fentanyl 25mcg is equivalent to 60-134 mg of oral Morphine.
- Not recommended for acute pain and rapidly changing pain because it takes about 24 hours to reach maximum effect and cannot be titrated rapidly.
- Titration every 6-7 days (2 patches) and refer to CPS conversion table for dose conversion from oral to transdermal and titration.
- The dosing interval for the transdermal system is usually 72 hours but due to inter-individual pharmacokinetic variability, some patients may require a dosing interval of 48 hours.

Patients with Fever
- Serum Fentanyl concentrations could theoretically increase by approximately one-third for patients with a body temperature of 40°C due to temperature-dependent increases in Fentanyl release from the system and increased skin permeability. Patients who develop fever should be monitored for opioid side effects and have their Fentanyl dose adjusted if necessary.

Outpatient prescription available in 12, 25, 50, 75 & 100mcg patches delivering respectively 12.5mcg, 25mcg, 50mcg, 75mcg and 100mcg of Fentanyl per hour for 72 hours.

Name Brand: Duragesic™ & generics
PAIN MANAGEMENT - Supportive Therapy

Adjunctive analgesia treatment in adult patients with advanced cancer who experience moderate-to-severe pain during the highest tolerated dose of strong opioid therapy for persistent background pain

THC/CBD

- THC (delta-9-tetrahydrocannabinol)/CBD (cannabidiol) are the two principal ingredients in the product known as Sativex™.
- Sativex™ has a dosing rate of one spray every four hours on the first day, up to a maximum of four sprays on the first day and gradually titrate upward as needed and as tolerated.
- Sativex™ is contraindicated in patients with a known or suspected allergy to Cannabinoids, Propylene Glycol, Ethanol or Peppermint Oil.
- Patients with serious cardiovascular disease such as ischemic heart disease, arrhythmias, poorly controlled hypertension or severe heart failure, history of schizophrenia or any other psychotic disorder should avoid using this product.
- Use with caution in patients with a history of substance abuse, including alcohol abuse or dependence
- Outpatient prescription available in 5.5mL amber glass vial containing up to 51 sprays/actuation. Each spray contains 2.7mg THC and 2.5mg CBD.
- Sativex™ is packed as 4 vials in each carton.

TOXICITIES:

Renal Failure
Methadone
- No adjustment necessary in renal impairment unless CrCl < 0.17mL/sec: administer 50 to 75% of normal dose.

CLINICAL MONITORING:

Methadone
- CYP3A4 inhibitors (Azole antifungals, Erythromycin, Clarithromycin, Diltiazem, Verapamil etc.) may increase levels/effects of Methadone. Use cautiously with other drugs that prolong the QTc (Amitriptyline, Imipramine, Haloperidol, Sotalol, Quinidine, Domperidone, Clarithromycin etc.)
- CYP3A4 inducers (Carbamazepine, Phenobarbital, Phenytoin, Rifampicin, Protease Inhibitors etc.) may decrease levels/effects of Methadone, larger doses may be required.
- Methadone may reduce levels/effects of CYP2D6 prodrug substrates (ex. Codeine, Hydrocodone, Oxycodone and Tramadol).

Fentanyl
- Fentanyl is a major substrate of CYP3A4.
- Potent inhibitors of CYP3A4 (Azole antifungals, Clarithromycin, Erythromycin, Doxycycline, Protease Inhibitors, Verapamil, Diltiazem, Imatinib etc) may increase levels/effects of Fentanyl.
- Potent inducers of CYP3A4 (Carbamazepine, Phenytoin, Phenobarbital, Rifampine, St John’s Wort etc) may decrease effects/levels of Fentanyl.
- MAO inhibitors during the previous 14-day period is not recommended. Conversely, the use of MAO inhibitors in patients who have received Fentanyl in the previous 14-day period is not recommended.

THC/CBD
- Tachycardia, and transient changes in blood pressure, including episodes of postural hypotension changes of mood, mouth irritations decrease in cognitive performances and memory, decrease in ability to control drives and impulses, and alteration of the perception of reality, particularly altered time sense
- Additive effects when coadministered with sedatives, alcohol, drugs with sedating or psychotropic effects. Potential for drug interactions, THC inhibits CYP1A2, CYP2C9, CYP2C19, CYP3A4 and CBD inhibits CYP1A2, CYP2C9, CYP2C19, CYP3A4 and CYP2D6. Caution with Fentanyl and Amitriptyline.

REFERENCES:
- Compendium of Pharmaceuticals and Specialties (CPS), Canadian Pharmacist Association 2007.

Date revised: 12/17/2008
**PAMIDRONATE Therapy**

*Hypercalcemia (Cancer or Therapy-related)*

**PAMIDRONATE**

60-90mg  IV  Day 1

- If Corrected Serum Calcium = 2.7-3.5 mmol/L, give 60mg.
- If Corrected Serum Calcium > 3.5 mmol/L, give 90mg.

**First Dose:**
- Mix in **500mL 5% Dextrose or Normal Saline** and Infuse over **4 hours**.

**Subsequent Doses:**
- Admix into **250mL Normal Saline** in an Intramate LV50 pump and Infuse over **5 hours** at home.

**REPEAT EVERY 14 to 28 DAYS Until Normalization of Serum Calcium Levels**

**TESTS:**

<table>
<thead>
<tr>
<th>Baseline Tests</th>
<th>Ca</th>
<th>Cr</th>
<th>Urea</th>
<th>Albumin</th>
</tr>
</thead>
</table>

**PATIENT VISITS and APPOINTMENT TYPE:**

- **First dose:** 4hrs  Type C
- **Subsequent doses:** 15min  Type A

**CLINICAL MONITORING:**

Clinical Monitoring Criteria
- Serum electrolytes, including calcium.

**Hypocalcemia**

0. Serum Calcium > 2.10 mmol/L
1. Serum Calcium = 2.10 to 1.93 mmol/L
2. Serum Calcium = 1.92 to 1.74 mmol/L
3. Serum Calcium = 1.73 to 1.51 mmol/L
4. Serum Calcium < 1.50 mmol/L

Rated on assessment of anti-hypercalcemia response and at periodic visits or in response to patient complaint. **Expected Clinical Outcomes**

- Assessment of Serum Calcium at 3 to 7 days after treatment; rating of response by Response Criteria.
- No retreatment if patient is normocalcemic, or only mildly hypercalcemic (use clinical judgement).

**Hypercalcemia**- Response Criteria

0. Serum Calcium < 2.64 mmol/L
1. Serum Calcium = 2.64 to 2.88 mmol/L
2. Serum Calcium = 2.89 to 3.12 mmol/L
3. Serum Calcium = 3.13 to 3.37 mmol/L
4. Serum Calcium > 3.37 mmol/L

Rated on assessment of anti-hypercalcemia response and at periodic visits or in response to patient complaint.

- Creatinine should be monitored regularly.
- Consider a reduced initial dose or an infusion time of at least 4 hours in patients with pre-existing renal impairment (CrCl<30ml/min).
- Use is not recommended for the treatment of bone metastases in patients with severe renal impairment.
- In patients who develop renal deterioration during bisphosphonate therapy (>44umol/L in patients with normal baseline or >88umol/L in patients with abnormal baseline), consider holding dose. Resumption of therapy (at the same dose) may be considered when serum creatinine returns to within 10% of baseline.

**FORMULAE:**

**Corrected Serum Calcium (mmol/L)**

\[ \text{Corrected Serum Calcium} = \text{Measured Serum Calcium} + \left[ \frac{40 - \text{serum albumin}}{0.02} \right] \]

\[ \text{CrCl - Cockcroft & Gault (mL/sec)} \]

Male: \[
\left( \frac{140 - \text{age(yrs)}}{\text{TBW(Kg)}} \right) \times \frac{\text{TBW(Kg)}}{\left( 50 \times \text{SCr(umol/L)} \right)}
\]

Female: \[
\left( \frac{140 - \text{age(yrs)}}{\text{TBW(Kg)}} \right) \times \frac{\text{TBW(Kg)}}{\left( 50 \times \text{SCr(umol/L)} \right)} \times 0.85
\]

**INTERNAL CODE:**

- PAMID60*SC
- PAMID90*SC

CCO Eligibility Form Required  [ ]  Non-Formulary Form Required  [ ]

*Date revised: 08/29/2008*
STRONTIUM-89 Supportive Therapy

Pain Associated with Bony Lesions from Cancer

STRONTIUM-89

4mCi IV Day 1
- Inject over 5 minutes, then observe for 30 minutes (may be dosed as 2MBq/kg; normal dose 111-150MBq).
- Dose reduction to 2mCi for patients with a superscar.
- IV administration by strict protocol for environmental radiation protection and under the direct supervision of a radiation oncologist or nuclear medicine physician.
- Due to the short half-life of the commercial product, drug acquisition (through the Pharmacy) and patient treatment schedule must be carefully planned. Treatment should occur within 1-2 days of receipt of the product at JCC.

SINGLE TREATMENT; MAY REPEAT IN 3 MONTHS OR LONGER IF SYMPTOMS RECUR

TESTS:
Baseline Tests: WBC HB PLT Cr
-1 Month: WBC HB PLT

PATIENT VISITS and APPOINTMENT TYPE:
Day 1: 60min Type D

TOXICITIES:
Hematologic
- Confirm adequate hematology values BEFORE dose is ordered.

SUGGESTED ACTION

REFERENCES:
- Brundage et al; Use of Strontium 89 in Endocrine-Refractory Prostate Cancer Metastatic to Bone; Cancer Prevention and Control; Volume 2; pp79-87;1998.
- McEwan, A; Use of Radionuclides for the Palliation of Bone Metastases; Seminars in Radiation Oncology; Volume 10; pp103-114;2000.
- Pagliaro et al; A Phase II/III Study of Strontium-89 Combined with Gemcitabine in the Treatment of Patients with Androgen Independent Prostate Carcinoma and Bone Metastases; Cancer; Volume 97; pp 2988 - 2994; 2003.
- Porter et al; Results Of A Randomized Phase-III Trial To Evaluate The Efficacy of Strontium-89 Adjuvant To Local Field External Beam Irradiation In The Management of Endocrine Resistant Metastatic Prostate Cancer; International Journal of Radiation Oncology, Biology, and Physics; Volume 25;pp805-813;1993.
- Quilty et al; A Comparison of the Palliative Effects of Strontium-89 And External Beam Radiotherapy in Metastatic Prostate Cancer, Radiotherapy and Oncology; Volume 31;pp33-40;1993.

Date revised: 03/07/2005
Zoledronic Acid Supportive Therapy

Hypercalcemia - Cancer or Therapy related

**Zoledronic Acid** 4mg IV Day 1

- Mix in **100mL bag 5% Dextrose or Normal Saline**.
- Infuse over a minimum of **15 minutes**.
- If corrected Serum Calcium > 3.0mmol/L, give 4mg dose.
- If calcium does not return or remain normal after initial treatment, may retreat with 4mg dose. The efficacy and safety of retreatment with 4mg has not been assessed in prospective studies therefore renal function must be assessed prior to each re-administration.

Dosing for mild to moderate renal impairment:
1. If baseline CrCl > 60mL/min, give 4mg dose.
2. If baseline CrCl 50-60mL/min, give 3.5mg dose.
3. If baseline CrCl 40-49mL/min, give 3.3mg dose.
4. If baseline CrCl 30-39mL/min, give 3mg dose.
- Do not mix with calcium-containing infusion solutions (eg. Lactated Ringer’s solution).

**TESTS:**
Baseline Tests Ca  Cr  Urea  Albumin

**PATIENT VISITS and APPOINTMENT TYPE:**
→ Day 1:  30min Type B

**TOXICITIES:**
Renal Failure
- During treatment, serum creatinine should be measured before each dose and treatment should be withheld for renal deterioration.

In the clinical studies, renal deterioration was defined as follows:
- For patients with normal baseline creatinine (< 123umol/L), an increase of 44umol/L.
- For patients with abnormal baseline creatinine (> 123umol/L), an increase of 88umol/L.
- In the clinical studies, treatment was resumed (at the same dose) when the creatinine returned to within 10% of the baseline value.

**CLINICAL MONITORING:**
Clinical Monitoring Criteria
- Serum electrolytes, including calcium

**Hypocalcemia**
0. Serum Calcium > 2.10 mmol/L
1. Serum Calcium = 2.10 to 1.93 mmol/L
2. Serum Calcium = 1.92 to 1.74 mmol/L
3. Serum Calcium = 1.73 to 1.51 mmol/L
4. Serum Calcium < 1.50 mmol/L

Rated on assessment of anti-hypocalcemia response and at periodic visits or in response to patient complaint.

**Expected Clinical Outcomes**
- Assessment of Serum Calcium at 3 to 7 days after treatment; rating of response by Response Criteria.
- No retreatment if patient is normocalcemic, or only mildly hypercalcemic (use clinical judgement).

**Hypercalcemia - Response Criteria**
0. Serum Calcium < 2.64 mmol/L
1. Serum Calcium = 2.64 to 2.88 mmol/L
2. Serum Calcium = 2.89 to 3.12 mmol/L
3. Serum Calcium = 3.13 to 3.37 mmol/L
4. Serum Calcium > 3.37 mmol/L

- Rated on assessment of anti-hypercalcemia response and at periodic visits or in response to patient complaint.

**FORMULAE:**
Corrected Serum Calcium (mmol/L) = Measured Serum Calcium + [(40 - serum albumin) x 0.02]
CrCl - Cockcroft & Gault (mL/sec) = [140-age(years)] x TBW(Kg) / [50 x SCr(umol/L)]
CrCl - Cockcroft & Gault (mL/sec) = [140-age(years)] x TBW(Kg) / [50 x SCr(umol/L)] x 0.85
Creatinine CI (mL/min) = mL/min = 60 x CrCl mL/sec

**INTERNAL CODE:**
OPIS CODE: Zoledronic Acid

CCO Eligibility Form Required  Non-Formulary Form Required  Date revised: 10/13/2005

Supportive Care
The printing of the Regional Cancer Program Formulary was made possible by a primary unrestricted educational grant from ORTHO BIOTECH.

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JANSEN-ORTHO INC.

The Juravinski Cancer Centre
699 Concession Street, Hamilton, ON L8V 5C3
Phone: (905) 387-9495 Website: http://www.hrcc.on.ca/Welcome.htm
RECAP Glossary of Terms

Cancer Regimen Information

**Status** – A regimen may be *Active*, *Inactive* or *Closed to Accrual*.

*Active*: The drug or regimen is listed in the formulary and is considered one of the treatment choices for that disease site.

*Inactive*: The drug or regimen is archived because it is no longer widely used for that disease site.

*Closed to Accrual*: This refers to clinical trials regimens that are no longer accepting new patients.

**Category** – A regimen may be designated as Formulary, Non Formulary, CCO New Drug Funding Program or a Clinical Trial.

*Formulary*: A regimen that has received approval for use and Formulary listing by the JCC Formulary and Therapeutics Committee. It is recognized that up to two drugs may be deleted from an existing formulary regimen and remain within the formulary.

*Non-Formulary*: A regimen that has not been approved for listing in the formulary or a formulary regimen to which a drug has been added.

*CCO New Drug Funding Program*: A regimen which requires eligibility confirmation for reimbursement by the CCO New Drug Funding Program.

*Clinical Trial*: These regimens are designed to test the usefulness of new drugs, new approaches to surgery or radiation therapy, or new combinations of treatments.

**STR Colour** – The Systemic Therapy Record (STR) for JCC patients are colour coded to reflect whether the regimen is a *single day* (green), *multiple day* (grey) or *oral regimen* (ivory).

**Site Group** – Refers to the primary disease location for which the regimen is used.

**Classification** – Is the type of regimen treatment being applied (e.g., Chemotherapy, Chemoradiotherapy, Radioimmunotherapy, Supportive Therapy, Targeted Therapy).

**Site Group Affiliation** – A regimen may be associated with site groups in addition to the primary site group.

BR = Breast
CN = Central Nervous System
GI = Gastro Intestinal
GU = Gastro Urinary
GY = Gynecology
HN = Head & Neck
LU = Lung
ME = Melanoma
SA = Sarcoma
SK = Skin
UK = Unknown
ALL = All sites
CCO New Drug Funding Program (NDFP) - New and expensive drugs identified by CCO and requires the completion of an eligibility form for reimbursement by CCO under the program.

Non-Formulary Regimen Request - This form is used for drugs or regimens that are not in the formulary but an oncologist wishes to use the drug/regimen at then Centre. The head of medical oncology must approve the drug/regimen before it may be used.

Ambulatory Code – The OPIS Code related to the specific regimen.

Inpatient Code – The Meditech Code related to the specific regimen.

Regimen Title – Descriptive terms assigned to the regimen.

Regimen Indication – Provides an indication of the type of treatment (e.g., Advanced Breast Cancer).

General

Internal Code – Additional code a regimen may be assigned.

Internal Code – Description of the internal code.

Hydration – Pre, Concurrent and Post Hydration are included as required.

Antimicrobial Prophylaxis – Included in specific regimens where required.

Regimen

Order Group # – Used in OPIS 2000 to group drugs to facilitate order entry at specific points within the course of the regimen.

Order Group Directive – Description of the time frame within the course of treatment.

Type – Kind of entry (e.g., Chemo, Pre-meds, Radiation and Supportive).

Drug – Generic name of the drug.

Dosage – Dosage.

Schedule – When the drug is given (e.g., Day 1).

Rounding – Rounding to the closest measurable dosage.

Route – The form in which the drug is given to the patient (e.g., Oral, Intravenous).

Administration – The way in which the medication is administered (e.g., Admix in 500ml of normal saline and infuse over 1hr).

Cycle Schedule – Specifies the time interval and frequency in which the regimen is repeated.
Test Tab

Baseline Tests – Tests performed prior to treatment.

Schedule Tests – Tests performed at specified treatment times within the cycle.

Antiemetics

Ambulatory Pre-Chemo – Antiemetics ordered for ambulatory patients prior to chemotherapy. They may be taken at home or administered at the Cancer Centre.

Take Home Antiemetic – Antiemetics ordered for ambulatory patients after chemotherapy. They are taken at home.

In-patient Antiemetic – Antiemetics ordered for in-patients.

Supplementary

Ancillary Treatment – Other recommended treatment used to help enhance the drug therapy or prevent undue effects of the drug therapy (e.g., cryo-therapy).

Clinical Monitoring – Provides monitoring grades for specific side effects for each regimen.

Special Precautions – Other specific parameters to observe and/or monitor patient treatment.

Hypersensitivity Procedures – Methods for treating reactions and re-treatment of patients.

Formulae - Calculations associated with a particular regimen.

Admin Time – Time required to administer treatment on a specified day within the regimen.

Type – Code indicating assigned nursing times (e.g., A=15min, B=30min, C=45min etc.).

Toxicities

Toxicity – Provides information on hematological, gastrointestinal, hepatic, cutaneous, neurological and renal toxicities and guidelines for drug dosage modification based on the values of specific lab tests (e.g., bilirubin, creatinine clearance).

In-Patient Specifics

Lab Parameters – Identifies the parameters within which the regimen may be started and/or continued.

Blood Products – Specifies the timing and type of blood products administered.

Growth Factors – Specifies the timing and type of growth factors used.

Procedures – Specifies the timing and type of procedure (e.g., bone marrow transplant).
CT Specifics

CT Code – Internal code which may be assigned to the study.

Nurse – Clinical Trial Nurse assigned to the study.

Principal Investigator – Designated researcher associated with the study.

Study Title (full) – Complete study title.

Study Notes – Additional description of study (e.g., randomization).

Alerts – Special warnings regarding the study.

Dose Modifications – Changes in dosage due to the clinical status of the patient.

Pharmacokinetics – Specific lab tests that may be required as part of the study.

Clinical Trial Formulae - Calculations associated with a particular study regimen.

Comments

References – Evidence based references associated with the regimen.

Notes – Additional regimen relevant information.

History

Approval Date – The date the regimen was approved as part of the Formulary.

Entry Date – The date the regimen was entered into the software.

Revision Date – The date the regimen was last revised by the Pharmacy Department.