

**Regimen Monograph**

[Regimen Name](#) | [Drug Regimen](#) | [Cycle Frequency](#) | [Premedication and Supportive Measures](#) | [Dose Modifications](#) | [Adverse Effects](#) | [Interactions](#) | [Drug Administration and Special Precautions](#) | [Recommended Clinical Monitoring](#) | [Administrative Information](#) | [References](#) | [Other Notes](#) | [Disclaimer](#)

**A - Regimen Name**

# PEME Regimen

**Pemetrexed****Disease Site** Lung - Non-Small Cell**Intent** Adjuvant  
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**

- Treatment of locally advanced or metastatic non-squamous non-small cell lung cancer after prior therapy
- Maintenance treatment of locally advanced or metastatic non-squamous non-small cell lung cancer, in patients without disease progression, immediately after first-line platinum doublet therapy
- Monotherapy after completion of 3 cycles of cisplatin or carboplatin plus pemetrexed concurrent with radiotherapy

[back to top](#)

## B - Drug Regimen

[pemetrexed](#)

500 mg /m<sup>2</sup>

IV

Day 1

[back to top](#)

## C - Cycle Frequency

### REPEAT EVERY 21 DAYS

Advanced Setting: Until disease progression or unacceptable toxicity

Consolidation after CISPPEME(RT) or CRBPPEME(RT): For a usual total of 4 cycles

[back to top](#)

## D - Premedication and Supportive Measures

**Antiemetic Regimen:** Low

### Other Supportive Care:

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

### Premedication:

- Vitamin supplementation starting  $\geq$  1 week prior to first pemetrexed dose; continue until 3 weeks after last dose to reduce treatment-related toxicities:
  - Folic acid 0.4 mg - 1 mg PO daily
  - Vitamin B<sub>12</sub> 1000 mcg IM q9 weeks
- Dexamethasone (e.g. 4 mg PO BID) beginning on the day before chemotherapy for a total of 3 days to reduce the incidence and severity of cutaneous reactions.

[back to top](#)

## E - Dose Modifications

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

- NSAIDs should be held for at least 2-5 days prior to, and at least 2 days after pemetrexed infusion (see Interactions section).

- Patients should not begin a new treatment cycle unless:
  - ◊ ANC  $\geq 1.5 \times 10^9/L$
  - ◊ Platelets  $\geq 100 \times 10^9/L$
  - ◊ Creatinine clearance is  $\geq 45$  mL/min

### **Dosage with toxicity**

#### **Hematologic:**

<b>Worst toxicity in previous cycle</b>	<b>Grade</b>	<b>Pemetrexed (% previous dose)*</b>
Thrombocytopenic bleeding		50%
ANC	Grade 4	75%
Platelets	$\geq$ Grade 3	
Recurrent myelosuppression after 2 dose reductions	$\geq$ Grade 3	Discontinue

\*Start next cycle only when ANC  $\geq 1.5 \times 10^9/L$ , platelets  $\geq 100 \times 10^9/L$  and related organ/non-hematologic toxicity  $\leq$  grade 2 (or recovery to baseline).

#### **Non-hematologic:**

<b>Worst toxicity in previous cycle</b>	<b>Grade</b>	<b>Pemetrexed (% previous dose)*</b>
Neurotoxicity	Grade 2	100%
	$\geq$ Grade 3	Discontinue
Mucositis	$\geq$ Grade 3	50%
Diarrhea	$\geq$ Grade 3 or requiring hospitalization	75%
Pneumonitis	Any	Hold and investigate; discontinue if confirmed
All other related organ / non-hematologic toxicity	Grade 3	75%
	Grade 4	Discontinue
Stevens-Johnson syndrome	Any	
Toxic epidermal necrolysis		

Recurrent non-hematologic toxicity after 2 dose reductions	≥ Grade 3	
--	-----------	--

\*Start next cycle only when ANC  $\geq 1.5 \times 10^9/L$ , platelets  $\geq 100 \times 10^9/L$  and related organ/non-hematologic toxicity  $\leq$  grade 2 (or recovery to baseline).

### **Hepatic Impairment**

Pemetrexed is not extensively metabolized in the liver. No specific studies have been performed in patients with moderate or severe hepatic impairment. Pemetrexed should be used with caution in patients with hepatic impairment.

### **Renal Impairment**

Use with caution as pemetrexed exposure is increased in renal impairment.

Creatinine clearance (mL/min)	Pemetrexed (% of previous dose)
$\geq 45$	100%*
$< 45$	Discontinue

\* Exercise caution with co-administration of NSAIDs for patients with CrCl 45-79mL/min

### **Dosage in the Elderly**

No dose adjustments are needed but patients should be monitored closely. In maintenance therapy, more frequent myelosuppression, renal and severe GI adverse events were noted in patients  $\geq 65$  years of age. There was no observed effect of age on pemetrexed pharmacokinetics over the range of 26 to 80 years.

[back to top](#)

## F - Adverse Effects

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

(Continued on next page)

Common (25-49%)	Less common (10-24%)	Uncommon (< 10%), but may be severe or life-threatening
<ul style="list-style-type: none"> <li>• Fatigue</li> <li>• Nausea, vomiting</li> </ul>	<ul style="list-style-type: none"> <li>• Anorexia</li> <li>• Mucositis (including esophagitis, may be severe)</li> <li>• Myelosuppression ± infection, bleeding</li> <li>• Rash (may be severe)</li> <li>• Diarrhea (may be severe)</li> <li>• ↑ LFTs (may be severe)</li> </ul>	<ul style="list-style-type: none"> <li>• Neuropathy</li> <li>• Eye disorders (including conjunctivitis and increased lacrimation)</li> <li>• Creatinine increased</li> <li>• Arrhythmia</li> <li>• Arterial / venous thromboembolism</li> <li>• GI perforation</li> <li>• Hypersensitivity</li> <li>• Radiation recall reaction</li> <li>• Hemolysis</li> <li>• Pneumonitis</li> </ul>

[back to top](#)

## G - Interactions

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

- Hold NSAIDs with short half-lives (eg. ibuprofen) for at least 2 days before to at least 2 days after pemetrexed administration in patients with mild to moderate renal impairment (CrCl 45–79 mL/min).
- Hold NSAIDs with long half-lives (eg. piroxicam) for at least 5 days before to at least 2 days after pemetrexed administration.

[back to top](#)

---

## H - Drug Administration and Special Precautions

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

### Administration:

- Reconstitute as directed with Normal Saline (preservative free).
- Dilute drug to a total volume of 100mL with normal saline only and infuse intravenously over 10 minutes.
- Reconstituted solution maybe colourless to yellow or green-yellow.
- 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 with a known hypersensitivity to the drug/excipients.
- Concomitant use of yellow fever vaccine.

### Other Warning/Precautions:

- Exercise caution in patients with pre-existing cardiovascular risk factors.
- Patients with moderate-severe renal dysfunction (CrCl < 45 mL/min).
- Avoid the use of live or live-attenuated vaccines.

### Pregnancy/Lactation:

- Pemetrexed is not recommended for use 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.

- 
- Pemetrexed may cause irreversible infertility.
    - Sperm preservation should be considered prior to starting treatment in males.

[back to top](#)

## 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, before each cycle, on days 8 and 15 of each cycle (for nadir and recovery), and as clinically indicated
- Liver function tests; baseline and at each visit
- Renal function tests; baseline and at each visit
- Clinical toxicity assessment for fatigue, pneumonitis, thromboembolism, mucositis, diarrhea, neurotoxicity, infection, bleeding and rash; at each visit
- Grade toxicity using the current [NCI-CTCAE \(Common Terminology Criteria for Adverse Events\) version](#)

[back to top](#)

## J - Administrative Information

Approximate Patient Visit	0.5 hour
Pharmacy Workload (average time per visit)	21.349 minutes
Nursing Workload (average time per visit)	36.667 minutes

[back to top](#)

## K - References

Choy H, Schwartzberg LS, Dakhil SR, et al. Phase 2 study of pemetrexed plus carboplatin, or pemetrexed plus cisplatin with concurrent radiation therapy followed by pemetrexed consolidation in

---

patients with favourable-prognosis inoperable stage IIIA/B non-small-cell lung cancer. J Thorac Oncol.2018;8: 1308-1316.

Ciuleanu T, Brodowicz T, Zielinski C, et al. Maintenance pemetrexed plus best supportive care versus placebo plus best supportive care for non-small-cell lung cancer: a randomized, double-blind, phase 3 study. Lancet 2009; 374: 1432-40.

Govindan R, Bogart J, Stinchcombe T, et al. Randomized phase II study of pemetrexed, carboplatin, and thoracic radiation with or without cetuximab in patients with locally advanced unresectable non-small-cell lung cancer: cancer and leukemia group B trial 30407. J Clin Oncol. 2011;29:3120-3125.

Hanna N, Shepherd FA, Fossella FV, et al. Randomized phase III trial of pemetrexed versus docetaxel in patients with non-small cell lung cancer previously treated with chemotherapy. J Clin Oncol 2004; 22(9): 1589-97.

Paz-Ares L, de Marinis F, Dediu M, et al. Maintenance therapy with pemetrexed plus best supportive care versus placebo plus best supportive care after induction therapy with pemetrexed plus cisplatin for advanced non-squamous non-small-cell lung cancer (PARAMOUNT): a double-blind, phase 3, randomised controlled trial. Lancet Oncol 2012;13(3):247-55.

Senan S, Brade A, Wang L, et al. PROCLAIM: Randomized Phase III Trial of Pemetrexed-Cisplatin or Etoposide-Cisplatin Plus Thoracic Radiation Therapy Followed by Consolidation Chemotherapy in Locally Advanced Nonsquamous Non–Small-Cell Lung Cancer. J Clin Oncol. 2016;34:953-962. Pemetrexed drug monograph, Cancer Care Ontario.

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

- [Systemic Treatment for Patients with Advanced Non-Small Cell Lung Cancer](#)
- [The Use of Systemic Treatment in the Maintenance of Patients with Non-small Cell Lung Cancer](#)

**August 2021** Modified Rationale and Uses section

[back to top](#)

### **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 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.

While care has been taken in the preparation of the information contained in the Formulary, 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.

CCO and the Formulary's content providers shall have no liability, whether direct, indirect, consequential, contingent, special, or incidental, related to or arising from the information in the Formulary or its use thereof, whether based on breach of contract or tort (including negligence), and even if advised of the possibility thereof. Anyone using the information in the Formulary does so at his or her own risk, and by using such information, agrees to indemnify CCO and its content providers from any and all liability, loss, damages, costs and expenses (including legal fees and expenses) arising from such person's use of the information in the Formulary.

[back to top](#)