

## Regimen Monograph

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## A - Regimen Name

# BEVA Regimen

**Bevacizumab**

**Disease Site**      Gynecologic  
                                 Ovary

**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**      For the treatment of patients with high risk or recurrent epithelial ovarian, fallopian or primary peritoneal cancer following platinum-based chemotherapy.

NDFP funding applies to use following treatment with carboplatin/paclitaxel only. See NDFP for detailed funding criteria.

**Supplementary Public Funding**      [bevacizumab](#)  
New Drug Funding Program (Bevacizumab (Biosimilar) with Paclitaxel and Carboplatin - Front-line Treatment (Previously Untreated) Ovarian, Fallopian Tube, and Primary Peritoneal Cancer) ([NDFP Website](#)) (**Funded after treatment with paclitaxel-carboplatin only**)

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## B - Drug Regimen

Different bevacizumab products are **not interchangeable**.

**After treatment with CRBPPACL+BEVA\*:**

<a href="#">bevacizumab</a>	7.5 mg /kg	IV	Day 1
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\*after 6 cycles of carboplatin/paclitaxel, 5 in combination with bevacizumab (see CRBPPACL+BEVA regimen), continue with single-agent bevacizumab.

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## C - Cycle Frequency

**REPEAT EVERY 21 DAYS**

For up to 12 additional cycles unless disease progression or unacceptable toxicity occurs

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## D - Premedication and Supportive Measures

**Antiemetic Regimen:** Minimal

**Other Supportive Care:**

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

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.

### **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		Any internal fistula
	GI Perforation or fistula		
	PRES, hypertensive encephalopathy		
	Arterial thromboembolism	Pulmonary embolism	Venous thromboembolism (including pulmonary embolism)
	Symptomatic cardiac failure		
	Recurrent hemoptysis > 2.5 mL	Bleeding (any)	Bleeding (any)

Intracranial bleeding		
<p>* may restart when &lt; 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](#).

<b>Grade</b>	<b>Management</b>	<b>Re-challenge</b>
1 or 2	<ul style="list-style-type: none"> <li>• Stop or slow the infusion rate.</li> <li>• Manage the symptoms.</li> </ul> <p><b>Restart:</b></p> <ul style="list-style-type: none"> <li>• Once symptoms resolve, the infusion can be restarted at a slower rate, unless a serious reaction occurred.</li> </ul>	<ul style="list-style-type: none"> <li>• No specific recommendations can be made at this time</li> </ul>
3 or 4	<ul style="list-style-type: none"> <li>• Stop treatment.</li> <li>• Aggressively manage symptoms.</li> </ul>	

### **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. Bevacizumab may exacerbate common toxicities of chemotherapy (i.e. hand foot syndrome, neurotoxicity) when given in combination.

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

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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 7.5mg/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
- 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
- Use caution if given with bisphosphonates or other anti-angiogenic agents, given risk of ONJ
- The safety and efficacy of concurrent radiotherapy and bevacizumab has not been established

**Pregnancy/Lactation:**

- Bevacizumab is not recommended for use in pregnancy. Cases of fetal abnormalities have been reported. Adequate contraception (including at least 2 contraceptive methods) should be used by both sexes during treatment, and for at least **6 months** after the last dose.
- Breastfeeding is not recommended during treatment and for at least **6 months** following the last dose.
- Fertility effects: Long-term effects unknown. Discuss fertility preservation with women of reproductive potential prior to starting treatment.

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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.

Recommended Clinical Monitoring

- Blood pressure; Baseline and every 2-3 weeks during therapy; more frequently in patients who develop hypertension
- CBC; Baseline and at each visit
- Urine dipstick, 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, infection, myelosuppression, thromboembolism, delayed 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

- 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
- Liver and renal function tests; Baseline and at each visit
- INR in 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**

Aghajanian C, Blank SV, Goff BA, et al. OCEANS: A randomized, double-blind, placebo-controlled phase III trial of chemotherapy with or without bevacizumab in patients with platinum-sensitive recurrent epithelial ovarian, primary peritoneal, or fallopian tube cancer. J Clin Oncol. 2012 Jun



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10;30(17):2039-45.

Bevacizumab drug monograph, Cancer Care Ontario

Perren TJ, Swart AM, Pfisterer J, et al; ICON7 Investigators. A phase 3 trial of bevacizumab in ovarian cancer. *N Engl J Med*. 2011 Dec 29;365(26):2484-96.

### **PEBC Advice Documents or Guidelines**

- [Systemic Therapy for Recurrent Epithelial Ovarian Cancer](#)

**September 2022** Removed unfunded tag for bevacizumab; removed information related to CRBPGEMC+BEVA

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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 information's quality, accuracy, currency, completeness, or reliability, and Cancer Care Ontario disclaims all liability for the use of this information, and for any claims, actions, demands or suits that arise from such use.*

*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.

*The information set out in the drug monographs, regimen monographs, appendices and symptom management information (for health professionals) contained in the Drug Formulary (the "Formulary") is intended for healthcare providers and is to be used for informational purposes only. The information is not intended to cover all possible uses, directions, precautions, drug interactions or adverse effects of a particular drug, nor should it be construed to indicate that use of a particular drug is safe, appropriate or effective for a given condition. The information in the Formulary is not intended to constitute or be a substitute for medical advice and should not be relied upon in any such regard. All uses of the Formulary are subject to clinical judgment and actual prescribing patterns may not follow the information provided in the Formulary.*

*The format and content of the drug monographs, regimen monographs, appendices and symptom management*

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*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.*

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