**Regimen Monograph**



## A - Regimen Name

# CYCLTOPO Regimen

**Topotecan-Cyclophosphamide**

| | |
|---|---|
| **Disease Site** | Sarcoma - Ewing's<br>Sarcoma - Soft Tissue |
| **Intent** | Palliative |
| **Regimen Category** | **Evidence-Informed :**<br><br>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

| | | | |
|---|---|---|---|
| **cyclophosphamide** | 250 mg /m² | IV | Days 1 to 5 |
| **topotecan** | 0.75 mg /m² | IV | Days 1 to 5 |

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## C - Cycle Frequency

**REPEAT EVERY 21 DAYS**

Until disease progression or unacceptable toxicity

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## D - Premedication and Supportive Measures

**Antiemetic Regimen:** Moderate

**Other Supportive Care:**

- Consider prophylactic growth factor support (according to local practice) especially for heavily pretreated patients.
- Ensure patient receives appropriate PO/IV hydration.

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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

| Toxicity | Topotecan (% previous dose)* | Cyclophosphamide (% previous dose)* |
|---|---|---|
| Grade 4 neutropenia ≥ 7 days, or<br>Febrile neutropenia, or<br>Previous delay due to neutropenia | ↓ 20% | ↓ 20% |
| Platelets ≤ 25 X $10^9$/L or bleeding | ↓ 20% | ↓ 20% |
| Grade 3 non-hematological toxicities | ↓ 20% | ↓ 20% |
| Grade 4 non-hematological toxicities | Discontinue | Discontinue |
| Cystitis | No change | Consider dose reduction |

*Do not retreat until major organ toxicities ≤ grade 2, neutrophils ≥ 1.5 X $10^9$/L; platelets ≥ 100 X $10^9$/L, and hemoglobin ≥ 90 g/L (after transfusion if necessary).

### Hepatic Impairment

| Topotecan | Cyclophosphamide |
|---|---|
| No adjustments required for bilirubin < 171 µmol/L | No adjustments required |

### Renal Impairment

| Creatinine Clearance (mL/min) | Topotecan (% previous dose) | Cyclophosphamide (% previous dose) |
|---|---|---|
| >40 | 100% | 100% |
| >30-40 | 50% | |
| 20-30 | | 50-75% |
| 10-<20 | DISCONTINUE | |
| <10 | | 50% or OMIT |

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## F - Adverse Effects

Refer to cyclophosphamide, topotecan 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)<br>• Alopecia<br>• Diarrhea (may be severe)<br>• Constipation, abdominal pain<br>• Mucositis<br>• Nausea and vomiting<br>• Dyspnea/cough (may be severe)<br>• Anorexia<br>• Headache, pain<br>• Rash (may be severe)<br>• Fatigue | • Hypersensitivity<br>• GI obstruction<br>• Pneumonitis<br>• ↑ LFTs<br>• Arterial/venous thromboembolism<br>• Cardiotoxicity<br>• ↑ QTc<br>• Nephrotoxicity, SIADH<br>• Pancreatitis<br>• Tumour lysis syndrome<br>• Secondary malignancies<br>• Cystitis |

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## G - Interactions

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

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## H - Drug Administration and Special Precautions

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

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## I - Recommended Clinical Monitoring

Recommended Clinical Monitoring

- Baseline and regular CBC – counts must be assessed prior to each cycle.
- Clinical toxicity assessment of infection GI, pulmonary, dermatologic, GU effects.
- Baseline and regular hepatic and renal function tests and urinalysis
- 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 hours |
| Pharmacy Workload (average time per visit) | 24.841 minutes |
| Nursing Workload (average time per visit) | 41.667 minutes |

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## K - References

Hunold A, Weddeling N, Paulussen M, et al. Topotecan and cyclophosphamide in patients with refractory or relapsed Ewing tumors. Pediatric Blood & Cancer 2006; 47: 795–800.

Saylors RL, Stine KC, Sullivan J, et al. Cyclophosphamide plus topotecan in children With recurrent or refractory solid tumors: A Pediatric Oncology Group Phase II Study. J Clin Oncol 2001; 19: 3463-9.

**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.*

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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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