

Systemic Therapy Update



BC Cancer Agency

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- **[Website Resources and Contact Information](#)**

EDITOR'S CHOICE

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

The **Lung Tumour Group and the Systemic Therapy Program** have expanded the use of **Pemetrexed** to the following indications in patients with advanced non-small cell lung cancer (NSCLC) of non-squamous cell histology:

1. First-line chemotherapy option as a platinum doublet regimen (ULUAVPP)
2. Single agent maintenance therapy in patients with no disease progression after 4 cycles of platinum-based doublet not containing pemetrexed (ULUAVPMTN)

Previously, standard first-line chemotherapy for stage IIIB/IV NSCLC included platinum-based doublet combinations with taxanes, vinorelbine and gemcitabine. In a phase III trial, first-line therapy with cisplatin and pemetrexed was shown to improve overall survival compared to cisplatin plus gemcitabine (11.8 vs. 10.4 months) in patients with advanced NSCLC of non-squamous cell histology. Cisplatin and pemetrexed were also associated with lower rates of grade 3 or 4 hematologic toxicities and nausea.

ULUAVPMTN is the first maintenance therapy approved by the BCCA for patients with stage IIIB/IV NSCLC who have not progressed after first-line chemotherapy. A phase III trial showed that compared to placebo, maintenance pemetrexed resulted in delayed progression (4.3 vs. 2.6 months) and improved overall survival (13.4 vs. 10.6 months) in patients who did not have disease progression after at least 4 cycles of platinum-based doublet chemotherapy. When confined to non-squamous cell histology patients, there was an increase of 5.2-months in overall survival (15.5 vs. 10.3 months).

Reference:

1. Scagliotti GV, Parikh P, von Pawel J, et al. Phase III study comparing cisplatin plus gemcitabine with cisplatin plus pemetrexed in chemotherapy-naïve patients with advanced-stage non-small-cell lung cancer. *J Clin Oncol* 2008;26(21):3543-51.
2. Syrigos KN, Vansteenkiste J, Parikh P, et al. Prognostic and predictive factors in a randomized phase III trial comparing cisplatin-pemetrexed versus cisplatin-gemcitabine in advanced non-small-cell lung cancer. *Ann Oncol* 2010;21(3):556-61.
3. Ciuleanu T, Brodowicz T, Zielinski C, et al. Maintenance pemetrexed plus best supportive care versus placebo plus best supportive care for non-small-cell lung cancer: a randomised, double-blind, phase 3 study. *Lancet* 2009;374:1432-40.

The **Genitourinary Tumour Group and the Systemic Therapy Program** have introduced **Everolimus** as a new therapy option for patients with advanced renal cell carcinoma after failure of multi-target kinase inhibitors (sunitinib, sorafenib). Access via the manufacturer's AfiniTRAC Reimbursement Support Program is officially terminated on 31 January 2011. Patients enrolled in this program prior to and including 31 January 2011 will continue to receive everolimus through the AfiniTRAC Program. For more details, see UGUEVER (www.bccancer.bc.ca/HPI/ChemotherapyProtocols/Genitourinary)

Like temsirolimus, everolimus is an mTOR inhibitor indicated for the second-line treatment of patients with metastatic renal cell carcinoma (RCC) refractory to either sunitinib or sorafenib. The recommended dosage is 10 mg orally daily on an empty stomach or after a small, fat-free meal. In a phase III trial, everolimus significantly prolonged progression-free survival compared to placebo in patients who failed sunitinib and/or sorafenib (4.0 mo vs. 1.9 mo, respectively).¹ No statistically significant difference was observed in overall survival or objective response. As with temsirolimus, pulmonary toxicity has been reported with everolimus. For more information on everolimus toxicity, see November 2010 issue of the Update (www.bccancer.bc.ca/HPI/ChemotherapyProtocols/stupdate) and the UGUEVER protocol.

Reference:

Motzer *et al.* Efficacy of everolimus in advanced renal cell carcinoma: a double-blind, randomized, placebo-controlled phase III trial. *Lancet* 2008;372:449-56.

BENEFIT DRUG LIST

The following programs have been added on the benefit list effective 1 February 2011:

- **Everolimus** (case-by-case) for advanced renal cell carcinoma after failure of tyrosine kinase inhibitors (UGUEVER)
- **Gemcitabine** (class II) in combination with cisplatin as neoadjuvant therapy for urothelial carcinoma (GUNAJPG)
- **Pemetrexed** (case-by-case)
 - combination with platinum as first-line treatment of advanced non-small cell lung cancer (ULUAVPP)
 - maintenance therapy of advanced non-small cell lung cancer after first-line chemotherapy (ULUAVPMTN)
- **Rituximab** (class II) as pre-emptive rituximab therapy of Epstein-Barr virus related post-transplant lymphoproliferative disease (BMTLPDRIT)

Methyltestosterone has been deleted from the Benefit Drug List as it is no longer available in Canada.

CANCER MANAGEMENT GUIDELINES – FLUOROURACIL INFUSION OVERDOSE

An interim guidance on the **Management of Fluorouracil Infusion Overdose** has been developed by the Gastrointestinal Tumour Group (www.bccancer.bc.ca/HPI/CancerManagementGuidelines/Gastrointestinal/5FUOD). Thomson Reuter Health Care Inc. in collaboration with the Systemic Therapy Safety Committee of the Canadian Association of Provincial Cancer Agencies are in the process of developing a POISONDEX® treatment protocol for 5-FU infusion overdose. These protocols will be available across all poison control centres in Canada, tentatively around April or May 2011.

PROVINCIAL SYSTEMIC THERAPY PROGRAM POLICIES

Labelling of Vinca Alkaloid Preparations (Policy V-40) has been revised with updated references.

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
BMTLPDRIT	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Pre-Emptive Rituximab Therapy of Epstein-Barr Virus (EBV) Related Post-Transplant Lymphoproliferative Disease
GICART	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	Curative therapy for cancer of the anal canal using combined Mitomycin, Capecitabine and Radiation Therapy
GIENAFUPRT	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	Neo-adjuvant Combined Modality Therapy for Operable Esophageal and Esophageal-stomach Junction Cancer using Cisplatin, Infusional Fluorouracil and Radiation Therapy.
GIGAIRT	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	Combined Modality Adjuvant Therapy For Completely Resected Stomach Cancer Using Fluorouracil And Folinic Acid (Leucovorin) And Radiation Therapy
GOBEP	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	Therapy of Non-Dysgerminomatous Ovarian Germ Cell Cancer Using Bleomycin, Etoposide, and Cisplatin
UGUEVER	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	Therapy for Advanced Renal Cancer Using Everolimus
ULUAVPP	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	First-Line Treatment of Advanced Non-Small Cell Lung Cancer with Platinum and Pemetrexed
ULUAVPMTN	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	Maintenance Therapy of Advanced Non-Small Cell Lung Cancer With Pemetrexed
LUMMPP	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	Treatment of Malignant Mesothelioma with Platinum and Pemetrexed
LUMMPP (Carboplatin Option)	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	Treatment of Malignant Mesothelioma with Platinum and Pemetrexed (Carboplatin Option)

CODE	Protocol	PPPO	Patient Handout	Protocol Title
LUOTPE (Carboplatin Option)	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	Treatment of Thymoma/Thymic Carcinoma Carboplatin and Etoposide
LUOTPERT (Carboplatin Option)	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	Treatment of Thymoma/Thymic Carcinoma with Carboplatin, Etoposide and Radiation

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

CODE	Protocol	PPPO	Patient Handout	Changes	Protocol Title
BRAVABR	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<i>Drug administration procedure clarified</i>	Palliative Therapy for Metastatic Breast Cancer using Nanoparticle, Albumin-bound (nab)-Paclitaxel (ABRAXANE®)
BRAVCMFPO	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<i>Drug administration sequence clarified</i>	Palliative therapy for advanced breast cancer using Cyclophosphamide (oral), Methotrexate and Fluorouracil
GOBEP	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<i>Hydration added</i>	Therapy of Non-Dysgerminomatous Ovarian Germ Cell Cancer Using Bleomycin, Etoposide, and Cisplatin
GOOVCARB	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<i>LFT removed from baseline tests, creatinine clarified</i>	First or Second Line Therapy for Invasive Epithelial Ovarian Cancer using Single-Agent Carboplatin
GOSADG	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<i>Liver function tests clarified</i>	Treatment of Uterine Sarcoma Cancer Using Docetaxel and Gemcitabine
GUNAJPG	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<i>Revised to class II benefit status</i>	Neo-Adjuvant Therapy for Urothelial Carcinoma Using Cisplatin and Gemcitabine
ULKCMLD	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<i>BCR/ABL transcripts added to Tests</i>	Treatment of Chronic Myeloid Leukemia and Ph+ Acute Lymphoblastic Leukemia Using Dasatinib
LKCMLI	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<i>BCR/ABL transcripts added to Tests</i>	Therapy for Chronic Myeloid Leukemia and Ph+ Acute Lymphoblastic Leukemia Using Imatinib
ULKCMLN	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<i>BCR/ABL transcripts added to Tests, caution added to Administration</i>	Treatment of Chronic Myeloid Leukemia Using Nilotinib
ULKMDSA	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<i>Tests clarified</i>	Therapy of IPSS Intermediate-2 or High-Risk Myelodysplastic Syndrome with Azacitidine
LUAVDOC	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<i>Eligibility clarified</i>	Second-Line Treatment of Advanced Non-Small Cell Lung Cancer (NSCLC) with Docetaxel

CODE	Protocol	PPPO	Patient Handout	Changes	Protocol Title
ULUAVGEF	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<i>Deleted</i>	Third-Line Treatment of Advanced Non-Small Cell Lung Cancer (NSCLC) with Gefitinib
LUAVPEM	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<i>Eligibility clarified</i>	Second-Line Treatment of Advanced Non-Small Cell Lung Cancer (NSCLC) With Pemetrexed
LULAPERT	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<i>Dose modifications for etoposide clarified</i>	Treatment Of Locally Advanced Non-Small Cell Lung Cancer Using Cisplatin And Etoposide With Radiation Therapy
LUOTPE	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<i>Dose modifications for etoposide clarified</i>	Treatment Of Thymoma With Cisplatin And Etoposide
LUOTPERT	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<i>Dose modifications for etoposide clarified</i>	Treatment Of Thymoma Using Cisplatin And Etoposide With Radiation Therapy
LUPUPE	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<i>Dose modifications for etoposide clarified</i>	Treatment Of Cancer Of Unknown Primary Involving The Thorax With Cisplatin And Etoposide
LUSCPE	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<i>Dose modifications for etoposide clarified</i>	Therapy Of Extensive Stage Small Cell Lung Cancer (SCLC) With Cisplatin And Etoposide
LUSCPERT	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<i>Dose modifications for etoposide clarified</i>	Therapy Of Limited Stage Small Cell Lung Cancer Using Cisplatin And Etoposide With Radiation
LYABVD	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<i>Lab test requirement and diluent volume clarified</i>	Treatment of Hodgkin's Disease with Doxorubicin, Bleomycin, Vinblastine, and Dacarbazine
LYCHOP	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<i>Diluent volume clarified for optional use of etoposide</i>	Treatment of Lymphoma with Doxorubicin, Cyclophosphamide, Vincristine and Prednisone
LYCHOPR	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<i>Diluent volume clarified for optional use of etoposide</i>	Treatment of Lymphoma with Doxorubicin, Cyclophosphamide, Vincristine, Prednisone and Rituximab
LYCVPPABO	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<i>Diluent volume clarified for optional use of etoposide</i>	Treatment of Hodgkin's Disease with Cyclophosphamide, Vinblastine, Procarbazine And Prednisone
LYIVACR	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<i>Diluent volume clarified for etoposide</i>	Treatment of Burkitt's Lymphoma and Leukemia (ALL-L3) with Ifosfamide, Mesna, Etoposide, Cytarabine (IVAC) and Rituximab
SAAVGEMD	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<i>Infusion time clarified</i>	Second or Third Line Therapy for Soft Tissue Sarcomas using Gemcitabine and Docetaxel

REVISED LYMPHOMA PROTOCOLS FOR NEW CONTACT PHYSICIAN

CODE	Protocol Title
LYABVD	Treatment of Hodgkin's Disease with Doxorubicin, Bleomycin, Vinblastine, and Dacarbazine
LYCCOP	Treatment of Hodgkin's disease using Cyclophosphamide, Vincristine, Prednisone
LYCDA	Treatment of Hairy Cell Leukemia with Cladribine
LYCHLOR	Therapy for Low Grade Lymphoma and Chronic Lymphocytic Leukemia Using Chlorambucil
LYCSPA	Cyclosporine for Cytopenias Associated with Lymphoproliferative Disorder of Large Granular Lymphocytes
LYCYCLO	Therapy of Lymphoma, Hodgkin's Disease, Chronic Lymphocytic Leukemia or Multiple Myeloma Using Cyclophosphamide
LYFLU	Treatment of Low-Grade Lymphoma or Chronic Lymphocytic Leukemia with Fludarabine
LYGDP	Treatment of Lymphoma with Gemcitabine, Dexamethasone and Cisplatin (GDP)
ULYGDP	Treatment of Lymphoma with Gemcitabine, Dexamethasone and Cisplatin (GDP) with Rituximab
LYIT	Treatment of Lymphoma using Intrathecal Methotrexate and Cytarabine
LYPALL	Lymphoma Palliative Chemotherapy
LYRITB	Summary for Palliative Therapy For Lymphoma Using Radioimmunotherapy Tositumomab-Priming for I ¹³¹ Tositumomab
LYRITUX	Treatment of Lymphoma with single agent Rituximab
LYRITZ	Palliative Therapy For Lymphoma Using Radioimmunotherapy Rituximab-Priming for Ibritumomab ⁹⁰ Y

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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
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