Regimen Monograph

A - Regimen Name

CISPPEME Regimen

CISplatin-Pemetrexed

Disease Site	Lung - Non-Small Cell
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 treatment of locally advanced or metastatic non-squamous non-small cell lung cancer (NSCLC)

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B - Drug Regimen

pemetrexed	500 mg /m²	IV in 100mL NS over 10 minutes	Day 1
CISplatin	75 mg /m²	IV over 2 hours; 30 minutes after end of Pemetrexed	Day 1

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C - Cycle Frequency

REPEAT EVERY 21 DAYS

For a usual total of 4 to 6 cycles in responding patients, unless disease progression or unacceptable toxicity occurs

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D - Premedication and Supportive Measures

Antiemetic Regimen: High

Other Supportive Care:

- Pemetrexed:
- Vitamin B12 1000mcg IM every 9 weeks, Folic acid 0.4 - 1 mg PO daily (both starting ≥ 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)

- Cisplatin:
- Standard regimens for Cisplatin premedication and hydration should be followed. Refer to Cisplatin 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

Worst toxicity in previous cycle	Pemetrexed (% previous dose)*	Cisplatin (% previous dose, if applicable)*
Thrombocytopenic bleeding	50%	50%
Grade 4 ANC or ≥ Grade 3 platelets	75%	75%
Grade 2 neurotoxicity	100%	50%
Grade 3 or 4 mucositis	50%	100%
Diarrhea requiring hospitalization, or grade 3 or 4	75%	75%
Grade 3 or 4 neurotoxicity	Discontinue	
Symptoms suggesting pneumonitis	Hold and investigate; discontinue if confirmed	
Other Grade 3 related organ / non-hematologic toxicity	75%	75%
Other Grade 4 related organ / non-hematologic toxicity	Discontinue	
Grade 3 or 4 toxicity after 2 prior dose reductions, any occurrence of Stevens-Johnson syndrome, Toxic epidermal necrolysis	Discontinue	
*Start next cycle only when ANC ≥ 1.5 x 10^9/L, platelets ≥ 100 x 10^9/L and related organ/non-hematologic toxicity ≤ 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. Refer to the dose modification table above.
CISplatin: No adjustment required.

Renal Impairment

Creatinine clearance (mL/min)	Cisplatin (% previous dose)	Pemetrexed (% previous dose)
61-79	100%	100%; but use NSAIDs with extreme caution
45-60	75%	
30-<45	50%	Discontinue
<30	Discontinue	Discontinue

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F - Adverse Effects

Refer to pemetrexed, CISplatin drug monograph(s) for additional details of adverse effects

Most Common Side Effects	Less Common Side Effects, but may be Severe or Life-Threatening
• Nausea, vomiting • Myelosuppression ± bleeding, infection (may be severe) • Fatigue • Diarrhea (may be severe) • Mucositis • Anorexia • Neurotoxicity (including ototoxicity, may be severe) • Nephrotoxicity (may be severe) • Rash (may be severe)	• Pneumonitis • Arterial thromboembolism • Venous thromboembolism • Arrhythmia • Hemolysis • Hypersensitivity • GI perforation • ↑ LFTs

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G - Interactions

Refer to pemetrexed, CISplatin drug monograph(s) for additional details

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H - Drug Administration and Special Precautions

Refer to pemetrexed, CISplatin drug monograph(s) for additional details

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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

- Clinical toxicity assessment (including neurologic, ototoxicity, fatigue, diarrhea, mucositis, thromboembolism, bleeding, infection, pneumonitis, rash); at each visit
- CBC before each cycle, including nadir counts
- Baseline and regular renal function tests (including electrolytes and magnesium) and urinalysis
- Baseline and regular liver functions tests

- Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for Adverse Events) version

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J - Administrative Information

Approximate Patient Visit	4-6 hours
Pharmacy Workload (average time per visit)	41.935 minutes
Nursing Workload (average time per visit)	46.667 minutes

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K - References

Cisplatin, pemetrexed drug monographs, Cancer Care Ontario.

Scagliotti GV, Park K, Patil S, et al. Survival without toxicity for cisplatin plus pemetrexed versus cisplatin plus gemcitabine in chemonaıve patients with advanced non-small cell lung cancer: A risk-benefit analysis of a large phase III study. Eur J Cancer 2009; 45: 2298 -303.

Scagliotti G, Parikh P, von Pawal J et al. Phase III Study Comparing Cisplatin Plus Gemcitabine With Cisplatin Plus Pemetrexed in Chemotherapy-Naïve Patients With Advanced-Stage Non–Small-Cell Lung Cancer. JCO 2008; 26: 3543-51.

PEBC Advice Documents or Guidelines

- Systemic Treatment for Patients with Advanced Non-Small Cell Lung Cancer

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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.

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