



INSIDE THIS ISSUE

- [New US Guidelines on Cytotoxic Exposures](#)
- [Highlights of Protocol Changes](#)
- [Benefit Drug List](#) – Docetaxel
- [List of New and Revised Protocols](#) – BRAJFEC, BRLAACD, UGICAPOX, GIFUA, HNDE, GOCXADV, UGOCXCAD, UGOCXCAT, GOENDCAD, GOENDCAT, GOOVCADR, GOOVCADX, UGOOVGAGE, GOOVCATR, GOOVCATX, GOOVETO, GOOVGEM, GOOVTAX3, GOOVTOP, UGOOVVIN, LUPG, LYABVD, ULYALEM, LYCCOP, LYCDA, LYCHLOR, LYCHOP, LYCHOP-R, LYCSPA, LYCVP, LYCVPPABO, LYCYCLO, LYECV, LYFLU, LYGDP, LYHDMTXP, LYHDMTXR, LYIT, ULYMFBEX, LYODBEP, LYPALL, LYRITUX, LYSCNCC, LYTHALID, UMYBORTEZ, MYMP, SAAJAP, SAAVAP
- [Pre-Printed Order Update](#) – BRAJACT, GIFUR3, ULYALEM, SAAJAP, SAAVAP
- [Cancer Drug Manual](#) – Drug Monographs Updated
- [Patient Education](#) – Drug Information Handouts Updated
- [Drug Update](#) – Valrubicin Shortage, Thiotepa
- [Cancer Management Guidelines](#)
- [Focus on Grapefruit Juice and Drug Interactions](#)
- [Provincial Systemic Therapy Policies](#)
- [Library/Cancer Information Centre](#)

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

NEW US GUIDELINES ON CYTOTOXIC EXPOSURES

The US National Institute for Occupational Safety and Health (NIOSH) is the federal agency responsible for conducting research and making recommendations for the prevention of work-related injury and illness. NIOSH is part of the Centers for Disease Control and Prevention (CDC) in the Department of Health and Human Services. After several years of work, they have released a prepublication copy of an alert entitled "Preventing occupational exposures to antineoplastic and hazardous drugs in healthcare settings". The purpose of the alert is to increase awareness among healthcare workers and their employers about the health risks posed by working with hazardous drugs and to provide them with measures for protecting their health. "Prepublication" means that the technical and policy contents of the alert are final but that the text has not undergone final editing and formatting for publication. Therefore, the substantive message of this document will not change, even though the wording in the final printed copy may differ somewhat from the web version.

The full document is 93 pages long and available at <http://www.cdc.gov/niosh/docs/2004-HazDrugAlert/>.

The BC Cancer Agency is undertaking a formal review of the document and will make recommendations regarding practice changes.



HIGHLIGHTS OF PROTOCOL CHANGES

Protocols The *Breast* Tumour Group has introduced a new protocol for the treatment of locally advanced breast cancer using doxorubicin and cyclophosphamide (AC) and sequential docetaxel (BRLAACD).

Revised Protocols The *Lymphoma* Tumour Group has revised all the treatment protocols to include management of hepatitis B reactivation (for more details, see the April 2004 issue of the Systemic Therapy Update). In addition, several protocols have been revised to include clarification of the maximum number of treatment cycles (LYCVP, LYCYCLO, LYFLU, LYODBEP, ULYMFBEX, UMYBORTEZ) while the high dose methotrexate protocols for intracerebral lymphoma (LYHDMTXP, LYHDMTXR) have been revised with dosing now prorated to renal function.

The *Gynecological* Tumour Group has revised a number of protocols to clarify the number of maximum number of treatment cycles (GOCXADV, UGOCXCAD, UGOCXCAT, GOENDCAD, GOENDCAT, GOOVCADR, GOOVCADX, UGOOVAGE, GOOVCATR, GOOVCATX, GOOVETO, GOOVGEM, GOOVTAX3, GOOVTOP, UGOOVVIN).

BENEFIT DRUG LIST

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

✚ **Docetaxel** in combination with doxorubicin and cyclophosphamide as treatment of locally advanced breast cancer (BRLAACD)

This new indication has been added to 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.

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
- **BRLAACD** revised (requirement for undesignated approval replaced by class II benefit drug): Treatment of locally advanced breast cancer using doxorubicin and cyclophosphamide followed by docetaxel (Taxotere®)
- **UGICAPOX** revised (number of cycle extended): Palliative combination chemotherapy for metastatic colorectal cancer using oxaliplatin, and capecitabine
- **GIFUA** revised (mitomycin dose clarified): Curative combined modality therapy for carcinoma of the anal canal using mitomycin, infusional fluorouracil and radiation therapy
- **HNDE** revised (lab tests clarified): Therapy for recurrent and metastatic nasopharyngeal cancer using cisplatin and etoposide
- **GOCXADV** revised (maximum number of cycles clarified): Treatment of advanced/recurrent non-small cell cancer of the cervix with cisplatin and etoposide
- **UGOCXCAD** revised (maximum number of cycles clarified): Treatment of advanced/recurrent non-small cell cancer of the cervix with carboplatin and docetaxel in ambulatory care settings



- **UGOCXCAT** revised (maximum number of cycles clarified): Primary treatment of advanced/recurrent non-small cell cancer of the cervix with carboplatin and paclitaxel in ambulatory care settings
- **GOENDCAD** revised (maximum number of cycles clarified): Treatment of primarily advanced or recurrent endometrial cancer using carboplatin and docetaxel
- **GOENDCAT** revised (maximum number of cycles clarified): Treatment of primarily advanced or recurrent endometrial cancer using carboplatin and paclitaxel (GO 95 01)
- **GOOVCADR** revised (maximum number of cycles clarified): Second line treatment using docetaxel and carboplatin for epithelial ovarian cancer relapsing after primary treatment
- **GOOVCADX** revised (maximum number of cycles clarified): Primary treatment of visible residual (extreme risk) invasive epithelial ovarian cancer
- **UGOOVCAGE** revised (maximum number of cycles clarified): Treatment of advanced ovarian cancer in patients who have progressed or recurred following first-line platinum-based treatment using carboplatin and gemcitabine
- **GOOVCATR** revised (maximum number of cycles clarified): Second line treatment using paclitaxel and carboplatin for epithelial ovarian cancer relapsing after primary treatment
- **GOOVCATX** revised (maximum number of cycles clarified): Primary treatment of visible residual (extreme risk) invasive epithelial ovarian cancer in ambulatory care settings using paclitaxel and carboplatin
- **GOOVETO** revised (maximum number of cycles clarified): Therapy for relapsed/progressive "ovarian" cancer using Etoposide
- **GOOVGEM** revised (maximum number of cycles clarified): Palliative chemotherapy for re-treatment of ovarian, tubal, and peritoneal cancer using gemcitabine
- **GOOVTAX3** revised (maximum number of cycles clarified): Treatment of progressive, platinum-refractory epithelial ovarian carcinoma, primary peritoneal carcinoma or fallopian tube carcinoma using paclitaxel (Taxol®)
- **GOOVTOP** revised (maximum number of cycles clarified): Treatment of relapsed/progressive epithelial ovarian, fallopian tube or primary peritoneal cancer using topotecan
- **UGOOVIN** revised (maximum number of cycles clarified): Palliative chemotherapy for re-treatment of ovarian, tubal, and peritoneal cancer using vinorelbine
- **LUPG** revised (pretreatment tests revised): Treatment of non-small cell lung cancer and malignant mesothelioma with cisplatin and gemcitabine
- **LYABVD** revised (hepatitis B reactivation management): Treatment of Hodgkin's disease with doxorubicin, bleomycin, vinblastine and dacarbazine
- **ULYALEM** revised (hepatitis B reactivation management): Treatment of fludarabine-refractory B-chronic lymphocytic leukemia (B-CLL) and T-prolymphocytic leukemia (T-PLL) with alemtuzumab
- **LYCCOP** revised (hepatitis B reactivation management): Treatment of Hodgkin's disease using cyclophosphamide, vincristine, prednisone
- **LYCDA** revised (hepatitis B reactivation management): Treatment of hairy cell leukemia with cladribine
- **LYCHLOR** revised (hepatitis B reactivation management): Therapy for low grade lymphoma and chronic lymphocytic leukemia using chlorambucil
- **LYCHOP** revised (hepatitis B reactivation management): Treatment of lymphoma with doxorubicin, cyclophosphamide, vincristine and prednisone
- **LYCHOP-R** revised (hepatitis B reactivation management): Treatment of lymphoma with doxorubicin, cyclophosphamide, vincristine, prednisone and rituximab
- **LYCSPA** revised (hepatitis B reactivation management): Cyclosporine for cytopenias associated with lymphoproliferative disorder of large granular lymphocytes
- **LYCVP** revised (maximum number of cycles, hepatitis B reactivation management): Advanced indolent lymphoma using cyclophosphamide, vincristine and prednisone

- **LYCVPPABO** revised (hepatitis B reactivation management): Treatment of Hodgkin's disease with cyclophosphamide, vinblastine, procarbazine and prednisone
- **LYCYCLO** revised (maximum number of cycles, hepatitis B reactivation management): Therapy of lymphoma, Hodgkin's disease, chronic lymphocytic leukemia or multiple myeloma using cyclophosphamide
- **LYECV** revised (hepatitis B reactivation management): Consolidation for lymphoma using etoposide and cyclophosphamide
- **LYFLU** revised (maximum number of cycles, hepatitis B reactivation management): Treatment of low-grade lymphoma or chronic lymphocytic leukemia with fludarabine
- **LYGDP** revised (hepatitis B reactivation management): Treatment of lymphoma with gemcitabine, dexamethasone and cisplatin
- **LYHDMTXP** revised (hepatitis B reactivation management, dosing, renal function monitoring, reference): Treatment of primary intracerebral lymphoma with high dose methotrexate
- **LYHDMXTR** revised (hepatitis B reactivation management, dosing, renal function monitoring, reference): Treatment of leptomeningeal lymphoma or recurrent intracerebral lymphoma with high dose methotrexate
- **LYIT** revised (hepatitis B reactivation management): Treatment of lymphoma using intrathecal methotrexate and cytarabine
- **ULYMFBEX** revised (maximum number of cycles, hepatitis B reactivation management): Treatment for refractory cutaneous T-cell lymphoma using bexarotene
- **LYODBEP** revised (cycle length, hepatitis B reactivation management): Treatment of Hodgkin's disease in elderly patients with vincristine, doxorubicin, bleomycin, etoposide and prednisone
- **LYPALL** revised (hepatitis B reactivation management): Lymphoma palliative chemotherapy
- **LYRITUX** revised (hepatitis B reactivation management): Treatment of lymphoma with single agent rituximab
- **LYSCNCC** revised (hepatitis B reactivation management): Treatment of Burkitt lymphoma with cyclophosphamide and methotrexate (leucovorin)
- **LYTHALID** revised (hepatitis B reactivation management): Therapy of multiple myeloma using thalidomide
- **UMYBORTEZ** revised (Special Access Programme requirement, maximum number of cycles, hepatitis B reactivation management): Treatment of multiple myeloma with bortezomib
- **MYMP** revised (hepatitis B reactivation management): Treatment of multiple myeloma using melphalan and prednisone
- **SAAJAP** revised (nabilone dose clarified): Adjuvant therapy for osteosarcoma using doxorubicin (Adriamycin®) and cisplatin
- **SAAVAP** revised (EKG tests deleted, nabilone dose clarified): Therapy of advanced osteosarcoma using doxorubicin (Adriamycin®) and cisplatin

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.

- **BRAJACT** revised (indication clarified): Adjuvant therapy for breast cancer using doxorubicin and cyclophosphamide followed by paclitaxel
- **GIFUR3** revised (appointment section): Combined modality adjuvant therapy for high risk rectal carcinoma using fluorouracil, folinic acid (leucovorin) and radiation therapy
- **ULYALEM** revised (appointment section): Treatment of fludarabine-refractory B-chronic lymphocytic leukemia (B-CLL) and T-prolymphocytic leukemia (T-PLL) with alemtuzumab

- **SAAJAP** revised (KCl concentration hydration fluid, labs, appointments): Adjuvant therapy for osteosarcoma using doxorubicin (Adriamycin®) and cisplatin
- **SAAVAP** revised (KCl concentration hydration fluid, labs, appointments): Therapy of advanced osteosarcoma using doxorubicin (Adriamycin®) and cisplatin

CANCER DRUG MANUAL

Drug Monographs Updated The following drug monographs and patient information handouts have been updated:

- **Daunorubicin** monograph and patient handout have been completely updated from the last revision of the Cancer Drug Manual 2nd edition.
- **Dexamethasone** patient handout for nausea and premedication has been completely revised to reflect the current practice of dosing schedule.
- **Etoposide** monograph and patient handout (oral capsule) has undergone limited revision to incorporate avoidance of grapefruit juice.
- **Ondansetron** patient handout for nausea has been completely revised to reflect the current practice of dosing schedule.
- **Letrozole** patient handout has undergone limited revision to incorporate suggested diarrhea management.
- **Procarbazine** patient handout has undergone limited revision to incorporate new description of which tyramine-containing food products should be avoided.

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: **dexamethasone**, **etoposide (oral)**, **letrozole**, **ondansetron**, and **procarbazine**, (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](#).

DRUG UPDATE

Valrubicin Shortage Valrubicin is used for the treatment of BCG-refractory bladder Tis (carcinoma in situ: "flat tumour") in patients who are unfit for cystectomy (GUBVAL). The current manufacturer is unable to supply valrubicin, and it is no longer available until further notice.

Thiotepa Shortage Thiotepa may be given as intravesical administration for the treatment of bladder cancer. The current manufacturer has discontinued this product and it is no longer available in Canada.

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 GRAPEFRUIT JUICE AND DRUG INTERACTIONS

Grapefruit juice has been implicated in a variety of drug interactions. Grapefruit juice inhibits the cytochrome P-450 enzyme system, resulting in the potential for drug interactions with other drugs metabolized by this

enzyme system. The effects of grapefruit juice are thought to be exerted primarily in the gastrointestinal tract, thus, only orally administered drugs have the potential to be affected.¹

There have been few clinical studies on the impact of grapefruit juice interactions with oral antineoplastic drugs. For example, etoposide is the only antineoplastic drug interaction with grapefruit juice documented in the Drug Interaction Facts® database (Facts and Comparisons, St Louis, Missouri, April 2004). The evidence of the impact of grapefruit juice on etoposide and several cancer drugs which are metabolized by cytochrome P-450 enzyme system was evaluated and is summarized below. For etoposide, a study looking at the co-administration of grapefruit juice with etoposide showed a reduction in etoposide levels. Interestingly, the cytochrome P-450 enzyme system does not seem to be involved as inhibition of this system should have led to increased, rather than decreased, bioavailability of etoposide. For tamoxifen, exemestane and imatinib, no studies were found. In these cases, the pharmacokinetic parameters of each drug were evaluated to see if a potential or theoretical drug interaction could be determined (see table).

Drug	Studies	Effect	Comment
tamoxifen	none	no real or theoretical interactions noted	
etoposide (oral) ²	co-administration of etoposide and grapefruit juice resulted in a reduction in bioavailability of the etoposide by 25%	potential reduction in effect	avoid combination
exemestane	none	potential for increased toxicity based on pharmacokinetic parameters	avoid combination
imatinib	none	no real or theoretical interactions noted	advise patient to follow manufacturer's recommendation and avoid grapefruit juice

Patients receiving oral prescriptions for etoposide or exemestane should be counselled to avoid grapefruit juice while on therapy. Patients on imatinib should be counselled as to the evidence for the manufacturer's recommendation. Tamoxifen does not appear to be affected by grapefruit juice and patients receiving this drug do not need to be counselled to avoid the combination.

Submitted by
 Saira Mithani, Pharm.D.
 Provincial Drug Information Specialist
 BC Cancer Agency

References

1. Kane GC, Lipsky JJ. Drug-grapefruit juice interactions. *Mayo Clin Proc* 2000;75(9):933-42.
2. Reif S, Nicolson MC, Bisset D, et al. Effect of grapefruit juice intake on etoposide bioavailability. *Eur J Clin Pharmacol* 2002;58(7):491-4.

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.

ACKNOWLEDGEMENT OF SUPPORT

Partnership with Abbott Laboratories The Systemic Therapy Program is pleased to announce the renewal and strengthening of our long term partnership with **Abbott Laboratories**. This partnership encompasses prostate cancer research and education support. The BC Cancer Agency, affiliated BC based research organizations and community researchers in BC will benefit from this partnership

Roche Oncology Grant The B.C. Cancer Agency would like to acknowledge **Roche Oncology** for an unrestricted grant of \$200,000 to go towards research that will continue to help the Lymphoma, Gastrointestinal, and Breast Cancer Tumour groups in its tradition to excel in providing optimal patient care.

EDITORIAL REVIEW BOARD

Mário de Lemos, MSc, PharmD (Editor)
Cicely Bryce, MD
Johanna Den Duyf, MA
Karen Janes, MSN

Beth Morrison, MLS
Jaya Venkatesh, MHA
Susan Walisser, BSc (Pharm)
Gigi Concon (Secretary)

IN TOUCH	www.bccancer.bc.ca	bulletin@bccancer.bc.ca
BC Cancer Agency	(604)-877-6000	Toll-Free 1-(800)-663-3333
Communities Oncology Network	Ext 2744	jvenkate@bccancer.bc.ca
Education Resource Nurse	Ext 2638	nursing@bccancer.bc.ca
Nursing Professional Practice	Ext 2623	ilundie@bccancer.bc.ca
Pharmacy Professional Practice	Ext 2247	gconcon@bccancer.bc.ca
Provincial Systemic Therapy Program	Ext 2247	gconcon@bccancer.bc.ca
Communities Oncology Network Pharmacist	Ext 6277	francish@bccancer.bc.ca
Drug Information	Ext 6275	druginfo@bccancer.bc.ca
Library / Cancer Information	Ext 2690	bethm@bccancer.bc.ca
Update Editor	Ext 2288	mdelemos@bccancer.bc.ca
Centre for the Southern Interior (CCSI)	(250) 712-3900	Toll-Free 1-(888)-563-7773
Fraser Valley Centre (FVCC)	(604)-930-2098	Toll-Free 1-(800)-523-2885
Vancouver Centre (VCC)	(604)-877-6000	Toll-Free 1-(800)-663-3333
Vancouver Island Centre (VICC)	(250) 519-5500	Toll-Free 1-(800)-670-3322

