Regimen Monograph

A - Regimen Name

CRBPPACL+BEVA+PEMB Regimen

CARBOplatin-PACLitaxel-Bevacizumab-Pembrolizumab

Disease Site

Gynecologic
Cervix

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.

This **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). 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.

Rationale and Uses

For treatment of patients with persistent, recurrent, or metastatic cervical cancer whose tumours express PD-L1 (CPS ≥1), as determined by a validated test.
Treatment is only for patients:

- who have not received prior systemic chemotherapy for metastatic or

advanced disease,
- who have a good performance status,
- whose disease is not amenable to curative treatment, and
- who do not have active central nervous system (CNS) metastases or significant autoimmune disease

Supplementary Public Funding

pembrolizumab
New Drug Funding Program (Pembrolizumab - Metastatic, Persistent, or Recurrent Carcinoma of the Cervix) (NDFP Website)

bevacizumab
New Drug Funding Program (Bevacizumab (Biosimilar) - Metastatic (Stage IVB), Persistent, or Recurrent Carcinoma of the Cervix) (NDFP Website)

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B - Drug Regimen

Different bevacizumab products are **not interchangeable**.

pembrolizumab^	2 mg /kg	IV (max 200 mg)	Day 1
PACLitaxel	175 mg /m²	IV	Day 1
CARBOplatin	AUC 5*	IV	Day 1
bevacizumab	15 mg /kg	IV	Day 1

^Dosing based on NDFP funding criteria. Alternative dosing schedule: pembrolizumab 4 mg/kg (max 400mg) IV q6 weeks.

*Adjust Carboplatin dose to AUC target (using Calvert formula) as outlined in "Other Notes" section

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C - Cycle Frequency

REPEAT EVERY 21 DAYS unless disease progression or unacceptable toxicity occurs

CRBPPACL+BEVA+PEMB* is usually given for 6 cycles. (Chemotherapy may be continued beyond 6 cycles for patients with ongoing benefit and without unacceptable side effects.)

Followed by BEVA+PEMB(MNT) or PEMB(MNT) for the maintenance phase of treatment (up to 35 doses of pembrolizumab in total given every 3 weeks, or 18 doses given every 6 weeks).

*If bevacizumab is discontinued due to toxicity, patients may receive pembrolizumab plus chemotherapy, followed by PEMB(MNT).
If CRBPPACL is discontinued for toxicity, patients may continue to receive BEVA+PEMB(MNT).

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D - Premedication and Supportive Measures

Antiemetic Regimen:

Moderate + NK1 antagonist (Carboplatin AUC ≥ 5)

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.

Pre-medications (prophylaxis for infusion reaction):

Paclitaxel*:

- Dexamethasone 20 mg PO 12- and 6-hours OR Dexamethasone 20 mg IV 30 minutes pre-infusion†
- Diphenhydramine 25-50 mg IV/PO 30-60 minutes pre-infusion
- Ranitidine 50 mg IV OR Famotidine 20 mg IV 30-60 minutes pre-infusion

*Consider discontinuing pre-medications for paclitaxel if there was no IR in the first 2 doses.

†Oral and IV dexamethasone are both effective at reducing overall IR rates. Some evidence suggests that oral dexamethasone may be more effective for reducing severe reactions; however, adverse effects and compliance remain a concern.

Carboplatin:

- There is insufficient evidence that routine prophylaxis with pre-medications reduce infusion reaction (IR) rates.
- Corticosteroids and H1-receptor antagonists ± H2-receptor antagonists **may** reduce IR rates for some patients (e.g. gynecological patients with a platinum-free interval (PFI) > 12 months or a history of drug allergy who are receiving carboplatin starting from the 7th cycle) but no optimal pre-medication regimen has been established.

Pembrolizumab:

- Routine pre-medication is not recommended.
- May consider antipyretic and H1-receptor antagonist in patients who experienced a grade 1-2 infusion reaction.

Other Supportive Care:

- Avoid the use of corticosteroids or immunosuppressants before starting pembrolizumab treatment. Corticosteroids may be used as premedication (e.g. antiemetic) when given with chemotherapy.

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J - Administrative Information

Approximate Patient Visit	6-7 hours
Pharmacy Workload (average time per visit)	46.146 minutes
Nursing Workload (average time per visit)	74.167 minutes

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K - References

CADTH reimbursement recommendation: Pembrolizumab (treatment of adult patients with persistent, recurrent, or metastatic cervical cancer whose tumours express PD-L1 (CPS ≥ 1), as determined by a validated test, in combination with chemotherapy with or without bevacizumab). December 2022.

Colombo N, Dubot C, Lorusso D, et al. Pembrolizumab for persistent, recurrent, or metastatic cervical cancer. N Engl J Med. 2021 Nov 11;385(20):1856-1867. doi: 10.1056/NEJMoa2112435

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L - Other Notes

Calvert Formula

DOSE (mg) = target AUC X (GFR + 25)

- AUC = product of serum concentration (mg/mL) and time (min)
- GFR (glomerular filtration rate) expressed as measured Creatinine Clearance or estimated from Serum Creatinine (by Cockcroft and Gault method or Jelliffe method)

(Calvert AH, Newell DR, Gumbrell LA, et al, Carboplatin dosage: Prospective evaluation of a simple formula based on renal function. J Clin Oncol, 1989; 7: 1748-1756)

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M - Disclaimer

Regimen Abstracts

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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.

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

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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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