



# Systemic Therapy Update

Volume 10, Number 5 *for health professionals who care for cancer patients* May 2007  
Website access at <http://www.bccancer.bc.ca/HPI/ChemotherapyProtocols/stupdate.htm>

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## EDITOR'S CHOICE

### PEMETREXED FOR NON-SMALL CELL LUNG CANCER (NSCLC)

The BC Cancer Agency is now funding pemetrexed (ALIMTA®) as single-agent therapy for the second-line treatment of advanced NSCLC (LUAVPEM) and listed as class II benefit drug. Until now, single-agent docetaxel (TAXOTERE®) constituted standard therapy in this situation (LUAVDOC). As of May 1, either option is available to patients with advanced NSCLC, who have had prior treatment with platinum-based chemotherapy. However, clinicians should note that, in any one patient, funding is available for *either* docetaxel *or* pemetrexed, but *not both*.

Docetaxel and pemetrexed are equally efficacious as second-line treatments for advanced NSCLC. Both agents are administered parenterally every 3 weeks. Key *differences* include:

	<i>docetaxel</i>	<i>pemetrexed</i>
<i>infusion time</i>	60 minutes	10 minutes
<i>pre-medication</i>	dexamethasone 8 mg PO BID for 3 days, given to prevent hypersensitivity reactions and fluid retention	dexamethasone 4 mg PO BID for 3 days, given to prevent rash <i>plus</i> folic acid, vitamin B12 (see next paragraph)
<i>major side effects</i>	neutropenia, febrile neutropenia, hospitalizations, filgrastim usage, neurotoxicity, alopecia	nausea, rashes, increases in ALT

Pemetrexed is an antifolate antimetabolite, and patients must also receive supplementation of folic acid and vitamin B12 to reduce toxicity:

- folic acid 0.4 mg PO once daily and
- vitamin B12 1000 mcg IM every 9 weeks

Supplementation must be initiated one week before the first pemetrexed dose, and must continue until three weeks after the last pemetrexed dose. Both agents are available without a prescription at any community pharmacy.

Non-steroidal anti-inflammatory drugs (NSAID's) may decrease the clearance of pemetrexed, and should be avoided in most patients. However, non-prescription doses of ibuprofen may be taken by those with good renal function (creatinine clearance  $\geq 80$  mL/min). Low doses of aspirin do not affect the pharmacokinetics of pemetrexed.

In the setting of advanced NSCLC, pemetrexed and docetaxel have similar efficacy, with different side effect profiles. In a randomized Phase III trial<sup>1</sup>, 571 patients with stage III/IV lung cancer, who had received one prior chemotherapy regimen for advanced disease, were randomized to receive treatment with pemetrexed 500 mg/m<sup>2</sup> or docetaxel 75 mg/m<sup>2</sup> every 21 days. Median survival time was 8.3 months for pemetrexed vs. 7.9 months for docetaxel (p=0.226). Patients receiving pemetrexed experienced more nausea, rashes, and increases in ALT. Patients receiving docetaxel experienced more neutropenia, febrile neutropenia, hospitalizations, G-CSF usage, neurotoxicity, and alopecia. Patient-reported quality of life was similar for both treatments.

More information on pemetrexed may be found in the October 2005 issue of the [Systemic Therapy Update](#). The new LUAVPEM protocol, pre-printed order, and patient information handout may be found at [www.bccancer.bc.ca](http://www.bccancer.bc.ca) > Health Professionals Info > Chemotherapy Protocols > [Lung](#). Note that information in the [Cancer Drug Manual](#) is currently based on mesothelioma trials, in which pemetrexed was given in combination with cisplatin. When given as a single agent, the toxicity profile of pemetrexed is greatly decreased. The Cancer Drug Manual is being updated to reflect this new information.

#### Reference

1. Hanna N, Shepherd FA, Fossella FV, et al. Randomized phase III trial of pemetrexed vs docetaxel in patients with non-small cell lung cancer previously treated with chemotherapy. *J Clin Oncol* 2004;22:1589-97.

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### CANCER DRUG MANUAL

**Cytarabine Monograph and Patient Handouts** These have been completely revised and updated. Expert review was provided by Dr. John Shepherd (Lymphoma Tumour Group).

Important additions include:

- details on intrathecal therapy and high-dose cytarabine reactions in the Side Effects paragraphs
- interactions with ciprofloxacin, digoxin, and fludarabine listed in the Interactions table
- information on headache and its management described in the intrathecal patient handout

Other changes include:

- expansion of the Dosage Guidelines to include CNMODPCV, CCNU, NCCNU, CNCC
- the infusion time required for intermittent infusions
- a clarification to the dosage in hepatic failure
- updates to the Chemotherapy Preparation and Stability Chart

**Mechlorethamine Monograph and Patient Handouts** These have been completely revised and updated. Expert review was provided by Dr. Christina Parsons (Radiation Oncology), Dr. Joseph Connors (Lymphoma Tumour Group), and Dr. Stephen Nantel (Leukemia/BMT Program of BC). Changes include an expanded Side Effects table including additional information regarding topical mechlorethamine reactions. As the incidence of allergic contact dermatitis is significantly decreased when mechlorethamine ointment is used compared to the solution, detailed information regarding the solution has been removed from the monograph. The

topical mechlorethamine patient handout is now specific for the ointment. The Chemotherapy Preparation and Stability Chart has also been updated.

**Methotrexate Intrathecal Patient Handout** Headache was discussed as a side effect of intrathecal cytarabine. Expert reviewers and Editorial Board physicians agreed that this side effect is often procedure-related, rather than drug-related, so it is reasonable to provide this information to any patient receiving intrathecal drug therapy.

**Chemotherapy Preparation and Stability Chart** has been revised to indicate the following:

- extended stability of diluted solution of docetaxel based on new data
- clarification of expiry date of diluted solution of etoposide to be consistent with the BCCA pharmacy policy
- clarification of pemetrexed dilution to be consistent with protocol and pre-printed order
- latex content has been deleted from the chart as it is felt that more up-to-date information can be obtained as the need arises directly from the manufacturer

**A note from the editors:** Cytarabine and mechlorethamine mark the end of a major updating of hematology drugs in the Cancer Drug Manual. Working through many new issues and a great deal of unfamiliar content, our writers demonstrated their usual skill, style, and tenacity. Our editorial assistant, Gigi Concon, proved that her patience really is limitless. Our reviewers and editorial board demonstrated their usual generosity of time and expertise, and several external reviewers (from the Leukemia/BMT Program of BC) graciously reviewed multiple documents with short deadlines. Many thanks to all involved.

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#### NURSING RESOURCES OF THE MONTH

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Rooney, M; and Wald, A. (2007). Interventions for the management of weight and body composition changes in women with breast cancer. *Clinical Journal of Oncology Nursing* 11(1), 41-52.

Reviews current evidence from weight intervention studies, including diet, exercise, and combined approaches for weight loss – or for prevention of weight gain. Along with published practice guidelines, the currently available information provides guidance for oncology nurses in the methods that can impact unhealthy weight conditions associated with breast cancer.

Limburg, C. (2007). Screening, prevention, detection, and treatment of cancer therapy-induced bone loss in patients with breast cancer. *Oncology Nursing Forum*, 34(1), 55-63.

Describes the physiological consequences associated with osteoporosis, discusses the life style habits that are risk factors for, and nursing management issues related to treatment for osteoporosis.

Both articles are available online to BCCA staff through Library Links on the BCCA internal network. If the links do not work or if you would like to request a copy, please contact your hospital or health library.

**The Breast Cancer Nursing Education Resource (BCNER)** The BCNER is a web-based education resource for BCCA and community nurses designed to enhance their knowledge of breast cancer patient's needs, care and treatment. The content emphasizes best practices, recent developments/BCCA policy changes, and controversies in the areas of diagnosis, biology and treatment, based on patient's needs at key points in the breast cancer journey. Information is based on BCCA standards, oncology nursing standards and external sources. A multidisciplinary team provided direction for the content, structure and format of the resource and supervision of the project's objective. Feedback and accuracy of content was sought from BCCA oncologists. A pilot evaluation was conducted with a representative group of nurses from oncology and community settings. This evaluation primarily determined the user's overall acceptance, format suitability and the relevance of the content to nursing clinical practice.

Recognizing the difficulty for nurses to access information in a timely manner in a busy clinical setting, the site can be used both at point of care, and in the nurse's own time. Initial pilot testing was positive, with nurses stating they say this as an ideal resource for the nurse who is orienting to the care of breast cancer patients.

Official launch of the site will be on May 9, 2007.

You can locate it at: <http://www.bccancer.bc.ca/HPI/CE/Nursing/default.htm>.

Any questions regarding the site or content may be directed to: [nursinged@bccancer.bc.ca](mailto:nursinged@bccancer.bc.ca).

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### **LIST OF NEW AND REVISED PROTOCOLS, Pre-Printed Orders and Patient Handouts**

The **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" approval are prefixed with the letter **U**. Note that when a protocol code has been changed (eg, LUDOC replaced by LUAVDOC), the new code (LUAVDOC) should be used to for subsequent treatments of the same patient.

#### **NEW PROTOCOLS, PPPOs AND PATIENT HANDOUTS (AFFECTED DOCUMENTS ARE CHECKED):**

CODE	Protocol	PPPO	Patient Handout	Protocol Name
GIPE	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	Palliative Therapy of Neuroendocrine Tumours using Cisplatin and Etoposide
LKCMLI	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	Treatment of Chronic Myeloid Leukemia Using Imatinib (GLEEVEC®)
LUAVDOC (REPLACING LUDOC)	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	Second-Line Treatment of Advanced Non-Small Cell Lung Cancer (NSCLC) with Docetaxel
LUAVPEM	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	Second-line Treatment of Advanced Non-Small Cell Lung Cancer (NSCLC) with Pemetrexed

#### **REVISED PROTOCOLS, PPPOs AND PATIENT HANDOUTS (AFFECTED DOCUMENTS ARE CHECKED):**

CODE	Protocol	PPPO	Patient Handout	Changes	Protocol Title
UGIFFIRB	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<i>Typo corrected with extra tick box for urinalysis</i>	Palliative Combination Chemotherapy for Metastatic Colorectal Cancer Using Irinotecan, Fluorouracil, Folinic Acid (Leucovorin) and Bevacizumab
LUAVCAV	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<i>Cyclophosphamide administration clarified</i>	Treatment of Extensive Small Cell Lung Cancer (SCLC) with Cyclophosphamide, Doxorubicin and Vincristine (CAV)
LUDOC				<i>Replaced by LUAVDOC</i>	Second-Line Treatment of Advanced Non-Small Cell Lung Cancer (NSCLC) with Docetaxel
LUMMPPEM	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<i>Return appointments clarified</i>	Treatment of Malignant Mesothelioma with Platinum and Pemetrexed

CODE	Protocol	PPPO	Patient Handout	Changes	Protocol Title
LYFLUDR	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<i>minor clarification on when to calculate creatinine clearance to be consistent with the protocol</i>	Treatment of Chronic Lymphocytic Leukemia or Prolymphocytic Leukemia with Fludarabine and Rituximab

### **SURVEY OF THE IMPACT OF PHARMACY COMMUNITIES ONCOLOGY NETWORK (CON) EDUCATORS**

In 2002, the BC Cancer Agency (BCCA) developed the 4 part-time positions of Pharmacy CON Educator, with one in each regional cancer centre. The mandate of these pharmacy educators is to address the oncology educational needs of CON pharmacists in their region. What has been the impact of the educator on the work of a CON pharmacist?

#### **Survey of the CON pharmacists**

In December 2006, 77 surveys addressing the impact of the educators were distributed to the CON pharmacists and 24 responses were received (31%). Nearly half of the respondents (44%) spent less than 25% of their time in oncology related pharmacy, with an additional 35% spending between 25-49% of their time.

About half of the respondents (52%) found that activities of the educators have improved the overall communication with the BCCA. There was an equal split from respondents as to whether or not the activities of the educator have had a direct impact on their practice. Other highlights from the survey are as follows.

#### Site visit

Each educator should make an annual visit to each CON site. Because of BCCA staffing shortages and travel issues, site visits have not occurred consistently. Approximately half of the respondents (57%) stated that they had received one visit in the previous year, with another 10% having received one visit in the previous two years. Overall, there was a positive level of satisfaction in 62% of the respondents on these visits. Some of the activities at these site visits include: introducing new BCCA policies and procedures, answering specific questions on chemotherapy delivery, reviewing chemotherapy process of the CON centre, meeting with oncology healthcare professionals, providing in-services, sharing BCCA information such as video-linked oncology rounds, etc.

A variety of suggestions regarding to types of future educational activities were made for the educators to provide during a site visit. The most common suggestion (29%) was to review the internal process for improvement (e.g., handling workload and workflow, preparing chemotherapy, or providing patient care.)

#### Pharmacy Guide to Chemotherapy Protocols

The educators developed the “*Pharmacy Guide to BC Cancer Agency Chemotherapy Protocols*” in 2003 to help pharmacists develop the skills to interpret and clinically apply the BCCA treatment protocol summaries. Most respondents (76%) stated their facility had a copy of the guide, while 57% stated they had read it. However, only 29% had submitted the case studies to obtain continuing education credits from UBC.

#### Other publications

Most respondents (67%) have read the regular contributions by the educators in the monthly Systemic Therapy Update newsletter.

In 2002, the educators developed a webpage on the BC Cancer Agency website.

([www.bccancer.bc.ca/RS/CommunitiesOncologyNetwork/Educators/Pharmacists/](http://www.bccancer.bc.ca/RS/CommunitiesOncologyNetwork/Educators/Pharmacists/)). However, 90% of the respondents have never accessed this page.

## Summary

Overall, the outcome was generally positive with the educators facilitating improved communication between the CON pharmacists and the BCCA. The majority of sites have received a visit from an educator within the last two years, and most were satisfied with the visit. The Pharmacy Guide to BCCA Chemotherapy Protocols is widely available and used by a substantial proportion of the respondents. Finally, most CON pharmacists have been reading the articles written by the educators in the Systemic Therapy Update.

Identified areas for future considerations are:

- to develop a process to assist a CON pharmacy site in re-evaluating their internal process of providing chemotherapy
- to assess the need for continued accreditation through UBC for the “Pharmacy Guide to BCCA Chemotherapy Protocols”
- to improve the Pharmacy CON Educator webpage on the BCCA website

The Pharmacy CON Educators would like to extend their thanks to those pharmacists who participated in the survey.

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## PROVINCIAL SYSTEMIC THERAPY POLICIES

**New Parenteral Drug Therapy Policy (III-90)** This new policy is meant to streamline the overlapping resources currently used for basic information and approved administration routes of parenteral drugs at the BCCA. Listed below are the key differences on how to look up this information between current practice and the new policy:

<i>Type of drug</i>	<i>Current practice</i>	<i>New policy</i>
Antineoplastic	Cancer Drug Manual, PDTM, or List of BCCA-Approved Parenteral Routes	Cancer Drug Manual
Non-antineoplastic	PDTM and List of BCCA-Approved Parenteral Routes	PDTM only
Clinical trial	PDTM, clinical trial protocol, pre-printed order	no change

PDTM = Parenteral Drug Therapy Manual, including white and yellow coloured monographs

In addition, the review and approval process for administration routes has also been simplified. For more details, see the full policy at [www.bccancer.bc.ca/HPI/ChemotherapyProtocols/Policies.htm](http://www.bccancer.bc.ca/HPI/ChemotherapyProtocols/Policies.htm).

## CONTINUING EDUCATION

**BC Cancer Agency Annual Cancer Conference 2007** Mark your calendar! This year’s conference will be held on 29 November – 1 December, at the Westin Bayshore Resort & Marina in Vancouver. The theme of the 2007 conference is “*Technology and Innovation – Bench to Bedside*”.

Stay tuned for more information about the conference.

## WEBSITE RESOURCES

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

REIMBURSEMENT AND FORMS: BENEFIT DRUG LIST, CLASS II, COMPASSIONATE ACCESS PROGRAM (UNDESIGNATED INDICATION)	<a href="http://www.bccancer.bc.ca/HPI/ChemotherapyProtocols/Forms">www.bccancer.bc.ca/HPI/ChemotherapyProtocols/Forms</a>
CANCER DRUG MANUAL	<a href="http://www.bccancer.bc.ca/cdm">www.bccancer.bc.ca/cdm</a>
CANCER MANAGEMENT GUIDELINES	<a href="http://www.bccancer.bc.ca/CaMgmtGuidelines">www.bccancer.bc.ca/CaMgmtGuidelines</a>
CANCER CHEMOTHERAPY PROTOCOLS	<a href="http://www.bccancer.bc.ca/ChemoProtocols">www.bccancer.bc.ca/ChemoProtocols</a>
CANCER CHEMOTHERAPY PRE-PRINTED ORDERS	<a href="http://www.bccancer.bc.ca/ChemoProtocols">www.bccancer.bc.ca/ChemoProtocols</a> under the index page of each tumour site
SYSTEMIC THERAPY PROGRAM POLICIES	<a href="http://www.bccancer.bc.ca/HPI/ChemotherapyProtocols/Policies">www.bccancer.bc.ca/HPI/ChemotherapyProtocols/Policies</a>
<a href="#">UNCONVENTIONAL CANCER THERAPIES MANUAL</a>	under Patient/Public Info, Unconventional Therapies

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