

## Regimen Monograph

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## A - Regimen Name

# CRBPPEME Regimen

**CARBO**platin-Pemetrexed

**Disease Site** Lung  
Mesothelioma (Pleural)

**Intent** Curative  
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** An alternative to cisplatin-pemetrexed for the treatment of patients with malignant pleural mesothelioma

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**B - Drug Regimen**

<a href="#">pemetrexed</a>	500 mg /m <sup>2</sup>	IV	Day 1
<a href="#">CARBOplatin</a>	AUC 5*	IV	Day 1

\* 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**

For a usual total of 6 cycles unless disease progression or unacceptable toxicity occurs

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**D - Premedication and Supportive Measures**

**Antiemetic Regimen:** Moderate + NK1 antagonist (Carboplatin AUC  $\geq 5$ )

**Febrile Neutropenia Risk:** Low

**Other Supportive Care:**

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

- Vitamin B12 1000mcg IM every 9 weeks, Folic acid 0.4 - 1 mg PO daily (both starting  $\geq 1$  week prior to pemetrexed administration continue throughout and 3 weeks after last dose of Pemetrexed).
- Dexamethasone 4mg PO BID for 3 days starting day before chemotherapy suggested for rash prophylaxis.
- Note: NSAIDs should be held for 2-5 days prior and 2 days after pemetrexed (refer to pemetrexed monograph)

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## E - Dose Modifications

Doses should be modified according to the protocol by which the patient is being treated. The following recommendations have been adapted from clinical trials or product monographs and could be considered.

### Dosage with toxicity

Do not start a new cycle until ANC  $\geq 1.5 \times 10^9/L$  and platelets  $\geq 100 \times 10^9/L$ . In clinical trials, treatment delays of up to 6 weeks were permitted for toxicity.

Worse toxicity in previous cycle (counts $\times 10^9/L$ )	Carboplatin (% previous dose)*	Pemetrexed (% previous dose)*
ANC $< 0.5$ and platelets $\geq 50$ or 1 <sup>st</sup> episode febrile neutropenia	75%	75%
Platelets $< 50$ and any ANC or 2 <sup>nd</sup> episode febrile neutropenia	50%**	50%**
Grade 3 related organ non-hematologic toxicity (except nausea and/or vomiting)	75%	75%
Grade 4 related organ non-hematologic toxicity	50% or Discontinue	50% or Discontinue
Symptoms suggesting pneumonitis	n/a	Hold and investigate; discontinue if confirmed.
Any occurrence of SJS/TEN	n/a	Discontinue

\*Do not retreat unless platelets  $\geq 100 \times 10^9/L$ , ANC  $\geq 1.5 \times 10^9/L$  and toxicities have recovered to  $\leq$  grade 1

\*\*If toxicity recurs a 3<sup>rd</sup> time, discontinue

### Hepatic Impairment

Pemetrexed is not extensively metabolized in the liver. No dosage adjustment is recommended, but use with caution. No dosage adjustment is recommended for carboplatin.

**Renal Impairment**

Patients with CrCl < 45 ml/min were excluded from clinical trials.

CrCl (ml/min)	Carboplatin	Pemetrexed
≥ 45 ml/min	Use Calvert formula, if appropriate	No change
< 45 ml/min	Discontinue	Discontinue

**Dosage in the Elderly**

Carboplatin: caution should be exercised and dose reduction considered as elderly patients may have more severe myelosuppression and neuropathy.

Pemetrexed: no dosage adjustments are needed, but elderly patients should be monitored closely as more myelosuppression, renal and severe GI effects were noted.

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**F - Adverse Effects**

Refer to [pemetrexed](#), [CARBOplatin](#) drug monograph(s) for additional details of adverse effects.

Very common (≥ 50%)	Common (25-49%)	Less common (10-24%)	Uncommon (< 10%), but may be severe or life-threatening
<ul style="list-style-type: none"> <li>Myelosuppression ± infection, bleeding (may be severe)</li> <li>Nausea, vomiting</li> </ul>	<ul style="list-style-type: none"> <li>Abnormal electrolyte(s) (↓ in Na, K, Ca, Mg)</li> <li>Fatigue</li> </ul>	<ul style="list-style-type: none"> <li>Anorexia</li> <li>Hearing impairment</li> <li>Mucositis</li> <li>Rash</li> <li>Diarrhea</li> </ul>	<ul style="list-style-type: none"> <li>Arrhythmia</li> <li>Arterial / venous thromboembolism</li> <li>Radiation recall reaction</li> <li>GI perforation</li> </ul>

		<ul style="list-style-type: none"> <li>• Nephrotoxicity (may be severe)</li> <li>• ↑ BUN</li> <li>• ↑ LFTs (transient)</li> </ul>	<ul style="list-style-type: none"> <li>• Hemolytic uremic syndrome</li> <li>• Hemolytic anemia</li> <li>• Hemolysis</li> <li>• Peripheral ischemia</li> <li>• Hypersensitivity</li> <li>• Secondary malignancy</li> <li>• Peripheral neuropathy</li> <li>• Visual disorders</li> <li>• Encephalopathy</li> <li>• Pneumonitis</li> </ul>	
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## G - Interactions

Refer to [pemetrexed](#), [CARBOplatin](#) drug monograph(s) for additional details.

- Nephrotoxic drugs (e.g. aminoglycosides) may increase the toxicity of pemetrexed and exacerbate nephro and ototoxicity; caution and monitor closely if used together
- NSAIDs may increase the toxicity of pemetrexed. Hold NSAIDs with shorter half-lives (e.g. ibuprofen) at least 2 days before to 2 days after pemetrexed. Hold NSAIDs with long half-lives (e.g. piroxicam) 5 days before to 2 days after pemetrexed.
- Phenytoin levels may be altered by carboplatin. Monitor levels and adjust the phenytoin dose as required.
- Use with warfarin may increase INR and the risk of bleeding. Monitor INR and adjust the warfarin dose as required.

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**H - Drug Administration and Special Precautions**

Refer to [pemetrexed](#), [CARBOplatin](#) drug monograph(s) for additional details.

**Administration****Carboplatin:**

- Mix in 100mL to 250mL bag (5% Dextrose or Normal Saline).
- Administer over 30 minutes, starting 30 minutes after the end of Pemetrexed.
- Incompatible with sets, needles or syringes containing aluminum – leads to precipitation and loss of potency.
- Protect from light.

**Pemetrexed:**

- Reconstitute as directed with Normal Saline.
- Dilute drug in 100mL (Normal Saline only); Infuse IV over 10 minutes.
- Incompatible with calcium-containing solutions.
- Do not co-administer with other drugs and diluents.
- Keep unopened vials at room temperature. Pemetrexed is not light sensitive.

**Contraindications**

- Patients who have a hypersensitivity to these drugs or other platinum-containing compounds
- Patients with severe renal impairment ( $\text{CrCl} < 45 \text{ ml/min}$ ), severe myelosuppression or bleeding tumours
- Avoid the use of live vaccines

**Warnings/precautions**

- Patients with abnormal renal function or who are receiving concomitant nephrotoxic drugs
- Patients who have received extensive prior treatment, have poor performance status and those over 65 years of age

- Patients with cardiovascular risk factors

### **Pregnancy/lactation**

- These drugs are not recommended in pregnancy.
- Adequate contraception should be used by both sexes during treatment, and for at least **6 months** after the last dose.
- Breastfeeding is not recommended
- Fertility Effects:
  - Carboplatin: Unknown
  - Pemetrexed: Yes (may be irreversible)

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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**

- CBC; baseline and before each cycle
- Liver function tests; baseline and regular
- Renal function tests; baseline and regular, including electrolytes
- Clinical toxicity assessment for neurotoxicity, ototoxicity, hypersensitivity, bleeding, infection, GI, and pulmonary effects; at each visit
- Grade toxicity using the current [NCI-CTCAE \(Common Terminology Criteria for Adverse Events\) version](#)

### **Suggested Clinical Monitoring**

INR for patients receiving warfarin; baseline and regular

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**J - Administrative Information**

Approximate Patient Visit	2 hours
Pharmacy Workload (average time per visit)	33.069 minutes
Nursing Workload (average time per visit)	49.167 minutes

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**K - References**

Carboplatin and pemetrexed drug monographs, Cancer Care Ontario.

Castagneto B, Botta M, Aitini E, et al. Phase II study of pemetrexed in combination with carboplatin in patients with malignant pleural mesothelioma (MPM). Ann Oncol. 2008 Feb;19(2):370-3.

Ceresoli GL, Zucali PA, Favaretto AG, et al. Phase II study of pemetrexed plus carboplatin in malignant pleural mesothelioma. J Clin Oncol. 2006 Mar 20;24(9):1443-8.

Santoro A, O'Brien ME, Stahel RA, et al. Pemetrexed plus cisplatin or pemetrexed plus carboplatin for chemo-naïve patients with malignant pleural mesothelioma: results of the International Expanded Access Program. J Thorac Oncol 2008;3(7):756-63.

**PEBC Advice Documents or Guidelines**

- [Endorsement of the 2018 ASCO Treatment of Malignant Pleural Mesothelioma Guideline](#)

**October 2024** No changes. Republished to display Cancer Type

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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**

*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.*

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