**Indication**

Palliative therapy for relapsed ovarian, fallopian tube or primary peritoneal cancer.

Second line treatment of partially platinum sensitive, platinum resistant or platinum refractory advanced ovarian cancer or in patients who are allergic to platinum based compounds and for whom Caelyx® and paclitaxel are not considered appropriate.

(NICE TA91)

**ICD-10 codes**

Codes prefixed with C48, 56 and 57.

**Regimen details**

<table>
<thead>
<tr>
<th>Day</th>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-5</td>
<td>Topotecan</td>
<td>1.5mg/m²*</td>
<td>IV infusion</td>
</tr>
</tbody>
</table>

* This dose and schedule may be too toxic for some patients, especially those heavily pre-treated with platinum based therapy. In such patients consider a reduced starting dose of 1.0-1.25mg/m².

Alternatively patients may be prescribed the modified weekly regimen as per the table below. This regimen has been shown to be equivalent, less toxic and more convenient than the 5 day schedule. Note: this dosing is unlicensed.

<table>
<thead>
<tr>
<th>Day</th>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
</tr>
</thead>
<tbody>
<tr>
<td>1, 8, 15</td>
<td>Topotecan</td>
<td>3.5mg/m²</td>
<td>IV infusion</td>
</tr>
</tbody>
</table>

**Cycle frequency**

21 days (or 28 days for the modified weekly regimen)

**Number of cycles**

6 cycles

**Administration**

Topotecan is administered in 50-100mL* sodium chloride 0.9% or glucose 5% over 30 minutes.

*the final concentration should be between 25-50 micrograms/mL.

**Pre-medication**

Nil

**Emetogenicity**

This regimen has a moderate - low emetogenic potential

**Additional supportive medication**

Loperamide. Patients should be advised of the risk and management of topotecan induced diarrhoea, including recognition of symptoms, use of loperamide and prophylactic antibiotics, fluid intake and the need for
hospitalisation. Supplies of antibiotics (ciprofloxacin 250-500mg BD) should be given in addition to loperamide and the patient should be advised if diarrhoea persists beyond 24 hours of loperamide treatment to commence the antibiotics.

**Extravasation**
Topotecan is an exfoliant (Group 4)

<table>
<thead>
<tr>
<th>Investigation</th>
<th>Validity period (or as per local policy)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FBC</td>
<td>14 days</td>
</tr>
<tr>
<td>U+E (including creatinine)</td>
<td>14 days</td>
</tr>
<tr>
<td>LFTs</td>
<td>14 days</td>
</tr>
<tr>
<td>CA125</td>
<td>28 days</td>
</tr>
</tbody>
</table>

**Investigations - pre subsequent cycles**

<table>
<thead>
<tr>
<th>Investigation</th>
<th>Validity period (or as per local policy)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FBC</td>
<td>96 hours</td>
</tr>
<tr>
<td>U+E (including creatinine)</td>
<td>7 days</td>
</tr>
<tr>
<td>LFTs</td>
<td>7 days</td>
</tr>
</tbody>
</table>

**Standard limits for administration to go ahead**
If blood results not within range, authorisation to administer must be given by prescriber/consultant.

<table>
<thead>
<tr>
<th>Investigation</th>
<th>Limit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neutrophils</td>
<td>( \geq 1.5 \times 10^9/L )</td>
</tr>
<tr>
<td>Platelets</td>
<td>( \geq 100 \times 10^9/L )</td>
</tr>
<tr>
<td>Creatinine Clearance (CrCl)</td>
<td>( \geq 40 \text{mL/min} )</td>
</tr>
<tr>
<td>Bilirubin</td>
<td>(&lt; 10 \times \text{ULN} )</td>
</tr>
</tbody>
</table>

**Dose modifications**

- **Haematological toxicity**
If neutrophils < \( 1.5 \times 10^9/L \) and/or platelets < \( 100 \times 10^9/L \) delay treatment for 1 week or until count recovery.

If any of the following are experienced, future doses should be reduced:
- Neutrophils < \( 0.5 \times 10^9/L \) for 7 days or more or severe neutropenia with fever
- Treatment delay due to neutropenia
- Platelets < \( 25 \times 10^9/L \) at any point during treatment

In the case of febrile neutropenia consider prophylactic antibiotics for all further cycles.

- **Renal impairment**

<table>
<thead>
<tr>
<th>CrCl (mL/min)</th>
<th>Topotecan dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \geq 40 )</td>
<td>100%</td>
</tr>
<tr>
<td>20-39</td>
<td>50%</td>
</tr>
<tr>
<td>&lt; 20</td>
<td>Contraindicated</td>
</tr>
</tbody>
</table>

- **Hepatic impairment**
There is a lack of information available for dosing in hepatic impairment, however topotecan is not recommended in severe hepatic impairment with bilirubin > 10 x ULN.
• **Other toxicities**
  For all other grade 3 toxicities (except alopecia and nausea/vomiting) delay treatment until resolved to ≤ grade 1 and resume with dose reduction of 0.25mg/day. If further toxicity occurs or grade 4 toxicity withhold treatment or consider an additional dose reduction (discuss with consultant).

If delays of > 3 weeks or > 2 dose reductions, discontinue treatment.

**Adverse effects** - for full details consult product literature/ reference texts

• **Serious side effects**
  Myelosuppression
  Interstitial lung disease
  Paraesthesia

• **Frequently occurring side effects**
  Myelosuppression
  Nausea and vomiting
  Constipation, diarrhoea*
  Fatigue
  Abdominal pain

* this can be severe, ensure patients are counselled on management of diarrhoea (see supportive medication)

• **Other side effects**
  Alopecia
  Headache
  Rash
  Stomatitis

**Significant drug interactions** – for full details consult product literature/ reference texts

**Warfarin/coumarin anticoagulants**: Avoid use due to elevations in INR. Switch to low molecular weight heparin during treatment.

**Clozapine**: increased risk of agranulocytosis; avoid concomitant use.

**Digoxin tablets**: reduced absorption (give digoxin as liquid form).

**P-glycoprotein inhibitors**: (cyclosporin, ketoconazole, ritonavir, saquinavir) increase exposure of topotecan.

**Phenytoin**: may increase topotecan clearance

**Additional comments**

Nil

**References**
