Etoposide and CISplatin 20mg/m² (EP) Therapy

INDICATIONS FOR USE:

<table>
<thead>
<tr>
<th>INDICATION</th>
<th>ICD10</th>
<th>Regimen Code</th>
<th>*Reimbursement Indicator</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment of good prognosis (IGCCCG criteria) metastatic germ cell tumours (both non-seminoma and seminoma)</td>
<td>C62</td>
<td>00301a</td>
<td></td>
</tr>
</tbody>
</table>

*If a reimbursement indicator (e.g. ODMS, CDS) is not defined, the drug and its detailed indication have not been 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.

Treatment with etoposide and CISplatin is administered on 5 consecutive days (days 1-5), of a 21 day cycle and repeated for 4 cycles or until disease progression or unacceptable toxicity develops.

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

<table>
<thead>
<tr>
<th>Admin Order</th>
<th>Day</th>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Diluent &amp; Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1-5</td>
<td>Etoposide</td>
<td>100mg/m²</td>
<td>IV infusion</td>
<td>1000ml 0.9% NaCl over 30-120 minutes b</td>
</tr>
<tr>
<td>2</td>
<td>1-5</td>
<td>CISplatin</td>
<td>20mg/m²</td>
<td>IV infusion</td>
<td>500 to 1000ml 0.9% NaCl over 1 hour (Pre hydration therapy required) a</td>
</tr>
</tbody>
</table>

*aPrehydration therapy required for CISplatin
See local hospital policy recommendations.
Suggested prehydration for CISplatin therapy:
1. Administer 10mmol magnesium sulphate (MgSO₄) (+/- KCl 20mmol/L if indicated) in 1000 mL sodium chloride 0.9% over 60 minutes.
2. Administer CISplatin as described above

*bHypotension following rapid IV administration has been reported.
Longer infusion times may be required based on the patient’s tolerance

ELIGIBILTY:
- Indications as above
- ECOG status 0-3

EXCLUSIONS:
- Hypersensitivity to etoposide, CISplatin or any of the excipients.
- CISplatin
  - Pre existing neuropathies ≥ grade 2
  - Creatinine clearance < 40 mL/min
  - Significant hearing impairment/tinnitus
- Severe liver impairment (etoposide)
The treatment plan must be initiated by a Consultant Medical Oncologist.

**Tests:**

- **Baseline tests:**
  - FBC, U&Es, LFTs, creatinine
  - Consider sperm banking for appropriate patients prior to initiation of therapy

- **Regular tests:**
  - FBC weekly during treatment
  - U&Es, LFTs, creatinine prior to each treatment 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:**

- Delay and dose reductions are not recommended as the efficacy of this treatment may be greatly compromised.
- All delays to treatment must be approved by prescribing consultant.
- Prophylactic use of G-CSF is not recommended.
- G-CSF is indicated in patients receiving their second or subsequent cycle of BEP who have had an episode of neutropenic fever or who have not recovered their neutrophil count by Day 5.
Renal and Hepatic Impairment:

<table>
<thead>
<tr>
<th>Drug</th>
<th>Renal Impairment</th>
<th>Hepatic Impairment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cr CI (ml/min)</td>
<td>Dose</td>
</tr>
<tr>
<td>Etoposide</td>
<td>&gt;50</td>
<td>100%</td>
</tr>
<tr>
<td></td>
<td>15-50</td>
<td>75%</td>
</tr>
</tbody>
</table>

Subsequent dosing should be based on patient tolerance and clinical effect. Data are not available in patients with CrCl < 15ml/min and further dose reductions should be considered in these patients.

<table>
<thead>
<tr>
<th></th>
<th>GFR (ml/min)</th>
<th>Dose of CISplatin</th>
<th>No dose reduction necessary</th>
</tr>
</thead>
<tbody>
<tr>
<td>CISplatin</td>
<td>≥ 60</td>
<td>100%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>*45-59</td>
<td>75%</td>
<td></td>
</tr>
<tr>
<td>&lt;45</td>
<td>Hold CISplatin or delay with additional IV fluids</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Due to the curative intent of this chemotherapy regimen, in cases where Cr CI falls between 45-59ml/min it may be appropriate to maintain dose of CISplatin but with extra hydration, longer infusion time and daily Creatinine measurements at the discretion of the prescribing consultant.

SUPPORTIVE CARE:

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

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

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.
- **Hypersensitivity**: Hypersensitivity reactions have been reported with etoposide and CISplatin. Monitor infusion of etoposide for the first 15 minutes for signs of hypotension.
- **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.

**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

**ATC CODE:**
- CISplatin L01XA01
- Etoposide L01CB01

**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>08/04/2016</td>
<td></td>
<td>Dr Maccon Keane</td>
</tr>
<tr>
<td>2</td>
<td>20/09/2017</td>
<td>Updated with new NCCP regimen template</td>
<td>Prof Maccon Keane</td>
</tr>
<tr>
<td>3</td>
<td>06/12/2017</td>
<td>Updated with revised CISplatin hydration regimen recommendations</td>
<td>Prof Maccon Keane</td>
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</tbody>
</table>

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.

1 ODMS – Oncology Drug Management System
2 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/](http://www.hse.ie/eng/services/list/5/cancer/profinfo/medonc/cdmp/)

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