



INSIDE THIS ISSUE

- [Editor's Choice](#): Provincial Pre-Printed Chemotherapy Orders, Focus on Bortezomib
- [Drug Update](#): Management of Oxaliplatin Extravasation
- [Cancer Management Guidelines](#) – Management of Anal Canal Cancer; PSA Screening for Prostate Cancer (Patient Information)
- [Cancer Drug Manual](#) – New Pemetrexed Monograph; Revised Monographs and Handouts (Aromatase Inhibitors, Oxaliplatin, Rituximab, Tamoxifen)
- [Nursing Update](#) – Articles of the Month, Telephone Guidelines, Continuing Education On-Line, Responsibilities Related to Checking Chemotherapy Orders
- [Patient Education](#) – Revised Handouts (Aromatase Inhibitors, Oxaliplatin, Pemetrexed, Rituximab, Tamoxifen)
- [Highlights of Protocol Revisions](#) – GI Protocols Using Oxaliplatin
- [List of New and Revised Protocols](#) – UGICAPOX, UGIFOLFOX, HNFUA, HNFUP, HNM, LUAVPG, LUMMPPEM, LYABVD, LYCHOP, LYCHOPR, LYCVP, LYCVPPABO, LYCVPR, LYFLUDR
- [List of New and Revised Pre-Printed Orders](#) – HNFUA, HNFUP, HNM, LUAVPG, LUMMPPEM, LYABVD, LYCHOP, LYCHOPR, LYCVP, LYCVPPABO, LYCVPR, LYFLUDR
- [Provincial Systemic Therapy Policies](#) – Extravasation Guidelines
- [Website Resources](#)

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

EDITOR'S CHOICE

BC CANCER AGENCY LAUNCHES PROVINCIAL PRE-PRINTED CHEMOTHERAPY ORDERS

Provincial pre-printed chemotherapy orders are now available on the BC Cancer Agency website under Chemotherapy Protocols. These standardized orders provide the essential elements for a comprehensive chemotherapy order and mirror the BC Cancer Agency chemotherapy treatment protocol with parameters for prescribing, preparing and administering the treatments.

The provincial pre-printed chemotherapy order should **always be used** in conjunction with the corresponding BC Cancer Agency chemotherapy treatment protocol and the relevant drug information. The Provincial Systemic Therapy Program (PSTP) recommends that all health care practitioners involved in chemotherapy delivery use the PSTP Policy entitled Chemotherapy Process as the guide to safe delivery of chemotherapy. This policy can be located on the BCCA website at: (www.bccancer.bc.ca/HPI/ChemotherapyProtocols/Policies)

Any health care professional using a BC Cancer Agency chemotherapy order to provide treatment for patients will be solely responsible for all aspects of the chemotherapy treatment including patient assessment, dose modification, drug and the dose verification, provision of prescriptions and administration of medications according to acceptable standards of care.

If there are any questions or concerns, please contact the BC Cancer Agency, Provincial Drug Information Coordinator at (604) 877-6098, local 2247.

FOCUS ON BORTEZOMIB (VELCADE®): A NOVEL ACTING AGENT FOR MULTIPLE MYELOMA

Bortezomib (also known as Velcade or PS-341) recently received a Notice of Compliance from Health Canada. It is currently not a BC Cancer Agency Benefit Drug and approval via undesignated request is needed prior to its use. Bortezomib is the first of a new class of drugs called proteasome inhibitors. Proteasomes are complexes that digest proteins that have been marked for digestion, including proteins that are involved in regulating the cell cycle. Inhibition of proteasomes disrupts the normal cell process, resulting in cell death.⁽¹⁾ Bortezomib is indicated for the treatment of multiple myeloma in patients whose disease has progressed with at least two previous chemotherapeutic regimens.^(2, 3) Bortezomib is also being studied for treatment of other cancers such as prostate, colorectal, lung, lymphoma and leukemia.⁽¹⁾

Prior to receiving approval from Health Canada, bortezomib was only available through the Special Access Program (S.A.P.) through specific clinical trials. Janssen-Ortho, the manufacturer of bortezomib, will continue to supply the drug for existing patients already on it through the S.A.P. program or specific clinical trials. The S.A.P. program and phase II trial are now closed to new patients.⁽⁴⁾ Oncologists should fill out undesignated request forms for new patients requiring bortezomib for treatment of myeloma. The Lymphoma Tumour Group now recommends that bortezomib be considered for patients with myeloma requiring systemic treatment after failure of alkylating agents, corticosteroids and thalidomide.

The recommended dose of bortezomib for multiple myeloma is 1.3 mg/m² twice weekly for 2 weeks on days 1, 4, 8 and 11. This is followed by a rest period of 10 days. The cycle is repeated every 21 days for a maximum of 6-8 cycles. A dose reduction to 1 mg/m² is recommended if bortezomib is given in combination with other chemotherapy; however, any such combinations are currently experimental and will only be used within clinical trials, which will provide specific dosing directions.⁽³⁾ Studies are under way to determine pharmacokinetics in patients with renal or hepatic impairment. Patients with renal or hepatic impairment should be closely monitored for signs of toxicity when treated with bortezomib.⁽⁵⁾ Patients with baseline creatinine clearance less than 30 ml/min should not be started on bortezomib without prior discussion with a member of the Lymphoma Tumour Group who has special experience with bortezomib in this situation.⁽³⁾

The most commonly reported adverse effects in clinical trials include asthenia, nausea, diarrhea, decreased appetite, constipation, thrombocytopenia, peripheral neuropathy, pyrexia, vomiting, and anemia.⁽²⁾ The majority of the side effects from bortezomib can be managed with standard interventions.⁽⁵⁾ Adverse events that led to the discontinuation of bortezomib in clinical trials included peripheral neuropathy, thrombocytopenia, diarrhea, and fatigue.⁽²⁾ Baseline thrombocytopenia was generally present in patients who went on to develop grade 3 thrombocytopenia. Because bortezomib has been tested in patients who had previously been given thalidomide, 80% of patients had baseline neuropathy prior to treatment with bortezomib. However, it can cause significant neuropathy even in patients without neuropathy at baseline.⁽⁶⁾

Several cytochrome P450 enzymes (CYP) metabolize bortezomib. CYP3A4 and 2C19 are considered to be the major enzymes involved. No formal drug interaction studies have been done for bortezomib. Caution should be used when bortezomib is given with agents that are known to be potent CYP3A4 inhibitors (eg, some macrolide antibiotics, fluoxetine, ketoconazole) and inducers (eg, carbamazepine, phenytoin, rifampin) or CYP 2C19 inhibitors (eg, fluconazole, fluoxetine, omeprazole) and inducers (eg, rifampin).⁽²⁾

Even though no formal drug interaction studies have been done for bortezomib, the adverse effect profile suggests caution should be used when coadministering some drugs. Medications that can lead to myelosuppression, such as melphalan, can increase myelosuppression with bortezomib.⁽⁷⁾ Hypoglycemia and hyperglycemia have been reported in diabetic patients taking oral antidiabetic agents. Diabetic patients should be closely monitored and may need dose adjustments for their antidiabetic medications.⁽⁷⁾ Medications commonly associated with neuropathy such as amiodarone, isoniazid, nitrofurantoin and statins can increase the incidence of neuropathy with bortezomib.⁽⁷⁾ Patients are also at a higher risk of developing neuropathy if they have been previously treated with chemotherapeutic agents that can cause neuropathy such as cisplatin, paclitaxel, vinca alkaloids and thalidomide.⁽⁵⁾ Patients taking antihypertensive medications may have an increased risk of

orthostatic hypotension with bortezomib.⁽⁵⁾ Anticoagulants, and drugs with antiplatelet action (ie, NSAIDs) may increase the risk of bleeding for patients with thrombocytopenia from bortezomib therapy.⁽⁷⁾

Pharmacies can order bortezomib directly from Janssen-Ortho, after the undesignated request is approved. Bortezomib is supplied in vials containing 3.5 mg of drug in powder form. Unreconstituted vials should be stored at room temperature and protected from light. Reconstitution with 3.5 ml of normal saline results in a 1 mg/ml solution. The 1 mg/ml solution can be stored for up to 8 hours at room temperature in the vial. It can also be stored in a syringe for up to 3 hours, but must not exceed 8 hours total time after reconstitution.⁽²⁾

References:

1. Vapiwala N. Protease Inhibitors. Oncolink July 22, 2004 ed. Pennsylvania: Abramson Cancer Center of the University of Pennsylvania; 2004. [cited from URL: <http://www.oncolink.upenn.edu/treatment/article.cfm?c=12&s=89&id=260>.
2. Janssen-Ortho Inc. Product Monograph Velcade. 2005:1-37.
3. B.C. Cancer Agency. BCCA Protocol Summary for the Treatment of Multiple Myeloma with Bortezomib. Vancouver, British Columbia; 2004. [cited from URL: <http://www.bccancer.bc.ca/HPI/ChemotherapyProtocols/Lymphoma/umybortez.htm>.
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7. Tariman JD, Lemoine C. Bortezomib. Clin J Oncol Nurs 2003;7(6):687-9.

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DRUG UPDATE

Management of Oxaliplatin Extravasation Oxaliplatin extravasation may cause severe local inflammation and potentially tissue necrosis. Hence, oxaliplatin would be better described as an **irritant** rather than having minimal or no vesicant potential. There have been five reports published involving a total of 25 cases of oxaliplatin extravasation in the literature.¹⁻⁴ Most cases involved local mild inflammatory reaction, but a few cases showed local inflammation with pain, swelling, and redness. No ulceration was reported, but tissue necrosis was described clinically or by imaging in three cases, although no biopsy was done.^{1,2,5} In addition, there was one case of phlebitis and two cases of abscess.^{1,2}

The usual management at the BC Cancer Agency for extravasation of vesicants includes application of cool compresses. In the case of oxaliplatin, this raises the concerns of exacerbating peripheral sensory neuropathy. Experience in the United Kingdom⁶ and Australia^{7,8} – where oxaliplatin has been commercially available – suggest that oxaliplatin extravasation should be managed with **warm** compresses.

In view of these data, the British Columbia Cancer Agency recently reclassified oxaliplatin as an irritant and replaced cool compresses with warm compresses as part of the general management of oxaliplatin extravasation. The relevant information has been incorporated into the Cancer Drug Manual Oxaliplatin monograph and handout, chemotherapy protocols (UGIFOLFOX) and Systemic Therapy policy on extravasation management.

References

1. Baur M, Kienzer HR, Rath T, et al. Extravasation of Oxaliplatin (Eloxatin^(R)) - Clinical Course. Onkologie 2000;23(5):468-71.
2. Kennedy JG, Donahue JP, Hoang B, et al. Vesicant characteristics of oxaliplatin following antecubital extravasation. Clin Oncol (R Coll Radiol) 2003;15(5):237-9.
3. Kretzschmar A, Thuss-Patience P, Pink D, et al. Extravasations of oxaliplatin. Proc Am Soc Clin Oncol 2002;21:A2900.
4. Kretzschmar A, Pink D, Thuss-Patience P, et al. Extravasations of oxaliplatin. J Clin Oncol 2003;21(21):4068-9.
5. Eckert R, Maier KP. Necrotizing panniculitis after extravasation of oxaliplatin. Ann Oncol 2002;13(Suppl 5):29 (abstract 103).
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CANCER MANAGEMENT GUIDELINES

The **Gastrointestinal Tumour Group** has revised the management guideline on anal canal cancer (<http://www.bccancer.bc.ca/HPI/CancerManagementGuidelines/Gastrointestinal/07.Anus/start.htm>).

The **Genitourinary Tumour Group** has reformatted the patient information on PSA screening for prostate cancer (www.bccancer.bc.ca/HPI/CancerManagementGuidelines/Genitourinary/Prostate/PSAScreening/default.htm).

CANCER DRUG MANUAL

New Pemetrexed Monograph has been developed. This is a new agent recently introduced for the treatment of malignant mesothelioma. The accompanying patient handout has also been updated.

Revised Monographs and Handouts Several drugs have been revised. The **oxaliplatin** monograph and handout have been revised to incorporate new information on extravasation hazard and management (see Drug Update for more details). The **rituximab** monograph has been updated to include special precautions regarding hepatitis B reactivation.

Several hormonal drug information for breast cancer (**anastrozole, exemestane, letrozole, tamoxifen**) have been revised. The side effects of these drugs have been updated based on the recently published adjuvant trials comparing these agents in breast cancer.

NURSING UPDATE

Nursing Articles of the Month Both these articles are available on-line for BCCA staff through the library links provided.

- Green J and Hacker E. (2005). Chemotherapy in the geriatric population. Clinical Journal of Oncology Nursing 8(6), 591–7. (<http://www.ons.org/publications/journals/CJON/Volume8/Issue6/0806591.asp>)
- Harris D and Knobf T. (2004). Assessing and managing chemotherapy induced mucositis pain. Clinical Journal of Oncology Nursing 8(6), 622–8. (<http://www.ons.org/publications/journals/CJON/Volume8/Issue6/0806622.asp>)

Telephone Guidelines Telephone Consultation Protocols are documents that were originally developed to address the nursing management of outpatient-related calls at BCCA. Twenty-one protocols describe the assessment, triaging of, and related teaching for patients experiencing side effects or complications of cancer and its treatment, including diarrhea, dyspnea, stomatitis, constipation, anemia, hypercalcemia, neutropenic sepsis, and superior vena cava syndrome.

These evidence-based protocols have many potential uses that extend far beyond telephone consultation. They are available to you through the following link: <http://www.bccancer.bc.ca/HPI/Nursing/References/TelConsultProtocols/default>

Continuing Education On-Line: Advancing the Assessment and Treatment of Oral Mucositis

This on-line education program through Oncology Education Services addresses the etiology and impact of mucositis, the patient's perspective, patient assessment, and discusses interventions and treatments for the condition. The program ends by responding to common questions and answers. You can access this program through this link: <http://oes.digiton.com/mucositis/>

Clarification of Nurses' Responsibilities Related to Checking Chemotherapy Orders

Changes have been made to BCCA Nursing Directive C-252 to ensure that any nurse who gives chemotherapy takes responsibility for a *full clinical check of both the orders and the drug(s) before ever administering the drug(s). Examples of where this would apply include:

- An RN hanging a subsequent bag of chemo after first bag has finished in an ongoing infusional treatment would complete an entire clinical check.
- An RN relieving another RN for a break would need to complete an entire clinical check before hanging the new bag of chemo.

- An RN giving treatment as part of a multi-day regime would complete a full clinical check on each day that a treatment is administered.

Please review the changes to the policy at this link: <http://www.bccancer.bc.ca/HPI/Nursing/References/NursingBCCA/C-252>

*The agency policy III-10, Chemotherapy Process that describes the full clinical check can be found here: <http://www.bccancer.bc.ca/HPI/ChemotherapyProtocols/Policies>

PATIENT EDUCATION

Patient Handout on Cancer Drugs The patient information handout for several drugs have been revised. (See under [Cancer Drug Manual](#)).

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](#).

HIGHLIGHTS OF PROTOCOL REVISIONS

The **Gastrointestinal Tumour Group** has revised the oxaliplatin-based protocols for metastatic colorectal cancer (UGICAPOX, UGIFOLFOX) to reflect the emerging evidence of extravasation hazard associated with oxaliplatin. For more details on this information, see under Drug Update section, page 2.

LIST OF NEW AND REVISED PROTOCOLS

The **BC Cancer Agency Protocol Summaries** are revised on a periodic basis. New and revised protocols for this month are listed below. Protocol codes for treatments requiring “Undesignated Indication” approval are prefixed with the letter U.

- **UGICAPOX** revised (extravasation hazard added to Precautions): Palliative combination chemotherapy for metastatic colorectal cancer using oxaliplatin, and capecitabine
- **UGIFOLFOX** revised (extravasation hazard added to Precautions): Palliative combination chemotherapy for metastatic colorectal cancer using oxaliplatin, 5-fluorouracil and folinic acid (leucovorin)
- **HNFUA** revised (liver function tests clarified, contact physician revised): Combined modality therapy for advanced head and neck cancer using mitomycin, fluorouracil and radiation therapy
- **HNFUP** revised (liver function tests clarified, contact physician revised): Cisplatin and fluorouracil (5-FU) for advanced head and neck cancer
- **HNM** revised (ANC revised for Dose Modification for grade I mucositis): Methotrexate for head and neck cancer
- **LUAVPG** revised (carboplatin AUC clarified): Treatment of advanced non-small cell lung cancer (NSCLC) with platinum and gemcitabine
- **LUMMPPEM** revised (timing of pemetrexed administration clarified): Treatment of malignant mesothelioma with platinum and pemetrexed (Alimta®)
- **LYABVD** revised (Tests revised, order of medications revised): Treatment of Hodgkin’s disease with doxorubicin, bleomycin, vinblastine, and dacarbazine
- **LYCHOP** revised (Tests revised, order of medications revised): Treatment of Lymphoma with doxorubicin, cyclophosphamide, vincristine and prednisone (CHOP)
- **LYCHOPR** revised (revised tests, revised premedications, revised order of medications, revised hypersensitivity section to delete routine vitals during Rituximab administration): Treatment of lymphoma with doxorubicin, cyclophosphamide, vincristine, prednisone and rituximab (CHOP-R)
- **LYCVP** revised (revised eligibility and tests, revised order of medications): Treatment of advanced indolent lymphoma using cyclophosphamide, vincristine, prednisone (CVP)
- **LYCVPPABO** revised (revised tests, revised order of medications): Treatment of Hodgkin’s disease with cyclophosphamide, vinblastine, procarbazine and prednisone

- **LYCVPR** revised (revised tests, revised premedications, revised order of medications, revised hypersensitivity section to delete routine vital signs during Rituximab administration): Treatment of advanced indolent lymphoma using cyclophosphamide, vincristine, prednisone and rituximab (CVP-R)
- **LYFLUDR** revised (revised tests, revised premedications, revised hypersensitivity section to delete routine vitals during Rituximab administration): Treatment of chronic lymphocytic leukemia with fludarabine and rituximab

LIST OF NEW AND REVISED PRE-PRINTED ORDERS

The **INDEX to BC Cancer Agency Pre-printed Orders** are revised on a periodic basis. New and revised protocols for this month are listed below. Protocol codes for treatments requiring “Undesignated Indication” approval are prefixed with the letter U.

- **HNFUA** revised (liver function tests clarified, contact physician revised): Combined modality therapy for advanced head and neck cancer using mitomycin, fluorouracil and radiation therapy
- **HNFUP** revised (liver function tests clarified, contact physician revised): Cisplatin and fluorouracil (5-FU) for advanced head and neck cancer
- **HNM** revised (ANC revised for Dose Modification for grade I mucositis): Methotrexate for head and neck cancer
- **LUAVPG** revised (carboplatin AUC clarified): Treatment of advanced non-small cell lung cancer (NSCLC) with platinum and gemcitabine
- **LUMMPPEM** revised (timing of pemetrexed administration clarified): Treatment of malignant mesothelioma with platinum and pemetrexed (Alimta®)
- **LYABVD** revised (Tests revised, order of medications revised): Treatment of Hodgkin’s disease with doxorubicin, bleomycin, vinblastine, and dacarbazine
- **LYCHOP** revised (Tests revised, order of medications revised): Treatment of lymphoma with doxorubicin, cyclophosphamide, vincristine and prednisone (CHOP)
- **LYCHOPR** revised (revised tests, revised premedications, revised order of medications, revised hypersensitivity section to delete routine vitals during Rituximab administration): Treatment of lymphoma with doxorubicin, cyclophosphamide, vincristine, prednisone and rituximab (CHOP-R)
- **LYCVP** revised (revised eligibility and tests, revised order of medications): Treatment of advanced indolent lymphoma using cyclophosphamide, vincristine, prednisone (CVP)
- **LYCVPPABO** revised (revised tests, revised order of medications): Treatment of Hodgkin’s disease with cyclophosphamide, vinblastine, procarbazine and prednisone
- **LYCVPR** revised (revised tests, revised premedications, revised order of medications, revised hypersensitivity section to delete routine vital signs during Rituximab administration): Treatment of advanced indolent lymphoma using cyclophosphamide, vincristine, prednisone and rituximab (CVP-R)
- **LYFLUDR** revised (revised tests, revised premedications, revised hypersensitivity section to delete routine vitals during Rituximab administration): Treatment of chronic lymphocytic leukemia with fludarabine and rituximab

PROVINCIAL SYSTEMIC THERAPY PROGRAM POLICIES

Revision for Extravasation of Chemotherapy The BC Cancer Agency Systemic Therapy Policy on the Prevention and Management of Extravasation of Chemotherapy (Policy III-20) has been revised in two areas. The first is the reclassification of oxaliplatin as an irritant and the use of warm compresses instead of cool compresses for extravasation (see Drug Update for more details).

The second revision clarifies the concentration of topical dimethylsulfoxide (DMSO). This is used as an antidote for anthracyclines extravasation. In the literature, the concentration commonly cited is 99%. However, the closest product in the market is a 99.7% solution available from Xenex (Sel-Win) in B.C. (tel: 1-800-663-1002).

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

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.

The Cancer Chemotherapy Pre-Printed Orders are available on the BC Cancer Agency website (www.bccancer.bc.ca/ChemoProtocols) under Health Professionals Info, Chemotherapy Protocols. Pre-Printed Orders are posted at the index page of each tumour site.

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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Protocol Summaries: (also available on our website www.bccancer.bc.ca)			Index of Protocol Summaries		
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