Regimen Monograph

A - Regimen Name

CISPETOP(3D) Regimen

CISplatin-Etoposide

Disease Site	Breast Gastrointestinal - Colorectal Gastrointestinal - Esophagus Gastrointestinal - Gastric / Stomach Gastrointestinal - Hepatobiliary / Liver / Bile Duct Gastrointestinal - Pancreas Genitourinary - Bladder / Urothelial Genitourinary - Prostate Gynecologic - Cervix Gynecologic - Endometrial Gynecologic - Ovary Head and Neck Lung - Small Cell
Intent	Adjuvant
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 small cell carcinoma

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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

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

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D - Premedication and Supportive Measures

Antiemetic Regimen: Moderate

Febrile Neutropenia Risk: Moderate

Other Supportive Care:

Also refer to CCO Antiemetic Summary

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E - Dose Modifications

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

Dosage with toxicity

Hematologic Toxicities: See appendix 6 for general recommendations.

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
If CrCl 10 – 50 mL/min	**REDUCE** Cisplatin* to **75%** or **50%** dose AND **REDUCE** Etoposide to **75%** dose
If CrCl < 10 ml/min	**REDUCE** Etoposide to **50%** dose, or **OMIT** dose AND **OMIT** Cisplatin* dose

*See Dosing section of CISPLATIN drug monograph (dosage reduction).

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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) • Ototoxicity • Myelosuppression +/- infection, bleeding • Anorexia • Diarrhea • Mucositis • Abnormal electrolytes	• Increased LFTs • Hypersensitivity • Arterial thromboembolism • Venous thromboembolism • Pneumonitis • Vasculitis

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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 stomatitis, neurotoxicity, ototoxicity); at each visit
- CBC; baseline and before each cycle. Interim counts should be done in first cycle and repeated if dose modifications necessary.
- Baseline and regular liver function tests
- Baseline and regular 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	2 to 3 hours
Pharmacy Workload (average time per visit)	17.790 minutes
Nursing Workload (average time per visit)	49.167 minutes

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K - References

Cisplatin, etoposide drug monographs, Cancer Care Ontario.

Breast:

Adegbola T, Connolly CE, Mortimer G. Small cell neuroendocrine carcinoma of the breast: a report of three cases and review of the literature. J Clin Pathol 2005; 58(7): 775–8.

Kanat O, Kilickap S, Korkmaz T, et al. Primary small cell carcinoma of the breast: report of seven cases and review of the literature. Tumori 2011;97(4):473-8.

Lung:

Evans WK, Osoba D, Feld R, et al, Etoposide (VP-16) and cisplatin: An effective treatment for relapse in small-cell lung cancer. J Clin Oncol, 1985; 3: 65-71

Fukuoka M, Furuse K, Saijo N, et al. Randomized trial of cyclophosphamide, doxorubicin, and vincristine versus cisplatin and etoposide versus alteration of these regimens in small cell lung cancer. JNCI, 1991; 83: 855-861

Maksymiuk AW, Jett JR, Earle JD, Su JQ, Diegert FA, Mailliard JA, et al. Sequencing and schedule effects of cisplatin plus etoposide in small-cell lung cancer: results of a North Central Cancer Treatment Group randomized clinical trial. J Clin Oncol 1994;12:70-6.

Roth BJ, Johnson DH, Einhorn LH, et al. Randomized study of cyclophosphamide, doxorubicin, and vincristine versus cisplatin and etoposide versus alteration of these two agents in extensive small cell lung cancer: a phase III trial of the Southeastern Cancer Study Group. J Clin Oncol, 1992; 10: 282-291

Endometrial:

Hunter RW, Williams KE, Buck M, et al. Metastatic small cell carcinoma of the endometrium: prolonged remission and possible cure following chemotherapy. Int J Gynecol Cancer. 1994;4(2):127-130.

Bladder:

Bex A, Nieuwenhuijzen JA, Kerst M, et al. Small cell carcinoma of bladder: a single-center prospective study of 25 cases treated in analogy to small cell lung cancer. Urology. 2005 Feb;65(2):295-9.

Siefker-Radtke AO, Kamat AM, Grossman HB, et al. Phase II clinical trial of neoadjuvant alternating doublet chemotherapy with ifosfamide/doxorubicin and etoposide/cisplatin in small-cell urothelial cancer. J Clin Oncol. 2009 Jun 1;27(16):2592-7.

August 2018 removed archived PEBC guideline

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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

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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