Regimen Monograph

A - Regimen Name

CISPETOP(3D) Regimen

CISplatin-Etoposide

Disease Site	Unknown Primary Poorly-Differentiated Cancer
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.

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B - Drug Regimen

CISplatin	25 mg /m²	IV	Days 1 to 3
etoposide	100 mg /m²	IV	Days 1 to 3

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C - Cycle Frequency

REPEAT EVERY 21 DAYS

Until disease progression or unacceptable toxicity; usually up to 6 cycles due to cumulative cisplatin toxicity

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D - Premedication and Supportive Measures

Antiemetic Regimen: Moderate

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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 may be considered.

Dosage with toxicity

Hematologic Toxicities: See Appendix 6 for general recommendations.

Hepatic Impairment

Bilirubin	**etoposide**
1-2 x ULN	↓ to **50%** dose
2-4 x ULN	↓ to **25%** dose
>4 x ULN	**OMIT**

Renal Impairment

Creatinine Clearance (mL/min)	CISplatin* (% previous dose)	etoposide (% previous dose)
10-50	↓ to **75%** or **50%** dose	↓ to **75%** dose
<10	**OMIT**	↓ to **50%** or **OMIT**

*See "Dose Modification" section of cisplatin drug monograph

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F - Adverse Effects

Refer to CISplatin, etoposide 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 • Alopecia • Nephrotoxicity (may be severe) • Neurotoxicity (includes ototoxicity) • Myelosuppression +/- infection, bleeding (may be severe) • Anorexia • Diarrhea • Mucositis • Abnormal electrolytes	• ↑ LFTs • Hypersensitivity • Hypotension • Arrhthymia • Arterial thromboembolism • Venous thromboembolism • Pneumonitis • Seizure • Encephalopathy • Vasculitis • Tumour lysis syndrome

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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

- CBC; Baseline and before each cycle
- Liver function tests; Baseline and before each cycle
- Renal function tests; Baseline and before each cycle
- Electrolytes, including magnesium, sodium, potassium, phosphate and calcium; Baseline and before each cycle
- Blood pressure; Baseline and at each treatment
- Audiogram; Baseline and as clinically indicated
- Clinical toxicity assessment of infection, bleeding, nausea/vomiting, neurotoxicity, ototoxicity, thromboembolism; at each visit

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

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J - Administrative Information

Approximate Patient Visit	2 to 3 hours

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K - References

Greco FA, Johnson DH, Hainsworth JD. Etoposide/cisplatin-based chemotherapy for patients with metastatic poorly differentiated carcinoma of unknown primary site. Seminars in Oncology 1992 Dec; 19(6 Suppl 13): 14-18.

Voog E, Merrouche Y, Trillet-Lenoir V, et al. Multicentric phase II study of cisplatin and etoposide in patients with metastatic carcinoma of unknown primary. Am J Clin Oncol 2000 Dec; 23(6): 614-616.

March 2017 modified adverse effects, cycle frequency and monitoring sections

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L - Other Notes

May be more effective if cisplatin given first, followed by etoposide (Maksymiak AW, J Clin Oncol, 1994; 12: 70-76)

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M - Disclaimer

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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