**Systemic Anti Cancer Treatment Protocol**

# Cyclophosphamide & Topotecan
## Sarcoma

**PROTOCOL REF: MPHACYTOSA**
**(Version No: 1.0)**

## Approved for use in:

Ewing's sarcoma – 2nd line onwards

Rhabdomyosarcoma

## Dosage:

| Drug | Dosage | Route | Frequency |
|---|---|---|---|
| Topotecan | 0.75mg/m$^2$ days 1 to 5 | IV | Every 21 days |
| Cyclophosphamide | 250mg/m$^2$ days 1 to 5 | IV | Every 21 days |

**Supportive treatments:**

**Anti –emetic risk - moderate**

Dexamethasone tablets, 4mg twice daily for 3 days

Domperidone 10mg oral tablets, up to 3 times a day or as required

If haemorrhagic cystitis develops, oral mesna can be added to the regimen, for example 400mg one hour before and then repeated at 2 hours and 4 hours after the cyclophosphamide.

## Extravasation risk:

Topotecan: exfoliant
Cyclophosphamide: neutral

## Administration:

| Day | Drug | Dosage | Route | Diluent and Rate |
|---|---|---|---|---|
| 1 | Dexamethasone<br>30 mins before chemotherapy | 8mg | PO | |
| 1 | Ondansetron<br>30 mins before chemotherapy | 16mg | PO | |
| 1 | **Topotecan** | 0.75mg/m$^2$ | IV | In 50mL sodium chloride 0.9% over 30 minutes |
| 1 | **Cyclophosphamide** | 250mg/m$^2$ | IV | IV bolus over 30 minutes |
| 2 | Dexamethasone<br>30 mins before chemotherapy | 8mg | PO | |
| 2 | Ondansetron<br>30 mins before chemotherapy | 16mg | PO | |
| 2 | **Topotecan** | 0.75mg/m$^2$ | IV | In 50mL sodium chloride 0.9% over 30 minutes |
| 2 | **Cyclophosphamide** | 250mg/m$^2$ | IV | IV bolus over 30 minutes |
| 3 | Dexamethasone<br>30 mins before chemotherapy | 8mg | PO | |
| 3 | Ondansetron<br>30 mins before chemotherapy | 16mg | PO | |
| 3 | **Topotecan** | 0.75mg/m$^2$ | IV | In 50mL sodium chloride 0.9% over 30 minutes |
| 3 | **Cyclophosphamide** | 250mg/m$^2$ | IV | IV bolus over 30 minutes |
| 4 | Dexamethasone<br>30 mins before chemotherapy | 8mg | PO | |
| 4 | Ondansetron<br>30 mins before chemotherapy | 16mg | PO | |
| 4 | **Topotecan** | 0.75mg/m$^2$ | IV | In 50mL sodium chloride 0.9% over 30 minutes |
| 4 | **Cyclophosphamide** | 250mg/m$^2$ | IV | IV bolus over 30 minutes |
| 5 | Dexamethasone<br>30 mins before chemotherapy | 8mg | PO | |
| 5 | Ondansetron<br>30 mins before chemotherapy | 16mg | PO | |
| 5 | **Topotecan** | 0.75mg/m$^2$ | IV | In 50mL sodium chloride 0.9% over 30 minutes |
| 5 | **Cyclophosphamide** | 250mg/m$^2$ | IV | IV bolus over 30 minutes |

## Main Toxicities:

Cyclophospahamide: myelosuppression, haemorragic cystitis, nausea, vomiting, diarrhoea, stomatitis, alopecia, infertility, anorexia, interstitial lung disease, hypersensitivity reaction (including rash), hyperbilirubinaemia

Topotecan: neutropenia, thrombocytopenia, anaemia, leucopenia, interstitial lung disease, nausea, vomiting, diarrhoea, constipation, mucositis, dyspepsia, hypersensitivity

## Investigations and treatment plan

| | Pre | Cycle 1 | Cycle 2 | Cycle 3 | Cycle 4 | Comments/ ongoing |
|---|---|---|---|---|---|---|
| Medical Assessment | X | X | X | X | X | Alternate cycle |
| Nursing Assessment | X | X | X | X | X | Every cycle |
| FBC | X | X | X | X | X | Day 1 only |
| U&E & LFT | X | X | X | X | X | Day 1 only |
| CT scan | X | | | | | As clinically indicated |
| Informed Consent | X | | | | | |
| PS recorded | X | X | X | X | X | Every cycle day 1 |
| Toxicities documented | X | X | X | X | X | Every visit |
| Weight recorded | X | X | X | X | X | Every cycle day 1 |

## Dose Modifications and Toxicity Management:

### Haematological toxicity

Proceed on day 1 if:-

| | |
|---|---|
| ANC ≥ 1.0 x $10^9$/L | Platelets ≥ 100 x $10^9$/L |

Delay 1 week on day 1 if:-

| | |
|---|---|
| ANC ≤ 0.9 x $10^9$/L | Platelets ≤ 99 x $10^9$/L |

If platelets or ANC still below required levels for treatment at week 2, delay treatment again and patient will need assessment and consideration of dose reduction.

**Non-haematological toxicity**

<table>
<tr><td>Renal</td><td>
<table>
<tr><th>CrCl mL/min</th><th>Topotecan dose</th><th>Cyclophosphamide dose</th></tr>
<tr><td>Above 40</td><td>100%</td><td>100%</td></tr>
<tr><td>20 to 39</td><td>50%</td><td>100%</td></tr>
<tr><td>10 to 20</td><td>Discontinue</td><td>75%</td></tr>
<tr><td>Less than 10</td><td>Discontinue</td><td>50%</td></tr>
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<tr><td>Hepatic</td><td>Cyclophosphamide - Usually no reductions required, discuss with consultant if severe impairment<br>Topotecan – no specific guidance, withhold if bilirubin more than 2 x ULN</td></tr>
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**Cockroft and Gault formula**

Male patients $\frac{1.23 \times (140 - \text{age}) \times \text{weight (kg)}}{\text{Serum Creatinine (micromol/L)}}$

Female patients $\frac{1.04 \times (140 - \text{age}) \times \text{weight (kg)}}{\text{Serum Creatinine (micromol/L)}}$

## References:

Hunold, A., Weddeling, N., Paulussen, M., Ranft, A., Liebscher, C. and Jürgens, H. (2006). Topotecan and cyclophosphamide in patients with refractory or relapsed Ewing tumors. *Pediatric Blood & Cancer*, 47(6), pp.795-800.

Farhat, R., Raad, R., Khoury, N., Feghaly, J., Eid, T., Muwakkit, S., Abboud, M., El-Solh, H. and Saab, R. (2013). Cyclophosphamide and Topotecan as First-line Salvage Therapy in Patients with Relapsed Ewing Sarcoma at a Single Institution. *Journal of Pediatric Hematology/Oncology*, 35(5), pp.356-360.