Systemic Therapy Update

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INSIDE THIS ISSUE

EDITOR'S CHOICE

HIGHLIGHTS OF CHANGES IN PROTOCOLS, PRE-PRINTED ORDERS AND PATIENT HANDOUTS

The **Breast Tumour Group** has revised the eligibility criteria for adjuvant chemotherapy protocols with **trastuzumab** to include patients with node-negative, T1b (>0.5 cm to ≤1 cm), HER2 positive breast cancer. Use of trastuzumab in patients with node-negative T1a disease (≤0.5 cm) still requires approval by the BCCA Compassionate Access Program (CAP). Changes to the management guidelines for adjuvant and metastatic HER2 positive breast cancer will be posted on the website shortly.

The **Leukemia/Bone Marrow Transplantation Program** has revised the eligibility criteria and dosing schedule for the use of **azacitidine** for myelodysplastic syndrome (MDS) in the ULKMDSA protocol. The protocol had previously used a 7-day administration schedule as per phase III clinical trials methodology. The BCCA and CON ambulatory centres, along with a number of cancer centres across Canada, are unable to accommodate this dosing schedule because few facilities provide chemotherapy services 7 days a week. Therefore, the protocol has been revised to include options to administer this agent as 5 days on, 2 days off, and 2 days on to allow a break on the weekend.

- Patients already approved for ULKMDSA will not require new CAP approval to switch to this alternative regimen.
- Every effort should be made to avoid scheduling over long weekends (e.g., over 3-4 days) or statutory holidays during the week. If unavoidable, it should aim to deliver a total of 7 days of treatment out of about 10 consecutive days; having breaks in therapy over these circumstances do not require CAP approval.

Pyridoxine Ineffective for Capecitabine-Related Hand-Foot Syndrome Based on the emerging evidence, pyridoxine has been removed as a prevention/treatment option for hand-foot syndrome (HFS) in the protocol and protocol-specific patient handouts. Similar changes will be implemented in the Cancer Drug Manual in February 2011.

Background
HFS is reported in up to 57% of patients receiving capecitabine. It can range from mild tingling to severe desquamation of the palms and soles. Although the exact pathogenesis is unknown, some data suggest that the capecitabine-activating enzyme, thymidine phosphorylase, is expressed at higher levels in the skin of the palms, which renders the area more sensitive to the effects of cytotoxic drugs.[1]

Because HFS closely resembles acrodynia, a disease caused by pyridoxine deficiency in rats, pyridoxine was introduced as an empiric treatment for capecitabine-induced HFS. A small number of case reports and retrospective studies previously supported this indication. However, a recent randomized controlled trial showed that pyridoxine was not effective in preventing and treating HFS compared to placebo.[2] Pyridoxine did not significantly reduce the frequency of HFS of any grade, and did not increase the patients' tolerance to higher cumulative doses of capecitabine. Similar results were also found in another randomized controlled trial that evaluated pyridoxine for the prevention of liposomal doxorubicin-associated HFS.[3]

References:

1. Levine LE, et al. Distinctive acral erythema occurring during therapy for severe myelogenous leukemia. Arch Dermatol. 1985;121:102-4.
2. Kang YK, et al. Pyridoxine is not effective to prevent hand-foot syndrome associated with capecitabine therapy: results of a randomized, double-blind, placebo-controlled study. J Clin Oncol 2010;28:3824-29.
3. Von Gruenigen V, et al. A double-blind, randomized trial of pyridoxine versus placebo for the prevention of pegylated liposomal doxorubicin-related hand-foot syndrome in gynecologic oncology patients. Cancer 2010;116:4735-43.

New Lung Protocol Patient Handouts New information handouts for nine protocols have been developed for patients undergoing chemotherapy and chemoradiation. The protocol-specific patient handouts match existing treatment protocols LUAVNP, LUAVPG, LULAPERT, LULAPERT, LUMMPG, LUOTCAV, LUOTPE, LUOTPERT and LUPUPE.

CANCER DRUG MANUAL

Irinotecan Monograph and **Patient Handout** have been revised to delete the diuretic interaction from the interaction table and interaction paragraph, respectively. Interactions with diuretics are no longer noted in current interaction references and obvious additive interactions are not included within the CDM monographs.

Dacarbazine Monograph and Patient Handout have been revised. The monograph now includes more details about metabolism and CYP 3A4 interactions in the Pharmacokinetics and Interactions tables. The Solution Preparation and Compatibility section has been revised to reflect current template standards. The patient handout has updated the information about myelosuppression in the Side Effect table. Myelosuppression information has been reviewed and revised to be consistent with the information found in the monograph.

Dexrazoxane Monograph has been revised to include information about a new formulation in the Supply and Storage section, as well as in the Chemotherapy Preparation and Stability Chart. Diluent will

no longer be supplied with the Dexrazoxane vial and a 500 mg vial is currently available. New reconstitution, dilution and administration instructions now apply. template standards (also see Systemic Therapy Update December 2010: www.bccancer.bc.ca/HPI/ChemotherapyProtocols/stupdate).

Quinagolide Monograph has been revised to update the manufacturer name and starter pack contents in the Supply and Storage section.

MEDICATION SAFETY UPDATE: MEDICATION RECONCILIATION IMPLEMENTATION AT BCCA

Medication reconciliation is an accreditation requirement for both the inpatient and ambulatory care clinic settings. Medication Reconciliation was implemented in the inpatient unit at Vancouver Centre in 2009, and is currently being piloted in select ambulatory clinics at each BCCA centre. Over the next year or two, medication reconciliation will be rolled out as an official process across BCCA.

What is Medication Reconciliation?
Medication Reconciliation is a formal process of:

1. Obtaining and verifying a complete and accurate list of a patient's current medications (prescription, non-prescription, complementary and alternative medications) taken on a regular basis at home – including name, dosage, frequency and route.
2. Using that list when writing admission, transfer, discharge, or ambulatory care clinic medication orders, and
3. Comparing the list against the patient's admission, transfer, discharge, or ambulatory care clinic orders, identifying and bringing any discrepancies to the attention of the prescriber and, if appropriate, making changes to the orders. Any resulting changes in orders are documented.[1]

Why is Medication Reconciliation Important?
With over 22,000 drug products on the market in Canada, keeping a clear record of each patient's home medications is a challenge.[2] It is also not surprising that with multiple changes in doses, schedules, and the added complexity of oncology medications, there is ample opportunity for drug-drug interactions and ineffective transfer of medication information.[3]

Research has shown that about 25% of ambulatory cancer patients are receiving at least one medication that is unnecessary at the end of life.[4] In addition, the lack of a structured medication reconciliation process in the ambulatory care setting is associated with patients using unnecessary medications and being at risk for experiencing clinically important drug-related problems**.**

What does the Medication Reconciliation process look like in the ambulatory care setting?
An electronic Medication Reconciliation form will be printed that will include the patient's medication history from the previous 6 months. PharmaNet is a computer database that keeps a record of prescriptions dispensed for patients in British Columbia and will be used to print the patient's medication history onto the Medication Reconciliation form.

- Prior to the patient's appointment, the patient will review the medication reconciliation form and add all non-prescription medications to the list
- Initially, clinical pharmacists will be verifying and reconciling the complete medication list with the patient in the ambulatory clinics. However, other healthcare professionals will be involved in this process once the Medication Reconciliation project is rolled out to other clinics.

References:

1. *Safer Healthcare Now!* Campaign "How-to Guide: Adverse Drug Events (Medication Reconciliation)" May 2007 (accessed December 2010).

2. Sketris IS, et al. Strategic opportunities for effective optimal prescribing and medication management. *Can J Clin Pharmacol* 2009;16(1):e103.
3. Varkey P, et al. Improving medication reconciliation in outpatient setting. *Jt Comm J Qual Patient Saf* 2007; 33(5):286.
4. Fede A, et al. Use of unnecessary medications by patients with advanced cancer: cross-sectional survey 2010; *Supp Care Cancer*, online first: DOI 10.1007/s00520-010-0947-1.

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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, revised or deleted protocols, PPPOs and patient handouts for this month are listed below. Protocol codes for treatments requiring "Compassionate Access Program" (previously Undesignated Indications 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
HNLAALTPRT	☑	☑	☑	Locally Advanced (Alternate) Head and Neck Cancer Using Cisplatin During Radiation Therapy
LUAVNP	☐	☐	☑	Treatment for Advanced Non-Small Cell Lung Cancer (NSCLC) with Cisplatin and Vinorelbine *(Carboplatin Option)*
LUAVPG	☐	☐	☑	Treatment of Advanced Non-Small Cell Lung Cancer (NSCLC) with Platinum and Gemcitabine *(Carboplatin Option)*
LULAPERT	☐	☐	☑	Treatment of Locally Advanced Non-Small Cell Lung Cancer Using Cisplatin and Etoposide with Radiation Therapy
LULAPERT	☐	☐	☑	Treatment of Locally Advanced Non-Small Cell Lung Cancer Using Cisplatin and Etoposide with Radiation Therapy *(Carboplatin Option)*
LUMMPG	☐	☐	☑	Treatment of Malignant Mesothelioma with Platinum and Gemcitabine *(Carboplatin Option)*
LUOTCAV	☐	☐	☑	Treatment of Thymoma/Thymic Carcinoma with Cyclophosphamide, Doxorubicin and Vincristine (CAV)
LUOTPE	☐	☐	☑	Treatment Of Thymoma With Cisplatin And Etoposide
LUOTPERT	☐	☐	☑	Treatment of Thymoma Using Cisplatin and Etoposide with Radiation Therapy
LUOTPERT	☐	☐	☑	Treatment of Thymoma Using Cisplatin and Etoposide with Radiation Therapy *(Carboplatin Option)*

CODE	Protocol	PPPO	Patient Handout	Protocol Title
LUPUPE	☐	☐	☑	Treatment of Cancer of Unknown Primary Involving the Thorax with Cisplatin and Etoposide
LUPUPE	☐	☐	☑	Treatment of Cancer of Unknown Primary Involving the Thorax with Cisplatin and Etoposide (Carboplatin Option)
SMTAM	☐	☑	☐	Therapy for Malignant Melanoma using Tamoxifen

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

CODE	Protocol	PPPO	Patient Handout	Changes	Protocol Title
BRAJACTT	☑	☐	☐	*Eligibility revised*	Adjuvant Therapy for Breast Cancer using Doxorubicin and Cyclophosphamide followed by Paclitaxel and Trastuzumab
BRAJACTTG	☑	☐	☐	*Eligibility revised*	Adjuvant Therapy for Breast Cancer Using Dose Dense Therapy: Doxorubicin and Cyclophosphamide Followed by Paclitaxel and Trastuzumab
UBRAJDCT	☑	☐	☐	*Eligibility revised*	Adjuvant Therapy for Breast Cancer Using Docetaxel, Carboplatin, and Trastuzumab
BRAJDTFEC	☑	☐	☐	*Eligibility revised*	Adjuvant Therapy for Breast Cancer Using Docetaxel and Trastuzumab, and Fluorouracil, Epirubicin and Cyclophosphamide
BRAJTR	☑	☐	☐	*Eligibility revised*	Adjuvant Therapy for Breast Cancer Using Trastuzumab (HERCEPTIN®) Following the Completion of Chemotherapy (Sequential)
GOCXCRT	☑	☐	☑	*Eligibility revised*	Treatment of High Risk Squamous Carcinoma, Adenocarcinoma, or Adenosquamous Carcinoma of the Cervix with Concurrent Cisplatin and Radiation
GOOVETO	☐	☑	☐	*Minor typo corrected*	Treatment of Relapsed/Progressing Epithelial Ovarian, Primary Peritoneal, or Fallopian Tube Carcinoma Using Etoposide
GOOVIPPC	☑	☐	☐	*Eligibility and management of hypersensitivity clarified*	Primary Treatment of Stage III less than or equal to 1 cm Visible Residual Invasive Epithelial Ovarian Cancer or Stage I Grade 3 or Stage II Grade 3 Papillary Serous Ovarian Cancer Using Intravenous and Intraperitoneal Paclitaxel and Intraperitoneal Carboplatin
GOSMCCRT	☑	☑	☐	*Cisplatin dose, hydration and return appointment schedule revised*	Treatment of Small Cell or Neuroendocrine Carcinoma of Gynecologic System Origin using Paclitaxel, Cisplatin, Etoposide and Carboplatin with Radiation
GUAVPG	☑	☑	☐	*Diluent volume for Gemcitabine clarified*	Palliative Therapy for Urothelial Carcinoma Using Cisplatin and Gemcitabine
GUMVAC	☑	☑	☐	*Administration of cisplatin revised*	Therapy for Transitional Cell Cancers of the Urothelium using Methotrexate, Vinblastine, Doxorubicin and Cisplatin

CODE	Protocol	PPPO	Patient Handout	Changes	Protocol Title
HNNLAPRT	☑	☑	☐	*Eligibility and labs clarified*	Treatment of Locally Advanced Nasopharyngeal Cancer with Concurrent Cisplatin and Radiation
HNPRT	☑	☑	☐	*Replaced by HNLAALTPRT*	Therapy For Advanced Head And Neck Cancer Using Cisplatin Before Or During Radiation Therapy
ULKMDSA	☑	☑	☐	*Eligibility and dosing schedule revised*	Therapy of Myelodysplastic Syndrome using Azacitidine
LUOTCAV	☑	☐	☐	*Number of treatment cycles clarified*	Treatment of Thymoma/Thymic Carcinoma with Cyclophosphamide, Doxorubicin and Vincristine (CAV)
LUOTPE	☑	☐	☐	*Number of treatment cycles clarified*	Treatment Of Thymoma With Cisplatin And Etoposide
LUSCPERT	☐	☐	☑	*Typo in protocol title corrected*	Therapy Of Limited Stage Small Cell Lung Cancer Using Cisplatin And Etoposide With Radiation
LUSCPERT	☐	☐	☑	*Typo in protocol title corrected*	Therapy Of Limited Stage Small Cell Lung Cancer Using Cisplatin And Etoposide With Radiation *(Carboplatin option)*
LUSCTOP	☑	☐	☑	*Number of treatment cycles clarified*	Second-line Treatment of Recurrent Small Cell Lung Cancer (SCLC) with Topotecan
UMYLENDEX	☐	☑	☑	*RevAid information revised*	Treatment of Multiple Myeloma Using Lenalidomide (REVLIMID®) and Dexamethasone
SCDRUGRX	☑	☐	☐	*Epinephrine dose and administration route revised, references added*	Management of Hypersensitivity Reactions to Chemotherapeutic Agents

REVISED PATIENT HANDOUTS RELATED TO DELETION OF PYRIDOXINE FOR CAPECITABINE-RELATED HAND-FOOT SYNDROME

CODE	Protocol Title
BRAVCAP	Therapy for Metastatic Breast Cancer Using Capecitabine
BRAVDCAP	Palliative Therapy for Metastatic Breast Cancer Using Docetaxel and Capecitabine
UGIAVTZCAP	Palliative therapy of Metastatic Neuroendocrine Cancer using Temozolomide and Capecitabine
UGICAPIRI	Palliative Combination Chemotherapy for Metastatic Colorectal Cancer Using Irinotecan and Capecitabine in Patients Unsuitable for GIFOLFIRI
UGICAPOX	Palliative Combination Chemotherapy for Metastatic Colorectal Cancer Using Oxaliplatin, and Capecitabine

CODE	Protocol Title
UGICIRB	Palliative Combination Chemotherapy for Metastatic Colorectal Cancer Using Irinotecan, Bevacizumab and Capecitabine
UGICOXB	Palliative Combination Chemotherapy for Metastatic Colorectal Cancer Using Oxaliplatin, Bevacizumab and Capecitabine
GIGAVECC	Palliative Therapy for Metastatic or Locally Advanced Gastric or Esophagogastric Cancer Using Epirubicin, Cisplatin and Capecitabine
GIGECC	Perioperative Treatment of Resectable Adenocarcinoma of the Stomach, Gastroesophageal Junction or Lower 1/3 Esophagus using Epirubicin, Cisplatin and Capecitabine
GIRINFRT	Combined Modality Adjuvant Therapy for High Risk Rectal Carcinoma using Capecitabine, Infusional Fluorouracil and Radiation Therapy

WEBSITE RESOURCES AND CONTACT INFORMATION

WEBSITE RESOURCES	www.bccancer.bc.ca
REIMBURSEMENT AND FORMS: BENEFIT DRUG LIST, CLASS II, BC CANCER AGENCY COMPASSIONATE ACCESS PROGRAM	www.bccancer.bc.ca/HPI/ChemotherapyProtocols/Forms
CANCER DRUG MANUAL	www.bccancer.bc.ca/cdm
CANCER MANAGEMENT GUIDELINES	www.bccancer.bc.ca/CaMgmtGuidelines
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