I N S I D E T H I S I S S U E

- Benefit Drug List
- Protocol Update – BRAJCEF, BRAJCEF-G, BRAVNAV, BRINFCEF, BRINFCEF-G, BRLACEF, BRLACEF-G, GIFFAD, UGIFOLFOX, GIFUFA, GIFUR2, GIGAI, GIRAI, GIRFF, GIRLAFF, UGUAJPG, GUAVPG, GUBCV, LUPAVESE, LUPAVESL, ULUPG, ULYMFBE, LYTALID, USMAJIFN
- Cancer Management Manual
- Pre-Printed Order Update – BRAVCAD, GUPMX, LYCCOP
- Patient Education Update – Bexarotene, Interferon-Alfa, Thalidomide
- Drug Update – Mitomycin for bladder carcinoma, Irinotecan interaction with St. John’s Wort
- Cancer Drug Manual – Interferon-Alfa, Mitomycin
- Nursing Practice Update – Nursing responsibility for oral assessment of patients on fluorouracil-based GI chemotherapy
- Focus On – Carboplatin hypersensitivity
- Provincial Systemic Therapy Program Policies – III-60 Physician coverage for medical emergencies during delivery of selected chemotherapy drugs
- Provincial Drug Information – New drug information specialist
- Communities Oncology Network
- Library/Cancer Information Centre – Unconventional Drug Therapies Manual
- Continuing Education – Presentation on Symptom Management, BC Cancer Agency Annual Cancer Conference

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

BENEFIT DRUG LIST

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

PROTOCOL UPDATE

INDEX TO BC CANCER AGENCY PROTOCOL SUMMARIES revised monthly (includes tumour group, protocol code, indication, drugs, last revision date and version). Protocol codes for treatments requiring “Undesignated Indication” approval prior to use are prefixed with the letter U.

- **BRAJCEF** revised (reformatted): Adjuvant therapy for breast cancer using cyclophosphamide, epirubicin and fluorouracil
- **BRAJCEF-G** new (for patients requiring filgrastim support on BRAJCEF): Adjuvant therapy for breast cancer using cyclophosphamide, epirubicin, fluorouracil and filgrastim (G-CSF)
- **BRAVNAV** revised (tests, premedications, precautions): Palliative therapy for metastatic breast cancer using vinorelbine (Navelbine®)
- **BRINFCEF** revised (reformatted): Therapy for inflammatory breast cancer using cyclophosphamide, epirubicin and fluorouracil
- **BRINFCEF-G** new (for patients requiring filgrastim support on BRINFCEF): Therapy for inflammatory breast cancer using cyclophosphamide, epirubicin, fluorouracil and filgrastim (G-CSF)
- **BRLACEF** revised (reformatted): Therapy for locally advanced breast cancer using cyclophosphamide, epirubicin and fluorouracil.
- **BRLACEF-G** new (for patients requiring filgrastim support on BRLACEF): Therapy for locally advanced breast cancer using cyclophosphamide, epirubicin, fluorouracil and filgrastim (G-CSF)
- **GIFFAD** revised (additional information on stomatitis and diarrhea): Adjuvant therapy for stage III and high risk stage II colon cancer using leucovorin and fluorouracil
- **UGIFOLFOX** (previously UGIFOLFOX6) new: Palliative combination chemotherapy for...
metastatic colorectal cancer using oxaliplatin, 5-fluorouracil and folinic acid (leucovorin)

- **GIFUFA** revised (additional information on stomatitis and diarrhea): Combined modality curative therapy for carcinoma of the anal canal using mitomycin, fluorouracil and radiation therapy
- **GIFUR2** revised (additional information on stomatitis and diarrhea): Combined modality adjuvant therapy for high risk rectal carcinoma using fluorouracil, leucovorin, and radiation therapy
- **GIGAI** revised (additional information on stomatitis and diarrhea, dose modification for stomatitis): combined modality adjuvant therapy for completely resected gastric adenocarcinoma using fluorouracil + folinic acid (leucovorin) + radiation therapy
- **GIRAI** revised (additional information on stomatitis and diarrhea): Adjuvant therapy for rectal carcinoma using fluorouracil + leucovorin + XRT
- **GIRFF** revised (additional information on stomatitis and diarrhea):
- **GIRLAIFF** revised (additional information on stomatitis and diarrhea): Adjuvant therapy for stage II and III rectal cancer previously treated with preoperative radiotherapy
- **UGUAJPG** revised (liver function and cisplatin prehydration clarified): Adjuvant therapy for urothelial carcinoma using cisplatin and gemcitabine
- **GUAVPG** revised (liver function and cisplatin prehydration clarified): Palliative therapy for urothelial carcinoma using cisplatin and gemcitabine
- **GUBCV** revised (CBC clarified, carboplatin administration clarified): Therapy for transitional cell cancers using carboplatin-vinblastine
- **LUPAVESE** revised (exclusions revised): Treatment For Extensive stage small cell lung cancer (SCLC) with cisplatin, doxorubicin, vincristine and etoposide (PAVE)
- **LUPAVESL** revised (exclusions revised): Treatment for limited stage small cell lung cancer (SCLC) with cisplatin, doxorubicin, vincristine and etoposide (PAVE), and cisplatin and etoposide (EP) concurrent with early thoracic irradiation
- **ULUPG** revised (cisplatin prehydration in renal dysfunction clarified): Treatment of malignant mesothelioma with cisplatin and gemcitabine
- **ULYMFEX** new: Treatment of cutaneous T-cell lymphoma (mycosis fungoides/Sézary syndrome) with bexarotene (Targretin®) (Note: approval from the Health Canada Special Access Programme required)
- **LYTHALID** revised (dose and administration guideline): Therapy of multiple myeloma using thalidomide
- **USMAJIFN** revised (monitoring, premedications, administration guideline, rest period): Adjuvant therapy of high-risk malignant melanoma with high dose interferon (HDIFN) α-2b (Note: for nursing issues related to this protocol, please contact 604-877 6098 local 2623).

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

### CANCER MANAGEMENT MANUAL

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

### 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.

- **BRAVCAD** new: Palliative therapy for metastatic breast cancer using docetaxel and capcitabine
- **GIFFAD** revised (dose calculation section revised for leucovorin): Adjuvant therapy for stage III and high risk stage II colon cancer using Leucovorin and Fluorouracil
- **GUPMX** revised (frequency of PSA tests): Palliative therapy for hormone-refractory prostate cancer using Mitoxantrone and Prednisone
LYCCOP new (replacing LYCOPP): Treatment of Hodgkin’s lymphoma using cyclophosphamide, vincristine and prednisone

**PATIENT EDUCATION UPDATE**

**Bexarotene Patient Information Handout** is now available. Bexarotene is a retinoid that selectively binds to and activates retinoid receptors. It inhibits the growth of tumour cell lines of hematopoietic and squamous cell origin and is used for the treatment of cutaneous T-cell lymphoma (e.g., mycosis fungoides, Sézary syndrome). Also see protocol ULYMFBEXA for more details.

**Interferon-Alfa Patient Information Handout** has been revised to reflect the adverse effect profile associated with the intravenous regimen.

**Thalidomide Patient Information Handout** has been revised to clarify instructions for missing doses.

Patient information handouts for cancer drugs are available on the BC Cancer Agency website (www.bccancer.bc.ca) under Health Professionals Info, Drug Database.

**DRUG UPDATE**

**Mitomycin for Bladder Carcinoma** The mitomycin monograph in the Cancer Drug Manual has been updated to include a broader range of acceptable concentrations for the bladder instillation of mitomycin. A recent trial using a 2mg/mL concentration of mitomycin found similar efficacy and side effects as has been reported with a 1mg/mL concentration. Physicians need to specify the concentration required when prescribing mitomycin instillations.

**Reference**

**Irinotecan Interaction with St John’s Wort**

St John's Wort (SJW) is a herbal product commonly used for the treatment of mild-moderate depression and has recently been reported to interact with the antineoplastic, irinotecan. SJW is an *inducer* of the cytochrome P450 (CYP) 3A4 enzyme system and of P-glycoprotein/MDR-1 (Multidrug resistance) expression.\(^1\,^2\)

Irinotecan’s metabolism is complex and involves several metabolic pathways, including an active metabolite, SN-38, and the involvement of CYP 3A4 and the P-glycoprotein.\(^1\) Recently, Mathijssen et al. reported the results of a crossover trial involving 5 patients who received irinotecan with and without St John’s Wort.\(^1\) A significant drug interaction between SJW and irinotecan was demonstrated which may result in decreased effectiveness of irinotecan. Concentrations of the active metabolite, SN-38, were decreased which manifested clinically as less myelosuppression. No differences in efficacy were seen but patients only received SJW with the irinotecan for one cycle of chemotherapy.\(^1\)

There is potential for SJW to interact with many other chemotherapeutic agents. Antineoplastics metabolized by CYP 3A4 include busulfan, doxorubicin, cyclophosphamide, docetaxel, imatinib, etoposide, ifosfamide, paclitaxel, teniposide, vinblastine, and vincristine.\(^3\) Hormonal agents metabolized by 3A4 system include anastrozole, tamoxifen, exemestane, flutamide, and letrozole.\(^3\) Other examples of inducers of CYP 3A4 are carbamazepine, phenobarbital, phenytoin, and rifampin.\(^3\)

Irinotecan has been shown to induce the action of P-glycoprotein.\(^2\) P-glycoprotein is an efflux pump which acts to remove any chemical the cell considers undesirable. Multidrug resistance has been shown to be one mechanism by which cancer cells develop resistance and may result from induction of P-glycoprotein. Other inducers of P-glycoprotein are rifampin, ritonavir and yohimbine.\(^4\)

**Conclusion**

St John’s Wort should not be combined with irinotecan or with other antineoplastics metabolized by the CYP 3A4 enzyme system or by P-glycoprotein.

**References**
1. Mathijssen RHJ, Verweij J, de Bruijn P, Loos WJ, Sparreboom A. Effects of St. John's Wort on irinotecan

By Dana Cole, BScPharm, PharmD
Drug Information Specialist,
Provincial Systemic Therapy Program,
BC Cancer Agency

NURSING PRACTICE UPDATE

Nursing Responsibility for Oral Assessment of Patients on Fluorouracil-Based GI Chemotherapy In the September issue of Systemic Update you read of the importance of identifying patients who are at risk for (or who are experiencing) oral mucositis as a result of fluorouracil (5-FU) based chemotherapy for GI cancers. In this issue we describe the specific assessment responsibilities of all nurses caring for this group of patients.

Nurses caring for patients receiving 5-FU based GI chemotherapy will incorporate the 3 following steps into their assessment process.

1. The RN will assess each GI patient prior to the administration of each dose of 5-FU based chemotherapy to identify
   ▪ any symptoms involving the patient’s mouth, tongue, and throat
   ▪ any change in ability to eat
   ▪ any change in the physical condition of mouth

2. The RN will report any changes from the baseline assessment to the Oncologist prior to the administration of chemotherapy.

3. The RN will document the details of the oral assessment daily prior to the administration of chemotherapy.

Questions to ask the patient during this assessment:
“Have you noted any changes in your mouth, tongue, or throat such as
   ▪ discomfort or pain on swallowing?
   ▪ burning sensation?
   ▪ changes in sense of taste?
   ▪ sensitivity to salty and spicy foods or drinks?

Are you able to eat a regular diet? Please describe any changes in your eating pattern.”

Physical exam
Using a flashlight and tongue blade, examine the patient’s lips, tongue, cheeks, upper and lower palate for:
   ▪ redness
   ▪ swelling
   ▪ tenderness of mucous membranes
   ▪ ulcerations

As we continue to develop our understanding of the significance of the problem of mucositis, adjustments to involved chemotherapy protocols will be made. Stay tuned for future ST Updates for further information. In the next issue we will discuss assessment tools to streamline and standardize nursing assessment of stomatitis. In the meantime do not hesitate to contact our Education Resource Nurse phone line (1-800-663-3333, local 2638) or our e-mail address nursinged@bccancer.bc.ca with questions or concerns related to the nursing care of these patients.

July Oliver,
Education Resource Nurse,
BCCA-Vancouver Centre,
For the Nursing Practice Committee

FOCUS ON CARBOPLATIN HYPERSONSIVITY

Carboplatin is a widely used chemotherapeutic agent for both first and second line treatment of ovarian cancer as well as pediatric malignancies, germ cell tumours, and endometrial cancer. Due to the decreased incidence of nephrotoxicity and neurotoxicity, as well as reduced emetogenic potential compared to cisplatin, carboplatin usage has increased dramatically over the past decade.1,2 Consequently, an increase in the incidence of hypersensitivity reactions (HSR) has become a
growing issue when utilizing carboplatin, particularly in the second line ovarian cancer setting.

The most outstanding feature associated with carboplatin hypersensitivity is the occurrence of the reaction after multiple exposures to the drug. Although a 2% incidence of allergic reactions has been reported with carboplatin alone, an increased rate of HSR of 15-27% has been seen in patients receiving more than 7 cycles of the drug. HSR range from mild to severe and potentially fatal and may include any of the following symptoms; pruritus, palmar erythema, urticarial or macular rash, facial and tongue edema, edema of infusion arm, abdominal cramps, diarrhea, nausea, vomiting, angina, tachycardia, anxiety, hypotension, and dyspnea. The ability to identify and distinguish a HSR associated with carboplatin is important as this drug is frequently administered with other chemotherapy agents, in particular, paclitaxel in the ovarian cancer setting. The following table outlines the differences that may be observed between a paclitaxel and carboplatin HSR.

<table>
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<tr>
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<th>Carboplatin</th>
<th>Paclitaxel</th>
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<tr>
<td><strong>Initial Onset</strong></td>
<td>after multiple courses</td>
<td>first or second course</td>
</tr>
<tr>
<td><strong>Onset of Symptoms</strong></td>
<td>highly variable (minutes to days)</td>
<td>within minutes of initiation of infusion</td>
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<tr>
<td><strong>Symptoms</strong></td>
<td>variable (itching, rash, chest tightness, emesis, blood pressure changes, facial swelling)</td>
<td>characteristic (chest tightness, dyspnea, angioedema, back pain, urticaria, blood pressure changes)</td>
</tr>
<tr>
<td><strong>Ability to Safely Retreat</strong></td>
<td>variable (based on severity of symptoms)</td>
<td>almost always</td>
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A type I IgE-mediated HSR appears to be the type of HSR associated with carboplatin although an anaphylactoid reaction mediated by the direct release of vasoactive substances such as histamine may be responsible in some cases. Various studies have been unable to identify any predisposing factors linked to a carboplatin HSR. Immediate management of a HSR of carboplatin may include administration of diphenhydramine 50 mg IV, hydrocortisone 100 mg IV, epinephrine 0.1-0.25 mg IV, salbutamol 5 mg via nebulizer, and oxygen as required or as outlined by institutional policy.

Treatment options following a carboplatin HSR may include oral premedications and/or intravenous carboplatin desensitization, switching to cisplatin, or a third line agent such as oral etoposide, gemcitabine or topotecan. A wide variety of retreatment and desensitization protocols have been attempted with varying degrees of success. Robinson et al compiled 23 attempts to retreat with carboplatin and reported 21 successful carboplatin administrations, which employed a wide range of protocols. Typically, attempts at re-treatment in patients with severe reactions are not suggested and an alternative agent should be chosen for this patient group.

Oral premedications are the most cost-effective method of attempting re-treatment. Various protocols are available in the literature and a common example follows:

**Premedications:**
Dexamethasone 20 mg po every 6 hours for 4 to 8 doses
Cimetidine 300-600 mg po every 8 hours for 3 to 6 doses
Diphenhydramine 25-50 mg every 6 hours for 4 to 8 doses
Optional:
Salbutamol MDI 2 puffs every 6 hours for 8 doses

**Immediately prior to infusion:**
Dexamethasone 20 mg IV
Cimetidine 300-600 mg IV
Diphenhydramine 25-50 mg IV
Optional:
Lorazepam 0.5 mg IV
Ondansetron 8 mg IV
May continue dexamethasone, cimetidine, diphenhydramine during infusion.

Intravenous desensitization involves gradually administering increasing concentrations of carboplatin as tolerated. Often, IV desensitization will be combined with an oral premedication schedule as above. A common desensitization schedule follows:

Mix calculated total dose in 100 mL D5W
Administer 0.1 mL of this solution in 100 mL D5W or 1 hour (1:1000 dilution).
If tolerated, administer 1 mL of the solution in 100 mL D5W over 1 hour (1:100 dilution).
If tolerated, administer 10 mL of the solution in 100 mL D5W over 1 hour (1:10 dilution).
If tolerated, administer the remaining solution over 1 hour (1:1 dilution).

The incidence of cross-allergy between carboplatin and cisplatin is unknown. The outcome of these cases are found sporadically throughout the literature. Dizon et al reported on six patients who received cisplatin after a documented allergy to carboplatin. Five of the six patients were successfully retreated with routine premedication and slower infusion rates as tolerated. However, there was one fatal outcome following the patient’s second cycle of cisplatin despite premedication and a successful first cycle. Cisplatin remains a viable treatment option for carboplatin sensitive patients, but as with other treatment options, the risks and benefits must be carefully considered in consultation with the patient.

Overall, caution must be exercised in patients receiving multiple courses of carboplatin due to the increased risk of a HSR. Although various reports describe re-treatment of patients with carboplatin HSRs, the number of patients reported is limited; therefore, it is difficult to reliably determine the success rate, risks, and optimal protocol for each individual patient. Each HSR must be assessed on a case-by-case basis to determine the appropriate course of treatment. Premedication and desensitization schedules may allow some patients to proceed with carboplatin or cisplatin therapy while alternative agents may be considered more appropriate for others.

References

Kimberly Kuik
Pharmacy CON Educator
BC Cancer Agency-Southern Interior Centre

Reviewed by Susan Ellard
Medical Oncologist
BC Cancer Agency-Southern Interior Centre

CANCER DRUG MANUAL

Interferon-Alfa monograph has been updated to reflect the option of using 50 mL infusion for IV administration.

Mitomycin monograph has been updated to include a broader range of acceptable concentrations for the bladder instillation of mitomycin. See Drug Update in this issue of the Update for more details.

The Cancer Drug Manual is available on the BC Cancer Agency website www.bccancer.bc.ca/cdm/.
PROVINCIAL SYSTEMIC THERAPY
PROGRAM POLICIES

Physician Coverage for Medical Emergencies During Delivery of Selected Chemotherapy Drugs

This patient care policy (III-60) has been revised regarding the management of medical emergencies arising during rituximab treatment.

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.

PROVINCIAL DRUG INFORMATION

New Provincial Drug Information Specialist

We are pleased to announce that Dr. Dana Cole has recently joined the BC Cancer Agency as a Drug Information Specialist for the Provincial Systemic Therapy Program. Dana will be working with Dr. Robin O’Brien to answer drug information requests from across the province. She will be working out of the Fraser Valley Centre in Surrey. Her other responsibilities include updating and maintaining the BCCA Cancer Drug Manual.

Dana has received her Bachelor of Science in Pharmacy from Dalhousie University, Halifax and her Pharm.D from UBC. She did her residency in Queen Elizabeth II Health Sciences Center, Victoria General, Halifax. Most recently, she was the Regional Clinical Coordinator at the Prince George Regional Hospital. She brings with her a wealth of skills and experience, which will enhance her role as the Drug Information Specialist. Her expertise in working at a CON Centre will be an asset to the Agency. Dana may be reached Monday to Friday at (604) 587-4308.

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.

CONTINUING EDUCATION

Presentation on Symptom Management

Karima Velji, an advanced practice nurse with an extensive background in cancer nursing practice, education, and research, will present "Implementing Research in Practice: Symptom Management" on Wednesday evening, 27 November, 2002. Please join us at one of the four regional cancer centres for a light dinner at 6 pm, followed by the video-linked presentation at 7 pm.

For more details, please call: Vancouver Island Centre - Jodi Graham (250) 519-5573; Centre for the Southern Interior - Dixie Rosher (250) 712-3975; Vancouver and Fraser Valley Centres - Isabel Lundie (604) 877-6098, local 2623.

BC Cancer Agency Annual Cancer Conference

will be held on 28, 29 and 30 of November at the Renaissance Harbourside Hotel in Vancouver. The program on the Thursday of 28 November will be the Implementation of Canadian Strategy of Cancer Control meeting (by invitation only), focusing on issues that relate to the Agency, with representations from physicians, nurses, nutritionists, pharmacists and social workers of the community cancer centres and cancer services. Note that this will replace the originally planned Partners in Cancer Care meeting.

The mornings of Friday and Saturday will be the Annual Oncologist / Scientist Cancer Conference. This is open to any healthcare professionals and is an academic evidence-based exploration of new scientific insights that hold potential to advance cancer care. In addition to the "hot topics", this year's theme will be "The Immune System and Cancer". This part of the conference is open to all professionals caring for cancer patients and is especially relevant to oncologists and cancer research scientists.

The Annual Provincial Oncology Professionals education and business meetings for - nursing, psychosocial oncology, nutrition will be held on, 29 November, while surgical oncology network,
radiation therapy and pharmacy will hold theirs on Saturday, 30 November. This part of the conference is also by invitation from the provincial oncology professional leader.

For more details, please call (604) 877-6098 local 2744. Also, More details on the Conference will be available on our website in early October.

**Call for Abstracts for Poster Presentations** The deadline for submission will be **21 October, 2002**. For more details, please contact Jaya Venkatesh, Provincial Business Affairs Coordinator, Provincial Systemic Therapy Program & Communities Oncology Network, BC Cancer Agency, email: jvenkate@bccancer.bc.ca or tel: (604) 877-6000 local 2732.

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We appreciate your comments. Write us at bulletin@bccancer.bc.ca
BC CANCER AGENCY SYSTEMIC THERAPY UPDATE FAX REQUEST FORM

FAX (604) 877-0585
bulletin@bccancer.bc.ca

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☐ Cancer Drug Manual Monographs (also available on our website www.bccancer.bc.ca)
☐ Interferon-Alfa
☐ Mitomycin
☐ Patient Education Handout (also available on our website www.bccancer.bc.ca)
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