



BC Cancer Agency

Systemic Therapy Update

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Website access at <http://www.bccancer.bc.ca/HPI/ChemotherapyProtocols/stupdate.htm>

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EDITOR'S CHOICE

SAFETY OF ERYTHROPOIESIS-STIMULATING AGENTS (ESAs) IN CANCER PATIENTS

The US Food and Drug Administration (FDA) has recently released new safety data on using the ESAs (e.g, **epoetin alfa** [EPREX®], **darbepoetin alfa** [ARANESP®]) to target haemoglobin levels greater than 120 g/L in cancer patients.¹

In two studies of patients not on active chemotherapy, the use of ESAs was associated with shortened survival while no benefits were seen in reducing the need for blood transfusions.^{1,2} A third study showed that darbepoetin alfa was linked to increased disease progression and a trend towards increased mortality in patients undergoing radiotherapy.¹ Finally, increased mortality was also reported in a study of comparing pegylated epoetin alfa with darbepoetin alfa in patients receiving chemotherapy.¹

The latest safety evidence on patients not receiving active chemotherapy follows previous findings from two studies suggesting harm in patients receiving epoetin alfa to target high haemoglobin (> 120 g/L) while on active cancer treatment. One study reported decreased survival in patients on chemotherapy for metastatic breast cancer³ while another showed increased disease progression in patients on radiotherapy for advanced head and neck cancer.⁴ At the time, the FDA felt that ESAs were generally safe in anemic cancer patients.⁵

In Canada, epoetin alfa is approved for use to avoid blood transfusion in cancer patients with chemotherapy-induced anemia and in patients with disease-induced anemia, irrespective of whether they are receiving chemotherapy. In the US, use of ESAs in cancer patients is limited to those with chemotherapy-induced anemia. Labelling of ESAs in the US has been revised to reflect these new safety data¹; further labelling revisions may occur after the FDA's Oncologic Drugs Advisory Committee meeting in May. Health Canada is reviewing the impact of these data on the Canadian labelling of ESAs.

Overall, these data suggest that¹:

- use of ESAs offers no benefit and may shorten survival in anemic cancer patients who are not on chemotherapy
- use of ESAs to target haemoglobin > 120 g/L may shorten survival and time to disease progression in cancer patients

- the lowest dose possible should be used to gradually increase the haemoglobin concentration to avoid the need for transfusion.

ESAs are not BC Cancer Agency (BCCA) benefit drugs but are used by some cancer patients. The BCCA guidelines on epoetin alfa (SCEPO, www.bccancer.bc.ca/HPI/ChemotherapyProtocols/SupportiveCare/) is being revised to reflect the recent safety data.

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DRUG UPDATE – PEMETREXED FOR NON-SMALL CELL LUNG CANCER (NSCLC)

Pemetrexed (ALIMTA®) is an antifolate antimetabolite which will be funded by the BC Cancer Agency starting 1 May 2007 as a single agent therapy for the second-line treatment of NSCLC. Randomized controlled data have shown that single agent pemetrexed is associated with similar survival to docetaxel while having less hematologic toxicity in this population (see the October 2005 issue of the Systemic Therapy Update for more focused review of this topic).

CANCER DRUG MANUAL

Carmustine Monograph and Patient Handouts These have been completely revised, and a new patient handout has been created for the implantable carmustine-impregnated wafer. Expert review was provided by Dr. Stephen Nantel (Leukemia/BMT Program of BC) and Dr. Brian Thiessen (Neuro-Oncology Tumour Group). Highlighted changes include:

- addition of information on the implantable carmustine-impregnated wafer
- addition of information on “BCNU pneumonitis,” a potentially fatal side effect seen after autologous BMT (note: BCNU is common synonym for carmustine, based on the trade name BiCNU®)
- in the carmustine injection patient handout, the bullet describing breathing problems has been moved up to the emergency section

Lomustine Monograph and Patient Handout These have been completely revised and updated. Expert review was provided by Dr. Brian Thiessen (Neuro-Oncology Tumour Group). Highlighted changes include:

- expansion of the Side Effects table, including the clinically-significant side effect of anorexia
- removal of the Drug Interactions table
- expansion of the Dosage Guidelines to include CNMODPCV, CCNU, NCCNU, CNCCV protocols
- in the patient handout, inclusion of a statement about the possibility of receiving two or more different types and colours of capsules in the same container, and the addition of anorexia to the Side Effects table

Pamidronate and Clodronate Patient Handouts These have revised to emphasise that interaction with drugs which increase calcium level is only likely when the bisphosphonates are used for hypercalcemia rather than bone metastases.

Chemotherapy Preparation and Stability Chart has been revised to indicate the following:

- bevacizumab – new stability data correlated with a concentration range (1.4-1.65 mg/mL) to allow the use of larger infusion bag volume for larger doses
- idarubicin – stability data for the new pre-mixed solution vial
- melphalan – clarification to emphasise that administration should be *completed* within 60 minutes from the time of initial reconstitution because of rapid decomposition

DRUG UPDATE – DISPENSING MELPHALAN TABLET IN PLASTIC VIALS

The BC Cancer Agency recommends that melphalan tablets be dispensed in plastic vials. Melphalan tablets (ALKERAN®, GlaxoSmithKline) have traditionally been dispensed in glass vials, based on the manufacturer’s recommendation. However, the tablets were reformulated in 2002, and this new formulation does not carry the same recommendation. Standard pharmacy vials are plastic, inexpensive, and widely available in a variety of formats such as “snap caps.” Since no literature could be found to support the continued use of glass vials, all centres are now dispensing melphalan tablets in plastic vials.

It should be noted that the current formulation requires refrigeration; this information has not changed.

For more information, contact: Provincial Drug Information, BC Cancer Agency at druginfo@bccancer.bc.ca.

LIST OF NEW AND REVISED PROTOCOLS, PRE-PRINTED ORDERS AND PATIENT HANDOUTS

The **BC Cancer Agency Protocol Summaries, Provincial Pre-Printed Orders (PPPOs) and Patient Handouts** are revised periodically. New and revised protocols, PPPOs and patient handouts for this month are listed below. Protocol codes for treatments requiring “Compassionate Access Program” approval are prefixed with the letter U.

New protocols, PPPOs and Patient Handouts (affected documents are checked):

Code	Protocol	PPPO	Patient Handout	Protocol Name
PUM	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	Palliative Therapy for Metastatic Carcinomas Using Mitomycin
SAMV	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	Palliative Therapy for Aggressive Fibromatosis Using Weekly or Alternate Week Methotrexate and Vinblastine Intravenously
SCPAINSU	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	Incident Pain Therapy Using Sufentanil Via Sublingual Route

Revised protocols, PPPOs and patient handouts (affected documents are checked):

Code	Protocol	PPPO	Patient Handout	Changes	Protocol Title
BRAJTR	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<i>Typo corrected</i>	Adjuvant Therapy for Breast Cancer using Trastuzumab (HERCEPTIN®) following the Completion of Chemotherapy (Sequential)
GIFUA	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<i>Return appointment orders changed</i>	Curative Combined Modality Therapy for Carcinoma of the Anal Canal using Mitomycin, Infusional Fluorouracil and Radiation Therapy

Code	Protocol	PPPO	Patient Handout	Changes	Protocol Title
GIFURC	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<i>Administration of capecitabine clarified</i>	Combined Modality Adjuvant Therapy for High Risk Rectal Carcinoma using Fluorouracil, Folinic Acid (Leucovorin), Capecitabine and Radiation Therapy

CONTINUING EDUCATION

BC Cancer Agency Annual Cancer Conference 2007 Mark your calendar! This year's conference will be held on 29 November – 1 December, at the Westin Bayshore Resort & Marina in Vancouver. The theme of the 2007 conference is *“Technology and Innovation – Bench to Bedside”*.

Stay tuned for more information about the conference.

WEBSITE RESOURCES

The following are available on the BC Cancer Agency website (www.bccancer.bc.ca) under the Health PROFESSIONALS INFO SECTION:

Reimbursement and Forms: Benefit Drug List, Class II, Compassionate Access Program (Undesignated Indication)	www.bccancer.bc.ca/HPI/ChemotherapyProtocols/Forms
Cancer Drug Manual	www.bccancer.bc.ca/cdm
Cancer Management Guidelines	www.bccancer.bc.ca/CaMgmtGuidelines
Cancer Chemotherapy Protocols	www.bccancer.bc.ca/ChemoProtocols
Cancer Chemotherapy Pre-Printed Orders	www.bccancer.bc.ca/ChemoProtocols under the index page of each tumour site
Systemic Therapy Program Policies	www.bccancer.bc.ca/HPI/ChemotherapyProtocols/Policies
Unconventional Cancer Therapies Manual	under Patient/Public Info, Unconventional Therapies

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