Regimen Monograph

A - Regimen Name

CISPETOP(RT) Regimen

CISplatin-Etoposide

Disease Site	Lung - Non-Small Cell Lung - Small Cell
Intent	Neoadjuvant 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.

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B - Drug Regimen

CISplatin	50 mg /m²	IV	Days 1, 8, 29, 36
etoposide	50 mg /m²	IV	Days 1 to 5 and 29 to 33

Concurrent with RADIOTHERAPY

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C - Cycle Frequency

8 WEEK CYCLE

One cycle during concurrent radiotherapy
Some centres give an additional 8-week cycle of cisplatin and etoposide after completion of radiation

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D - Premedication and Supportive Measures

Antiemetic Regimen: Moderate (D1, 8, 29, 36)
Low (D2-5, 30-33)

Febrile Neutropenia Risk: High

Consider G-CSF prophylaxis for patients at high risk of febrile neutropenia. See G-CSF recommendations.

Other Supportive Care:

Also refer to CCO Antiemetic Recommendations.

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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 are in use at some centres.

Dosage with toxicity

Hematologic Toxicities: Refer to Appendix 6 for general recommendations.

In clinical trials,

- Cisplatin was **omitted** on day 8 or 36 for grade 4 neutropenia or febrile neutropenia, during

concurrent chemoradiotherapy. A break in radiation was allowed for grade 4 neutropenia.

- Cisplatin and etoposide were **delayed** 1 week on day 29 for an ANC < 1.5 x 10^9/L or a platelet count < 100 x 10^9/L.
- Etoposide was **reduced** to 4 days, if febrile neutropenia occurred during the previous cycle.

Non-Hematologic Toxicities

In clinical trials:

- Cisplatin was **omitted** on day 8 or 36 for grade 4 esophagitis. A break in radiation was allowed for severe esophagitis requiring parenteral alimentation.
- Cisplatin and etoposide were **delayed** 1 week on day 29 for > grade 3 non-hematological toxicity.

Hepatic Impairment

Bilirubin	**Action**
1. If Bilirubin 1-2 x ULN	**REDUCE** Etoposide to **50%** dose
2. If Bilirubin 2-4 x ULN	**REDUCE** Etoposide to **25%** dose
3. If Bilirubin > 4 x ULN	**OMIT** Etoposide

Renal Impairment

Creatinine Clearance	**Action**
1. If CrCl 10 – 50 mL/min	**OMIT** Cisplatin* and **REDUCE** Etoposide to **75%** dose
2. If CrCl < 10 mL/min	**REDUCE** Etoposide to **50%** dose, and **OMIT** Cisplatin* dose

*In clinical trials:

Cisplatin was omitted if the serum creatinine was > 1.7 mg/dL and the calculated creatinine clearance was < 45 mL/min. After a one week delay, cisplatin was reduced to 25 mg/m^2, if the serum creatinine was > 1.7 mg/dL but < 2 mg/dL and the calculated creatinine clearance was > 45 mL/min.

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F - Adverse Effects

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

Most Frequently Occurring Adverse Effects

- Nausea and Vomiting
- Nephrotoxicity
- Neurotoxicity and ototoxicity
- Myelosuppression
- Fatigue

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G - Interactions

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

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H - Drug Administration and Special Precautions

Refer to CISplatin, etoposide 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 neurotoxicity, ototoxicity); at each visit
- CBC before each cycle. Interim counts should be done in first cycle and repeated if dose modifications necessary
- Baseline and regular liver and renal function tests (including electrolytes and magnesium) and urinalysis
- Blood pressure monitoring during infusion

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

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J - Administrative Information

Approximate Patient Visit	Days 1, 8, 29, 36: 4 hours; Etoposide only: 1 hour
Pharmacy Workload (average time per visit)	13.451 minutes
Nursing Workload (average time per visit)	40.833 minutes

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K - References

Albain KS, Swann RS, Rusch VR, et al. Radiotherapy plus chemotherapy with or without surgical resection for stage III non-small-cell lung cancer: a phase III randomised controlled trial. Lancet 2009; 374: 379-86.

Cisplatin and etoposide drug monographs, Cancer Care Ontario.

PEBC Advice Documents or Guidelines

- Treatment of Patients with Stage III (N2 or N3) Non-Small Cell Lung Cancer
- Initial Management of Small Cell Lung Cancer (Limited and Extensive Stage) and the Role of Thoracic Radiotherapy and First-Line Chemotherapy

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M - Disclaimer

Regimen Abstracts

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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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