**Topotecan Monotherapy – Weekly**

### INDICATIONS FOR USE:

<table>
<thead>
<tr>
<th>INDICATION</th>
<th>ICD10</th>
<th>Regimen Code</th>
<th>*Reimbursement Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment of patients with metastatic carcinoma of the ovary after failure of first-line or subsequent therapy</td>
<td>C56</td>
<td>00312a</td>
<td>Hospital</td>
</tr>
<tr>
<td>Treatment of patients with metastatic carcinoma of the fallopian tubes after failure of first-line or subsequent therapy</td>
<td>C57</td>
<td>00312b</td>
<td>Hospital</td>
</tr>
<tr>
<td>Treatment of patients with metastatic peritoneal carcinoma after failure of first-line or subsequent therapy</td>
<td>C48</td>
<td>00312c</td>
<td>Hospital</td>
</tr>
</tbody>
</table>

*If the reimbursement status is not defined, the indication has yet to be assessed through the formal HSE reimbursement process.

### TREATMENT:

The starting dose of the drugs detailed below may be adjusted downward by the prescribing clinician, using their independent medical judgement, to consider each patient's individual clinical circumstances.

Topotecan is administered on days 1, 8 and 15 of a 28 day cycle until disease progression or unacceptable toxicity develops.

<table>
<thead>
<tr>
<th>Day</th>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Diluent &amp; Rate</th>
<th>Cycle</th>
</tr>
</thead>
<tbody>
<tr>
<td>1, 8 and 15</td>
<td>Topotecan</td>
<td>4mg/m²</td>
<td>IV infusion</td>
<td>b 250ml 0.9% NaCl over 30 minutes</td>
<td>Every 28 days</td>
</tr>
</tbody>
</table>

* Topotecan should be diluted to a final concentration of between 25 and 50 microgram/ml.

### ELIGIBILITY:

- Indications as above
- Life expectancy > 3 months
- ECOG status 0-2*
- Adequate organ function; ANC > 1.5 x10⁹ cells/L, platelets 100 x10⁹/L
  
  *Selected patients with ECOG status 3 due to disease burden may be eligible at consultant discretion and with planned close monitoring for toxicity and clinical benefit and prophylactic GCSF support

### EXCLUSIONS:

- Hypersensitivity to topotecan or any of the excipients
- Breast Feeding

### PRESCRIPTIVE AUTHORITY:

The treatment plan must be initiated by a Consultant Medical Oncologist

### TESTS:

**Baseline tests:**
- FBC, renal and liver profile

**Regular tests:**
- FBC, renal and liver profile before each cycle

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Disease monitoring:
Disease monitoring should be in line with the patient’s treatment plan and any other test/s as directed by the supervising Consultant.

DOSE MODIFICATIONS:
- Any dose modification should be discussed with a Consultant.

Haematological:
G-CSF may be used to maintain neutrophil counts or dose reduction may be used as shown in table 1 for cycles 2-6

Table 1: Dose modification of topotecan in haematological toxicity

<table>
<thead>
<tr>
<th>ANC (x10^9/L)</th>
<th>Platelets (x10^9/L)</th>
<th>Haemoglobin level</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 1</td>
<td>and ≥ 100</td>
<td>≥ 9 g/dl (after transfusion if necessary)</td>
<td>100% Dose</td>
</tr>
<tr>
<td>0.5 to 0.99</td>
<td>and/or &lt;100</td>
<td>&lt; 9g/dl</td>
<td>Delay treatment until recovery. Following recovery from neutropenia, reduce dose by 0.25 mg/m^2/day to 1.25 mg/m^2/day (or subsequently down to 1mg/m^2/day if necessary).</td>
</tr>
<tr>
<td>&lt;0.5 for ≥ 7 days and/or &lt; 25</td>
<td></td>
<td></td>
<td>Reduce dose by 0.25 mg/m^2/day to 1.25mg/m^2/day (or subsequently down to 1mg/m^2/day if necessary).</td>
</tr>
</tbody>
</table>

Renal and Hepatic Impairment:
Table 2: Dose modification of topotecan in renal and hepatic impairment

<table>
<thead>
<tr>
<th>Renal Impairment</th>
<th>Dose</th>
<th>Hepatic Impairment</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>CrCl (ml/min)</td>
<td></td>
<td>Bilirubin (micromol/L)</td>
<td></td>
</tr>
<tr>
<td>&gt;40</td>
<td>100%</td>
<td>&lt;170</td>
<td>100%</td>
</tr>
<tr>
<td>20-39</td>
<td>50%</td>
<td>&gt;170</td>
<td>Clinical decision</td>
</tr>
<tr>
<td>&lt;20</td>
<td>Contra-indicated</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Management of adverse events:
Table 3: Dose Modification of topotecan for Adverse Events

<table>
<thead>
<tr>
<th>Adverse reactions</th>
<th>Recommended dose modification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade ≥ 3 (except nausea)</td>
<td>Decrease dose by 25%</td>
</tr>
<tr>
<td>Interstitial lung disease</td>
<td>Discontinue</td>
</tr>
</tbody>
</table>

SUPPORTIVE CARE:
EMETOGENIC POTENTIAL: Low (Refer to local policy).

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PREMEDICATIONS: None

OTHER SUPPORTIVE CARE:
No specific recommendations

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS
The adverse effects listed are not exhaustive. Please refer to the relevant Summary of Product Characteristics for full details.

- **Neutropenia**: Fever or other evidence of infection must be assessed promptly and treated aggressively.
- **Neutropenic enterocolitis**: Topotecan-induced neutropenia may lead to neutropenic enterocolitis. This should be considered in patients presenting with neutropenia, fever, and abdominal pain.
- **Interstitial lung disease**: Topotecan has been associated with reports of interstitial lung disease (ILD), some of which have been fatal. Underlying risk factors include history of ILD, pulmonary fibrosis, lung cancer, thoracic exposure to radiation and use of pneumotoxic drugs and/or colony stimulating factors.

Patients should be monitored for pulmonary symptoms indicative of ILD (e.g. cough, fever, dyspnoea and/or hypoxia), and topotecan should be discontinued if a new diagnosis of ILD is confirmed.

DRUG INTERACTIONS:

- Increased toxicity of topotecan possible with p-glycoprotein inhibitors due to reduced clearance.
- Concurrent use of topotecan and platinums (e.g. CISplatin and CARBOplatin) may result in severe myelosuppression. Administration of platinums before topotecan resulted in worse thrombocytopenia and neutropenia than topotecan preceeding platinums.
- Current drug interaction databases should be consulted for more information.

ATC CODE:
Topotecan - L01XX17

REFERENCES:

<table>
<thead>
<tr>
<th>Version</th>
<th>Date</th>
<th>Amendment</th>
<th>Approved By</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>4/4/2016</td>
<td></td>
<td>Prof Maccon Keane</td>
</tr>
<tr>
<td>2</td>
<td>18/04/2018</td>
<td>Updated with new NCCP regimen template, standardization of treatment table and dosing in renal and hepatic impairment</td>
<td>Prof Maccon Keane</td>
</tr>
</tbody>
</table>

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.
NCCP Regimen: Topotecan Monotherapy - Weekly

Published: 08/04/2016
Review: 18/04/2020
Version number: 2

Tumour Group: Gynaecology/Lung
NCCP Regimen Code: 00312
ISMO Contributor: Prof Maccon Keane

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1 This regimen is outside its licensed indication in Ireland. Patients should be informed of the unlicensed nature of this indication and consented to treatment in line with the hospital’s policy on the use of unlicensed medication and unlicensed or “off label” indications. Prescribers should be aware of their responsibility in communicating any relevant information to the patient and also in ensuring that the unlicensed or “off label” indication has been acknowledged by the hospital’s Drugs and Therapeutics Committee, or equivalent, in line with hospital policy.

2 ODMS – Oncology Drug Management System
CDS – Community Drug Schemes (CDS) including the High Tech arrangements of the PCRS community drug schemes
Further details on the Cancer Drug Management Programme is available at; http://www.hse.ie/eng/services/list/5/cancer/profinfo/medonc/cdmp/