Regimen Monograph

A - Regimen Name

CISPTOPO Regimen

Topotecan-CISplatin

Disease Site	Gynecologic - Cervix
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	Patients with metastatic, recurrent cervical cancer should be offered the opportunity to participate in randomized trials. If trials are not available, cisplatin in combination with topotecan should be offered to women for whom first line treatment with chemotherapy is indicated

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B - Drug Regimen

topotecan	0.75 mg /m²	IV	Days 1 to 3
CISplatin	50 mg /m²	IV	Day 1 (give after topotecan)

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C - Cycle Frequency

REPEAT EVERY 21 DAYS

Until evidence of stable disease, metastatic progression or limited by toxicity

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D - Premedication and Supportive Measures

Antiemetic Regimen: Moderate (D1)
Low (D2,3)

Other Supportive Care:
Standard regimens for Cisplatin premedication and hydration should be followed. Refer to Cisplatin monograph

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

See Appendix 6 for general recommendations.

Prior to the first cycle, patients must have a baseline neutrophil count of ≥ 1.5 x 10^9/L, a platelet count of ≥ 100 x 10^9/L, and a hemoglobin level of ≥ 90 g/L.

Do not retreat with topotecan and cisplatin, unless absolute neutrophil count recovers to ≥ 1.5 X 10^9/L and platelet count ≥ 100 X 10^9/L. Treatment to be delayed until blood counts have returned to acceptable levels.

Severe hematological toxicities should be managed by dose modification and the use of granulocyte-colony–stimulating factors (G-CSFs) in subsequent cycles.

At the time of retreatment, chemotherapy doses were adjusted based on nadir blood counts and interval toxicity:

<table>
<tr><th>Toxicity (Grade/ Counts x 10^9)</th><th></th><th>Toxicity (Grade/ Counts x10^9)</th><th>Topotecan[1]</th><th>Cisplatin [1]</th></tr>
<tr><td>Platelets 25-50</td><td>and/or</td><td>ANC 0.5-1</td><td rowspan="2">↓ by 20%[2]</td><td rowspan="2">↓ by 20%</td></tr>
<tr><td colspan="3">Febrile Neutropenia</td></tr>
<tr><td>Platelets < 25</td><td>and/or</td><td>ANC < 0.5</td><td>↓ by 40%</td><td>↓ by 40%</td></tr>
<tr><td colspan="3">Grade 2 Neurotoxicity</td><td>No change</td><td>Consider ↓</td></tr>
<tr><td colspan="3">Grade 3 Neurotoxicity</td><td>No change</td><td>Hold and ↓ by 20%</td></tr>
<tr><td colspan="3">Grade 3 other non-hematological</td><td>Hold and ↓ by 20%</td><td>Hold and ↓ by 20%</td></tr>
<tr><td colspan="3">Grade 4 other non-hematological</td><td>Discontinue</td><td>Discontinue</td></tr>
<tr><td colspan="5">[1] Do not retreat until toxicity ≤ grade 2 and ANC ≥ 1.5 X 10^9 /L and platelet count ≥ 100 X 10^9 /L.
[2] Consider growth factor support if febrile neutropenia recurs after dose ↓</td></tr>
</table>

Hepatic Impairment

Bilirubin (µmol/L)	Cisplatin (% previous dose)	Topotecan dose
<171	No dose adjustment required	No dose adjustment required
≥ 171		No data found

Renal Impairment

Creatinine clearance (mL/min)	Cisplatin (% previous dose)	Topotecan (% previous dose)
40-50	50-75%	No change
20 - <40		50%
10 - <20	OMIT	CONTRAINDICATED
<10		

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F - Adverse Effects

Refer to topotecan, 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
• Myelosuppression ± infection and bleeding (may be severe) • Nausea and vomiting • Neurotoxicity and ototoxicity • Nephrotoxicity ± electrolyte abnormality (may be severe) • Alopecia • Fatigue • Diarrhea (may be severe) • Rash (may be severe) • Stomatitis	• Interstitial lung disease • Arterial thromboembolism • Hemolysis, thrombotic microangiopathy

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G - Interactions

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

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H - Drug Administration and Special Precautions

Refer to topotecan, 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 gastrointestinal, infection, bleeding, pulmonary, skin toxicity, neurotoxicity and ototoxicity).
- 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 (including electrolytes and magnesium) 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	Day 1: 3-4 hours; Days 2-3: 0.5 hour
Pharmacy Workload (average time per visit)	17.887 minutes
Nursing Workload (average time per visit)	53.333 minutes

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K - References

Cisplatin and topotecan drug monographs, Cancer Care Ontario.

Long HJ, III, Bundy BN, Grendys EC, et al. Randomized phase III trial of cisplatin with or without topotecan in carcinoma of the uterine cervix: a Gynecologic Oncology Group Study. J Clin Oncol. 2005;23(21):4626-33.

PEBC Advice Documents or Guidelines

- Systemic Treatment for Recurrent, Metastatic, or Persistent Cervical Cancer

June 2021 Removed "unfunded" flag for topotecan

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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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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.

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