Systemic Therapy Update

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EDITOR'S CHOICE

NEW PROGRAMS

Effective 1 February 2018, the BC Cancer Provincial Systemic Therapy Program has approved the following programs.

Gastrointestinal and Lung:

Everolimus for Advanced Neuroendocrine Tumours of Gastrointestinal (UGINETEV) and Lung Origins (ULUNETEV) – The BC Cancer Gastrointestinal and Lung Tumour Groups are introducing everolimus for well differentiated, non-functional neuroendocrine tumours (NET) of either gastrointestinal or lung origin. Patients should have unresectable, locally advanced or metastatic disease. In a phase III trial, everolimus was associated with improved overall survival (25.8 vs. 20.2 mos) and progression free survival (11.0 vs. 3.9 mos) and a trend towards better overall survival compared to placebo. The most common toxicities were stomatitis, rash, diarrhea, hyperglycemia, thrombocytopenia and infection. Note that for the rare cases of NET of unknown primary or other origins, patients will be treated under the UGINETEV protocol.

Reference:
Yao JC, et al. Everolimus for the treatment of advanced, non-functional neuroendocrine tumours of the lung or gastrointestinal tract (RADIANT-4): a randomised, placebo-controlled, phase 3 study. Lancet 2016;387:968–77.

EDITOR'S CHOICE

Lung:

Pembrolizumab for Advanced Non-Small Cell Lung Cancer (NSCLC) (ULUAVPMBF, ULUAVPMB) – The BC Cancer Lung Tumour Group is introducing pembrolizumab as the new immunotherapy for patients with advanced NSCLC. Tumour histology should be negative for EGFR mutation and ALK mutation, as well as positive for PD-L1 expression.

In the first-line setting, pembrolizumab has been shown to improve overall survival at 6 months (80.2% vs. 72.4%, hazard ratio 0.60) and median progression free survival (10.3 vs. 6.0 mos) compared to conventional chemotherapy.[1] In the second-line setting, pembrolizumab was also associated with increased overall survival (14.9 vs. 8.2 mos) and progression free survival (5.0 vs. 4.1 mos) compared to docetaxel in patients with who have failed platinum-based chemotherapy.[2] Toxicities are similar to those seen when pembrolizumab is used for other indications.

References:
1. Reck M, et al. Pembrolizumab versus chemotherapy for PD-L1-postive non-small cell lung cancer. N Engl J Med 2016;375:1823-3.
2. Herbst RS, et al. Pembrolizumab versus docetaxel for previously treated, PD-L1-positive, advanced non-small cell lung cancer (KEYNOTE-010): a randomised controlled trial. Lancet.2016;387(10027):1540-50.

Head and Neck:

Paclitaxel and Platinum for Advanced Squamous Cell Cancer of the Head and Neck (SCCHN) (HNAVPC) – The BC Cancer Head and Neck Tumour Group is introducing paclitaxel and cisplatin or carboplatin as an alternate first-line treatment for patients with unresectable, locoregionally recurrent or metastatic SCCHN. Studies have shown that this regimen is associated with response rate of 26-39% with a median overall survival of 7-8 months.[1-3]

References:
1. Gibson MK, et. al. Randomized phase III evaluation of cisplatin plus fluorouracil versus cisplatin plus paclitaxel in advanced head and neck cancer (E1395): An intergroup trial of the Eastern Cooperative Oncology Group. J Clin Oncol 2005;23(15):3562-7.
2. Stathopoulos GP, et. al. Effectiveness of paclitaxel and carboplatin combination in heavily pretreated patients with head and neck cancers. Eur J Cancer 1997;33(11):1780-83.
3. Clark JI, et. al. Phase II evaluation of paclitaxel in combination with carboplatin in advanced head and neck carcinoma. Cancer 2001;92:2334-2340.

Leukemia/Bone Marrow Transplant (BMT):

Ruxolitinib for Polycythemia Vera (ULKPCVRUX) – The Leukemia/BMT Group is introducing ruxolitinib as a treatment for polycythemia vera. This treatment option is for patients with disease resistant to hydroxyurea (greater than 2 g/day dose for 3 months) or with severe intolerance to hydroxyurea (e.g., leg ulcer, grade 3 or 4 toxicities). In a phase III trial, ruxolitinib compared to best supportive care was associated with a higher rate of reduction in spleen volume and hematocrit control without the need for phlebotomy (20.9% vs. 0.9%). There were also a better complete hematological response (23.6% vs. 8.9%) and improvement in quality of life. Common toxicities include anemia, thrombocytopenia, and increased incidence of herpes zoster infections.

Reference:
Vannucchi AM, et al. Ruxolitinib versus standard therapy for the treatment of polycythemia vera. N Engl J Med 2015;372:426-35.

CANCER DRUG MANUAL

REVISED MONOGRAPHS AND PATIENT HANDOUTS

Clodronate Monograph
- *Side Effects:* updated paragraph about osteonecrosis of the jaw

Pamidronate Monograph
- *Side Effects:* updated paragraph about osteonecrosis of the jaw
- *Dosing:* updated BC Cancer standard regimens and protocols

Zoledronic acid Monograph
- *Dosing:* updated BC Cancer standard regimens and protocols

Thalidomide Monograph
- *Dosing:* remove instructions for opening capsules for patients who cannot swallow (no longer recommended)

Lenalidomide Monograph
- *Cautions:* add thyroid toxicity and monitoring
- *Side Effects:* add DRESS syndrome, Stevens-Johnson syndrome, toxic epidermal necrolysis, and thyroid toxicity

Paclitaxel Monograph
- *Supply and Storage:* updated available brands
- *Parenteral Administration:* add recommendation regarding inline filter

Paclitaxel Patient Handout
- remove detailed premedication bullet as instructions no longer consistent with BC Cancer protocols

Ponatinib Monograph
- *Supply and Storage:* delete 45 mg tablet as no longer marketed

EDITORIAL BOARD CHANGES

The Cancer Drug Manual writing team would like to bid farewell to our writer **Amber Tew** who will be returning to her pharmacist position at the Sindi Ahluwalia Hawkins Centre for the Southern Interior in Kelowna. The team would like to thank Amber for her many contributions during her tenure. We would also like to extend a warm welcome to the new writer **Lisa Wanbon** who is a clinical pharmacist at the BC Cancer Vancouver Island Centre in Victoria. Welcome Lisa!

The Cancer Drug Manual writing team would also like to bid farewell to exiting board member **Clarissa Cheng** (Clinical Pharmacy Specialist - Oncology Pharmacist, Burnaby Regional Cancer Centre) as she steps down from the Editorial Review Board. The team would like to thank Clarissa for her many contributions during her years of service on the Board and we wish her all the best in her future endeavours.

Provincial Systemic Therapy Program

Revised Policy of Treatment Delivery Process (III-10)

The BC Cancer Provincial Systemic Therapy Program has updated the policy on the treatment delivery process (Systemic Therapy Policy III-10) effective 1 February 2018. Answers to some of the frequently asked questions are as below:

1. What is Policy III-10?

- Policy III-10 defines the standards and processes for health care providers involved in providing systemic cancer drug treatments, to ensure the safe prescribing and assessment, preparation, dispensing and administration of oncology drug treatments to BC Cancer patients. It is developed in accordance with Accreditation Canada standards, provincially legislated requirements, approved BC Cancer policies, the BC Cancer tumour group protocols, and medical oncology/radiation oncology clinical trials.

2. How was Policy III-10 reviewed?

- An interdisciplinary working group (physicians, nurses and pharmacists) was created under the direction of BC Cancer Provincial Systemic Therapy Program to review and update Policy III-10 to reflect current practice and standards.
- The draft document then underwent several rounds of review by BC Cancer Professional Practice Groups (Medicine, Nursing and Pharmacy) and Committees (Medication Safety Subcommittee, Provincial Systemic Therapy Program Committee, Quality Council and Medical Advisory Council).
- The revised policy has been endorsed by the BC Cancer Systemic Therapy Program Committee and Quality Council.

3. How will the Clinical System Transformation (CST) Project affect Policy III-10?

- The overarching principles of safe systemic therapy delivery outlined in Policy III-10 should be applicable to all cancer centres regardless of the adoption of computerized prescriber order entry and closed-loop medication management processes.
- While the revised Policy III-10 will be used to inform CST build, CST design and resulting workflow changes will also impact future direction of systemic therapy delivery. Policy III-10 is subject to change as per CST development.

4. To whom does the policy apply?

- The policy is in effect throughout BC Cancer centres. It has not been designed for use in any other healthcare institution. While BC Cancer has a provincial mandate with respect to the development of high standards of patient care, it has no jurisdiction over the delivery of patient care in any other healthcare institution. The use of this policy by any other healthcare institution to direct patient care is the sole responsibility of that institution.

5. What are some of the changes to Policy III-10?

- See table below.

Category	Change
Overall Format	How information is presented to improve flow
Terminology	Introduction of the term "Cancer Drug Treatments" to encompass chemotherapy, immunotherapy, hormonal therapy etc.
Highlight of changes to individual sections	
Authorized prescribers	Whole section updated
Prescription requirements	Whole section updated with consideration to Accreditation Canada requirements, other best practice standards and recent BC Cancer policy changes, e.g. • Linkage with: o New BC Cancer Medication Order Requirements o BC Cancer Allergy Status documentation policy • Telephone orders: o Added details to comply with Accreditation Standard • Fax prescription: New language
Prescription order form section	Height and Weight • Updated to meet Accreditation language • Added details regarding frequency of review and what is considered significant weight change where dosing reassessment should be considered. Body Surface Area (BSA) • Round to two decimal places (CST build) BSA and Weight based dosing, clarified: • When dosing recalculation is required based on weight change • 5 % variance allowance refers to dose calculation check
Laboratory/Diagnostic test requirements	Updated the wording of whole section
Follow-up requirements	• Created new section. • Added linkage to Patient Safety Learning System (PSLS) process for reporting adverse drug reactions
Prescriber process	• Reformatted this section to make prescriber process and responsibilities clearer. • Added note about pregnancy status assessment.
Pharmacy and Nursing Processes	• Combined pharmacy and nursing sections as many checking steps are identical. • Separated out discipline specific requirements as appropriate
Patient Education and Information Process	• Updated language and website links • What's new: o Statement: "Information about medications is discussed with patients and documented prior to the initial dose and when the dose is adjusted." (Accreditation Canada Standard) o Link to new guidelines for handling cancer drugs and body fluids in the home.

BENEFIT DRUG LIST

NEW PROGRAMS

Effective 1 February 2018, these treatment programs have been added to the BC Cancer Benefit Drug List:

Protocol Title	Protocol Code	Benefit Status
Treatment of advanced neuroendocrine tumours of gastrointestinal origin (non-functional) using **everolimus**	**UGINETEV**	**Restricted**
Treatment of platinum resistant epithelial ovarian cancer with **bevacizumab** and **gemcitabine**	**UGOOVBEVG**	**Restricted**
Treatment of platinum resistant epithelial ovarian cancer with **bevacizumab** and **vinorelbine**	**UGOOVBEVV**	**Restricted**
Treatment for unresectable, locoregionally recurrent or metastatic squamous cell carcinoma of the head and neck using **paclitaxel** and **cisplatin** or **carboplatin**	**HNAVPC**	**Class I**
Treatment of polycythemia vera with **ruxolitinib**	**ULKPCVRUX**	**Restricted**
First-line treatment of advanced non-small cell lung cancer using **pembrolizumab**	**ULUAVPMBF**	**Restricted**
Second-line treatment of advanced non-small cell lung cancer using **pembrolizumab**	**ULUAVPMB**	**Restricted**
Treatment of advanced neuroendocrine tumours of lung origin (non-functional) using **everolimus**	**ULUNETEV**	**Restricted**

REVISED PROGRAMS

Effective 1 February 2018, the benefit status of the following treatment programs have been revised:

Protocol Title	Protocol Code	Benefit Status
Treatment of acute bone pain secondary to breast cancer metastases using IV **zoledronic acid**	**BRAVZOL**	Class I (Previously Restricted)

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

BC Cancer 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 treatment requiring BC Cancer Compassionate Access Program approval are prefixed with the letter "U".

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

CODE	Protocol	PPPO	Patient Handout	Protocol Title
UGINETEV	☑	☑	☑	Treatment of advanced neuroendocrine tumours of gastrointestinal origin (non-functional) using everolimus

NEW PROTOCOLS, PPPOS AND PATIENT HANDOUTS (AFFECTED DOCUMENTS ARE CHECKED)				
CODE	**Protocol**	**PPPO**	**Patient Handout**	**Protocol Title**
UGOOVBEVG	☑	☑	☐	Treatment of platinum resistant epithelial ovarian cancer with bevacizumab and gemcitabine
UGOOVBEVV	☑	☑	☐	Treatment of platinum resistant epithelial ovarian cancer with bevacizumab and vinorelbine
HNAVPC	☑	☑	☑	Treatment for unresectable, locoregionally recurrent or metastatic squamous cell carcinoma of the head and neck using paclitaxel and cisplatin or carboplatin
ULKPCVRUX	☑	☑	☐	Treatment of polycythemia vera with ruxolitinib
ULUAVPMBF	☑	☑	☑	First-line treatment of advanced non-small cell lung cancer using pembrolizumab
ULUAVPMB	☑	☑	☑	Second-line treatment of advanced non-small cell lung cancer using pembrolizumab
ULUNETEV	☑	☑	☐	Treatment of advanced neuroendocrine tumours of lung origin (non-functional) using everolimus

REVISED PROTOCOLS, PPPOS AND PATIENT HANDOUTS (AFFECTED DOCUMENTS ARE CHECKED)					
CODE	**Protocol**	**PPPO**	**Patient Handout**	**Changes**	**Protocol Title**
BRAJAC	☐	☐	☑	*General revision for consistency*	Adjuvant therapy for breast cancer using doxorubicin and cyclophosphamide
BRAVZOL	☑	☑	☐	*CAP requirement deleted*	Treatment of acute bone pain secondary to breast cancer metastases using IV zoledronic acid
GIFOLFIRI	☑	☑	☐	*Minor typo corrected*	Palliative combination chemotherapy for metastatic colorectal cancer using irinotecan, fluorouracil and leucovorin
GIFUC	☑	☑	☐	*Infusion device standardized, institution logo and name updated*	Palliative chemotherapy for upper gastrointestinal tract cancer (gastric, esophageal, gall bladder, pancreas carcinoma and cholangiocarcinoma) and metastatic anal using infusional fluorouracil and cisplatin
UGIPNEVER	☑	☑	☑	*Exclusion, prophylaxis, toxicity, references, institution name and logo updated; tests standardized*	Palliative treatment of advanced pancreatic neuroendocrine tumours using everolimus
GOENDAI	☑	☐	☐	*Eligibility clarified*	Advanced therapy for endometrial cancer using an aromatase inhibitor
GOTDLR	☑	☑	☐	*Tests clarified*	Therapy for low risk gestational trophoblastic cancer using dactinomycin and methotrexate
GOSADG	☐	☑	☐	*Tests clarified*	Treatment of uterine sarcoma cancer using docetaxel and gemcitabine

REVISED PROTOCOLS, PPPOS AND PATIENT HANDOUTS (AFFECTED DOCUMENTS ARE CHECKED)					
CODE	**Protocol**	**PPPO**	**Patient Handout**	**Changes**	**Protocol Title**
HNLACETRT	☑	☑	☐	*Tests and monitoring clarified*	Combined cetuximab and radiation treatment for locally advanced squamous cell carcinoma of the head and neck
HNLAPRT	☐	☑	☐	*Tests clarified*	Combined chemotherapy cisplatin and radiation treatment for locally advanced squamous cell carcinoma of the head and neck
HNNAVPC	☑	☑	☐	*Tests and dose modifications clarified*	Recurrent or metastatic nasopharyngeal carcinoma with carboplatin and paclitaxel
HNNLAPRT	☑	☐	☐	*TMN staging removed*	Treatment of locally advanced nasopharyngeal cancer with concurrent cisplatin and radiation
UHNOTLEN	☑	☑	☐	*Eligibility and tests clarified*	Therapy for locally recurrent or metastatic, RAI-refractory differentiated thyroid cancer using lenvatinib
LUAVDC	☑	☐	☐	*Eligibility clarified*	First-line treatment of advanced non-small cell lung cancer with cisplatin and docetaxel
LUAVERL	☑	☐	☐	*Title and eligibility clarified*	Second- or third-line treatment of advanced non-small cell lung cancer with erlotinib
ULUAVNIV	☑	☐	☐	*Exclusions clarified*	Treatment of advanced non-small cell lung cancer using nivolumab
LUAVNP	☑	☐	☐	*Eligibility updated*	Treatment for advanced non-small cell lung cancer with cisplatin and vinorelbine
LUAVPC	☑	☐	☐	*Eligibility updated*	First-line treatment of advanced non-small cell lung cancer with carboplatin and paclitaxel
LUAVPEM	☑	☐	☐	*Title and eligibility clarified*	Second-line treatment of advanced non-small cell lung cancer with pemetrexed
LUAVPG	☑	☐	☐	*Eligibility updated*	Treatment of advanced non-small cell lung cancer with platinum and gemcitabine
LUAVPP	☑	☐	☐	*Eligibility updated*	First-line treatment of advanced non-small cell lung cancer with platinum and pemetrexed
LUAVVIN	☑	☐	☐	*Eligibility updated*	Treatment of advanced non-small cell lung cancer with vinorelbine in elderly patients
ULKMDSA	☐	☑	☐	*Minor formatting*	Therapy of myelodysplastic syndrome using azacitidine
LYCHOPR	☑	☐	☐	*Minor typo corrected*	Treatment of lymphoma with doxorubicin, cyclophosphamide, vincristine, prednisone and rituximab
LYCHOPRMTX	☑	☐	☐	*Minor typo corrected*	Central nervous system prophylaxis with high dose methotrexate, CHOP and rituximab in diffuse large B-cell lymphoma
ULYFIBRU	☑	☑	☐	*Tests clarified*	Treatment of previously untreated chronic lymphocytic leukemia or small lymphocytic lymphoma with chromosome 17 p deletion using ibrutinib
ULYIBRU	☑	☑	☐	*Tests clarified*	Treatment of relapsed/refractory chronic lymphocytic leukemia or small lymphocytic lymphoma using ibrutinib
ULYIDELAR	☐	☑	☐	*Space for height and weight added*	Treatment of relapsed/refractory chronic lymphocytic leukemia or small lymphocytic lymphoma using idelalisib and rituximab

REVISED PROTOCOLS, PPPOS AND PATIENT HANDOUTS (AFFECTED DOCUMENTS ARE CHECKED)					
CODE	**Protocol**	**PPPO**	**Patient Handout**	**Changes**	**Protocol Title**
SMIMI	☐	☑	☐	*Minor formatting*	Topical immunotherapy for in-transit melanoma metastases, cutaneous lymphoma, basal cell carcinoma using imiquimod

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Library/Cancer Information	604-675-8003 Toll Free 888-675-8001 x 8003		requests@bccancer.bc.ca
Pharmacy Professional Practice	604-877-6000 x 672247		mlin@bccancer.bc.ca
Nursing Professional Practice	604-877-6000 x 672623		ilundie@bccancer.bc.ca
OSCAR	888-355-0355	604-708-2051	oscar@bccancer.bc.ca
Compassionate Access Program (CAP)	604-877-6277	604-708-2026	cap_bcca@bccancer.bc.ca
Pharmacy Chemotherapy Certification	250-712-3900 x 686741		rxchemocert@bccancer.bc.ca
BC Cancer-Abbotsford Centre	604-851-4710 Toll Free 877-547-3777		
BC Cancer-Centre for the North	250-645-7300 Toll Free 888-775-7300		
BC Cancer-Fraser Valley Centre	604-930-2098 Toll Free 800-523-2885		
BC Cancer-Sindi Ahluwalia Hawkins Centre for the Southern Interior	250-712-3900 Toll Free 888-563-7773		
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