**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>Small cell lung cancer (SCLC) limited disease</td>
<td>C34</td>
<td>00279a</td>
<td>Hospital</td>
</tr>
</tbody>
</table>

**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.*

CISplatin is administered on day 1 and etoposide is administered on three consecutive days (Days 1-3) of a 21 day cycle for 4 cycles.

Facilities to treat anaphylaxis MUST be present when the chemotherapy is administered.

Usual plan is for radiotherapy to start with the first cycle of chemotherapy, although radiotherapy may be started with later cycles dependent on clinical circumstances.

Regimen may be administered every 28 days at discretion of prescribing consultant.

<table>
<thead>
<tr>
<th>Admin Order</th>
<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</td>
<td>1, 2 &amp; 3</td>
<td>Etoposide</td>
<td>100mg/m²</td>
<td>IV Infusion</td>
<td>1000ml 0.9% NaCl over 1 hour</td>
<td>Every 21 days for 4 cycles</td>
</tr>
<tr>
<td>2</td>
<td>1</td>
<td>CISplatin</td>
<td>75mg/m²</td>
<td>IV Infusion</td>
<td>1000ml 0.9% NaCl over 2 hours</td>
<td>Every 21 days for 4 cycles</td>
</tr>
</tbody>
</table>

**PRE and post hydration therapy required for CISplatin**

See local hospital policy recommendations.

**Suggested prehydration for CISplatin therapy:**

- The administration of etoposide in 1000ml 0.9% NaCl over 1 hour as detailed above may be considered as pre-hydration for CISplatin
- Administer CISplatin as described above

**Post hydration:**

- Administer 10mmol magnesium sulphate (MgSO₄) and 20mmol potassium chloride (KCl) in 1000 ml 0.9% NaCl over 2 hours

*Mannitol* 10% may be used to as per local policy to induce diuresis, although there is no conclusive evidence that this is required. The routine use of furosemide to increase urine flow is not recommended unless there is evidence of fluid overload.(2,3)

**ELIGIBILITY:**

- Indications as above
- ECOG status 0-2
- Suitable candidate for thoracic radiation

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EXCLUSIONS:
- Hypersensitivity to etoposide, CISplatin or any of the excipients.
- CISplatin
  - Pre existing neuropathies ≥ grade 2
  - Creatinine clearance < 60 mL/min
  - Significant hearing impairment/tinnitus
- Severe liver impairment (etoposide)
- Pregnancy
- Breast Feeding

PRESCRIPTIVE AUTHORITY:
The treatment plan must be initiated by a Consultant Medical Oncologist.

TESTS:
Baseline tests:
- Blood, renal and liver profile
- Audiology and creatinine clearance if clinically indicated

Regular tests:
- Blood, renal and liver profile prior to each cycle

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:
Table 1: Dose modification of etoposide for haematological toxicity

<table>
<thead>
<tr>
<th>ANC (x 10^9/L)</th>
<th>Platelets (x 10^9/L)</th>
<th>Dose Etoposide</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 1.5 and</td>
<td>≥ 100</td>
<td>100%</td>
</tr>
<tr>
<td>1-1.49 or</td>
<td>75-99</td>
<td>75%</td>
</tr>
<tr>
<td>&lt; 1 or</td>
<td>&lt; 75</td>
<td>DELAY</td>
</tr>
</tbody>
</table>
Renal and Hepatic Impairment:

Table 2: Dose modification in renal and hepatic impairment

<table>
<thead>
<tr>
<th>Drug</th>
<th>Renal impairment</th>
<th>Hepatic Impairment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Etoposide</td>
<td>CrCl (ml/min)</td>
<td>Dose</td>
</tr>
<tr>
<td>&gt;50</td>
<td>100%</td>
<td>26-51 or &gt;51</td>
</tr>
<tr>
<td>15-50</td>
<td>75%</td>
<td>&gt;51</td>
</tr>
<tr>
<td>&lt;15</td>
<td>50%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Subsequent dosing should be based on patient tolerance and clinical effect.</td>
<td></td>
</tr>
</tbody>
</table>

CISplatin

<table>
<thead>
<tr>
<th>CrCl (ml/min)</th>
<th>Dose</th>
<th>No dose reduction necessary</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;60</td>
<td>100%</td>
<td></td>
</tr>
<tr>
<td>45-59</td>
<td>75%</td>
<td></td>
</tr>
<tr>
<td>&lt;45</td>
<td>Consider CARBOplatin/Clinical decision</td>
<td></td>
</tr>
</tbody>
</table>

Non-Haematological Toxicity:

Table 3: Dose modification schedule based on adverse events

<table>
<thead>
<tr>
<th>Adverse reactions</th>
<th>Recommended dose modification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade ≥ 2 peripheral neuropathy</td>
<td>Substitute CARBOplatin AUC 5 or 50% reduction of CISplatin dose after recovery to grade ≤ 1; 100% dose of etoposide.</td>
</tr>
<tr>
<td>Grade 3 (Other than mucositis or alopecia)</td>
<td>Delay until recovery to Grade 1. Then reduce dose of CISplatin and etoposide to 75%.</td>
</tr>
</tbody>
</table>

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL:

CISplatin: High (Refer to local policy).
Etoposide: Low (Refer to local policy).

PREMEDICATIONS:
Hydration prior and post CISplatin administration (Refer to local policy or see recommendations above).

OTHER SUPPORTIVE CARE: No specific recommendations
NCCP Chemotherapy Regimen

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 appropriately. Avoid aminoglycoside antibiotics.
- **Renal Toxicity**: Nephrotoxicity is common with CISplatin. Strongly encourage oral hydration. If oral hydration is not possible (e.g. excessive nausea), IV hydration is indicated. Avoid nephrotoxic drugs such as aminoglycoside antibiotics where possible. Where treatment with nephrotoxic drugs must be used, monitor renal function.
- **Ototoxicity and sensory neural damage**: These are associated with CISplatin therapy. They should be assessed by history prior to each cycle.
- **Hypersensitivity**: Hypersensitivity reactions have been reported with etoposide and CISplatin. Monitor infusion of etoposide for the first 15 minutes for signs of hypotension.

DRUG INTERACTIONS:

- CISplatin may potentiate the nephrotoxic and ototoxic effects of loop diuretics and aminoglycosides so concurrent use should be avoided.
- Concomitant CISplatin therapy is associated with reduced total body clearance of etoposide.
- CYP3A4 inducers may increase the clearance of etoposide.
- CYP3A4 and p-gp inhibitors may decrease the clearance of etoposide
- Current drug interaction databases should be consulted for more information

REFERENCES:

4. Park K, Sun J, Kim, S. et al. Phase III trial of concurrent thoracic radiotherapy (TRT) with either the first cycle or the third cycle of CISplatin and etoposide chemotherapy to determine the optimal timing of TRT for limited-disease small cell lung cancer. J Clin Oncol 2012 (suppl; abstr 7004)
NCCP Chemotherapy Regimen


<table>
<thead>
<tr>
<th>Version</th>
<th>Date</th>
<th>Amendment</th>
<th>Approved By</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>10/09/2015</td>
<td></td>
<td>Dr Maccon Keane</td>
</tr>
<tr>
<td>2</td>
<td>20/09/2017</td>
<td>Updated title and dosing in renal impairment, applied new NCCP regimen template</td>
<td>Prof Maccon Keane</td>
</tr>
<tr>
<td>3</td>
<td>09/01/2019</td>
<td>Updated CISplatin hydration protocol</td>
<td>Prof Maccon Keane</td>
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<tr>
<td>4</td>
<td>04/09/2019</td>
<td>Reviewed. Update of etoposide renal dosing</td>
<td>Prof Maccon Keane</td>
</tr>
<tr>
<td>5</td>
<td>24/06/2021</td>
<td>Reviewed. Updated CISplatin hydration protocol.</td>
<td>Prof Maccon Keane</td>
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</tbody>
</table>

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.

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