

CYCLOPHOSPHAMIDE TOPOTECAN

INDICATION (ICD10) C40, C41, C49

1. Recurrent and primary refractory Ewing sarcoma. PS 0, 1, 2

REGIMEN

Days 1 to 5

TOPOTECAN 0.75mg/m² in 50ml sodium chloride 0.9% IV infusion over 30 minutes

CYCLOPHOSPHAMIDE 250mg/m² in 250ml sodium chloride 0.9% IV infusion over 60 minutes

CYCLE FREQUENCY AND NUMBER OF CYCLES

Every 21 days for 6 cycles

ANTI-EMETICS

Moderate emetic risk days 1, 2, 3, 4 and 5

CONCURRENT MEDICATION REQUIRED

Cyclophosphamide	Ensure mesna administered, using separate lumen from cyclophosphamide. Ensure adequate oral fluid intake.
Topotecan	None required
GCSF	To maintain dose intensity (starting at least 24 hours after chemotherapy)

EXTRAVASATION AND TYPE OF LINE / FILTERS

Cyclophosphamide – neutral

Topotecan - exfoliant

Peripheral line

INVESTIGATIONS

Blood results required before SACT administration

FBC, U&E and LFTs every cycle

Neutrophils x 10⁹/L ≥1.0

Platelets x 10⁹/L ≥75

Ideally DTPA GFR should be used

Creatinine clearance (GFR) calculated, at the Consultants discretion

Serum creatinine

Baseline weight and every cycle

MAIN TOXICITIES AND ADVERSE REACTIONS

Cyclophosphamide	may irritate bladder, drink copious volumes of water. Haemorrhagic cystitis: Microscopic haematuria give 2000mL/m ² /day fluid + mesna100mg/m ² every 8 hours Macroscopic haematuria: stop cyclophosphamide – next cycle admit for hydration (2L/m ² /24 hours) + mesna
Topotecan	Interstitial lung disease Haematological toxicity

INTERACTIONS WHICH MAY REQUIRE DOSE MODIFICATIONS

(not exhaustive list check SPC/BNF/Stockleys)

Cyclophosphamide	Cytochrome P450 enzyme inducers (e.g. rifampicin, carbamazepine, phenytoin, St Johns Wort, corticosteroids): may increase active cyclophosphamide metabolites. Allopurinol, Cimetidine and protease inhibitors: may increase active metabolites. Aprepitant, Ciprofloxacin, Fluconazole, Itraconazole: may reduce activation of cyclophosphamide and alter the effectiveness of treatment. Grapefruit juice: decreased or delayed activation of cyclophosphamide. Patients should be advised to avoid grapefruit juice.
Topotecan	Amiodarone, verapamil, azithromycin, clarithromycin, ciclosporin, azoles, vemurafenib may increase exposure to topotecan

DOSE MODIFICATIONS

Haematological

Topotecan

Day 21 despite GCSF delayed >14 days:

First delay give 80% topotecan

repeated delay give 60% topotecan

Hepatic impairment

Topotecan

Bilirubin >170µmol/L – clinical decision.

Renal impairment

Cyclophosphamide

CrCl 10-29ml/min	Consider giving 75% dose
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Topotecan

CrCl >40ml/min	give 100% dose
CrCl 20-39ml/min	give 50% dose
CrCl <20ml/min	not recommended

REFERENCES

- Saylors RL, 3rd, Stine KC, Sullivan J, Kepner JL, Wall DA, Bernstein ML, 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(15):3463-9.