

Systemic Therapy Update



BC Cancer Agency

CARE + RESEARCH

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For Health Professionals Who Care For Cancer Patients

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- **Website Resources and Contact Information**

EDITOR'S CHOICE

NEW PROGRAM

The Provincial Systemic Therapy Program has approved the following new program effective 01 June 2013:

Lymphoma:

- **Bendamustine and Rituximab for First-Line Indolent Non-Hodgkin Lymphoma (NHL) and Mantle Cell Lymphoma (ULYBENDR)** – The combination of bendamustine and rituximab is replacing the current first-line treatment standard of LCVPR (cyclophosphamide, vincristine, prednisone and rituximab) and LYCHOPR (doxorubicin, cyclophosphamide, vincristine, prednisone and rituximab) for advanced stage indolent NHL and mantle cell lymphoma (both transplant eligible and ineligible). In a phase III trial comparing bendamustine and rituximab versus CHOP-R for untreated indolent NHL and mantle cell lymphoma, bendamustine and rituximab was associated with superior median progression free survival (69.5 mo vs. 31.2 mo) and complete response rate (39.8% vs. 30%). [*Rummel et al. Lancet 2013;381:1203-10*] The combination was also associated with lower rates of neutropenia, infectious complications, paresthesias, stomatitis and alopecia, but higher rates of allergic reactions and skin rash.

EDITOR'S CHOICE

Bendamustine is also available for the treatment of relapsed/refractory indolent NHL, mantle cell lymphoma, chronic lymphocytic leukemia and Hodgkin lymphoma. Please see eligibility criteria specified in the chemotherapy protocol for further details.

REVISED PROGRAM

The Provincial Systemic Therapy Program has revised the following program effective 01 June 2013:

Breast:

- **Extended Duration of Upfront Tamoxifen for Up to 10 Years for Adjuvant Breast Cancer (BRAJTAM)**
– Tamoxifen is now approved for to 10 years for hormone receptor positive, low grade, T1N0 invasive breast cancer. Long-term follow-up of the ATLAS study showed that women treated with 10 years of tamoxifen had a significantly lower risk of breast cancer recurrence than those treated for 5 years (HR 0.84, 95% CI 0.76-0.94). [Davies et al. *Lancet* 2013;381:805-816] Ten years of tamoxifen was also associated with an absolute mortality benefit of 2.8% during years 5 to 14 (12.2% vs. 15%). Side effects were consistent with the known side effects of tamoxifen.

MEDICATION SAFETY CORNER

LOOK-ALIKE PRODUCT ALERT – PHENYLEPHRINE VS. DIPHENHYDRAMINE

Phenylephrine and diphenhydrAMINE were discovered to be mistakenly stocked side by side in a BCCA patient care area. As can be seen in the diagram below, the two products look identical.



As a result of this discovery, the following actions have been implemented across BCCA regional centres:

- All look-alike phenylephrine boxes have been removed from patient care areas
- Alternative supplier's product with distinct labeling has been sourced and purchased
- Product complaint has been filed with the manufacturer to ensure labeling changes will be made

In the event that unsafe drug product labeling is discovered, it is recommended that the product(s) be isolated, and the local Pharmacy department be contacted immediately or further evaluation. Remember that use of the 7 "rights" prior to administering medications will help further reduce the risk for

MEDICATION SAFETY CORNER

medication errors.

1. Right medication
2. Right patient
3. Right dose
4. Right time
5. Right route
6. Right reason
7. Right documentation

DRUG UPDATE

CHANGE IN CARBOPLATIN DILUENT TO NORMAL SALINE

Effective 01 June 2013, the standard default diluent solution for carboplatin has been changed to 0.9% sodium chloride (normal saline [NS]) from dextrose 5% (D5W) in all BCCA chemotherapy protocols and pre-printed orders.

D5W was traditionally the preferred diluent for carboplatin because the drug appeared to be more stable in D5W (no decomposition) than in NS (5% decomposition).^{1,2,3} More significantly, there was *in vitro* evidence to suggest that some carboplatin could be converted to cisplatin as a result of decomposition.² However, further evidence showed that the amount of carboplatin converted to cisplatin is considered negligible (less than 0.7% over 24 h).⁴ Therefore, current recommendations state that carboplatin may be diluted in either NS or D5W.⁵⁻⁸ Since NS is the standard default diluent solution at the BCCA, all carboplatin-containing protocols and pre-printed orders have been revised to indicate NS as the standard diluent solution. All previously written pre-printed orders using D5W as the carboplatin diluent will be autosubstituted with NS to ensure a seamless transition.

References:

1. van der Vijgh WJ. Clinical pharmacokinetics of carboplatin. *Clin Pharmacokinet* 1991;21(4):242-61.
2. Benaji B, Dine T, Luyckx M, et al. Stability and compatibility of cisplatin and carboplatin with PVC infusion bags. *J Clin Pharm Ther* 1994;19(2):95-100.
3. Cheung YW, Craddock JC, Vishnuvajjala BR, et al. Stability of cisplatin, iproplatin, carboplatin, and tetraplatin in commonly used intravenous solutions. *Am J Hosp Pharm* 1987;44(1):124-130.
4. Perrone RK, Kaplan MA, Bogardus JB. Extent of cisplatin formation in carboplatin admixtures. *Am J Hosp Pharm* 1989;46(2):258-259.
5. Hospira Healthcare Corporation. CARBOPLATIN® injection product monograph. Saint-Laurent, Quebec; 1 June 2007.
6. Novopharm Ltd. Carboplatin product monograph. Toronto, Ontario; undated.
7. Bristol-Myers Squibb. Paraplatin (carboplatin aqueous solution) injection. Princeton, New Jersey; January 2004.
8. AHFS Drug Information® (database on the Internet). Carboplatin. Lexi-Comp Inc., 1 January 2009. Available at: <http://online.lexi.com>. Accessed 30 April 2013.

CANCER DRUG MANUAL

REVISED MONOGRAPHS AND PATIENT HANDOUTS

CANCER DRUG MANUAL

Highlights of key changes and/or updates to the Monographs and Patients Handouts are listed below:

- **Asparaginase Monograph**
 - *Parenteral Administration* – maximum volume for IM administration clarified
- **Brentuximab Interim Monograph**
 - *Special Precautions* – added progressive multifocal leukoencephalopathy to contraindications
 - *Side Effects* – added new paragraph on tumour lysis syndrome
 - *Interactions* – created this section to include CYP 3A4/5 interactions
- **Nilotinib Monograph**
 - *Side Effects* – added information on atherosclerotic-related disease to reflect a recent Health Canada warning
- **Thalidomide Monograph**
 - *Special Precautions* – updated information on RevAid® program (previously known as STEPS program)
 - *Side Effects* – added information on thromboembolic events to reflect a recent Health Canada warning

EDITORIAL BOARD MEMBERSHIP

The Cancer Drug Manual Writing Team and Editorial Board would like to bid farewell to exiting Editorial Board members, Drs. Pippa Hawley and Enny Oetomo, as they step down from the board. The team would like to extend its sincere thanks for their many contributions to the board. Ms. Mandeep Bains, CON Pharmacy Educator – Vancouver Centre, will be rejoining the Editorial Board in Dr. Oetomo's place. Welcome back Mandeep!

BENEFIT DRUG LIST

NEW PROGRAM

The following program change has been added to the Benefit Drug List effective 01 June 2013:

Protocol Title	Protocol Code	Benefit Status
Treatment of Non-Hodgkin Lymphoma with Bendamustine and RiTUXimab	ULYBENDR	Restricted

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
HNNAVPG	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	Treatment of Locoregionally Recurrent and/or Metastatic Nasopharyngeal Cancer with CISplatin and Gemcitabine
ULYBENDR	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	Treatment of Non-Hodgkin Lymphoma with Bendamustine and ritUXimab

REVISED PROTOCOLS, PPPOs AND PATIENT HANDOUTS (AFFECTED DOCUMENTS ARE CHECKED):					
CODE	Protocol	PPPO	Patient Handout	Changes	Protocol Title
BRAJTAM	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<i>Eligibility</i> revised	Adjuvant Therapy for Breast Cancer using Tamoxifen
GIENACTRT	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	Typo corrected in <i>Class II Indication</i>	Neoadjuvant Treatment of Esophageal and Gastroesophageal Carcinomas Using CARBOplatin, PACLitaxel and Radiation Therapy
HNLAPRT	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Electrolytes added to <i>Tests</i>	Combined Chemotherapy (CISplatin) and Radiation Treatment for Locally Advanced Squamous Cell Carcinoma of the Head and Neck
HNNAVP	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<i>Hematologic Dose Modification</i> clarified	Palliative Chemotherapy for Advanced Head and Neck Nasopharyngeal Carcinoma with Weekly CISplatin
LYABVD	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<i>Blood tests</i> schedule clarified	Treatment of Hodgkin's disease with DOXOrubicin, Bleomycin, vinBLAstine and Dacarbazine

All chemotherapy protocols and PPPOs that use carboplatin have been updated to: (1) reflect the change in CARBOplatin diluent and (2) to reformat all non-TALLman lettering drug names to lower case:

CODE	Protocol Title
BRAJDCARBT	Adjuvant Therapy for Breast Cancer Using DOCEtaxel, CARBOplatin, and Trastuzumab
BRAVTPCARB	Palliative Therapy for Metastatic Breast Cancer using Trastuzumab, PACLitaxel and CARBOplatin as First-Line Treatment for Advanced Breast Cancer
CNCARV	CARBOplatin and Etoposide in the Treatment of Recurrent Ependymoma
CNTAMCAR	Second and Third Line Treatment of Recurrent Gliomas with CARBOplatin and High Dose Tamoxifen

CODE	Protocol Title
GIENACTRT	Neoadjuvant Treatment of Esophageal and Gastroesophageal Carcinomas Using CARBOplatin, PACLitaxel and Radiation Therapy
GOCXCAD	Treatment of Advanced/Recurrent Non-Small Cell Cancer of the Cervix with CARBOplatin and DOCEtaxel in Ambulatory Care Settings
GOCXCAT	Primary Treatment of Advanced/Recurrent Non-Small Cell Cancer of the Cervix with CARBOplatin and PACLitaxel in Ambulatory Care Settings
GOENDCAD	Treatment of Primary Advanced or Recurrent Endometrial Cancer Using CARBOplatin and DOCEtaxel
GOENDCAT	Treatment of Primary Advanced or Recurrent Endometrial Cancer Using CARBOplatin and PACLitaxel
GOOVCADM	Primary Treatment of Invasive Epithelial Ovarian, Fallopian Tube and Primary Peritoneal Cancer, with No Visible Residual Tumour (Moderate-High Risk) Using CARBOplatin and DOCEtaxel
GOOVCADR	Second Line Treatment Using DOCEtaxel and CARBOplatin for Epithelial Ovarian Cancer Relapsing after Primary Treatment
GOOVCADX	Primary Treatment of Visible Residual (Extreme Risk) Invasive Epithelial Ovarian Cancer Using CARBOplatin and DOCEtaxel
GOOVCAG	Treatment of Advanced Ovarian Cancer in Patients Who Have Progressed or Recurred Following First-line Platinum-based Treatment Using CARBOplatin and Gemcitabine
GOOVCARB	First or Second Line Therapy for Invasive Epithelial Ovarian Cancer using Single-Agent CARBOplatin
GOOVCATM	Primary Treatment of Invasive Epithelial Ovarian, Fallopian Tube and Primary Peritoneal Cancer, with No Visible Residual Tumour (Moderate-High Risk) Using CARBOplatin and PACLitaxel
GOOVCATR	Second Line Treatment Using PACLitaxel and CARBOplatin for Epithelial Ovarian Cancer Relapsing After Primary Treatment
GOOVCATX	Primary Treatment of Visible Residual (Extreme Risk) Invasive Epithelial Ovarian Cancer in Ambulatory Care Settings Using PACLitaxel and CARBOplatin
UGOOVDDCAT	Treatment of Advanced Epithelial Ovarian, Primary Peritoneal, or Fallopian Tube Carcinoma Using CARBOplatin and Weekly PACLitaxel
GOOVI PPC	Primary Treatment of Stage III Less Than or Equal to 1 cm Visible Residual Invasive Epithelial Ovarian Cancer or Stage 1 Grade 3 or Stage II Grade 3 Papillary Serous Ovarian Cancer Using Intravenous and Intraperitoneal PACLitaxel and Intraperitoneal CARBOplatin
GOOVLDC	Second Line Treatment for Epithelial Ovarian Cancer Relapsing After Primary Treatment Using Pegylated Liposomal DOXOrubicin (PLD) and CARBOplatin
GOSMCCRT	Treatment of Small Cell or Neuroendocrine Carcinoma of Gynecologic System Origin using PACLitaxel, CISplatin, Etoposide and CARBOplatin with Radiation
GUAVPG	Palliative Therapy for Urothelial Carcinoma Using CISplatin and Gemcitabine
GUBCV	Therapy for Transitional Cell Cancers Using CARBOplatin-VinBLAstine
GUSCARB	Adjuvant Therapy for Stage I High Risk Seminoma Using CARBOplatin
GUSCPERT	Therapy of Genitourinary Small Cell Tumors with a Platin and Etoposide with Radiation
HNLACAFRT	Combined Chemotherapy (CARBOplatin and Fluorouracil) and Radiation Treatment for Locally Advanced Squamous Cell Carcinoma of the Head and Neck
UHNNAVPC	Treatment of Recurrent or Metastatic Nasopharyngeal Carcinoma with CARBOplatin and PACLitaxel
LUAJPC	Adjuvant CARBOplatin and PACLitaxel Following Resection of Stage I, II and IIIA Non-Small Cell Lung Cancer
LUAVNP	Treatment for Advanced Non-Small Cell Lung Cancer (NSCLC) with CISplatin and Vinorelbine
LUAVPC	First-Line Treatment of Advanced Non-Small Cell Lung Cancer (NSCLC) with CARBOplatin and PACLitaxel
LUAVPG	Treatment of Advanced Non-Small Cell Lung Cancer (NSCLC) with Platinum and Gemcitabine

CODE	Protocol Title
ULUAVPP	First-Line Treatment of Advanced Non-Small Cell Lung Cancer with Platinum and Pemetrexed
LULAPERT	Treatment of Locally Advanced Non-Small Cell Lung Cancer Using CISplatin and Etoposide with Radiation Therapy
LUMMPP	Treatment of Malignant Mesothelioma with Platinum and Pemetrexed
LUOTPE	Treatment of Thymoma with CISplatin and Etoposide
LUOTPERT	Treatment of Thymoma Using CISplatin and Etoposide with Radiation Therapy
LUPUPE	Treatment of Cancer of Unknown Primary Involving the Thorax with CISplatin and Etoposide
LUSCPE	Therapy of Extensive Stage Small Cell Lung Cancer (SCLC) with CISplatin and Etoposide
LUSCPERT	Therapy of Limited Stage Small Cell Lung Cancer Using CISplatin and Etoposide with Radiation
LUSCPI	Second-Line Treatment of Extensive Stage Small Cell Lung Cancer (SCLC) with Irinotecan With or Without Platinum
ULYRICE	Treatment of Advanced Stage Large B-Cell Non-Hodgkin's Lymphoma with Ifosfamide, CARBOplatin, Etoposide and riTUXimab
PUCAT	Primary Treatment of Cancer of Unknown Primary Origin Using CARBOplatin and PACLitaxel

WEBSITE RESOURCES AND CONTACT INFORMATION

WEBSITE RESOURCES	www.bccancer.bc.ca
Systemic Therapy Update	www.bccancer.bc.ca/HPI/ChemotherapyProtocols/stupdate
Reimbursement & Forms: Benefit Drug List, Class II, 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
Cancer Chemotherapy Protocols, Pre-printed Orders, Protocol Patient Handouts	www.bccancer.bc.ca/ChemoProtocols
Systemic Therapy Program Policies	www.bccancer.bc.ca/HPI/ChemotherapyProtocols/Policies
CON Pharmacy Educators	http://www.bccancer.bc.ca/HPI/Pharmacy/ContactUs.htm

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BCCA-Sindi Ahluwalia Hawkins Centre for the Southern Interior	250.712.3900 Toll Free 888.563.7773		
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