

# Systemic Therapy Update

Volume 4, Number 6

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

#### **BENEFIT DRUG LIST**

The following new programs have been funded by the Provincial Systemic Therapy Program effective 1 June, 2001:

**Dexamethasone Injectable** for treatment of lymphoma (not reimbursed for anti-emetic use or pre-paclitaxel use).

**Thalidomide** for multiple myeloma unresponsive to melphalan, prednisone, pamidronate and dexamethasone.

Dexamethasone is now approved as class I and thalidomide as class II on the benefit list. A Class II form must be completed and submitted to the Provincial Systemic Therapy Program before the drug will be dispensed at a regional cancer centre or reimbursed to a community hospital. In addition, Health Canada Special Access Programme approval is required to obtain supply of thalidomide from the manufacturer (see Drug Update section for more details).

Susan O'Reilly, MB, FRCPC Provincial Systemic Program Leader

Benefit Drug List and Class II forms are available on the website <a href="http://bccancer.com/providerhome.cfm">http://bccancer.com/providerhome.cfm</a>.

#### PROTOCOL UPDATE

Protocol codes for treatments requiring "Undesignated Indication" approval prior to use are prefixed with the letter  ${\bf U}$ .

- INDEX to BCCA Protocol Summaries revised monthly (includes tumour group, protocol code, indication, drugs, last revision date and version)
- BRAJAC revised (tests): Adjuvant therapy for breast cancer using doxorubicin and cyclophosphamide
- BRAJCAF revised (tests): Adjuvant therapy for breast cancer using cyclophosphamide, doxorubicin and fluorouracil
- BRAVCLOD revised (creatinine clarified):
   Therapy of bone metastases in breast cancer using oral clodronate
- **LYABVD** revised (filgrastim use): Treatment of Hodgkin's disease with doxorubicin, bleomycin, vinblastine, and dacarbazine
- **LYCHOP** revised (vincristine dose, filgrastim use): Treatment of lymphoma with doxorubicin, cyclophosphamide, vincristine and prednisone
- LYCHOP-R revised (vincristine dose, rituximab preparation, filgrastim use, precautions): Treatment of lymphoma with

- doxorubicin, cyclophosphamide, vincristine, prednisone and rituximab
- LYCOPP revised (vincristine dose): Treatment of Hodgkin's disease using cyclophosphamide, vincristine, procarbazine and prednisone
- LYCVP revised (reformatted, doses revised): Advanced indolent lymphoma using cyclophosphamide, vincristine, prednisone
- LYECV revised (vincristine dose):
   Consolidation for lymphoma using etoposide, cyclophosphamide and vincristine
- LYFLU revised (eligibility): Treatment of low grade lymphoma or chronic lymphocytic leukemia with fludarabine
- **LYODBEP** revised (vincristine dose, filgrastim use): Treatment of Hodgkin's disease with vincristine, doxorubicin, bleomycin, etoposide and prednisone
- LYRITUX revised (rituximab preparation, filgrastim use, precautions): Treatment of lymphoma with single agent rituximab
- **LYTHALID** new: Therapy of multiple myeloma using thalidomide

Most protocols are available on the BCCA website <a href="http://www.bccancer.bc.ca/ccp/">http://www.bccancer.bc.ca/ccp/</a>.

#### **CANCER MANAGEMENT MANUAL**

The Cancer Management Manual is available on BCCA website <a href="www.bccancer.bc.ca/cmm/">www.bccancer.bc.ca/cmm/</a>.

#### PRE-PRINTED ORDER UPDATE

Pre-printed orders should always be checked with the most current BCCA protocol summaries. The Vancouver Cancer Centre has prepared the following chemotherapy pre-printed orders, which can be used as a guide for reference:

- **BRAJCMF** (pre-printed order entitled BRCMFIV) revised (booking): Adjuvant therapy for premenopausal high risk breast cancer using cyclophosphamide (IV), methotrexate and fluorouracil
- BRAVCMF (pre-printed order entitled BRCMFIV) revised (booking): Palliative therapy for advanced breast cancer using cyclophosphamide, methotrexate and fluorouracil

- UBRAVTR revised (booking section):
   Palliative therapy for metastatic breast cancer using trastuzumab (Herceptin®).
- CNTEMOZ revised (capsule sizes added): Temozolomide as second line chemotherapy for recurrent malignant gliomas
- **GIENDO1** revised (lab and appointments): Palliative therapy for pancreatic endocrine tumours using streptozocin and doxorubicin
- **GIFUINF** revised (booking): Palliative therapy for metastatic colorectal adenocarcinoma using fluorouracil infusional chemotherapy
- **GIIR** revised (booking): Second-line palliative treatment for fluorouracil-refractory metastatic colorectal cancer using irinotecan
- GIRFUFA revised (booking): First-line palliative combination chemotherapy for metastatic colorectal cancer using irinotecan, fluorouracil and folinic acid (leucovorin)
- GIPGEM revised (lab and appointments):
   Palliative therapy for pancreatic adenocarcinoma cancer using gemcitabine
- **GUBEP** revised (pre-printed orders entitled GUBEP [in+out], GUBEP [out], GUBEP [in]): Therapy for intermediate risk nonseminomatous testicular cancer using bleomycin, etoposide and cisplatin
- **GUEP** revised (pre-printed orders entitled GUEP [in+out], GUEP [out], GUEP [in]): Therapy for nonseminoma germ cell cancer using etoposide-cisplatin
- **GUFUP** new: Combined modality therapy for squamous cell cancer of the genitourinary system using fluorouracil and cisplatin
- **LUNAVP** revised (lab section): Palliative therapy of non-small cell lung cancer using cisplatin and vinorelbine
- LYCHOP-R revised: Treatment of lymphoma with doxorubicin, cyclophosphamide, vincristine, prednisone and rituximab
- LYECV revised (filgrastim dose): Consolidation for lymphoma using etoposide and cyclophosphamide
- **LYIT** new: Treatment of lymphoma using intrathecal methotrexate and cytarabine
- LYRITUX revised: Treatment of lymphoma with single agent rituximab

- MYHDC new: Single dose cyclophosphamide priming therapy for multiple myeloma prior to autologous stem cell transplant
- MOIT revised: Solid tumours using intrathecal methotrexate and/or thiotepa and/or cytarabine
- SAAI revised: Therapy for advanced soft tissue sarcoma using doxorubicin, ifosfamide-mesna

An index to the orders can be obtained by Fax-Back.

#### **PATIENT EDUCATION**

**Thalidomide** patient handout is now available via H-drive at regional cancer centres or Fax-Back.

**BRAJCEF** patient handout has been revised. This handout is specific for the BCCA protocol of adjuvant therapy for breast cancer using cyclophosphamide, epirubicin and fluorouracil.

Patient handouts are available for a number of cancer drugs not in the BCCA Cancer Drug Manual or on the BCCA website, and for a number of BCCA treatment protocols. These are listed at the end of the Update and can be obtained via H-drive at regional cancer centres or Fax-Back.

#### **DRUG UPDATE**

#### Thalidomide Approval and Drug Ordering

As of 1 June, 2001, thalidomide has been added as a class II drug of the benefit list and no longer needs Undesignated Approval prior to use. However, thalidomide continues to require prior approval from the Health Canada Special Access Program (SAP). Once approved, the SAP arranges the provision of thalidomide to the local hospital pharmacy, which is responsible for the cost and subsequent claim to BCCA for reimbursement. To facilitate these processes, a "Request for Thalidomide from Celgene and SAP Program of Health Canada" form is available via Fax-Back. Note that BCCA regional cancer centres are only responsible for the provision of thalidomide if it is to be dispensed directly to the patient from that regional cancer centre.

Caution with Irinotecan-Fluorouracil (GIIRFUFA) regimen The enrollment in two NCIC clinical trials was recently suspended because of preliminary safety information about the number

and pattern of deaths of patients on the weekly irinotecan plus bolus fluorouracil and leucovorin (folinic acid) arms (GIIRFUFA or Saltz regimen). Although not statistically different, the mortality rate within 60 days of treatment initiation was higher with this regimen than in the other arms of these studies. It was also higher than that seen in the large clinical trial used to establish this protocol as an effective treatment for metastatic colorectal cancer. There was a higher than anticipated incidence of serious adverse events related to sepsis, diarrhea and thromboses.

Vigilant monitoring of all patients receiving this protocol is required and the dose modification guidelines outlined in the current protocol should be observed with particular attention paid to those required during the first cycle of therapy. In addition, at this time, consideration should be given to starting some patients at a reduced dosage level of irinotecan 100 mg/m<sup>2</sup>, fluorouracil 400 mg/m<sup>2</sup> and leucovorin 20 mg/m<sup>2</sup>. Any amendments to the GIIRFUFA protocol will be announced in a future Systemic Update. For further information see the Early Release Correspondence by DJ Sargent et al. posted the **NEJM** website (http://www.nejm.org/) 17 May, 2001.

Erythropoietin (Eprex®) In the April issue of the Update, we reported the recent decision by Pharmacare not to fund erythropoietin as a Pharmacare benefit drug for the treatment of anemia in cancer patients. As the BCCA oncology drug budget does not cover supportive care medication, the BCCA Systemic Therapy Program has requested Pharmacare to reconsider this decision urgently. The request provided justifications for the use of erythropoietin in these patients and details on how it could be used in a financially responsible, monitorable fashion by a small number of hematologists and oncologists in BC. The justifications for the use of erythropoietin in these patients include:

- 1. Anemia due to cancer or cancer treatment is common<sup>1</sup> and often symptomatic.<sup>2</sup>
- 2. Anemia of cancer is frequently caused by deficient erythropoietin production.<sup>3-5</sup> The use of erythropoietin for the anemia of cancer is similar to the use of other agents for other deficiencies, such as erythropoietin (anemia of

- chronic renal failure), thyroxine (hypothyroidism), insulin (diabetes), etc.
- 3. Blood transfusion as an alternative treatment is expensive, <sup>6-9</sup> labour intensive, and inconvenient for patients. It also has potential complications (eg, transfusion reactions, AIDS, hepatitis) <sup>6-8</sup> which are contrary to the spirit of the Krever Commission of Inquiry on the Blood System of Canada on the use of safer alternatives to blood products whenever possible.<sup>3</sup>
- 4. Erythropoietin has been shown to reverse anemia of cancer in about half of the patients in randomised controlled trials. <sup>2,10-14</sup>

Representatives from the Systemic Therapy Program pointed out that the most efficient way to determine if erythropoietin will reverse the anemia in a specific cancer patient is to give it for a two-month trial. Patients who will benefit experience a clear rise in hemoglobin. If that is not seen, erythropoietin should be discontinued. Pharmacare is still considering this proposal and has not reached a decision whether to accept it. (References available on request: mdelemos@bccancer.bc.ca.)

**Bleomycin Preparation** A review of current practice standards has confirmed that the BCCA administration guideline is to continue to dilute bleomycin in 50 mL normal saline and that no test dose is required.

**Rituximab Preparation** The recommended concentration of diluted rituximab solution has been changed from a maximum of 1 mg/mL to 1-4 mg/mL. Therefore, changes have been made to the LYCHOP-R and LYRITUX protocols to decrease the diluted volume of single dose rituximab from 1000 mL to 500 mL. Because rituximab is administered on a mg/hr basis, the administration time remains the same but the administration rate (ie, mL/hr) will be halved due to a more concentrated solution. See the newly revised rituximab protocols (LYCHOP-R, LYRITUX) for more details.

**Vincristine Dose** When vincristine was brought into multi-agent chemotherapy protocols for lymphoma treatment, it was originally given at the maximum dose that was acceptably tolerated for a weekly schedule, 1.4 mg/m² without any cap.

When MOPP became accepted as the treatment of advanced Hodgkin's lymphoma, it was given for 12 months, i.e., 24 doses of vincristine. It became clear that unacceptable neurotoxicity frequently developed and arbitrarily the cooperative groups began to cap the dose at 2.0 mg. This has never made physiologic sense because it tends to underdose large patients and fully dose small patients.

Currently, we no longer use MOPP-type protocols but rather regimens such as (LY)CHOP and (LY)CVP where vincristine is seldom given for more than 6 to 8 doses. At this low cumulative dose, unacceptable neurotoxicity is seldom encountered. In recognition of this, for many years the BCCA Lymphoma Tumor Group has advocated a dose of 1.2 mg/m² without any upper limit. This has the virtue of being based on body surface area and therefore, indirectly, volume of distribution. Gradually the international consensus is moving to such non-capped dosing.

To be most in line with recommendations elsewhere in the world, the Lymphoma Tumor Group has decided that it would be best to use the most widely accepted standard 1.4 mg/m<sup>2</sup> but still avoid any capping of the dose (see Protocol Update section). Of course, dose reductions should be made appropriately when neurotoxicity is encountered as provided in the guidelines that are part of each protocol containing vincristine. In addition, vincristine should be used with great care in patients who have pre-existing conditions that would contribute to gastrointestinal hypomotility, such as recent surgery, or narcotic medications which may interact with the vincristine and cause unacceptable constipation.

#### **CANCER DRUG MANUAL**

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

# PROVINCIAL SYSTEMIC THERAPY PROGRAM POLICIES

BCCA Systemic Therapy Policies are available at <a href="https://hittps://h

#### **COMMUNITIES ONCOLOGY NETWORK**

**2000/2001 Workload Statistics** for all the Community Cancer Centres are now available on the website at www.bccancer.com/providerhome.cfm.

#### LIBRARY/CANCER INFORMATION CENTRE

**Unconventional Cancer Therapies Manual** is available on our website <a href="www.bccancer.bc.ca/uct">www.bccancer.bc.ca/uct</a>. The manual consists of 46 short monographs on the more popular alternative cancer therapies, and includes tips for the patient and family on how alternative therapies can be evaluated. For each therapy (eg, Essiac, vitamins, teas, shark cartilage, etc.), the manual provides proponent/advocate claims, balanced by evidence-based professional evaluation/critique quotations from the literature.

#### **SUPPORTIVE CARE**

**Filgrastim Assistance Program** AMGEN, the manufacturer of filgrastim (Neupogen), has launched a filgrastim assistance program in BC. The Neupogen Care Program for British Columbia has a toll-free, 24-hours, 7 days a week, phone line (1-888-706-4717) answered by reimbursement specialists who can help investigate if the patient is covered by private or provincial drug plan and whether financing is needed for co-payments and deductibles. For more information, call toll-free 1-800-665-4273 local 511.

#### **BCCA WEBSITE**

New BCCA website to launch in late June Visit the BCCA website in late June and early July and you will see a link to the new website. Both the current and new websites will run concurrently for 2-3 weeks, to allow healthcare providers around the province to get to know the new site and to bookmark commonly used sections. You are encouraged to visit and tour this site often, so that when the current website comes down in July, you have found your way through the new site. For more information, contact webmaster@bccancer.bc.ca.

#### **CONTINUING EDUCATION**

Canadian Association of Nurses in Oncology Annual Conference will be held in Quebec City on 23-26 September 2001. For more details, please contact: Canadian Association of Nurses in Oncology, tel: (416) 596-6565, fax: (416) 596-1808, or email: <a href="mailto:canoacio@interlog.com">canoacio@interlog.com</a>.

**BCCA Annual Cancer Conference** will be held at the Wall Centre, Vancouver, on 22-24 November 2001. The conference will include presentations for physicians, nurses, and pharmacists. For more details, please contact Jack Chritchley at (604) 877 6183.

#### **ERRATUM**

**Exemestane Patient Education Handout** was incorrectly listed on the handouts available in the May issue of the Update. The development of this handout is currently in progress.

#### **Editorial Review Board**

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## **BCCA SYSTEMIC THERAPY UPDATE FAX REQUEST FORM**

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☐ Fax	( )	Attn:				
UPDATES Please ☑ Fax-Back information below:						
☐ All items						
Patient Handouts:						
anagrelide		anastrozole		bicalutamide		
□ BRAJAC		BRAJCAF		BRAJCEF		
☐ BRAJCMF		BRAJCMFPO		BRAJTAM		
□ BRAVCAF		BRAVCMF		BRAVTAM		
cabergoline		capecitabine		clodronate		
docetaxel (Taxotere)		gemcitabine		irinotecan		
letrozole		octreotide (Sandostatin LAR)		pamidronate		
raltitrexed		rituximab		temozolomide		
☐ thalidomide		topotecan		trastuzumab (Herceptin)		
vinorelbine						
Pre-Printed Orders:						
BRAJCMF		BRAVCMF		UBRAVTR		
☐ CNTEMOZ		GIENDO1		GIFUINF		
GIIR		GIIRFUFA		GIPGEM		
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				and thalidomide request form		
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Class 2 Form (01 June 2001)						
Filgrastim Usage Form (01 June 2001)						
Systemic Therapy Update Index						
☐ Jan-Dec 2000						

# **REGIONAL CANCER CENTRE ACCESS**

BULLETIN UPDATES	LOCATION		
Patient Handouts:	H:\everyone\systemic\chemo\Pt_Educ		
Anagrelide	BRAVCMF	Octreotide (Sandostatin LAR)	
Anastrozole	BRAVTAM	Pamidronate	
Bicalutamide	Cabergoline	Raltitrexed	
BRAJAC	Capecitabine	Rituximab	
BRAJCAF	Clodronate	Temozolomide	
BRAJCEF	<u>Docetaxel</u>	<u>Thalidomide</u>	
BRAJCMF	<u>Gemcitabine</u>	<u>Topotecan</u>	
BRAJCMFPO	<u>Irinotecan</u>	<u>Trastuzumab</u>	
BRAJTAM	<u>Letrozole</u>	<u>Vinorelbine</u>	
BRAVCAF			
Pre-Printed Orders	H:\everyone\systemic\chemo\Orders\VCC		
Index of Pre-Printed Orders		<u>Index.doc</u>	
BRAJCMF	<u>GIIRFUFA</u>	<u>LYECV</u>	
BRAVCMF	GIPGEM	<u>LYIT</u>	
<u>UBRAVTR</u>	GUBEP,GUBEP (out),GUBEP (in)	<u>LYRITUX</u>	
<u>CNTEMOZ</u>	GUEP, GUEP (out), GUEP (in)	<u>MYHDC</u>	
GIENDO1	<u>GUFUP</u>	<u>MOIT</u>	
GIFUINF	<u>LUNAVP</u>	<u>SAAI</u>	
GIIR	<u>LYCHOP-R</u>		
Protocol Summaries	H:\everyone\systemic\chemo\Protocol\"tumour site"		
Index of Protocol Summaries	Index NT or Index W6		
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BRAJCAF	<u>LYCVP</u>	<u>LYRITUX</u>	
BRAVCLOD	<u>LYCOPP</u>	LYTHALID, thalidomide request form	
LYABVD	LYECV		
LYCHOP	<u>LYFLU</u>		
Reimbursement	H:\everyone\systemic\chemo\Reimburs		
Benefit Drug List (1 June 2001)	BenefitList.doc		
Class 2 Form (1 June 2001)	Class2.doc		
Filgrastim (G-CSF) (1 June 2001)	GCSF_form.doc		

For easy access, double-click your systemic chemo icon.
We appreciate your comments. Write us at <a href="mailto:bulletin@bccancer.bc.ca">bulletin@bccancer.bc.ca</a>

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