BC Cancer Agency
CARE & RESEARCH

Systemic Therapy Update

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Website access at http://www.bccancer.bc.ca/HPI/ChemotherapyProtocols/stupdate.htm

INSIDE THIS ISSUE

BENEFIT DRUG LIST

The following indications have been added to the Benefit Drug List as class II drugs:

- **Gemcitabine** palliative therapy for metastatic breast cancer (BRAVGEM)
- **Irinotecan** high risk renal tumors in pediatric patients (COG protocol AREN0321)
- **Irinotecan** high risk rhabdomyosarcoma in pediatric patients (COG protocol ARSTO431)

FREQUENTLY ASKED QUESTIONS: CORTICOSTEROID USE DURING CHEMOTHERAPY

The following are some of the frequently asked questions by healthcare professionals around the province on the use of corticosteroids in patients receiving chemotherapy.

1. **Does being put on dexamethasone or prednisone during chemotherapy pose any risks to patients? Would this depend on the dose or duration of the corticosteroid?**

Corticosteroids such as dexamethasone and prednisone may be used for different purposes in patients with cancer. They are used for cancer treatment, as an anti-emetic, or are already in use for a pre-existing non-cancer condition. Cancers that are often treated with corticosteroids include lymphoid cancers (lymphoma, myeloma, chronic lymphocytic leukemia) and metastatic hormone refractory prostate cancer.

Corticosteroids expose the patient to multiple potential adverse effects. Although the risk of adverse effects exists whether a corticosteroid is used to treat a cancer or as an anti-emetic, each indication for a corticosteroid should be considered individually for its potential benefits and harms. In general, a higher dose and prolonged exposure are associated with a higher risk of complications. Monitoring patients for adverse effects is important, and dosage adjustments can be made based on the patient's ability to tolerate prescribed corticosteroid doses.

Adverse effects that tend to be problematic for patients taking dexamethasone as an anti-emetic include hyperglycemia in patients without pre-existing diabetes, loss of blood glucose control in patients with pre-existing diabetes, stomach upset and hyperacidity, palpitations, or insomnia.

Prednisone or dexamethasone taken continuously for longer periods of time, or for short, high-dose treatment courses that are repeated regularly (e.g., dexamethasone 40 mg daily for 4 days, or prednisone 75 mg daily for 5 days), may also be associated with adverse effects such as osteoporosis, weight gain, electrolyte imbalances, hypertension, opportunistic infections, glaucoma, severe mood swings (e.g., mania and/or depression), and suppression of the hypothalamic-pituitary-adrenal axis.

2. Can a patient who is already taking prednisone also take dexamethasone when on chemotherapy?

If a patient is already taking prednisone for a pre-existing condition other than cancer, the prednisone should be continued without change while the dexamethasone is being taken. Circumstances are more complex in patients taking prednisone as part of their cancer treatment and are also prescribed dexamethasone as an anti-emetic. Each corticosteroid or each indication should be considered individually. Often the dose or duration may help the clinician in deciding how to approach this type of situation. In general, if a patient is taking prednisone as part of their cancer treatment (e.g., CHOP for lymphoma, or GUPDOC for prostate), and dexamethasone has been prescribed as an anti-emetic, both agents should be continued. If one corticosteroid is discontinued or dropped simply because another has been started, there is a chance that the original corticosteroid will not be resumed when required.

3. How long should it take for side effects of dexamethasone to subside after it is used as an anti-emetic?

Side-effects related to anti-emetic doses of dexamethasone can be expected to subside within 24 to 48 hours after taking the last dose. Suppression of the hypothalamic-pituitary-adrenal axis is not a concern with a short course of dexamethasone used as an anti-emetic.

With input from Dr. J. Connors and Lynn Ferrier.

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CANCER DRUG MANUAL

Procarbazine Monograph and Patient Handout have been completely revised and updated. Expert review was provided by Drs. Brian Thiessen (Neuro-oncology Tumour Group) and Joseph Connors (Lymphoma Tumour Group). Highlights of monograph changes include:

- expansion of monoamine oxidase inhibition precautions
- nausea and vomiting details being added:
  -nausea and vomiting is dose-dependent and it may be minimized by increasing the dose of procarbazine over several days;
  -tolerance to nausea may commonly occur within a few days;

-emetogenic potential of procarbazine at doses of 100 mg/m^2 is considered low to moderate
- addition of secondary malignancy side effects including lung cancer, acute myelocytic leukemia, and malignant myelosclerosis; the risk of secondary lung cancer appears to be increased by tobacco use
- updated drug interactions section to include methotrexate, digoxin, antidiabetics, levodopa and ginseng as interacting agents

Highlights of handout changes include:

- addition of a recommendation to avoid smoking while on procarbazine due to the risk of secondary lung cancer
- addition of sun sensitivity and skin rashes as side effects and their management
- expanded details regarding alcohol avoidance while on procarbazine which includes details regarding the potential disulfiram-like reaction with all alcohol
- details regarding tyramine interaction due monoamine oxidase inhibition with certain types of alcohol (red wines, vermouth, and tap beer)

TEMSIROLIMUS MEDICATION PREPARATION: SAFETY ALERT

The Institute for Safe Medication Practices (ISMP) issued a Safety Alert regarding the preparation of Temsirolimus in May of this year after some potential problems were identified.[i]

Temsirolimus (Torisel®) injection is used for the treatment of advanced renal cell carcinoma. As a product it is distributed in a kit that contains two vials: a vial of active drug labelled as 25 mg/ml along with a second vial that contains 1.8 ml of diluent.

The active drug although it is labelled as 25 mg/ml, it is supplied as 30 mg in a total volume of 1.2 mL. The final fixed dose is 25 mg.

To prepare the drug for administration, the diluent is added to the vial of active drug to yield a total volume of 3 mL or a final concentration of 10 mg/mL. Although not explicitly stated in the package insert, there is a 20% overfill meant to accommodate withdrawal of medication from the vial. The full 30 mg amount in the vial is not meant to be withdrawn. The 25 mg dose (2.5 mL) should be drawn up and added to 250 ml of 0.9% sodium chloride and infused over 30-60 minutes. The final product should be prepared in a non-PVC IV bag and administered using non-PVC tubing that includes an inline filter.

The ISMP report describes an incidence where an error occurred with the preparation of Temsirolimus. In the case reported, the pharmacy staff did not realize that by adding the diluent to the vial containing active drug, the resulting concentration was now 10 mg/mL instead of 25 mg/mL, as marked on the vial label. When the dose was drawn up, only 1 mL (10 mg) was removed instead of 2.5 mL (25 mg). When the pharmacist checked the final product, the amount drawn up (1 mL) was compared with the Temsirolimus vial (labelled 25 mg/mL) and concluded that the correct dose had been withdrawn. This resulted in the patient receiving less than the ordered dose (i.e. 10 mg instead of the intended 25 mg). The report goes on to suggest a change in the vial labelling to state 30 mg/3 mL (10 mg/mL) after dilution with enclosed diluent. FDA is aware of the situation.

A recent Department of Veterans Affairs bulletin to VA employees (www.ismp.org/sc?k=pbm) provided information about staff being aware of the different Temsirolimus concentrations before and after dilution. The bulletin recommended that pharmacists keep the package insert with the full instructions for dilution of Temsirolimus with both active drug and diluent vials, since no instructions appear on the vials themselves. It also suggests creating warning systems to notify staff of the change in concentration when preparing the final dilution of Temsirolimus (i.e., computer alerts during the ordering/ verifying process and/or warning stickers on packaging).

[1] ISMP Safety Alert! Acute Care, Volume 13, Issue 9, May 8, 2008.

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HIGHLIGHTS OF CHANGES IN PROTOCOLS AND PRE-PRINTED ORDERS

The ***Gastrointestinal Tumour Group*** has deleted the comment about antibiotics and colony-stimulation factors from Neutropenia under Precautions in irinotecan-based protocols.

The ***Lymphoma Tumour Group*** has revised the visual observation for potential hypersensitivity reactions to rituximab to ensure consistency across the protocols pre-printed orders. Rituximab can cause allergic type reactions during the IV infusion such as hypotension, wheezing, rash, flushing, alarm, pruritus, sneezing, cough, fever or faintness. For first dose, patients are to be under constant visual observation during all dose increases and for 30 minutes after infusion is completed. For all subsequent doses, visual observation is not required.

LIST OF NEW AND REVISED PROTOCOLS, PRE-PRINTED ORDERS AND PATIENT HANDOUTS

BC Cancer Agency Protocol Summaries, Provincial Pre-Printed Orders (PPPOs) and Patient Handouts are revised periodically. New and revised protocols, PPPOs and patient handouts for this month are listed below. Protocol codes for treatments requiring "Compassionate Access Program" (previously Undesignated Indication Request) approval are prefixed with the letter **U**.

NEW PROTOCOLS, PPPOS AND PATIENT HANDOUTS (AFFECTED DOCUMENTS ARE CHECKED):

CODE	Protocol	PPPO	Patient Handout	Protocol Title
BRAVGEM	☑	☑	☑	Palliative Therapy for Metastatic Breast Cancer using Gemcitabine
GUAVPG	☐	☐	☑	Palliative Therapy for Urothelial Carcinoma Using Cisplatin and Gemcitabine

REVISED PROTOCOLS, PPPOS AND PATIENT HANDOUTS (AFFECTED DOCUMENTS ARE CHECKED):

CODE	Protocol	PPPO	Patient Handout	Changes	Protocol Title
BRAVTRNAV	☑	☐	☐	*Exclusion criteria modified*	Therapy for Metastatic Breast Cancer using Trastuzumab (HERCEPTIN®) and Vinorelbine
CNCCV	☑	☐	☐	*Tests, Premedications and Dose Modifications revised)*	Adjuvant Lomustine, Cisplatin and Vincristine in Adult High-Risk Medulloblastoma or other Primitive Neuro-Ectodermal Tumour (PNET)

CODE	Protocol	PPPO	Patient Handout	Changes	Protocol Title
UGICAPIRI	☑	☐	☐	*Comment about antibiotics and colony-stimulation factors deleted from Neutropenia under Precautions, contact physician revised*	First Line Palliative Combination Chemotherapy for Metastatic Colorectal Cancer Using Irinotecan and Capecitabine in Patients Unsuitable for GIFOLFIRI
UGICIRB	☑	☐	☐	*Comment about antibiotics and colony-stimulation factors deleted from Neutropenia under Precautions, contact physician revised*	Palliative Combination Chemotherapy for Metastatic Colorectal Cancer Using Irinotecan, Bevacizumab and Capecitabine
UGIFFIRB	☑	☐	☐	*Comment about antibiotics and colony-stimulation factors deleted from Neutropenia under Precautions, contact physician revised*	Palliative Combination Chemotherapy for Metastatic Colorectal Cancer Using Irinotecan, Fluorouracil, Folinic Acid (Leucovorin) and Bevacizumab
GIFOLFIRI	☑	☐	☐	*Comment about antibiotics and colony-stimulation factors deleted from Neutropenia under Precautions, contact physician revised*	First Line Palliative Combination Chemotherapy for Metastatic Colorectal Cancer Using Irinotecan, Fluorouracil and Folinic Acid (Leucovorin)
GIPGEM	☑	☐	☐	*Gall bladder and cholangiocarcinoma added to indications, references added*	Palliative Chemotherapy for Pancreatic Adenocarcinoma, Gallbladder Cancer, and Cholangiocarcinoma Using Gemcitabine
UGIRAJFFOX	☐	☑	☐	*Platelet threshold clarified*	Adjuvant Combination Chemotherapy for Stage III Rectal Cancer Using Oxaliplatin, 5-Fluorouracil and Folinic Acid (Leucovorin)
UGISORAF	☑	☐	☐	*Child-Pugh B status deleted from Eligibility*	Therapy for Advanced Hepatocellular Carcinoma Using Sorafenib
GOCXCRT	☐	☑	☐	*Appointment section clarified*	Treatment of High Risk Squamous Carcinoma, Adenocarcinoma, or Adenosquamous Carcinoma of the Cervix with Concurrent Cisplatin and Radiation
HNAVGEM	☐	☑	☐	*ANC value clarified*	Treatment of Loco-regionally Recurrent/Metastatic Nasopharyngeal Cancer not Amenable for Local Curative Therapy with Gemcitabine
LYCHOPR	☑	☑	☐	*Visual observation for potential hypersensitivity reactions to rituximab revised*	Treatment of Lymphoma with Doxorubicin, Cyclophosphamide, Vincristine, Prednisone and Rituximab (CHOP-R)
LYCVPR	☑	☑	☐	*Visual observation for potential hypersensitivity reactions to rituximab revised*	Treatment of Advanced Indolent Lymphoma using Cyclophosphamide, Vincristine, Prednisone and Rituximab (CVP-R)

CODE	Protocol	PPPO	Patient Handout	Changes	Protocol Title
LYCYCLO	☑	☐	☐	*Lab tests required prior to first treatment revised*	Therapy of Lymphoma, Hodgkin's Lymphoma, Chronic Lymphocytic Leukemia or Multiple Myeloma Using Cyclophosphamide
LYFLUDR	☑	☑	☐	*Visual observation for potential hypersensitivity reactions to rituximab revised*	Treatment of Chronic Lymphocytic Leukemia or Prolymphocytic Leukemia with Fludarabine and Rituximab
UGUSUNI	☐	☑	☐	*Tablet replaced by capsule*	Palliative Therapy for Renal Cell Carcinoma Using Sunitinib
LYHDMTXP	☑	☐	☐	*Cotrimoxazole precaution added, methotrexate dosing revised to mg/m^2*	Treatment of Primary Intracerebral Lymphoma with High Dose Methotrexate
LYHDMTXR	☑	☐	☐	*Cotrimoxazole precaution added, methotrexate dosing revised to mg/m^2*	Treatment of Leptomeningeal Lymphoma or Recurrent Intracerebral Lymphoma with High Dose Methotrexate
ULYMFBEX	☑	☐	☐	*Hepatitis B Reactivation precaution removed*	Treatment of Cutaneous T-cell Lymphoma (Mycosis Fungoides/Sézary syndrome) with Bexarotene
ULYRICE	☑	☑	☐	*Visual observation for potential hypersensitivity reactions to rituximab revised*	Treatment of Relapsed or Refractory Advanced Stage Aggressive B-Cell Non-Hodgkin's Lymphoma with Ifosfamide, Carboplatin, Etoposide and Rituximab
LYRITUX	☑	☑	☐	*Visual observation for potential hypersensitivity reactions to rituximab revised*	Treatment of Lymphoma with Single Agent Rituximab
ULYRMTN	☑	☑	☐	*Visual observation for potential hypersensitivity reactions to rituximab revised*	Maintenance Rituximab for Indolent Lymphoma
MYPAM	☑	☑	☐	*Serum creatinine, renal dysfunction and symptomatic hypocalcemia added to protocol, treatment and appointment scheduling clarified in PPPO*	Treatment of Multiple Myeloma with Pamidronate
SAAVA	☑	☐	☐	*Number of treatment cycles clarified*	Doxorubicin for use in Patients with Advanced Soft Tissue Sarcoma

CONTINUING EDUCATION

BC Cancer Agency Annual Cancer Conference 2008 will be held on **20-22 November** at the Westin Bayshore Resort & Marina in Vancouver. This year's theme will be ***Survivorship: Creating It, Managing It***.

Stay tuned for more information about this exciting conference.

EDITOR'S NOTE

This is a combined July-August issue of the Systemic Therapy Update. The next issue will be in September.

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, COMPASSIONATE ACCESS PROGRAM (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

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	nursinged@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	lkovacic@bcancer.bc.ca
DRUG INFORMATION	Ext 6275	druginfo@bccancer.bc.ca
LIBRARY/CANCER INFORMATION	1-(888)-675-8001 Ext 8003	requests@bccancer.bc.ca
OSCAR HELP DESK	1-(888)-355-0355 Fax (604) 708-2051	oscar@bccancer.bc.ca
COMPASSIONATE ACCESS PROGRAM OFFICE (FORMERLY UNDESIGNATED DRUG APPLICATION OFFICE)	Ext 6277 Fax (604) 708-2026	cap_bcca@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