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>Treatment of locally advanced nasopharyngeal cancer</td>
<td>C11</td>
<td>00517a</td>
<td>Hospital</td>
</tr>
</tbody>
</table>

*If the reimbursement status is not defined, the drug 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.

Gemcitabine is administered on day 1 and day 8 and CISplatin is administered on day 1 of a 21 day cycle for 4-6 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>
<th>Cycle</th>
</tr>
</thead>
<tbody>
<tr>
<td>Admin. Order</td>
<td>Day</td>
<td>Drug</td>
<td>Dose</td>
<td>Route</td>
<td>Diluent &amp; Rate</td>
<td>Cycle</td>
</tr>
<tr>
<td>1</td>
<td>1</td>
<td>Gemcitabine</td>
<td>1250mg/m²</td>
<td>IV infusion</td>
<td>250ml NaCl 0.9% over 30mins</td>
<td>Every 21 days</td>
</tr>
<tr>
<td>2</td>
<td>1</td>
<td>*CISplatin</td>
<td>80mg/m²</td>
<td>IV infusion</td>
<td>1000ml NaCl 0.9% over 120mins</td>
<td>Every 21 days</td>
</tr>
</tbody>
</table>

*Pre and post 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 1000mL sodium chloride 0.9% over 60 minutes.
2. Administer CISplatin as described above.
3. Post hydration: Administer 1000 ml 0.9% NaCl over 60 mins.

Mannitol 10% may be used 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 (4,5).

ELIGIBILITY:

- Indications as above
- ECOG 0-2
- Adequate marrow reserve (ANC > 1.5 x 10⁹/L, platelets > 100x10⁹/L)

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**EXCLUSIONS:**
- Hypersensitivity to Gemcitabine, CISplatin or any of the excipients
- CISplatin
  - Pre existing neuropathies ≥ grade 2
  - Creatinine clearance < 60 mL/min
  - Significant hearing impairment/tinnitus
- Breast Feeding

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

**TESTS:**

**Baseline tests:**
- FBC, renal and liver profile
- Audiometry and creatinine clearance as clinically indicated

**Regular tests:**
- Day 1: FBC, renal and liver profile
- Day 8: FBC, creatinine

**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:**
Prior to commencing a new treatment cycle (i.e day 1), ANC must be $\geq 1 \times 10^9/L$ and platelets $\geq 100 \times 10^9/L$.

**Table 1: Dose modifications for gemcitabine within a cycle (i.e day 8)**

<table>
<thead>
<tr>
<th>ANC (x $10^9$/L)</th>
<th>Platelet count (x $10^9$/L)</th>
<th>Other toxicity</th>
<th>Recommended dose of Gemcitabine</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\geq 1$</td>
<td>and $\geq 100$</td>
<td></td>
<td>100 %</td>
</tr>
<tr>
<td>0.5–1</td>
<td>or 50-100</td>
<td></td>
<td>75%</td>
</tr>
<tr>
<td>$&lt; 0.5$</td>
<td>or $&lt; 50$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ANC &lt; 0.5 for $\geq 5$ days or ANC &lt; 0.1 for $\geq 3$ days or Any incidence of febrile neutropenia</td>
<td>or $&lt; 25$</td>
<td>cycle delay of &gt;1 week due to any toxicity</td>
<td>Reduce dose to 75% of the original cycle initiation dose for all subsequent cycles.</td>
</tr>
</tbody>
</table>
NCCP Chemotherapy Regimen

Renal and Hepatic Impairment:

Table 2: Dose modification of CI$S$platin and Gemcitabine in 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 Cl (ml/min)</td>
<td>Dose</td>
</tr>
<tr>
<td>CI$S$platin</td>
<td>&gt;60</td>
<td>100%</td>
</tr>
<tr>
<td></td>
<td>45-59</td>
<td>75%</td>
</tr>
<tr>
<td></td>
<td>&lt;45</td>
<td>Consider CARBOplatin-</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Clinical decision</td>
</tr>
<tr>
<td>Gemcitabine</td>
<td>≥30</td>
<td>100%</td>
</tr>
<tr>
<td></td>
<td>&lt;30</td>
<td>Consider dose reduction</td>
</tr>
<tr>
<td></td>
<td></td>
<td>clinical decision</td>
</tr>
</tbody>
</table>

Management of adverse events:

Table 3: Dose Modification of Gemcitabine and CI$S$platin for Adverse Events

<table>
<thead>
<tr>
<th>Adverse reactions</th>
<th>Recommended dose modification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade ≥ 3 Non-haematological toxicity (except nausea/vomiting)</td>
<td>Therapy with Gemcitabine and CI$S$platin should be withheld (until toxicity has resolved to grade ≤ 1) and may be resumed with dose reduction at discretion of prescribing consultant.</td>
</tr>
<tr>
<td>Grade ≥ 2 peripheral neuropathy</td>
<td>Substitute CARBOplatin AUC 5 or 50% reduction of CI$S$platin dose after recovery to grade ≤ 1. 100% dose of Gemcitabine</td>
</tr>
<tr>
<td>Grade ≥ 2 pneumonitis</td>
<td>Discontinue gemcitabine</td>
</tr>
</tbody>
</table>

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL:
CI$S$platin High (Refer to local policy)
Gemcitabine Low (Refer to local policy).

PREMEDICATIONS:
Pre and Post Hydration therapy required for CI$S$platin administration (Reference local policy or see recommendations above).

OTHER SUPPORTIVE CARE:
Patient should be encouraged to drink large quantities of liquids for 24 hours after the CI$S$platin infusion to ensure adequate urine secretion.

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**: Nephrotoxicity is common with CI$S$platin. Encourage oral hydration. Avoid nephrotoxic drugs such as aminoglycoside antibiotics. Irreversible renal failure associated with
NCCP Chemotherapy Regimen

Gemcitabine (1250mg/m²) and CISplatin (80mg/m²)-21 day regimen may occur (rare) with Gemcitabine. Use caution with pre-existing renal dysfunction.

- **Pulmonary Toxicity**: Acute shortness of breath may occur with gemcitabine. Discontinue treatment if drug-induced pneumonitis is suspected.
- **Cardiovascular**: Due to the risk of cardiac and/or vascular disorders with gemcitabine, particular caution must be exercised with patients presenting a history of cardiovascular events.

**DRUG INTERACTIONS:**

- CISplatin may potentiate the nephrotoxic and ototoxic effects of loop diuretics and aminoglycosides so concurrent use should be avoided.
- Current drug interaction databases should be consulted for more information.

**ATC CODE:**

<table>
<thead>
<tr>
<th>Drug</th>
<th>ATC Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gemcitabine</td>
<td>L01BC05</td>
</tr>
<tr>
<td>CISplatin</td>
<td>L01XA01</td>
</tr>
</tbody>
</table>

**REFERENCES:**


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<tr>
<th>Tumour Group: Head and Neck</th>
<th>Tumour Regimen Code: 00517</th>
</tr>
</thead>
<tbody>
<tr>
<td>ISMO Contributor: Prof Maccon Keane</td>
<td>Version number: 1</td>
</tr>
</tbody>
</table>

Published: 07/11/2018
Review: 07/11/2020
NCCP Regimen: Gemcitabine (1250mg/m²) and CISplatin (80mg/m²) - 21 day

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Tumour Group: Head and Neck
NCCP Regimen Code: 00517

Version Date Amendment Approved By
1 07/11/2018

Prof Maccon Keane

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.

This indication is outside the licensed indications for Gemcitabine in Ireland. Patients should be informed of the unlicensed nature of this indication and consented to treatment in line with the hospital’s policy on the use of unlicensed medication and unlicensed or “off label” indications. Prescribers should be aware of their responsibility in communicating any relevant information to the patient and also in ensuring that the unlicensed or “off label” indication has been acknowledged by the hospital’s Drugs and Therapeutics Committee, or equivalent, in line with hospital policy.

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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