BC Cancer Agency

# Systemic Therapy Update

Volume 9, Number 7 *for health professionals who care for cancer patients* July 2006
*Website access at http://www.bccancer.bc.ca/HPI/ChemotherapyProtocols/stupdate.htm*

INSIDE THIS ISSUE



## EDITOR'S CHOICE

### 2006/07 New Treatment Policy Announcement

The Provincial Systemic Therapy Program of the BC Cancer Agency is pleased to announce the funding of a number of new treatment programs. These funded programs will be implemented once the relevant treatment protocols, patient education materials and pre-printed orders have been developed by the Provincial Tumour Groups, the Provincial Pharmacy and the Regional Cancer Centres. Implementation of the new programs will be announced in the Systemic Therapy Update and the relevant supporting documentation will be made available on the BC Cancer Agency web site (www.bccancer.bc.ca) Listed below are also treatment programs under consideration for implementation and programs which are not funded for 2006/06 fiscal year.

Yours sincerely,

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## Funded Programs

Chronic Disease

| Tumour Group | Program | Special Application Process | Projected implementation date |
|---|---|---|---|
| **Lung** | Second and third line treatment of progressive advanced non-small cell lung cancer with **erlotinib** (ULUAVERL)*<br><br>(Note. Patients must have *progressive disease* on or after first- or second-line therapy. Maintenance erlotinib after responding to chemotherapy is inappropriate and does not improve survival. Patients should also not switch over between erlotinib and gefitinib.* It is explicitly not approved by the Systemic Therapy Program.) | **erlotinib (case-by-case via undesignated indication request)** | already implemented |
| **Gastrointestinal** | First line palliative combination chemotherapy for metastatic colorectal cancer using selected chemotherapy regimens and **bevacizumab** (UGIFFOXB, UGIFFIRB, UGICOXB, UGICIRB) | **bevacizumab (case-by-case via undesignated indication request)** | already implemented |
| **Neuro-oncology** | Concomitant and adjuvant **temozolomide** for newly diagnosed malignant gliomas (CNAJTMZ) | **temozolomide**<br><br>**(class II)** | already implemented |
| **Lymphoma and myeloma** | Treatment of multiple myeloma with **bortezomib** (UMYBORTEZ) | **bortezomib – (compassionate access via undesignated indication request)** | already implemented |
| **Lymphoma and myeloma** | Maintenance **rituximab** for indolent lymphoma (ULYRMTN) | **rituximab (compassionate access via undesignated indication request)** | already implemented |

* See Drug Update in this issue for more information on new restrictions for prescribing gefitinib.

Curative/Adjuvant

| Tumour Group | Program | Special Application Process | Projected implementation date |
|---|---|---|---|
| **Breast** | Adjuvant therapy for breast cancer using fluorouracil, epirubicin and cyclophosphamide and **docetaxel** (BRAJFECD) | **docetaxel (class II)** | July 2006 |

| Tumour Group | Program | Special Application Process | Projected implementation date |
|---|---|---|---|
| **Breast (cont'd)** | Adjuvant therapy for breast cancer using cyclophosphamide, doxorubicin and **docetaxel** (BRAJTAC) | **docetaxel (class II)** | July 2006 |
| **Gynecological** | Treatment of primary advanced or recurrent endometrial cancer using **carboplatin** and **paclitaxel** (GOENDCAT) | **none** | implemented |

**Programs under consideration for implementation for 2006/07 fiscal year**

| Tumour Group | Program |
|---|---|
| **Gynecological** | **Pegylated liposomal doxorubicin (Caelyx®)** for advanced ovarian cancer after failing standard first line treatment |
| **Gastrointestinal** | **Capecitabine** to replace bolus fluorouracil in the adjuvant management of high risk rectal cancer |
| **Lung** | **Pemetrexed** as second line treatment for advanced non-small cell lung cancer |

**Programs not funded for 2006/07 fiscal year**

| Tumour Group | Program |
|---|---|
| **Bone Marrow Transplant/Leukemia** | Low dose **thalidomide** for myelodysplasia or idiopathic myelofibrosis |
| **Gastrointestinal** | Adjuvant combination chemotherapy for stage II colon cancer using **oxaliplatin**, fluorouracil and folinic acid (FOLFOX) |
| **Gastrointestinal** | DCF (**docetaxel**, cisplatin, and 5-fluorouracil) as first line chemotherapy for unresectable (locally advanced) and metastatic gastric adenocarcinoma. |
| **Gastrointestinal** | Second line palliative combination chemotherapy for metastatic colorectal cancer using selected chemotherapy regimens and **bevacizumab** |
| **Gastrointestinal** | Third line therapy with **cetuximab** and **irinotecan** for metastatic colorectal cancer. *(Note: cetuximab currently not marketed in Canada)* |
| **Head and neck** | **Cetuximab** together with radiotherapy for patients with locally advanced head and neck cancer patients who are unsuitable for the combination of radiotherapy and high dose cisplatinum. *(Note: cetuximab currently not marketed in Canada)* |

## CHANGES IN THALIDOMIDE ACCESS

Effective 10 July 2006, thalidomide will no longer be funded by the BC Cancer Agency for any ***new*** patients treated for multiple myeloma unresponsive to standard treatments (UMYTHALID). This does NOT affect patients who are currently being treated with thalidomide. This revised policy in thalidomide access brings the practice in BC in line with most of the provinces in Canada.

The following outlines the necessary process for patients newly prescribed with thalidomide obtain supply of the drug:

- Health Canada Special Access Programme
- Financial coverage for the drug cost by the Canadian Thalidomide® Access Program (1-888-611-6817)
- BC Cancer Agency Undesignated Indication Request Approval

A summary of this process will be made available on the BC Cancer Agency website at www.bccancer.bc.ca/HPI/ChemotherapyProtocols/Forms.

For further information, please contact the Undesignated Indication Request office at (604) 877-6277 or 1-800-663-3333 local 6277.

## CANCER DRUG MANUAL

**Bortezomib Monograph and Handout** These have been developed for this new agent, currently licensed as second line treatment for multiple myeloma. See Drug Update inside this issue on how to access the use of this drug. General information on bortezomib was previously reviewed in the April 2005 issue of Systemic Therapy Update.

**Fluorouracil (Topical) Handout** has been completely revised and was reviewed by Dr Harvey Lui of the Skin Cancer Tumour Group. Changes include clarification of the indication, as well as updating the management section in the side effect table. This revised handout will also replace the current information in the Cancer Management Guidelines for non-melanoma skin cancer.

**Clodronate (Oral) Handout** A limited revision has been made to clarify administration instructions. Oral absorption of clodronate is minimal and is best when clodronate is taken *before* eating. Watch for more information about clodronate absorption in next month's Systemic Therapy Update.

**Hydroxyurea Monograph** Based on a recent Health Canada alert, this has been revised to include rare occurrence of cutaneous vasculitic toxicities, including vasculitic ulcerations and gangrene. These toxicities have been reported in patients with myeloproliferative disorders during therapy with hydroxyurea, particularly those with a history of, or currently receiving, interferon therapy.

**Deletion of Drugs** Monographs and patient handouts for the following agents have been deleted from the Cancer Drug Manual because they are no longer commercially available in Canada:

- Diethylstilbestrol
- Fluoxymesterone
- Levamisole
- Plicamycin
- Vindesine

## DRUG UPDATE

**Restriction on Use of Gefitinib (Iressa®)** On 5 June 2006, Health Canada issued two new restrictions to the use of gefitinib as third line treatment for locally advanced or metastatic non-small cell lung cancer (NSCLC). First, no new patients should be prescribed gefitinib for this indication. Secondly, gefitinib should only be used in patients currently benefiting from it and whose tumours are EGFR expression status positive or unknown. To obtain further supply, these patients will need to be entered into the Iressa® Patient Registry. If a patient's tumour is EGFR expression negative and they are experiencing benefit from treatment with gefitinib, they should continue with their treatment and consult with their clinician at the earliest opportunity as to the appropriate course of action.

These changes were based on the recent evidence that gefitinib does not confer significant survival benefit. The conditional approval of gefitinib by Health Canada was originally based on two phase-II trials (IDEAL 1,

IDEAL 2),[1,2] which showed significant tumour response and symptom improvement. Subsequently, the ISEL trial[3] was conducted to investigate the impact of gefitinib on survival. This was a double-blind, placebo-controlled, randomized, phase III trial of 1692 patients with locally advanced or metastatic NSCLC. Patients either had disease refractory to or were intolerant of at least one prior chemotherapy regimen. Recent analysis of this study revealed no significant improvement in overall survival compared to placebo.

Iressa® Patient Registry

Patients currently on gefitinib therapy must be entered into the Iressa® Patient Registry by their pharmacists. The registration process will have two phases. The first phase (5 Jun – 1 October, 2006) will be a communication and early registration period. Information about the program will be distributed and pharmacists should begin to register patients currently on gefitinib therapy. Also during this time, McKesson Canada will become the sole distributor for gefitinib; registry staff will direct pharmacists without a McKesson account to the appropriate distribution centre. The second phase (starting 1 October 2006) begins the official launch of the Iressa® Patient Registry. All existing or new patients must be registered by this date in order to access further drug supply.

To register a patient, the pharmacist:

- must provide the patient with Health Canada's Public Advisory and Patient Information bulletins dated 5 June 2006,
- must complete the patient registration form and fax it to the registry, where the patient will be assigned a unique ID number,
- will use this ID number to submit a medication order form to the registry; a one-month supply of medication will be sent by McKesson (Note: a new request must be submitted for each monthly refill).

McKesson will mail registration kits to pharmacies at the end of June. For more information, or to register a patient, call the Iressa® Patient Registry at 1-866-473-7720.

The ULUGEF protocol has been updated to reflect these changes.

**References**

1. Fukuoka M, Yano S, Giaccone G, et al. Multi-institutional randomized phase II trial of gefitinib for previously treated patients with advanced non-small-cell lung cancer.[comment]. J Clin Oncol 2003;21(12):2237-46.
2. Kris MG, Natale RB, Herbst RS, et al. Efficacy of gefitinib, an inhibitor of the epidermal growth factor receptor tyrosine kinase, in symptomatic patients with non-small cell lung cancer: a randomized trial. JAMA 2003;290(16):2149-58.
3. Thatcher N, Chang A, Parikh P, et al. Gefitinib plus best supportive care in previously treated patients with refractory advanced non-small-cell lung cancer: results from a randomised, placebo-controlled, multicentre study (Iressa Survival Evaluation in Lung Cancer). Lancet 2005;366(9496):1527-37.

**Changes to Anti-Androgen Policy** Effective 1 July, 2006, bicalutamide 50mg OD will replace flutamide 250mg t.i.d. as the preferred anti-androgen for prostate cancer. Apart from more convenient once-daily administration, it is also better tolerated and is now available at an equivalent cost. Patients currently on flutamide may switch to bicalutamide at the physician's discretion. Patients who are intolerant to bicalutamide may be switched to other anti-androgens (flutamide, [class1] or nilutamide if flutamide intolerant [Class 2])

Indications include:

- Flare protection during the first month of LHRH agonist treatment
- Biochemical (PSA) or clinical progression in patients medically or surgically castrated. A three month trial with continuation only if there is a decrease in the serum PSA. Second-line treatment should not be continued in the face of progressive disease although permanent castration (surgical or medical) is recommended to avoid stimulation by androgens.
- During neoadjuvant therapy prior to radical radiation therapy, an antiandrogen will be added if there is a PSA rise, or if an inadequate PSA response is observed (defined as failure to achieve a PSA of <1 ng/ml after 4 months of adequate therapy as defined by castrate testosterone levels).

Monotherapy with bicalutamide 150mg/day is *not approved*. The drug does not have a licence for this use in Canada as a result of efficacy and safety concerns.

All three nonsteroidal antiandrogens (bicalutamide, flutamide, and nilutamide) are equally efficacious. Side effects of bicalutamide include diarrhea, nipple tenderness and gynecomastia. Side effects of flutamide include diarrhea, abnormalities in liver function enzymes, and occasional jaundice; liver function tests should be monitored periodically if used continuously for long (over 3 months) periods of time. Side effects of nilutamide include night blindness, alcohol intolerance and rarely, interstitial pneumonitis.

**Bortezomib (Velcade®) Newly Marketed** Bortezomib has been approved by Health Canada for second-line treatment of multiple myeloma since April 2006 (see new monograph and handout in the Cancer Drug Manual section). This means that Health Canada approval via the Special Access Programme is no longer required for its use. However, undesignated approval by the BC Cancer Agency continues to be needed for each new patient undergoing this treatment.

Note that the use of thalidomide, another second-line agent, continues to require Health Canada approval via the Special Access Programme. For more details on these two agents, see protocols UMYBORTEZ and MYTHALID, as well as the Cancer Management Guidelines.

## BENEFIT DRUG LIST

**Deletion of Drugs** The following agents have been deleted from the BC Cancer Agency Benefit List because they are no longer commercially available in Canada:

- Fluoxymesterone
- Levamisole
- Plicamycin
- Valrubicin
- Vindesine

In addition, thalidomide has been deleted from the formulary (see Editor's Choice in this issue for more information).

## PROVINCIAL SYSTEMIC THERAPY PROGRAM POLICY

**Extravasation Management Policy (III-20)** typo on bortezomib classification has been corrected (classified as "irritant" rather than "none").

**Physician Coverage for Medical Emergencies ("Hot Drugs") Policy (III-60)** the list of drugs reviewed for this policy has been clarified.

## 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**.

**New protocol**:

| Code | Protocol Name |
|---|---|
| **BRAVGEMD** | Palliative therapy for metastatic breast cancer using gemcitabine and docetaxel |

**Revised protocols**:

| Code | Changes | Protocol Name |
|---|---|---|
| **BRAJFECD** | *undesignated indication approval replaced by class II benefit* | Adjuvant therapy for breast cancer using fluorouracil, epirubicin and cyclophosphamide and docetaxel |
| **BRAJTAC** | *undesignated indication approval replaced by class II benefit* | Adjuvant therapy for breast cancer using cyclophosphamide, doxorubicin and docetaxel |
| **BRAJTR** | *CBC & diff, platelets optional prior to each treatment* | Adjuvant therapy for breast cancer using trastuzumab (Herceptin®) following the completion of chemotherapy (sequential) |
| **UGICIRB** | *eligibility revised, proteinuria and hypertension management clarified* | Palliative combination chemotherapy for metastatic colorectal cancer using irinotecan, bevacizumab and capecitabine |
| **UGICOXB** | *eligibility revised, proteinuria and hypertension management clarified* | Palliative combination chemotherapy for metastatic colorectal cancer using oxaliplatin, capecitabine and bevacizumab |
| **GIENDO2** | *premedications and liver function tests clarified* | Palliative therapy for pancreatic endocrine tumours using streptozocin and doxorubicin |
| **UGIFFIRB** | *eligibility revised, proteinuria and hypertension management clarified* | Palliative combination chemotherapy for metastatic colorectal cancer using irinotecan, fluorouracil, folinic acid (leucovorin) and bevacizumab |
| **UGIFFOXB** | *eligibility revised, proteinuria and hypertension management clarified* | Palliative combination chemotherapy for metastatic colorectal cancer using oxaliplatin, 5-fluorouracil, folinic acid (leucovorin) and bevacizumab |
| **GOOVETO** | *administration of oral etoposide with meals deleted* | Treatment of relapsed/progressive ovarian, fallopian tube or primary peritoneal cancer with etoposide |
| **GUBVAL** | *deleted* | Palliative therapy for BCG-refractory bladder Tis in patients unfit for cystectomy using intravesical valrubicin |
| **GUKIFN** | *tests section added* | Alpha-interferon (a-IFN) for advanced renal cell carcinoma |
| **GUPNSAA** | *benefit status for bicalutamide revised* | Non-steroidal treatment of prostate cancer |
| **ULUAVERL** | *approval process revised* | Treatment of advanced non-small cell lung cancer (NSCLC) with erlotinib (Tarceva®) |
| **ULUGEF** | *access process revised* | Third-line treatment for advanced non-small cell lung cancer (NSCLC) with gefitinib |
| **ULYALEM** | *need for Special Access Programme approval deleted from Eligibility* | Treatment of fludarabine-refractory B-chronic lymphocytic leukemia (B-CLL) and T-prolymphocytic leukemia (T-PLL) with alemtuzumab |
| **SMAJIFN** | *timing of radiotherapy revised in Exclusions* | Adjuvant therapy of high risk malignant melanoma with high dose interferon (HDIFN) ∝-2b |
| **UMYTHALID** | *benefit status changed* | Therapy of multiple myeloma using thalidomide<br><br>To access thalidomide, see flowchart at:<br>www.bccancer.bc.ca/HPI/ChemotherapyProtocols/Forms |

| | | |
|---|---|---|
| **SCEPO** | *baseline hemoglobin revised, reference added* | Guidelines for selecting and monitoring oncology patients for epoetin alfa (erythropoietin) therapy |

## LIST OF NEW AND REVISED PRE-PRINTED ORDERS

The **INDEX to BC Cancer Agency Pre-printed Orders** are revised on a periodic basis. The revised pre-printed orders for this month are listed below.

**New pre-printed orders**:

| Code | Protocol Name |
|---|---|
| **BRAVGEMD** | Palliative therapy for metastatic breast cancer using gemcitabine and docetaxel |

**Revised pre-printed orders**:

| Code | Changes | Protocol Name |
|---|---|---|
| **BRAJACTG** | *typo corrected* | Adjuvant therapy for breast cancer using dose dense therapy: doxorubicin and cyclophosphamide followed by paclitaxel |
| **BRAJFECD** | *undesignated indication approval replaced by class II benefit* | Adjuvant therapy for breast cancer using fluorouracil, epirubicin and cyclophosphamide and docetaxel |
| **BRAJTAC** | *undesignated indication approval replaced by class II benefit* | Adjuvant therapy for breast cancer using cyclophosphamide, doxorubicin and docetaxel |
| **BRAJTR** | *CBC & diff and platelets are now optional prior to each treatment* | Adjuvant therapy for breast cancer using trastuzumab (Herceptin®) following the completion of chemotherapy (sequential) |
| **UGICIRB** | *eligibility revised, proteinuria and hypertension management clarified* | Palliative combination chemotherapy for metastatic colorectal cancer using irinotecan, bevacizumab and capecitabine |
| **UGICOXB** | *eligibility revised, proteinuria and hypertension management clarified* | Palliative combination chemotherapy for metastatic colorectal cancer using oxaliplatin, capecitabine and bevacizumab |
| **GIENDO2** | *liver function tests clarified* | Palliative therapy for pancreatic endocrine tumours using streptozocin and doxorubicin |
| **UGIFFIRB** | *eligibility revised, proteinuria and hypertension management clarified* | Palliative combination chemotherapy for metastatic colorectal cancer using irinotecan, fluorouracil, folinic acid (leucovorin) and bevacizumab |
| **UGIFFOXB** | *eligibility revised, proteinuria and hypertension management clarified* | Palliative combination chemotherapy for metastatic colorectal cancer using oxaliplatin, 5-fluorouracil, folinic acid (leucovorin) and bevacizumab |
| **GIFUR** | *replacing GIFUR2 and GIFUR3* | Combined modality adjuvant therapy for high risk rectal carcinoma using fluorouracil, folinic acid (leucovorin) and radiation therapy |
| **GIFUR2** | *replaced by GIFUR* | Combined modality adjuvant therapy for high risk rectal carcinoma using fluorouracil, leucovorin, and radiation therapy |
| **GIFUR3** | *replaced by GIFUR* | Combined modality adjuvant therapy for high risk rectal carcinoma using fluorouracil, folinic acid (leucovorin) and radiation therapy |
| **GIGAI** | *timing of chemotherapy before radiation clarified* | Combined modality adjuvant therapy for completely resected gastric adenocarcinoma using fluorouracil + folinic acid (leucovorin) + radiation therapy |

| **Revised pre-printed orders**: | | |
|---|---|---|
| **Code** | **Changes** | **Protocol Name** |
| **GUKIFN** | *tests section added* | Alpha-interferon (a-IFN) for advanced renal cell carcinoma |
| **GUPDOC** | *Clarification of blood work parameters* | Palliative Therapy for Metastatic Hormone Refractory Prostate Cancer Using Docetaxel and Prednisone |
| **HNRADC** | *magnesium added to tests* | Treatment of locally advanced nasopharyngeal cancer with concurrent cisplatin and radiation |
| **UMYTHALID** | *benefit status changed* | Therapy of multiple myeloma using thalidomide<br><br>To access thalidomide, see flowchart at:<br>www.bccancer.bc.ca/HPI/ChemotherapyProtocols/Forms |

## NURSING ARTICLES OF THE MONTH

Shuey, K., and Payne, Y. (2005). Malignant Pleural Effusion. Clinical Journal of Oncology Nursing (9) 5, 529-532. The first in a series of Oncologic emergencies, to be continued over the next months.

Wilkes, G. (2005). Palmar-Plantar Erythrodysesthesia. Clinical Journal of Oncology Nursing (9)1, 103-106. A good review of pathophysiology of and interventions for hand-foot syndrome based on a case study.

These articles are available through the BCCA library or through your regional health librarian.

## 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, 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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