**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>Locally advanced or metastatic head and neck cancer</td>
<td>C76</td>
<td>00314</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. CISplatin and 5-Fluorouracil are administered on days 1-4 of a 28 day cycle until disease progression or unacceptable toxicity develops. Facilities to treat anaphylaxis MUST be present when the chemotherapy is administered on Day 1.

<table>
<thead>
<tr>
<th>Admin. Order</th>
<th>Day</th>
<th>Drug</th>
<th>Dose</th>
<th>Route and Method of Administration</th>
<th>Diluent &amp; Rate</th>
<th>Cycle</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1-4</td>
<td>CISplatin</td>
<td>25mg/m²²</td>
<td>IV infusion</td>
<td>1000ml 0.9% NaCl over 2 hours</td>
<td>Every 28 days</td>
</tr>
<tr>
<td>2</td>
<td>1-4</td>
<td>5-Fluorouracil</td>
<td>1000mg/m²²/ day</td>
<td>IV infusion</td>
<td>1000ml 0.9% NaCl over 22 hours</td>
<td>Every 28 days</td>
</tr>
</tbody>
</table>

*Pre hydration 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.

Administer CISplatin as described above

**Eligibility:**

- Indications as above
- ECOG status 0-2
- Adequate organ function; ANC > 1.5 x10⁹ cells/L, platelets 100 x10⁹/L serum creatinines ≤ 1.5 x ULN, transaminases ≤5 xULN, bilirubin ≤1.5 x ULN

**Exclusions:**

- Hypersensitivity to CISplatin, 5-fluorouracil or any of the excipients
- Lactation
- Pre existing neuropathies ≥ grade 2
- Severe liver impairment
- Moderate/severe renal impairment (creatinine clearance < 60 mL/min)
- Significant hearing impairment/ tinnitus

**Prescriptive Authority:**

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

Baseline tests:
- FBC, Renal and liver profile
- ECG (if patient has compromised cardiac function).
- Audiology and creatinine clearance if clinically indicated

Regular tests:
- FBC, Renal and liver profile before 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 for haematological toxicity

<table>
<thead>
<tr>
<th>ANC (x 10^9/L) (on day of chemotherapy)</th>
<th>Platelets (x 10^9/L) (at any stage during cycle)</th>
<th>Dose of 5-Fluorouracil</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-1.5</td>
<td>or 75-100</td>
<td>750mg/m^2/day x 4 days</td>
</tr>
<tr>
<td>&lt;1</td>
<td>or &lt;75</td>
<td>375mg/m^2/day x 4 days</td>
</tr>
</tbody>
</table>

Renal and Hepatic Impairment:

Table 2: Dose modification for renal and hepatic impairment

<table>
<thead>
<tr>
<th>Drug</th>
<th>GFR (ml/min)</th>
<th>Dose</th>
<th>Renal Impairment</th>
<th>Hepatic Impairment</th>
</tr>
</thead>
<tbody>
<tr>
<td>CISplatin</td>
<td>≥60</td>
<td>100%</td>
<td>No dose reduction necessary</td>
<td></td>
</tr>
<tr>
<td></td>
<td>45-59</td>
<td>75%</td>
<td></td>
<td>Consider using CARBOplatin</td>
</tr>
<tr>
<td></td>
<td>&lt;45</td>
<td>Clinical decision. Moderate hepatic impairment; reduce initial dose by 1/3. Severe hepatic impairment, reduce initial dose by 1/2.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5-Fluorouracil</td>
<td>Consider dose reduction in severe renal impairment only</td>
<td>Bilirubin</td>
<td>AST</td>
<td>Dose</td>
</tr>
<tr>
<td></td>
<td>&lt;85</td>
<td>&lt;180</td>
<td>100%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>&gt;85 or &gt;180</td>
<td></td>
<td>Contra-indicated</td>
<td>Clinical decision. Moderate hepatic impairment; reduce initial dose by 1/3. Severe hepatic impairment, reduce initial dose by 1/2.</td>
</tr>
</tbody>
</table>

Non-haematological toxicity

Table 3: Dose modification schedule for CISplatin based on adverse events

<table>
<thead>
<tr>
<th>Adverse reaction</th>
<th>Recommended dose modification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade ≥ 2 peripheral neuropathy</td>
<td>Omit CISplatin and consider substituting CISplatin with CARBOplatin</td>
</tr>
</tbody>
</table>
SUPPORTIVE CARE:

EMETOGENIC POTENTIAL: High (Refer to local policy).

PREMEDICATIONS: Hydration prior 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.

- **Neutropenia:** Fever or other evidence of infection must be assessed promptly and treated appropriately.
- **Renal toxicity:** Renal toxicity is common with CISplatin. Encourage oral hydration.
- **Ototoxicity and sensory neural damage** should be assessed by history prior to each cycle.
- **Myocardial ischaemia and angina:** Cardiotoxicity is a serious complication during treatment with fluorouracil. Patients, especially those with a prior history of cardiac disease or other risk factors, treated with fluorouracil, should be carefully monitored during therapy.
- **Dihydropyrimidine dehydrogenase (DPD) deficiency:** Rare, life-threatening toxicities such as stomatitis, mucositis, neutropenia, neurotoxicity and diarrhoea have been reported following administration of fluoropyrimidines (e.g. fluorouracil and capecitabine). Severe unexplained toxicities require investigation prior to continuing with treatment.

DRUG INTERACTIONS:

- Avoid concurrent use of CISplatin with nephrotoxic drugs (e.g. aminoglycosides, frusemide, NSAIDS) due to additive nephrotoxicity. If necessary monitor renal function closely.
- Marked elevations of prothrombin time and INR have been reported in patients stabilized on warfarin therapy following initiation of fluorouracil regimes.
- Concurrent administration of fluorouracil and phenytoin may result in increased serum levels of phenytoin.
- Caution should be taken when using fluorouracil in conjunction with medications which may affect dihydropyrimidine dehydrogenase activity.
- Current drug interaction databases should be consulted for more information.

ATC CODE:

CISplatin - L01XA01
5-Fluorouracil - L01BC02

REFERENCES:


The information contained in this document is a statement of consensus of NCCP and ISMO or IHS professionals regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibly of the prescribing clinician. and is subject to HSE’s terms of use available at [http://www.hse.ie/eng/Disclaimer](http://www.hse.ie/eng/Disclaimer)

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NCCP Chemotherapy Regimen

3. Cisplatin 1mg/ml Concentrate for Solution for Infusion Summary of Product Characteristics

<table>
<thead>
<tr>
<th>Version</th>
<th>Date</th>
<th>Amendment</th>
<th>Approved By</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3/05/2016</td>
<td>Applied new NCCP regimen template. Updated treatment table, revised CISplatin hydration regimen recommendations and standardised dosing in renal and hepatic impairment.</td>
<td>Prof Maccon Keane</td>
</tr>
<tr>
<td>2</td>
<td>2/05/2018</td>
<td>Amended treatment table, revised CISplatin hydration regimen recommendations and standardised dosing in renal and hepatic impairment.</td>
<td>Prof Maccon Keane</td>
</tr>
</tbody>
</table>

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.

1 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/profinfomedonc/cdmp/

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