

Regimen Monograph

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A - Regimen Name

BEVA Regimen

Bevacizumab**Disease Site** Central Nervous System**Intent** Palliative**Regimen Category** **Evidence-Informed :**

Regimen is considered appropriate as part of the standard care of patients; meaningfully improves outcomes (survival, quality of life), tolerability or costs compared to alternatives (recommended by the Disease Site Team and national consensus body e.g. pan-Canadian Oncology Drug Review, pCODR). Recommendation is based on an appropriately conducted phase III clinical trial relevant to the Canadian context OR (where phase III trials are not feasible) an appropriately sized phase II trial. Regimens where one or more drugs are not approved by Health Canada for any indication will be identified under Rationale and Use.

Rationale and Uses Single agent treatment of patients with glioblastoma (WHO Grade IV) after relapse or disease progression, following prior therapy.[back to top](#)**B - Drug Regimen**Different bevacizumab products are **not interchangeable**.**[bevacizumab](#)** 10 mg /kg IV Day 1**(This drug is not currently publicly funded for this regimen and intent)**

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C - Cycle Frequency

REPEAT EVERY 14 DAYS

Until disease progression or unacceptable toxicity

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D - Premedication and Supportive Measures

Antiemetic Regimen: Minimal

- Also refer to [CCO Antiemetic Recommendations](#).

Screen for hepatitis B virus in all cancer patients starting systemic treatment. Refer to the [hepatitis B virus screening and management](#) guideline.

Routine primary prophylaxis for infusion reactions is not recommended; the use of secondary prophylaxis pre-medications should be based on clinical judgement

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E - Dose Modifications

Doses should be modified according to the protocol by which the patient is being treated.

Bevacizumab should not be initiated in patients with recurrent hemoptysis, uncontrolled hypertension or wounds that require healing.

Prior to treatment, a dental evaluation should be performed and major dental procedures completed.

Bevacizumab should not be initiated for at least 28 days following major surgery or until wound healing has occurred; hold for 28 days prior to major elective surgery.

Dosage with toxicity

Dose reductions are not recommended. Bevacizumab should be held or discontinued based on toxicity.

Bevacizumab action	Toxicity		
	Any grade	Grade 3	Grade 4
Hold:	Uncontrolled hypertension		
	Delayed wound healing		
	Proteinuria \geq 2g/ 24 hours*		
	Surgery**		
Discontinue:		Hypertension not controlled with medical management	Hypertension
	Wound dehiscence, poor healing requiring medical intervention; necrotizing fasciitis		
	Nephrotic syndrome; non- recovery of proteinuria \geq 2g/24 hours		
	Tracheo-esophageal fistula, other non-GI fistulae		Fistula
	GI Perforation or fistula		
	PRES, hypertensive encephalopathy		
	Arterial thromboembolism	Pulmonary embolism	Venous thromboembolism (including pulmonary embolism)
	Symptomatic cardiac failure		
	Hemoptysis > 2.5 mL	Bleeding	Bleeding
	Intracranial bleeding		
<p>* may restart when < 2g/24hrs ** for 28 days PRIOR (if surgery elective) and AFTER major surgery, or until wound healed</p>			

Management of Infusion Reactions

Also refer to the CCO guideline for detailed description of [Management of Cancer Medication-Related Infusion Reactions](#).

Grade	Management	Re-challenge
1 or 2	<ul style="list-style-type: none"> • Stop or slow the infusion rate. • Manage the symptoms. <p>Restart:</p> <ul style="list-style-type: none"> • Once symptoms resolve, the infusion can be restarted at a slower rate, unless a serious reaction occurred. 	<ul style="list-style-type: none"> • No specific recommendations can be made at this time
3 or 4	<ul style="list-style-type: none"> • Stop treatment. • Aggressively manage symptoms. 	<ul style="list-style-type: none"> • Discontinue permanently (do not rechallenge)

Hepatic Impairment

Has not been studied. Not a major route of bevacizumab metabolism or excretion.

Renal Impairment

Has not been studied. Not a major route of bevacizumab metabolism or excretion.

Dosage in the Elderly

Use with caution; patients > 65 years old have an increased risk of arterial thrombotic events as well as myelosuppression, fatigue, proteinuria, hypertension, dizziness, dysphonia, anorexia and GI effects (except gastrointestinal perforation).

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F - Adverse Effects

Refer to [bevacizumab](#) drug monograph(s) for additional details of adverse effects. The adverse effects below were reported with and without concurrent chemotherapy use.

Common (25-49%)	Less common (10-24%)	Uncommon (< 10%), but may be severe or life-threatening
<ul style="list-style-type: none"> • Bleeding • Fatigue • Hypertension (may be severe) • Proteinuria (may be severe) • Headache 	<ul style="list-style-type: none"> • Diarrhea • Venous thromboembolism (may be severe) • Nausea, vomiting • Constipation • Insomnia • Musculoskeletal pain • Cough, dyspnea • Rash (may be severe) • Anorexia • Infection • Dysphonia • Cardiotoxicity (may be severe) 	<ul style="list-style-type: none"> • Arterial thromboembolism • Artery aneurysm / dissection • Hemorrhage (severe) • Myelosuppression • Arrhythmia • Pulmonary hypertension • Hypersensitivity • GI obstruction/perforation • Fistulas • Necrotizing fasciitis • Osteonecrosis (jaw, other) • RPLS/PRES • Thrombotic microangiopathy • Delayed wound healing

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G - Interactions

Refer to [bevacizumab](#) drug monograph(s) for additional details.

- Avoid use with sunitinib as hemolytic anemia has been reported.

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H - Drug Administration and Special Precautions

Refer to [bevacizumab](#) drug monograph(s) for additional details.

Different bevacizumab products are **not interchangeable**.

Administration:

- DO NOT ADMINISTER AS AN IV PUSH OR BOLUS.
- Bevacizumab infusions should **NOT** be administered or mixed with dextrose or glucose solutions due to potential for drug degradation.
- Mix in 100 mL bag NS. (Final concentration should be 1.4 -16.5 mg/mL).
- Compatible with PVC or polyolefin bags.
- Do not shake. Should not be mixed or diluted with other drugs.
- Infuse over 90 minutes as loading dose, if well tolerated next infusion can be given over 60 minutes; if well tolerated, can thereafter be given over 30 minutes as maintenance dose.
- Bevacizumab rapid infusion (over 10 minutes) has safely been administered with no significant increase in IRs for (5mg/kg and 7.5 mg/kg doses)
- Refrigerate unopened vials and protect from light; do not freeze.

Also refer to the CCO guideline for detailed description of [Management of Cancer Medication-Related Infusion Reactions](#).

Contraindications:

- Patients with known hypersensitivity to bevacizumab or its components
- Patients with known hypersensitivity to Chinese hamster ovary cell product or to other recombinant human or humanized antibodies
- Patients with untreated CNS metastases

Other Warnings/Precautions:

- Elderly patients
- Patients with a history of arterial thromboembolism or significant cardiovascular disease or cardiac failure
- Patients with coagulopathies (congenital, acquired or therapeutic)
- Patients with recurrent hemoptysis (>2.5ml), serious hemorrhage, or with *squamous* NSCLC
- Patients with colorectal cancer and colorectal stents; increased risk of GI perforation has been reported; use with caution.
- Hypertension should be controlled prior to starting treatment
- Use caution if given with bisphosphonates or other anti-angiogenic agents; increased risk of ONJ
- The safety and efficacy of concurrent radiotherapy and bevacizumab has not been established.

Pregnancy/Lactation:

- This regimen is not recommended for use in pregnancy. Adequate contraception should be used by patients and their partners while on treatment and after the last treatment dose. Recommended methods and duration of contraception may differ depending on the treatment. Refer to the drug monograph(s) for more information.
- Breastfeeding is not recommended during this treatment and after the last treatment dose. Refer to the drug monograph(s) for recommendations after the last treatment dose (if available).
- Fertility effects: Bevacizumab may cause ovarian failure. Prior to starting treatment, discuss fertility preservation with patients who can become pregnant.

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I - Recommended Clinical Monitoring

Treating physicians may decide to monitor more or less frequently for individual patients but should always consider recommendations from the product monograph.

Refer to the [hepatitis B virus screening and management](#) guideline for monitoring during and after treatment.

Recommended Clinical Monitoring

- CBC; baseline and at each visit
- Blood pressure; baseline and every 2-3 weeks during therapy and more frequently in patients who develop hypertension
- Urine dipstick, a 24 hour urine collection is recommended for patients with a 2+ or greater urine dipstick; baseline and at each visit
- Dental evaluation; baseline
- Clinical assessment of hypersensitivity, perforation, fistula, GI symptoms, ONJ, hemorrhage, thromboembolism, wound healing, hypertension, neurologic and cardiac effects; at each visit
- Grade toxicity using the current [NCI-CTCAE \(Common Terminology Criteria for Adverse Events\) version](#)

Suggested Clinical Monitoring

- Liver and renal function tests; Baseline and at each visit
- Cardiac function tests (Echo, RNA and/or MUGA scans) especially in patients who are close to the lifetime cumulative dose of anthracyclines/anthracenediones; Baseline and as clinically indicated
- INR for patients receiving warfarin; Baseline and as clinically indicated

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J - Administrative Information

Approximate Patient Visit	First dose: 1.5 hours; Second dose: 1 hour; Subsequent: 0.5 hour
Pharmacy Workload (average time per visit)	17.013 minutes
Nursing Workload (average time per visit)	42.5 minutes

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K - References

Bevacizumab drug monograph, Ontario Health (Cancer Care Ontario).

Friedman HS, Prados MD, Wen PY, et al. Bevacizumab Alone and in Combination With Irinotecan in Recurrent Glioblastoma. *J Clin Oncol* 2009; 27(28): 4733-40.

Kreisl TN, Kim L, Moore K, et al. Phase II Trial of Single-Agent Bevacizumab Followed by Bevacizumab Plus Irinotecan at Tumor Progression in Recurrent Glioblastoma. *J Clin Oncol* 2009; 27(5): 740-5.

Reidy DL, Chung KY, Timoney JP, et al. Bevacizumab 5 mg/kg can be infused safely over 10 minutes. *Journal of Clinical Oncology* 2007; 25: 2691-5.

PEBC Advice Documents or Guidelines

- [An Endorsement of the ASCO-SNO Guideline on Therapy for Diffuse Astrocytic and Oligodendroglial Tumors in Adults](#)

July 2024 Updated Dose Modifications, Adverse Effects and Pregnancy/Lactation sections

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M - Disclaimer

Regimen Abstracts

A Regimen Abstract is an abbreviated version of a Regimen Monograph and contains only top level information on usage, dosing, schedule, cycle length and special notes (if available). It is intended for healthcare providers and is to be used for informational purposes only. It is not intended to constitute or be a substitute for medical advice, and all uses of the Regimen Abstract are subject to clinical judgment. Such information is provided on an "as-is" basis, without any representation, warranty, or condition, whether express, or implied, statutory or otherwise, as to the

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Information in regimen abstracts is accurate to the extent of the ST-QBP regimen master listings, and has not undergone the full review process of a regimen monograph. Full regimen monographs will be published for each ST-QBP regimen as they are developed.

Regimen Monographs

Refer to the [New Drug Funding Program](#) or [Ontario Public Drug Programs](#) websites for the most up-to-date public funding information.

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The format and content of the drug monographs, regimen monographs, appendices and symptom management information contained in the Formulary will change as they are reviewed and revised on a periodic basis. The date of last revision will be visible on each page of the monograph and regimen. Since standards of usage are constantly evolving, it is advised that the Formulary not be used as the sole source of information. It is strongly recommended that original references or product monograph be consulted prior to using a chemotherapy regimen for the first time.

Some Formulary documents, such as the medication information sheets, regimen information sheets and symptom management information (for patients), are intended for patients. Patients should always consult with their healthcare provider if they have questions regarding any information set out in the Formulary documents.

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