BC Cancer Agency

Systemic Therapy Update

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Website access at http://www.bccancer.bc.ca/STUpdate/

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FAX request form and IN TOUCH phone list are provided if additional information is needed.

EDITOR'S CHOICE

HIGHLIGHTS OF PROTOCOL REVISIONS

The **Gastrointestinal Tumour Group** has reviewed and updated the irinotecan (UGICAPIRI, GIFOLFIRI, UGIIRFUFA, GIIRINALT) and oxaliplatin protocols (UGICAPOX, UGIFOLFOX). This is to ensure that the recommended methods of drug administration are accurate and efficient, the dosing information is accurate and clearly defined, and that the dose modification information is presented in a clear and concise manner. These revisions should help support healthcare providers throughout the province to deliver the therapies to patients with gastrointestinal tumours appropriately through the correct interpretation of the treatment protocols.

CANCER DRUG MANUAL

Limited Revision of Chlorambucil and Pamidronate Monographs The **chlorambucil** monograph has been revised to clarify the different implications of myelosuppression between patients with hematological malignancies and solid tumours. This is an extension to the recent changes to patient information handouts on drugs used for hematological malignancies (see January 2005 issue and below).

The **pamidronate** monograph has been revised to include the recent Health Canada caution of reported cases of osteonecrosis of the jaw (ONJ). This adverse event has been reported in patients treated with pamidronate and zoledronic acid, mostly associated with dental procedures (eg, tooth extraction) and signs of local infection (eg, osteomyelitis). Patients developed painful bone exposure in the mandible and/or maxilla that were unresponsive to surgical or medical treatments. Patients with concomitant risk factors (eg, cancer, chemotherapy, radiotherapy, corticosteroids, poor oral hygiene) should be considered for appropriate preventive dentistry before pamidronate treatment. They should also avoid invasive dental procedures during pamidronate treatment if possible.

Limited Revision of Thalidomide Patient Information The **thalidomide** patient information handout has been revised to include caution on blood clots to reflect the potential for venous thrombosis.

Changes to Patient Handouts for Hematological Drugs Recently, drugs which are used to treat hematological malignancies were identified for revision (see January 2005 issue). This was to address the issue of how to clearly communicate the myelosuppressive effects of these drugs in patients with hematological

malignancies and solid tumours. Due to the nature of hematological malignancies, and the chronic dosing schedules sometimes used, the blood count information given – which was based on similar statements for solid tumour patients – was generally unclear and potentially causing confusion in this group of patients. Hence, our goal was to modify the handouts so that they would be useful to patients with hematological malignancies as well as those with solid tumours. This proved to be a very challenging area.

In myeloproliferative disorders, the white blood cell (WBC) and platelet counts may be high at the start of treatment and the **intention** is to **decrease** cell counts. During treatment, these patients **may not** be susceptible to infections because they are not necessarily immunocompromised. In addition, these patients may have high overall platelet count before treatment but nevertheless have bleeding problems due to low number of actual functional platelets. During treatment, these patients **may have** their bleeding problems improve while the platelet count decreases because of reduced proliferation of dysfunctional platelets. The WBC and the platelet counts may **not** return to the normal range, because these cells were **not** normal to begin with.

In some cases, such as in refractory acute myelogenous leukemia, patients with hematological malignancies may be cytopenic before treatment except during leukemic blasts. Hence, warning about cytopenia during treatment is not appropriate as it may cause undue concern, with the risk that the patient may stop taking the medication. In other cases such as chronic lymphocytic leukemia, while the WBC count may be high at the beginning of treatment and the treatment intent is to reduce the count, the actual neutrophil count may fluctuate up and down. Some patients may not be knowledgeable about the different types of WBC and again this information may be confusing.

Finally, dosing for haematological malignancies may be chronic and based on blood counts. Hence, information on nadirs does not have the same importance as that with cyclical dosing for solid tumours.

The drugs that we chose to modify are busulfan, chlorambucil, cytarabine, hydroxyurea, mercaptopurine, methotrexate (oral) and thioguanine. The handout modifications include:

1. Providing a separate table for WCB and platelet information.
2. Including the blood count statement *"Changes in blood counts*
   This drug may cause temporary changes in your blood counts. Your doctor will be following these changes carefully by performing blood tests. Adjustment of your treatment may be needed in certain circumstances. If you are receiving an oral chemotherapy pill, do not stop the drug unless advised to do so by a doctor (preferably your cancer specialist)."
3. Adding the word "normal" before WBC and platelets.
4. Removing the cyclical information from the WBC and platelet sections.

Chlorambucil was more complicated than the other drugs on the list because although it is used in hematological malignancies, it is also used commonly in other tumour groups such as in lymphomas. We proceeded with the proposed changes to the chlorambucil handout, but in addition we modified the chlorambucil monograph by expanding the paragraph on myelosuppression. The nadir information is always present in the Cancer Drug Manual drug monographs and can be easily accessed by a health professional if required.

We hope that these modifications will provide useful information to our patients.

Submitted by:
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Reviewed by:
Mário de Lemos, PharmD
Cancer Drug Manual Editor

The Cancer Drug Manual is available on the BC Cancer Agency website www.bccancer.bc.ca/cdm/.

PATIENT EDUCATION

Patient Handouts on Cancer Drugs The patient information handout for thalidomide has been revised. See under Cancer Drug Manual for more details.

Patient information handouts for cancer drugs are available on the BC Cancer Agency website (www.bccancer.bc.ca/DrugDatabasePt/) under Health Professionals Info, Cancer Drug Manual, Drug

Information for the Patient. For treatment protocol specific information, go to the BC Cancer Agency website (www.bccancer.bc.ca) under Health Professionals Info, Chemotherapy Protocols, Information for the Patient.

DRUG UPDATE

Non-lyophilized Cyclophosphamide Bristol-Myers Squibb (BMS) has recently replaced their lyophilized cyclophosphamide product with a non-lyophilized formulation. However, BMS cannot provide stability information for the new formulation when further diluted in NS. This created a problem as the practice at the BC Cancer Agency is to dilute cyclophosphamide in NS for IV infusion, based on the stability data with the previous (lyophilized) product.

An in-house study conducted by BMS in 1990 showed that non-lyophilized Cytoxin® was stable in NS at a concentration of 0.1 mg/mL for 2 days at room temperature and 28 days when refrigerated. Currently, BMS in Canada and the US are trying to determine if the product used in that study is the same product manufactured today. However, Lawrence Trissel, director of Clinical Pharmaceutics Research Program at MD Anderson Cancer Center and a leading authority on IV admixtures, has recommended that the same expiration times may be used for both the lyophilized and the non-lyophilized products. This is based on the reasoning that the same cyclophosphamide molecule is used and no buffers have been added to change the pH and thus the stability.

Therefore, the Provincial Pharmacy Professional Practice Council of the BC Cancer Agency recommends no change in the current practice of diluting cyclophosphamide in NS for IV infusion.

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Update on Special Ordering Procedures Chart The chart for drugs with special order procedures (eg, Health Canada Special Access Programme drugs) has been updated. Some new products have been added (aprepitant, arsenic, bevacizumab, bortezomib, cetuximab, denileukin diftiox, thiotepa) while some others have been modified (pemetrexed, thalidomide). The chart is accessible from the BC Cancer Agency website (http://www.bccancer.bc.ca/ChemoProtocols/Forms/) under Health Professionals Info, Chemotherapy Protocols, Frequently Used Forms. CON centres can also get additional guidance on SAP applications from their Regional Cancer Centre Pharmacy.

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LIST OF NEW AND REVISED PROTOCOLS

The **INDEX to BC Cancer Agency Protocol Summaries** is revised monthly (includes tumour group, protocol code, indication, drugs, last revision date and version). Protocol codes for treatments requiring "Undesignated Indication" approval are prefixed with the letter **U**.

- **BRAVTR** revised (eligibility clarified): Palliative therapy for metastatic breast cancer using trastuzumab (Herceptin®)
- **BRAVTRNAV** revised (trastuzumab maintenance treatment clarified): Palliative therapy for metastatic breast cancer using trastuzumab (Herceptin®) and vinorelbine
- **UCNAJTMZ** revised (protocol code changed from UCNGBMTMZ): Concomitant and adjuvant temozolomide for newly diagnosed malignant gliomas
- **UCNGBMTMZ** revised (protocol code changed to UCNAJTMZ): Concomitant and adjuvant temozolomide for newly diagnosed malignant gliomas
- **(U)GICAPIRI** revised (INR statement standardized, cycle definition clarified): Palliative combination chemotherapy for metastatic colorectal cancer using irinotecan and capecitabine in patients unsuitable for GIFOLFIRI
- **(U)GICAPOX** revised (cycle definition clarified): Palliative combination chemotherapy for metastatic colorectal cancer using oxaliplatin, and capecitabine
- **GIFOLFIRI** revised (cycle definition clarified): Palliative combination chemotherapy for metastatic colorectal cancer using irinotecan, fluorouracil and folinic acid (leucovorin)

- **(U)GIFOLFOX** revised (cycle definition clarified): Palliative combination chemotherapy for metastatic colorectal cancer using oxaliplatin, 5-fluorouracil and folinic acid (leucovorin)
- **GIFUA** revised (options for concurrent radiation): Curative combined modality therapy for carcinoma of the anal canal using mitomycin, infusional fluorouracil and radiation therapy
- **GIIR** revised (cycle definition and liver function tests clarified): First- or second-line palliative chemotherapy for metastatic colorectal cancer using irinotecan
- **(U)GIIRFUFA** revised (liver function tests clarified): Palliative combination chemotherapy for metastatic colorectal cancer using irinotecan, fluorouracil and folinic acid (leucovorin)
- **GIIRINALT** revised (liver function tests clarified): Second-line treatment for 5-FU refractory metastatic colorectal cancer using weekly scheduled irinotecan
- **(U)GOOVCAG** revised (protocol code changed from UGOOVCAGE): Treatment of advanced ovarian cancer in patients who have progressed or recurred following first-line platinum-based treatment using carboplatin and gemcitabine
- **(U)GOOVCAGE** revised (protocol code changed to UGOOVCAG): Treatment of advanced ovarian cancer in patients who have progressed or recurred following first-line platinum-based treatment using carboplatin and gemcitabine
- **GUBCV** revised (bilirubin added to Tests): Therapy for transitional cell cancers using carboplatin-vinblastine
- **GUPMX** revised (typos corrected under Dose Modifications): Palliative therapy for hormone refractory prostate cancer using mitoxantrone and prednisone
- **(U)LUAJCAT** new: Adjuvant carboplatin and paclitaxel following resection of stage I, II and IIIA non-small cell lung cancer
- **(U)LUAJNP** new: Adjuvant cisplatin and vinorelbine following resection of stage I, II and IIIA non-small cell lung cancer
- **LUAVTOP** revised (dose adjustment for renal function clarified): Second-line Treatment of recurrent small cell lung cancer (SCLC) with topotecan
- **LUMMPG** revised (clarification of dosing adjustment of platinum): Treatment of malignant mesothelioma with platinum and gemcitabine
- **LUMMPPEM** revised (dose adjustment for renal function clarified): Treatment of malignant mesothelioma with platinum and pemetrexed (Alimta®)

PRE-PRINTED ORDER UPDATE

Pre-printed orders should always be checked with the most current BC Cancer Agency protocol summaries. The BC Cancer Agency Vancouver Centre has prepared chemotherapy pre-printed orders, which can be used as a guide for reference. An index to the orders can be obtained by Fax-back.

- **GIIR** revised (title and eligibility updated): First-or second-line palliative chemotherapy for metastatic colorectal cancer using irinotecan
- **BRAVCAD** revised (docetaxel infusion rate clarified): Palliative therapy for metastatic breast cancer using docetaxel and capecitabine
- **BRAVDOC** revised (docetaxel infusion rate clarified): Palliative therapy for metastatic breast cancer using docetaxel (Taxotere®)
- **BRAVDOC7** revised (docetaxel infusion rate clarified): Palliative therapy for metastatic breast cancer using weekly docetaxel (Taxotere®)
- **BRLAACD** revised (docetaxel infusion rate clarified): Treatment of locally advanced breast cancer using doxorubicin and cyclophosphamide followed by docetaxel (Taxotere®)
- **BRAVNAV** revised (typo corrected for ANC): Palliative Therapy for metastatic breast cancer using vinorelbine (Navelbine®)
- **BRAJACT** revised (dilution volume for cyclophosphamide clarified): Adjuvant therapy for breast cancer using doxorubicin and cyclophosphamide followed by paclitaxel
- **GIIR** revised (title and eligibility updated): First-or second-line palliative chemotherapy for metastatic colorectal cancer using irinotecan
- **GOCXCAD** revised (docetaxel infusion rate clarified, eligibility revised): Treatment of advanced/recurrent non-small cell cancer of the cervix with carboplatin and docetaxel in ambulatory care settings

- **GOENDCAD** revised (docetaxel infusion rate clarified): Treatment of primarily advanced or recurrent endometrial cancer using carboplatin and docetaxel
- **GOOVCADM** revised (docetaxel infusion rate clarified): Primary treatment of invasive epithelial ovarian, fallopian tube and primary peritoneal cancer, with no visible residual tumour (moderate-high risk)
- **GOOVCADR** revised (docetaxel infusion rate clarified): Second line treatment using docetaxel and carboplatin for epithelial ovarian cancer relapsing after primary treatment
- **GOOVCADX** revised (docetaxel infusion rate clarified): Primary treatment of visible residual (extreme risk) invasive epithelial ovarian cancer
- **GOOVDOC** revised (docetaxel infusion rate clarified, chair-side methylprednisolone replaced by hydrocortisone): Treatment of progressive, platinum-refractory epithelial ovarian carcinoma, primary peritoneal carcinoma or fallopian tube carcinoma using docetaxel
- **GUPDOC** revised (docetaxel infusion rate clarified, eligibility revised, chair-side methylprednisolone replaced by hydrocortisone): Palliative therapy for metastatic hormone refractory prostate cancer using docetaxel
- **LUCISDOC** revised (replacing ULUCISDOC, docetaxel infusion rate clarified, chair-side methylprednisolone replaced by hydrocortisone): First-line treatment of advanced non-small cell lung cancer (NSCLC) with cisplatin and docetaxel
- **LUDOC** revised (docetaxel infusion rate clarified): Second-line treatment for advanced non-small cell lung cancer (NSCLC) with docetaxel (Taxotere®)

WEBSITE RESOURCES

Reimbursement and Forms: The current Benefit Drug List, Class II forms and Undesignated Indication Application forms are available on the BC Cancer Agency website under Health Professionals Info, Chemotherapy Protocols, Frequently Used Forms (http://www.bccancer.bc.ca/HPI/ChemotherapyProtocols/Forms.htm).

Cancer Management Guidelines: The Cancer Management Guidelines are available on the BC Cancer Agency website (http://www.bccancer.bc.ca/CaMgmtGuidelines/) under Health Professionals Info, Cancer Management Guidelines.

The Cancer Chemotherapy Protocols are available on the BC Cancer Agency website (www.bccancer.bc.ca/ChemoProtocols) under Health Professionals Info, Chemotherapy Protocols.

Provincial Systemic Therapy Program Policies are available on the BC Cancer Agency website (www.bccancer.bc.ca) under Health Professionals Info, Chemotherapy Protocols, Policies and Procedures.

The Unconventional Cancer Therapies Manual is available on the BC Cancer Agency website www.bccancer.bc.ca under Patient/Public Info, Unconventional Therapies.

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Nursing Professional Practice	Ext 2623	ilundie@bccancer.bc.ca
Pharmacy Professional Practice	Ext 2247	gconcon@bccancer.bc.ca
Provincial Systemic Therapy Program	Ext 2247	gconcon@bccancer.bc.ca
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Fraser Valley Centre (FVCC)	(604)-930-2098	Toll-Free 1-(800)-523-2885
Vancouver Centre (VCC)	(604)-877-6000	Toll-Free 1-(800)-663-3333
Vancouver Island Centre (VICC)	(250) 519-5500	Toll-Free 1-(800)-670-3322

BC CANCER AGENCY SYSTEMIC THERAPY UPDATE REQUEST FORM

FAX (604) 877-0585
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UPDATES **Please ☑ Fax-Back information below**:

Most items have been hyperlinked for easy access

☐ All items for **February 2005 (Vol 8 № 2)**				
Cancer Drug Manual Monographs: (also available on our website www.bccancer.bc.ca)				
☐ Chlorambucil ☐ Pamidronate				
Patient Education Handout: (also available on our website www.bccancer.bc.ca)				
☐ Thalidomide				
Protocol Summaries: (also available on our website www.bccancer.bc.ca)			Index of Protocol Summaries	
☐ BRAVTR	☐ BRAVTRNAV	☐ UCNAJTMZ	☐ UCNGBMTMZ	☐ UGICAPIRI
☐ UGICAPOX	☐ GIFOLFIRI	☐ UGIFOLFOX	☐ GIFUA	☐ GIIR
☐ UGIIRFUFA	☐ GIIRINALT	☐ UGOOVCAG	☐ UGOOVCAGE	☐ GUBCV
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☐ GOOVCADM	☐ GOOVCADR	☐ GOOVCADX	☐ GOOVDOC	☐ GUPDOC
☐ LUCISDOC	☐ LUDOC			
Provincial Systemic Therapy Program Policies				
Reimbursement (also available on our website www.bccancer.bc.ca)				
☐ Benefit Drug List (01 January 2005)		☐ Class 2 Form (01 January 2005)		
Systemic Therapy Update Index (also available on our website www.bccancer.bc.ca)				
☐ Jan-Dec 2000	☐ Jan-Dec 2001	☐ Jan-Dec 2002	☐ Jan-Dec 2003	
☐ Jan-Dec 2004				