BC Cancer Agency

Systemic Therapy Update

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Website access at http://www.bccancer.bc.ca/STUpdate/

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

TREATMENT FOR LUNG CANCER – GEFITINIB (IRESSA®)

The BC Cancer Agency Provincial Systemic Therapy Program is pleased to announce the funding of ***gefitinib*** (Iressa, ZD 1839) as a new third-line monotherapy for patients with locally-advanced or metastatic non-small cell lung cancer (NSCLC). Gefitinib is an oral antineoplastic agent which has been available in Canada since the end of December 2003. Until now, this drug has been provided free of charge through the Iressa® Patient Assistance Program (IPAP) for patients who fit the Health Canada approved indication. Starting on 1 May 2004, IPAP will stop enrolling new patients. This has the following implications:

1. **Patients currently receiving gefitinib**: All patients will continue to receive free drug from IPAP until their therapy is stopped. Further supply of the drug can be obtained by faxing the completed Repeat Form to IPAP. The Repeat Form is available from IPAP (tel. 1-866-473-7720, fax. 1-866-706-2830). For BC Cancer Agency regional centres, this form can also be obtained from the h-drive systemic chemo reimbursement forms.
2. **New lung cancer patients starting gefitinib**: New patients who fit the criteria in the BC Cancer Agency gefitinib protocol for third-line treatment of NSCLC (ULUGEF) will be reimbursed by the BC Cancer Agency; a maximum of 60 days supply will be dispensed each time. Note that gefitinib should be discontinued if there is no clinical benefit after 4 weeks. More details on the eligibility criteria and treatment regimen can be found in the BC Cancer Agency protocol ULUGEF and the benefit drug list. Note that physicians must apply and obtain BCCA undesignated approval for each patient.
3. **New head and neck cancer patients**: New patients will *not* be reimbursed by the BC Cancer Agency at the present time.

For more information, call the BC Cancer Agency Undesignated Indication Requests at (604) 877-6277 or 1-800 633-3333 local 6277.

HIGHLIGHTS OF PROTOCOL CHANGES

Protocol The ***Lung*** Tumour Group has introduced a new protocol ULUGEF using ***gefitinib*** (Iressa®, ZD 1839) as a third-line monotherapy for locally-advanced or metastatic non-small cell lung cancer. For more details, see "**New Treatment for Lung Cancer – Gefitinib (Iressa, ZD 1839)**" at the beginning of this issue.

Revised Protocols Other protocol changes include the clarifications of dosing option of ***chlorambucil*** for low-grade ***lymphoma*** (LYCHLOR), dose modifications of ***melphalan*** for multiple ***myeloma*** (MYMP), treatment cycles of concurrent ***cisplatin*** with radiation for ***cervical*** cancer (GOCXRADC), and dose modifications in adjuvant ***FEC*** and ***CAF (days 1 and 8)*** regimens for ***breast*** cancer (BRAJFEC, BRAJCAFPO).

BENEFIT DRUG LIST

The following new program has been funded by the Provincial Systemic Therapy Program effective 1 May 2004:

- **Gefitinib** as third third-line treatment for advanced non-small cell lung cancer (ULUGEF)

This new indication is now added to the benefit list. An Undesignated Indication application must be completed for each patient 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.

The following was deleted from the Benefit List, effective May 1, 2004:

- **Diethylstilbestrol (DES) tablet and injectable**

DES was previously used with cyproterone for the treatment of patients with metastatic prostate cancer. This regimen has been largely replaced by luteinizing-hormone releasing hormone (LHRH) agonists (for more details, see March 2000 issue of the Systemic Therapy Update).

The current Benefit Drug List, Class II forms and Undesignated Indication Application forms are available on the BC Cancer Agency website (http://www.bccancer.bc.ca/ChemoProtocols/Forms/) under Health Professionals Info, Chemotherapy Protocols, Frequently Used Forms.

LIST OF NEW AND REVISED PROTOCOLS

The **INDEX to BC Cancer Agency Protocol Summaries** is revised monthly (includes tumour group, protocol code, indication, drugs, last revision date and version). Protocol codes for treatments requiring "Undesignated Indication" approval are prefixed with the letter **U**.

- **BRAJFEC** revised (dose modifications tables clarified): Adjuvant therapy for breast cancer using fluorouracil, epirubicin and cyclophosphamide
- **BRAJCAFPO** revised (dose modifications tables clarified): Adjuvant therapy for breast cancer using oral cyclophosphamide, doxorubicin and fluorouracil
- **GIFUR3** revised (minor typos corrected): Combined modality adjuvant therapy for high-risk rectal carcinoma using fluorouracil, folinic acid (leucovorin) and radiation therapy
- **GOCXRADC** revised (treatment cycles clarified): Treatment of high risk squamous cell carcinoma of cervix with concurrent cisplatin and radiation

- **ULUGEF** new: Third-line treatment for advanced non-small cell lung cancer (NSCLC) with gefitinib (Iressa®)
- **LYCHLOR** revised (dosing option clarified): Therapy for low-grade lymphoma and chronic lymphocytic leukemia using chlorambucil

- **MYMP** revised (minor typo corrected): Treatment of multiple myeloma using melphalan and prednisone

Protocols are available on the BC Cancer Agency website (http://www.bccancer.bc.ca/ChemoProtocols/) under Health Professionals Info, Chemotherapy Protocols.

PRE-PRINTED ORDER UPDATE

Pre-printed orders should always be checked with the most current BC Cancer Agency protocol summaries. The BC Cancer Agency Vancouver Centre has prepared chemotherapy pre-printed orders, which can be used as a guide for reference. An index to the orders can be obtained by Fax-back.

- **BRAJCAF-G** new: Adjuvant therapy for breast cancer using cyclophosphamide, doxorubicin, fluorouracil and filgrastim (G-CSF)
- **UGOOVVIN** revised (premeds and appointments sections): Palliative chemotherapy for re-treatment of ovarian, tubal, and peritoneal cancer using vinorelbine
- **GIFOLFIRI** revised (irinotecan/leucovorin administration and booking times): Palliative combination chemotherapy for metastatic colorectal cancer using irinotecan, fluorouracil and folinic acid (leucovorin)

- **HNCMT2** new: Combined chemotherapy and radiation treatment for locally-advanced squamous cell carcinoma of the head and neck

CANCER DRUG MANUAL

New Editorial Board Since January 2004, the Cancer Drug Manual has a new editorial board, with representatives from medical oncology (Dr. Mary MacNeil, Dr. Marianne Taylor), nursing (Karen Janes, Ruth Page, Christine Ransom), pharmacy (Linda Hamata, Saira Mithani, Susan Walisser), paediatric oncology (Jeff Davis, Roberta Esau) and the Communities Oncology Network (Dawn Annable, Clarissa Cheng). The editorial board is responsible for overseeing the general quality of the monographs and patient education materials in the manual. Since its first edition in 1990, the Cancer Drug Manual has been a unique reference source, which aims to provide timely, unbiased, concise, evaluative information on most oncology drugs for the practising health professionals.

Drug Monographs Updated Several monographs have recently been introduced: **amifostine (new)**, **anagrelide (new)**, **imatinib (new), thalidomide (new)** and **busulfan (completed updated)**. The corresponding patient information handouts have also been revised to incorporate the latest information.

Mário de Lemos, MSc, PharmD
Editor, Cancer Drug Manual

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

PATIENT EDUCATION

Drug Information Handouts Updated Several drug information handouts for patients have been revised: **amifostine**, **anagrelide**, busulfan, **imatinib** and **thalidomide** (see Cancer Drug Manual above for more details).

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.

CANCER MANAGEMENT GUIDELINES

The Cancer Management Guidelines are available on the BC Cancer Agency website (http://www.bccancer.bc.ca/CaMgmtGuidelines/) under Health Professionals Info, Cancer Management Guidelines.

FOCUS ON INFUSION REACTIONS FROM MONOCLONAL ANTIBODIES

Monoclonal antibodies (MoAbs) have become increasingly popular since their introduction into clinical practice in Canada in the 1990s. The following table outlines the MoAbs currently available in British Columbia for the treatment of adult malignancies:

Monoclonal Antibody	Target Antigen	BC Cancer Agency Protocol	Status	Uses (Approved or Investigational)
Alemtuzumab (Campath®)	CD52	(U)LYALEM	Special Access	▪ B-cell chronic lymphocytic leukemia ▪ Non-Hodgkin's lymphoma ▪ Prolymphocytic leukemia
Bevacizumab (Avastin®)	VEGF	None	Clinical Trials	▪ Breast cancer ▪ Colorectal cancer ▪ Peritoneal cancer
Cetuximab (Erbitux®)	EGFR	None	Clinical Trials	Colorectal cancer
Gemtuzumab ozogamicin (Mylotarg®)	CD33	None	Special Access	Acute myelogenous leukemia
Ibritumomab tiuxetan (Zevalin)*	CD20	None	Clinical Trials	Non-Hodgkin's lymphoma
Rituximab (Rituxan®)	CD20	▪ LYRITUX ▪ LYCHOP-R	Class II	▪ Follicular lymphoma ▪ Post-transplant lymphoproliferative disease ▪ Combination with CHOP for B-cell lymphoma
Tositumomab (Bexxar®)*	CD20		Clinical Trials	Non-Hodgkin's lymphoma
Trastuzumab (Herceptin®)	HER2	▪ BRAVTRAP ▪ BRAVTRNAV ▪ BRAVTRAP	Class II	Single or combination therapy for breast cancer overexpressing HER-2

*radiopharmaceuticals

Mild infusion reactions related to first infusion are one of the most common adverse effects of MoAbs. Symptoms include: headache, fever, chills, rigors, asthenia, rash, pruritus, urticaria, rhinitis, chest pain, nausea, vomiting, shortness of breath, hypotension, bronchospasm and hypoxia. Severe reactions can result in death. Infusion reactions are likely related to the release of cytokines from normal and neoplastic cells. These reactions most commonly occur within the first 30-120 minutes of the first infusion of the MoAb.

Risk factors for developing infusion reactions or having a poor outcome from an infusion reaction include the following:

- high number of circulating cells that express the antigen targeted by the MoAb,
- history of significant pulmonary or cardiac disease,
- rapid infusion rates.

All patients, especially those at risk for infusion reactions, should be monitored carefully during treatment with MoAbs, particularly with the first infusion. Infusion rate should be initiated slowly as outlined in the BC Cancer Agency protocols. All patients should be premedicated with diphenhydramine and acetaminophen, with additional corticosteroids in some cases (see specific BC Cancer Agency protocols for more details on required premedications).

MANAGEMENT OF INFUSION REACTIONS

- *Minor reactions*: can be treated with diphenhydramine and acetaminophen, while rigors can sometimes be managed with meperidine. Infusion can be continued despite minor reactions, either at the same or reduced rate.

- *Severe reactions*: infusions should be stopped if patients experience symptoms such as dyspnea, hypotension, rigors, chest pain or tachycardia. Bronchodilators, IV fluids and oxygen should be immediately available for supportive care. Infusions should not be restarted until there is complete resolution of the severe symptoms of the reaction, especially chest pain or bronchospasm.
- *Rechallenging*: despite an infusion reaction, many patients may be rechallenged on the same day and successfully treated with the MoAb without complications. For more severe reactions, patients may generally be rechallenged with the next scheduled dose. Note that restarting *rituximab* infusions *before* complete resolution of respiratory symptoms has been shown to be a risk factor for fatal outcome in postmarketing surveillance. Severe reactions are rare with trastuzumab.

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3. Dillman RO. Infusion reactions associated with the therapeutic use of monoclonal antibodies in the treatment of malignancy. Cancer Metastasis Rev 1999;18(4):465-71.
4. Kunkel L, Wong A, Maneatis T, et al. Optimizing the use of rituximab for treatment of B-cell non-Hodgkin's lymphoma: a benefit-risk update. Semin Oncol 2000;27(6 Suppl 12):53-61.
5. B.C. Cancer Agency Clinical Trials Database. Vancouver, British Columbia: BC Cancer Agency; April 2004.
6. B.C. Cancer Agency Breast Tumour Group. BCCA protocol summary for palliative therapy for metastatic breast cancer using trastuzumab (Herceptin®) (BRAVTR). Vancouver, British Columbia: BC Cancer Agency; 1 November 2002.
7. B.C. Cancer Agency Lymphoma Tumour Group. BCCA protocol summary for the treatment of lymphoma with single agent rituximab (LYRITUX). Vancouver, British Columbia: BC Cancer Agency; 01 June 2001.
8. B.C. Cancer Agency Lymphoma Tumour Group. BCCA protocol summary for the treatment of fludarabine-refractory B-chronic lymphocytic leukemia (B-CLL) and T-prolymphocytic leukemia (T-PLL) with alemtuzumab (ULYALEM). Vancouver, British Columbia: BC Cancer Agency; 01 October 2003.

NURSING UPDATE

Changes to BC Cancer Agency Nursing Directives and Procedures for Central Venous Catheters

A new Generic Directive (C-090) has been developed to describe points that are common to *all* central venous catheters. These points are grouped to address prevention of problems in 3 areas: infection, occlusion and air embolism. Related changes have also been made to the following procedures: C-080, C-086, and I-040. These changes reflect recommendations from research and from the Canadian Intravenous Nursing Association and the Intravenous Nurses Society. The move toward greater consistency between procedures and routines will also reduce the risk of error in clinical areas where nurses must develop skill in the care of multiple lines.

Below is a summary of the major changes:

- All *external central venous access devices* will be routinely flushed with 20 ml Normal Saline weekly.
- All *implanted venous access devices* will be routinely flushed with 20 ml Normal Saline monthly.
- In addition, all implanted and external venous access devices (except for GROSHONG® catheter PICC lines) will be flushed with 5 ml Heparin 10 units/ml in conjunction with the routine saline flush.
- All *venous access devices* (external or implanted) will also be flushed with 20 ml Normal Saline at any time when blood is in the line.
- Standardised volumes of alteplase for clearing occluded catheter lumens are noted in the procedures.
- The standard cleansing solution for skin and tubings will be Chlorhexadine 2% with 70% alcohol. (Options are noted for those with sensitivities).
- The standard dressing for CVCs will be a transparent semipermeable membrane dressing. (Options are noted for those with sensitivities).

- These changes have also been made to the patient teaching sheets for those patients who perform self-care for central venous catheters at home.

These changes will be implemented and accessible from **May 17** in the BC Cancer Agency Nursing Practice References found at **http://www.bccancer.bc.ca/HPI/Nursing/References/NursingBCCA/default**.

Submitted by

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Articles of the Month

1. Hawkins, R. (2001). Mastering the intricate maze of metastases. *Oncology Nursing Forum*. 28(6), 959-965.
2. Zack, E. (2001). Sentinel lymph node biopsy in breast cancer. Scientific rationale and patient care. *Oncology Nursing Forum* 28(6), 997- 1005.

PROVINCIAL SYSTEMIC THERAPY PROGRAM POLICIES

BC Cancer Agency Systemic Therapy Policies are available on the BC Cancer Agency website (www.bccancer.bc.ca) under Health Professionals Info, Chemotherapy Protocols, Policies and Procedures.

LIBRARY/CANCER INFORMATION CENTRE

Unconventional Cancer Therapies Manual is available on the BC Cancer Agency website www.bccancer.bc.ca under Patient/Public Info, Unconventional Therapies. The manual consists of 46 short monographs on the more commonly used unconventional cancer therapies (e.g., Essiac, vitamins, teas, shark cartilage) and includes tips for the patient and family on how unconventional therapies can be evaluated. For each therapy, the manual provides proponent/advocate claims, as well as evidence-based evaluation/critique quotations from the literature.

This manual is currently being revised and the Fourth Edition will be published in the near future.

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

Most items have been hyperlinked for easy access

☐ All items for **May 2004 (Vol 7 №5)**					
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