Regimen : Oral Topotecan for Small Cell Lung Cancer (NICE TA184)

### Indication
Treatment of relapsed small cell lung cancer when:
- retreatment with first line chemotherapy is inappropriate, **and**
- treatment with CAV (cyclophosphamide, doxorubicin and vincristine) combination therapy is contraindicated, and
- patient has Performance Status 0-2

### Regimen details

<table>
<thead>
<tr>
<th>Regimen details</th>
<th>Day</th>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1-5</td>
<td>Topotecan</td>
<td>2.3mg/m²/day*</td>
<td>Oral (Day 1 taken in chemo day unit)</td>
</tr>
</tbody>
</table>

### Administration
*Capsules are available in 0.25mg and 1mg.
Capsule(s) must be swallowed whole, and must not be crushed or chewed. They may be taken with or without food.
Capsules must be stored in a refrigerator between 2-8°C.

<table>
<thead>
<tr>
<th>BSA (m²)</th>
<th>Recommended Dose (mg/day)</th>
<th>Capsule</th>
<th>Number of Capsules per Day</th>
<th>Total Number of Capsules per Cycle</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.47-1.58</td>
<td>3.5</td>
<td>1mg</td>
<td>3</td>
<td>15</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.25mg</td>
<td>2</td>
<td>10</td>
</tr>
<tr>
<td>1.59-1.68</td>
<td>3.75</td>
<td>1mg</td>
<td>3</td>
<td>15</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.25mg</td>
<td>3</td>
<td>15</td>
</tr>
<tr>
<td>1.69-1.79</td>
<td>4</td>
<td>1mg</td>
<td>4</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.25mg</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>1.80-1.90</td>
<td>4.25</td>
<td>1mg</td>
<td>4</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.25mg</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>1.91-2.01</td>
<td>4.5</td>
<td>1mg</td>
<td>4</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.25mg</td>
<td>2</td>
<td>10</td>
</tr>
</tbody>
</table>

### Frequency
Every 21 days for up to 6 cycles

### Extravasation
N/A

### Premedication
None required

### Emetogenicity
This regimen has moderate emetogenic potential – refer to local protocol

### Additional recommended supportive medication
G-CSF recommended days 7-12 if patient has had neutropenic sepsis in a previous cycle.

### Pre-treatment evaluations
- FBC
- U+E (CrCl)
- LFT
Baseline – results valid for 14 days
Baseline – results valid for 14 days
Baseline – results valid for 14 days

### Regular investigations
- FBC
- U+E
- LFT
Results valid for 72 hours
Results valid for 7 days
Results valid for 7 days

### Standard limits for administration to go ahead
- Neutrophil count $\geq 1.0 \times 10^9$/L
- WCC $\geq 3.0 \times 10^9$/L
- Platelet count $\geq 100 \times 10^9$/L
- Haemoglobin $\geq 10$ g/dL
- Creatinine clearance $\geq 60$ ml/min
- Bilirubin $\leq$ ULN

*Only valid on day of printing*
### Dose modifications
For Grade 2-4 diarrhoea or any Grade 3/4 non-haematological toxicities (apart from alopecia), consider dose reductions similar to those for haematological toxicities i.e. dose reductions of 0.4mg/m² to a minimum dose of 1.5mg/m²/day.

### Haematological toxicity
- **WCC ≥ 3.0, neutrophils ≥ 1.0, platelets ≥ 100** – if cell counts lie below these values, delay by one week, rechecking FBC prior to administration and consider dose reduction by 0.4mg/m² for subsequent doses.

### Renal impairment
- **CrCl (ml/min)**
  - ≥60 ml/min: Dose 100%
  - 20-60ml/min: No dosage recommendations available-physician decision.
  - <20 ml/min: Contraindicated

### Hepatic impairment
There are no dosage recommendations available for patients with liver impairment-physician decision.
Topotecan is not recommended in patients with bilirubin >26micromol/L

### NCI Common toxicity criteria

<table>
<thead>
<tr>
<th>Toxicity</th>
<th>Definition</th>
<th>Dose adjustment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Diarrhoea</strong></td>
<td>≥ Grade 2</td>
<td>Treatment-emergent diarrhoea should be managed aggressively. Patients should be advised how to manage chemotherapy-induced diarrhoea, including, recognition of early warning signs, use of antidiarrhoeals and antibiotics, changes in fluid intake and diet, and the need for hospitalization.</td>
</tr>
<tr>
<td><strong>Febrile Neutropenia</strong></td>
<td>ANC &lt; 0.5 x 10⁹/l plus fever requiring IV antibiotics +/- hospitalisation</td>
<td>Reduce dose of next cycle by 0.4mg/m². (Lowest dose is usually considered 1.5mg/m²/day i.e. two dose reductions)</td>
</tr>
<tr>
<td><strong>Thrombocytopenia</strong></td>
<td>Platelet nadir of &lt; 25 x 10⁹/L</td>
<td>Reduce dose of next cycle by 0.4mg/m². (Lowest dose is usually considered 1.5mg/m²/day i.e. two dose reductions)</td>
</tr>
<tr>
<td><strong>Anaemia</strong></td>
<td>≥ Grade 2</td>
<td>Treatment should be deferred until Haemoglobin ≥ 9 g/dL (after transfusion if necessary) If Hb &lt; 10.0 and symptomatic, refer to prescribing doctor to consider blood transfusion.</td>
</tr>
</tbody>
</table>

### Adverse effects
- **Rare or serious side effects**
  - Neutropenia (very common)
  - Neutropenic colitis. Topotecan-induced neutropenia can cause neutropenic colitis (potentially fatal). In patients presenting with fever, neutropenia, and abdominal pain, the possibility of neutropenic colitis should be considered.
  - Interstitial lung disease (rare)
  - Diarrhoea (very common)*
  - Teratogenicity/fertility effects
  - *see NCI Common toxicity criteria above

- **Frequently occurring side effects**
  - Nausea and vomiting
  - Infection
  - Anaemia
  - Thrombocytopenia
  - Fatigue
  - Alopecia
Anorexia

Other

Constipation, stomatitis, pruritis and rash

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

- Clozapine: increased risk of agranulocytosis, avoid concomitant use
- Digoxin tablets: reduced absorption (resolved by giving the digoxin in liquid form)
- P-glycoprotein inhibitors (cyclosporin, ketoconazole, ritonavir, saquinavir): increased exposure of topotecan
- Phenytoin: may possibly increase Topotecan clearance

**Comments**

None

**Cumulative Doses**

None

**References**

- Summary of Product Characteristics Hycamtin® (Topotecan) 0.25mg and 1mg hard capsules (GlaxoSmithKline) [internet], accessed 10/11/2010 available from [http://www.medicines.org.uk/EMC/medicine/21246/SPC](http://www.medicines.org.uk/EMC/medicine/21246/SPC)