



For Health Professionals Who Care For Cancer Patients

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EDITOR'S CHOICE

AZACITIDINE – CHANGE IN MAXIMUM VOLUME OF SUBCUTANEOUS INJECTION

Effective 1 July 2018, all azacitidine-containing treatment protocols and pre-printed orders (ULKAMLAS, ULKMDSA), as well as the cancer drug manual monograph, will be revised to increase the maximum volume of subcutaneous injection to 4 mL.

Azacitidine is often administered at doses that require an injected volume greater than 2.5 mL, the conventional maximum volume for subcutaneous injection.^{1,2} Consequently, 3 to 4 injections are administered to nearly 80% of patients at each visit,³ which may impact negatively on tolerability and patient satisfaction.

This practice is unnecessary since an injected volume of 4 mL has been safely administered in pivotal trials.⁴⁻⁶ In addition, the conventional 2.5 mL threshold is supported by limited evidence.^{1,2} Although an injection of 1 mL is more painful than 0.5 mL, there is no further increase in pain with a 1.5 mL injection.⁷ This suggests that pain intensity does not increase linearly once volume exceeds 1 mL. By increasing the maximum volume to 4 mL, many patients would only require 2 injections per visit.

Please stay tuned for changes in the affected documents in the July issue of the Systemic Therapy Update.

References

1. Wikjord N, Harvey F. PCG M-100: Clinical Practice Document. Medication administration, subcutaneous (intermittent and continuous). Vancouver, BC: Palliative Care Unit, Vancouver Coastal Health; January 2011.
2. Palliative Care Clinical Practice Guidelines Committee. Management of subcutaneous injection site(s) in palliative care patients. Vancouver, BC: Senior Health Regional Palliative Care Program, Alberta Health Services; 20 October 2005.
3. Ferruccio LF, Murray C, Yee KW, Incekol D, Lee R, Paisley E, et al. Tolerability of Vidaza (azacitidine) subcutaneous administration using a

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- maximum volume of 3 ml per injection. *J Oncol Pharm Pract* 2016;22(4):605-10.
- Marcucci G, Silverman L, Eller M, et al. Bioavailability of azacitidine subcutaneous versus intravenous in patients with the myelodysplastic syndromes. *J Clin Pharmacol.* 2005;45(5):597-602.
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 - VIDAZA® product monograph. Mississauga, Ontario: Celgene Inc.; 23 November 2016. p. 31-40.
 - Jorgensen JT, Romsing J, Rasmussen M, et al. Pain assessment of subcutaneous injections. *Ann Pharmacother* 1996;30(7-8):729-32.

DRUG UPDATE

IV CLODRONATE DISCONTINUED

Effective immediately, clodronate injection has been discontinued by Bayer, the only manufacturer in Canada. Please note that oral clodronate is still available. All affected treatment protocols and pre-printed orders (BRAVCLOUD, BRAVPAM, SCHYPCAL) have been updated to remove IV clodronate.

Alternatives that may be considered include:

IV Clodronate-Containing Protocols	Alternative Treatment
BRAVCLOUD	Pamidronate 90 mg IV in 250 mL NS over 1 hour Clodronate 1600 mg PO once daily on an empty stomach (at least 1 hour before or 2 hours after eating)
BRAVPAM	Pamidronate 90 mg IV in 250 mL NS over 1 hour
SCHYPCAL	Pamidronate 60-90mg IV in 250 mL NS over 1 hour Zoledronic acid 4 mg IV in 100 mL NS over 15 minutes

BENEFIT DRUG LIST

DELETED PROGRAMS

The following treatment programs have been reviewed by the BC Cancer Tumour Groups and deleted from the BC Cancer [Benefit Drug List](#) effective 1 June 2018:

Protocol Title	Protocol Code
Palliative Therapy for Pancreatic Endocrine Tumours using Streptozocin and Doxorubicin	GIENDO2
Palliative Therapy of Advanced Colorectal Cancer using Leucovorin and Fluorouracil	GIFUFA
Adjuvant Chemotherapy of Gastric Cancer Patients with D2 Resection (Node Negative) or Ineligible for Adjuvant Chemoradiation, using Cisplatin and Capecitabine	GIGAJCC
Palliative Therapy for Kaposi's Sarcoma using Doxorubicin	KSAD

NEW MONOGRAPHS AND PATIENT HANDOUTS

The following drugs are NOT BC Cancer Benefit Drugs, and require application to the BC Cancer Compassionate Access Program. Their corresponding Interim Monographs and Patient Handouts are made available for reference only.

The **Avelumab Monograph** and **Patient Handout** have been developed with expert review provided by Dr. Christopher Lee (Medical Oncologist) and Robert Tillmanns (Pharmacist) of the BC Cancer Skin/Melanoma Tumour Group. Avelumab is a fully humanized IgG1 monoclonal antibody immune checkpoint inhibitor that binds to PD/L1 on tumour cells and tumour infiltrating cells, allowing the restoration of anti-tumour T-cell activity. It is indicated for the treatment of metastatic Merkel cell carcinoma and urothelial carcinoma. The usual dose is 10 mg/kg IV every 2 weeks.

Highlights of these documents include:

- Infusion reactions are common and include flushing, chills, hypotension, dyspnea, pyrexia, back pain, abdominal pain and urticaria. Premedication with an antihistamine plus acetaminophen is recommended for at least the first four doses.
- Immune-related reactions such as pneumonitis, hepatitis, colitis, endocrinopathies and nephritis have been reported and may be life-threatening. Prompt management is important and may include withholding avelumab and administering systemic corticosteroids and/or appropriate hormones.
- Other common side effects include fatigue, musculoskeletal pain, diarrhea, nausea, rash, peripheral edema and decreased appetite.

The **Vandetanib Monograph** and **Patient Handout** have been developed with expert review provided by Dr. Cheryl Ho (Medical Oncologist) and Karen Mason (Pharmacist) of the BC Cancer Head & Neck Tumour Group. Vandetanib is an oral, potent, selective inhibitor of vascular endothelial growth factor receptor-2 (VEGFR-2), epidermal growth factor receptor (EGFR), and rearranged during transfection (RET) receptor tyrosine kinases. It is indicated for the treatment of medullary thyroid cancer. The usual dose is 300 mg orally once daily, with or without food.

Highlights of these documents include:

- Common adverse drug reactions include diarrhea, rash, acneiform dermatitis and hypertension.
- QT prolongation, Torsades de pointes and sudden death have occurred with vandetanib; thus, must be prescribed and dispensed through the CAPRELSA® Restricted Distribution Program.
- Grapefruit and grapefruit juice should be avoided during treatment.

EDITORIAL BOARD CHANGES

The Cancer Drug Manual (CDM) Editorial Board would like to bid farewell to **Sanna Pellatt** (CON Pharmacy Educator, BC Cancer – Victoria) as she steps down from the Board. The Board would like to thank Sanna for her many contributions to the CDM over the years. **Mandeep Bains** (CON Pharmacy Educator, BC Cancer – Vancouver) will be rejoining the Board to represent the Communities Oncology

CANCER DRUG MANUAL

Network. Welcome back Mandeep!

Another longstanding board member, **Roberta Esau** (Clinical Pharmacy Specialist, BC Children's & Women's Health Centre), will be stepping down from the CDM Board as she enters retirement. The Board would like to acknowledge Roberta's many contributions to the CDM as a pediatric specialist, both as a board member and an expert reviewer. We wish her all the best in her retirement. **Dr. Jennifer Kendrick** (Clinical Pharmacy Specialist, BC Children's & Women's Health Centre) will be replacing Roberta in this capacity. Welcome Jennifer!

LIST OF 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".

REVISED PROTOCOLS, PPPOs AND PATIENT HANDOUTS (AFFECTED DOCUMENTS ARE CHECKED)					
CODE	Protocol	PPPO	Patient Handout	Changes	Protocol Title
BRAVCLOD	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<i>IV Clodronate deleted</i>	Therapy of Bone Metastases in Breast Cancer using Oral Clodronate
BRAVPAM	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<i>IV Clodronate deleted</i>	Treatment of Acute Bone Pain Secondary to Breast Cancer Metastases using IV Pamidronate
CNAJZRT	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<i>Treatment duration and Tests clarified</i>	Concomitant (Dual Modality) and Adjuvant Temozolomide for Newly Diagnosed Malignant Gliomas with Radiation
CNELTZRT	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<i>Treatment duration and Tests clarified</i>	Treatment of Elderly Newly Diagnosed Glioma Patient with Concurrent and Adjuvant Temozolomide and Radiation Therapy
CNMODPCV	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<i>Eligibility, Tests and Institutional Name updated</i>	Modified PCV Chemotherapy of Brain Tumours Using Procarbazine, Lomustine (CCNU) and Vincristine
GIGAVCCT	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<i>Tests and Institutional Name updated</i>	Palliative Treatment of Metastatic or Locally Advanced Gastric, Gastroesophageal Junction, or Esophageal Adenocarcinoma using Cisplatin, Capecitabine and Trastuzumab

REVISED PROTOCOLS, PPOs AND PATIENT HANDOUTS (AFFECTED DOCUMENTS ARE CHECKED)					
CODE	Protocol	PPO	Patient Handout	Changes	Protocol Title
GIGAVCFT	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<i>Tests and Institutional Name updated</i>	Palliative Treatment of Metastatic or Inoperable, Locally Advanced Gastric or Gastroesophageal Junction Adenocarcinoma Using Cisplatin, Infusional Fluorouracil and Trastuzumab
GIGAVEOCAP	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<i>Institutional Name, Tests, Dose Modifications and Patient Resource updated</i>	Palliative therapy for metastatic or locally advanced gastric or esophagogastric cancer using Epirubicin, Oxaliplatin and Capecitabine
GIGAVEOF	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<i>Institutional Name, Tests and Patient Resource updated</i>	Palliative Therapy for Metastatic or Locally Advanced Gastric or Esophagogastric Cancer using Epirubicin, Oxaliplatin and Infusional Fluorouracil
UGIGAVRAMT	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<i>Tumour Markers and Premedications Updated</i>	Second-Line Therapy for Metastatic or Locally Advanced Gastric or Gastroesophageal Junction Cancer Using Weekly Paclitaxel and Ramucirumab
UGIGFLODOC	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<i>Institutional Name and Patient Resource updated</i>	Perioperative Treatment of Resectable Adenocarcinoma of the Stomach, Gastroesophageal Junction or Lower 1/3 Esophagus using Docetaxel, Oxaliplatin, Infusional Fluorouracil, and Leucovorin
GIRCRT	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<i>Tests and Institutional Name updated</i>	Combined Modality Adjuvant Therapy for High-Risk Rectal Carcinoma using Capecitabine and Radiation Therapy
GIRINFRT	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<i>Tests and Institutional Name updated</i>	Combined Modality Adjuvant Therapy for High-Risk Rectal Carcinoma using Capecitabine, Infusional Fluorouracil and Radiation Therapy
UGISORAF	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<i>Tests, Renal and Hepatic Dysfunction, and QT Prolongation updated</i>	Therapy for Advanced Hepatocellular Carcinoma using Sorafenib
GUNAJPG	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<i>Minor typo corrected</i>	Neo-Adjuvant Therapy for Urothelial Carcinoma using Cisplatin and Gemcitabine
UHNAVIV	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<i>Dose clarified</i>	Palliative Therapy for Unresectable, Platinum-Refractory, Recurrent or Metastatic Squamous Cell Cancer of the Head and Neck using Nivolumab
ULUAVPMB	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<i>Tests updated</i>	Treatment of Advanced Non-Small Cell Lung Cancer Using Pembrolizumab
ULUAVPMBF	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<i>Tests updated</i>	First-Line Treatment of Advanced Non-Small Cell Lung Cancer Using Pembrolizumab

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

CODE	Protocol	PPO	Patient Handout	Changes	Protocol Title
USATEMBEV	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	Tests, Infusion time and Institutional Name updated	Therapy for Advanced Solitary Fibrous Tumours and Hemangiopericytoma Using Temozolomide and Bevacizumab
SCHYPICAL	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	IV Clodronate deleted	Guidelines for the Diagnosis and Management of Malignancy Related Hypercalcemia
SCPAINLI	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Contact Physician, Tests, Dosing and Institutional Name updated	Extreme Pain Therapy using Parenteral Lidocaine

WEBSITE RESOURCES AND CONTACT INFORMATION

CONTACT INFORMATION	PHONE	FAX	EMAIL
Systemic Therapy Update Editor	604-877-6000 x 673028		bulletin@bccancer.bc.ca
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To update contact information of any CON sites, please contact:			bulletin@bccancer.bc.ca
Oncology Drug Information	604-877-6275		druginfo@bccancer.bc.ca
Nurse Educators	604-877-6000 x 672638		nursinged@bccancer.bc.ca
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		mclin@bccancer.bc.ca
Provincial Professional Practice Nursing			BCCancerPPNAdmin@ehcnet.phsa.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 Oncology Certification	250-712-3900 x 686820		rxchemocert@bccancer.bc.ca
BC Cancer-Abbotsford	604-851-4710 Toll Free 877-547-3777		
BC Cancer-Prince George (Centre for the North)	250-645-7300 Toll Free 888-775-7300		
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