BC Cancer Agency

Systemic Therapy Update

INSIDE THIS ISSUE

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

BENEFIT DRUG LIST

Several new programs have been funded by the Provincial Systemic Therapy Program effective May 1, 1999. The following are now approved as Class I drugs:

- **CEF** (adjuvant cyclophosphamide, epirubicin, fluorouracil) for breast cancer in premenopausal women with 1 or more axillary node involvement (see protocol BRAJCEF)
- **Fludarabine** for first-line treatment of chronic lymphocytic leukemia and low-grade lymphoma (see protocol LYFLU)

The following are now approved as Class II drugs on the benefit list. A Class II form must be completed and submitted to the Provincial Systemic Therapy Program before the drugs will be dispensed at a radiation cancer centre or reimbursed to a community hospital.

- **Capecitabine** for metastatic breast cancer that has previously responded to an anthracycline and taxane (see protocol BRAVCAP)
- **Clodronate** oral for treatment of bone metastases associated with breast cancer (see protocol BRAVCLOD). Please note that there are 2 brands available (Bonefos®, Ostac®). Clodronate will be reimbursed at the current BCHS contract price for Bonefos® (Rhone-Poulenc Rorer).
- **Pamidronate** for treatment of multiple myeloma following chemotherapy (see protocol MYPAM)
- **Raltitrexed** for symptomatic advanced colorectal cancer in patients with previous fluorouracil toxicity (see protocol GIRALT)
- **Topotecan** for relapsed/progressive epithelial ovarian, fallopian tube or primary peritoneal cancer in patients who have previously responded to chemotherapy (see protocol GOOVTOP)

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

PROTOCOLS

Protocol codes for treatments requiring "Undesignated Indication" approval prior to use are prefixed with the letter **U**.

- **INDEX to BCCA Protocol Summaries** revised monthly (includes tumour group, protocol code, indication, drugs, last revision date and version)
- **BRAJCEF** revised (eligibility expanded to 1 or more lymph nodes positive) adjuvant therapy for breast cancer in premenopausal women with 1 or more involved axillary lymph nodes using cyclophosphamide, epirubicin and fluorouracil
- **BRAVCAP** new, therapy for metastatic breast cancer using capecitabine (Xeloda®) (Class II)

- **BRAVCLOD** new, therapy for bone metastases in breast cancer using clodronate (Class II)
- **GIFUA** revised (mitomycin schedule clarified) combined modality curative therapy for carcinoma of the anal canal using mitomycin, fluorouracil and radiation therapy
- **GIRALT** revised (reclassified to Class II) palliative treatment of symptomatic advanced or metastatic colorectal cancer using raltitrexed (Tomudex®) in patients with previous fluorouracil toxicity (Class II)
- **GOCXRADC (formerly GOCXCISR)**
  The protocol formerly known as GOCXCISR has been re-named GOCXRADC to distinguish its revised cisplatin regimen. GOCXRADC also incorporates a shorter post-hydration schedule, which will facilitate its delivery on an outpatient basis.
- **GOOVTOP** revised (reclassified to Class II) treatment of relapsed/progressive epithelial ovarian, fallopian tube or primary peritoneal cancer using topotecan
- **LYFLU** revised (eligibility revised to first-line, fludarabine reclassified to Class I) therapy for low grade lymphoma or chronic lymphocytic leukemia using fludarabine
- **MOIT** revised (cytarabine added) therapy for solid tumours using intrathecal methotrexate and/or thiotepa and/or cytarabine
- **MYPAM** revised (duration of treatment extended indefinitely) therapy for myeloma using pamidronate
- **UBRAVTRPA** revised (editorial change) palliative therapy for metastatic breast cancer using trastuzumab (Herceptin®) via Special Access Program and paclitaxel (Taxol®)

The following protocol summaries are **deleted,** as they are no longer used:

- **CNFUR96** therapy for refractory central nervous system malignancies with 96-hour fluorouracil infusions
- **CNLOGRA** therapy for symptomatic low-grade astrocytoma using lomustine
- **CNPLATFU** therapy of recurrent astrocytomas using cisplatin and 24-hour fluorouracil infusions

PATIENT HANDOUTS

- **BRAJCEF** revised (eligibility expanded)
- **Capecitabine** (Xeloda®) new
- **Clodronate** (Bonefos®, Ostac®) new
- **Pamidronate** (Aredia®) revised indications
- **Raltitrexed** (Tomudex®) new
- **Topotecan** (Hycamtin®) new
- **Trastuzumab** (Herceptin®) new

FOCUS ON ORAL CLODRONATE

Recommendation

The BCCA Breast Tumour Group recommends that **oral clodronate 1600 mg (4 x 400 mg capsules) once daily** be offered to all patients with bony metastases due to breast cancer (see protocol summary BRAVCLOD). For those who cannot tolerate oral clodronate, pamidronate 90 mg IV once monthly may be used. Patients who are currently receiving pamidronate without having had a trial of oral clodronate should be converted to oral clodronate starting 1 month after the last pamidronate treatment.

Rationale

Clodronate may slow progression of breast cancer in bone, reduce pain and prevent fractures. Clodronate and pamidronate are thought to be equally efficacious but clodronate is substantially cheaper and may be used orally. Therefore, oral clodronate is recommended and funded as first line treatment. Pamidronate may be used second line for those patients who are unable to take oral clodronate.

Oral Bioavailability

Clodronate has poor oral bioavailability (only 1-3% is absorbed from the gut) and bioavailability is reduced to zero in the presence of food, milk, antacids or minerals. Therefore, it must be taken with water on an empty stomach, at least 1 hour before eating or more than 2 hours after eating. Most patients find it convenient to take their clodronate on

awakening in the morning, at least 1 hour before breakfast, other medications or supplements of any kind including calcium.

GI Intolerance

Most patients tolerate oral clodronate well even though it is taken on an empty stomach. Nausea, vomiting, gastric pain and diarrhea have been reported in about 10% of patients. Starting treatment at 800 mg/day and slowly increasing to 1600 mg over 1-3 weeks may minimize the risk of GI disturbances. For those patients who still have problems, the following may be of benefit:

- split the dose (eg, 800 mg twice daily)
- reduce the dose until tolerated
- temporarily interrupt treatment

Symptomatic Hypocalcemia

Clodronate may lower serum calcium. However, symptomatic hypocalcemia is rare with clodronate in this patient population. Avoid the use of other agents that may lower calcium (eg, loop diuretics and corticosteroids). Calcium levels (along with serum albumin in order to calculate a corrected calcium level) may be indicated for those patients with symptoms of low calcium such as muscle spasms, depression and irritability.

Calcium supplements 1000-1500 mg per day and vitamin D may be required if symptomatic hypocalcemia occurs. Instruct patients to take clodronate at least 1 hour before or more than 2 hours after taking calcium in order to retain clodronate bioavailability.

Reimbursement

The BC Cancer Agency will reimburse community hospitals at the BCHS contract price for oral clodronate (currently Bonefos®, Rhone-Poulenc Rorer). A Class II Drug Registration Form must be submitted when treatment is initiated for oral clodronate. A second Class II form must be submitted if pamidronate is needed following an adequate trial of oral clodronate. Prescriptions may be written by family physicians.

BCCA Information Resources

- **BRAVCLOD** protocol summary
- **clodronate** patient handout
- **pamidronate** patient handout

Review Articles

- Bloomfield DJ. Should bisphosphonates be part of the standard therapy of patients with multiple myeloma or bone metastases from other cancers? An evidence-based review. J Clin Oncol 1998;16:1218-25.
- Plosker GL and Goa KL. Clodronate: a review of its pharmacological properties and therapeutic efficacy in resorptive bone disease. Drugs 1994;47:945-82.

PHARMACY CONTRACT UPDATE

Effective April 1, 1999, there are some changes to the BCHS contract, which will affect pharmacies receiving reimbursement. The following will be reimbursed at the current contract price:

- **cyproterone 50 mg tablets** - awarded to Berlex (distributed by Pharmascience).
- **etoposide IV 20 mg/mL** – awarded to Novopharm. The contract for etoposide capsules remains with Bristol-Myers Squibb.
- **5-fluorouracil 50 mg/mL** – awarded to Faulding.
- **interferon** – awarded to Schering (Intron A®). The tumour groups have agreed that both brands of interferon (Intron A® and Roferon®) are considered therapeutically equivalent and interchangeable. Patients currently receiving the Roche brand (Roferon®) can be switched to Intron A® at the same dosage. Schering will also provide a kit with injection supplies and a sharps container if the order is placed directly with Schering. Schering is in the process of changing the formulation of their interferon to provide a human albumin free product. In doing this, they are also changing the vials sizes and concentrations available. The H S A –free Intron A is available in 6 MU/mL and 10 MU/mL concentrations and can now be purchased directly from the manufacturer. Their currently available Intron A is a 5 MU/mL concentration. Roferon is available as a 3 MU/mL solution. It is essential that patients be informed of the change in brand and the

resulting change in volume that will need to be injected..

HEALTH CANADA APPROVALS

Ondansetron orally disintegrating tablet (Zofran ODT®, Glaxo Wellcome) was approved to prevent chemotherapy and radiation-induced nausea and vomiting, and postoperative nausea and vomiting. Ondansetron ODT is a supportive care medication and, therefore, is not on the BCCA benefit drug list.

IN TOUCH	www.bccancer.bc.ca	bulletin@bccancer.bc.ca
BC Cancer Agency	(604)-877-6000	Toll-Free 1-(800)-663-3333
Cancer Centre for the Southern Interior (CCSI)	(250) 712-3900	Toll-Free 1-(888)-563-7773
Fraser Valley Cancer Centre (FVCC)	(604)-930-2098	
Vancouver Cancer Centre (VCC)	(604)-877-6000	Toll-Free 1-(800)-663-3333
Vancouver Island Cancer Centre (VICC)	(250) 370-8228	Toll-Free 1-(800)-670-3322
Communities Oncology Network	(604) 877-6098 Ext 2744	Toll-Free 1-(800)-663-3333 Ext 2744
Nursing Professional Practice	(604)-877-6098 Ext 2623	Toll-Free 1-(800)-663-3333 Ext 2623
Pharmacy Professional Practice	(604)-877-6098 Ext 2247	Toll-Free 1-(800)-663-3333 Ext 2247
Provincial Systemic Program	(604)-877-6098 Ext 2247	Toll-Free 1-(800)-663-3333 Ext 2247
Francis Hu, CON Pharmacist	(604)-877-6098 Ext 2515	francish@bccancer.bc.ca
Robin O'Brien, Update Editor	(604)-877-6098 Ext 3028	robrien@bccancer.bc.ca

BCCA SYSTEMIC THERAPY UPDATE FAX REQUEST FORM

FAX (604) 877-6132
bulletin@bccancer.bc.ca

TO SUBSCRIBE: FAX OR EMAIL YOUR REQUEST OR CALL @ 877-6098 LOCAL 2247

FOR URGENT REQUESTS PLEASE CALL (604) 877-6098 LOCAL 2247

OR TOLL-FREE IN BC 1-800-663-3333 LOCAL 2247

PLEASE FEEL FREE TO MAKE COPIES FOR YOUR COLLEAGUES

I WOULD PREFER TO RECEIVE THIS INFORMATION VIA:

❑ E-mail (Word 6.0)	@
❑ Fax	( ) Attn:

UPDATES **Please ☑ Fax-Back information below:**

❑	All items	
	Patient Handouts:	
❑		BRAJCEF revised (eligibility expanded)
❑		Capecitabine (Xeloda ®) new
❑		Clodronate (Bonefos®, Ostac®) new
❑		Pamidronate (Aredia®) revised
❑		Raltitrexed (Tomudex®) new
❑		Topotecan (Hycamtin®) new
❑		Trastuzumab (Herceptin®) new
	Protocol Summaries:	
❑		BRAJCEF
❑		BRAVCAP
❑		BRAVCLOD
❑		GIFUA
❑		GIRALT
❑		GOCXRADC (formerly GOCXCISR)
❑		GOOVTOP
❑		LYFLU
❑		MOIT
❑		MYPAM
❑		UBRAVTRPA
❑		Index: Protocol Summaries (current month)
	Reimbursement	
❑		Benefit Drug List (01 May 99)
❑		Class 2 Form (01 May 99)
❑	Back Issues (circle)	1998 v.1 no. 1 Jun 2 July-Aug 3 Sep 4 Oct 5 Nov 6 Dec 1999 v.2 no. 1 Jan 2 Feb 3 Mar 4 Apr

Other:

RADIATION CANCER CENTRE ACCESS

BULLETIN UPDATES	LOCATION
Patient Handouts:	H:\everyone\systemic\chemo\Pt_Educ
BRAJCEF	H:\everyone\systemic\chemo\Pt_Educ\brajcef.doc
Capecitabine	H:\everyone\systemic\chemo\Pt_Educ\capecitabine.doc
Clodronate	H:\everyone\systemic\chemo\Pt_Educ\clodronate.doc
Pamidronate	H:\everyone\systemic\chemo\Pt_Educ\pamidronate.doc
Raltitrexed	H:\everyone\systemic\chemo\Pt_Educ\raltitrexed.doc
Topotecan	H:\everyone\systemic\chemo\Pt_Educ\topotecan.doc
Trastuzumab	H:\everyone\systemic\chemo\Pt_Educ\trastuzumab.doc
Protocol Summaries	H:\everyone\systemic\chemo\Protocol
BRAJCEF	H:\everyone\systemic\chemo\Protocol\breast\brajcef.doc
BRAVCAP	H:\everyone\systemic\chemo\Protocol\breast\bravcap.doc
BRAVCLOD	H:\everyone\systemic\chemo\Protocol\breast\bravclod.doc
GIFUA	H:\everyone\systemic\chemo\Protocol\GI\gifua.doc
GIRALT	H:\everyone\systemic\chemo\Protocol\GI\giralt.doc
GOCXRADC	H:\everyone\systemic\chemo\Protocol\Gyne\gocxradc.doc.doc
GOOVTOP	H:\everyone\systemic\chemo\Protocol\Gyne\goovtop.doc
LYFLU	H:\everyone\systemic\chemo\Protocol\Lymphoma & Myeloma\lyflu.doc
MOIT	H:\everyone\systemic\chemo\Protocol\Miscellaneous Origins\moit.doc
MYPAM	H:\everyone\systemic\chemo\Protocol\Lymphoma & Myeloma\mypam.doc
UBRAVTRPA	H:\everyone\systemic\chemo\Protocol\Breast\ubravtrpa.doc
Index of Protocol Summaries	H:\everyone\systemic\chemo\Protocol\Index\Index_NT or Index_W6
Reimbursement	H:\everyone\systemic\chemo\Reimburs
Benefit Drug List	H:\everyone\systemic\chemo\Reimburs\Benefit.doc
Class 2 Form	H:\everyone\systemic\chemo\Reimburs\Class2.doc

For easy access, double-click your systemic chemo icon.

We appreciate your comments. Write us at bulletin@bccancer.bc.ca