NCCP Chemotherapy Regimen

Gemcitabine (1000mg/m^2) and CISplatin (25mg/m^2)
Therapy- 21 day

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 pancreatic carcinoma</td>
<td>C25</td>
<td>00383a</td>
<td>Hospital</td>
</tr>
<tr>
<td>Locally advanced or metastatic biliary tree carcinoma</td>
<td>C22/C23</td>
<td>00383b</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.

Gemcitabine and CISplatin are administered on day 1 and day 8 of a 21 day cycle and treatment is continued 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>1</td>
<td>1 and 8</td>
<td>Gemcitabine</td>
<td>1000mg/m^2</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 and 8</td>
<td>CISplatin</td>
<td>25mg/m^2</td>
<td>IV infusion</td>
<td>500ml NaCl 0.9% over 120mins</td>
<td>Every 21 days</td>
</tr>
</tbody>
</table>

*Prehydration therapy required for CISplatin*

See local hospital policy recommendations.

Suggested prehydration for CISplatin therapy:

1. Administer 10mmol magnesium sulphate (MgSO_4) ((+/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 0-2
- Adequate marrow reserve (ANC > 1.5 x 10^9/L, platelets > 100x10^9/L)
- Total bilirubin ≤ 1.5 x ULN, liver enzymes ≤ 5 x ULN

NCCP Regimen: Gemcitabine and CISplatin (25mg/m^2)-21 day

Published: 15/11/2015
Review: 15/11/2019
Version number: 2

Tumour Group: Gastrointestinal
NCCP Regimen Code: 00383

ISM0 Contributor: Prof Maccon Keane

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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 responsibility of the prescribing clinician. and is subject to HSE’s terms of use available at http://www.hse.ie/eng/Disclaimer

This information is valid only on the day of printing, for any updates please check www.hse.ie/NCCPchemoregimens
EXCLUSIONS:
- Hypersensitivity to gemcitabine, CISplatin or any of the excipients
- Patients with inadequate renal function (CrCl < 45ml/min)
- 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:
Table 1: Dose modification of Gemcitabine in haematological toxicity

<table>
<thead>
<tr>
<th>ANC (x10^9 /L)</th>
<th>Platelets (x10^9 /L)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥1</td>
<td>≥ 100</td>
<td>100% Dose</td>
</tr>
<tr>
<td>0.5 to 0.99</td>
<td>or 75-100</td>
<td>75%</td>
</tr>
<tr>
<td>&lt;0.5</td>
<td>or &lt;75</td>
<td>Omit *</td>
</tr>
</tbody>
</table>

* CISplatin also omitted

Renal and Hepatic Impairment:
Table 2: Dose modification of CISplatin and Gemcitabine in renal and hepatic impairment

<table>
<thead>
<tr>
<th>Drug</th>
<th>Renal Impairment</th>
<th>Hepatic Impairment</th>
<th>Renal Impairment</th>
<th>Hepatic Impairment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cr Cl (ml/min)</td>
<td>Dose</td>
<td>No dose reductions necessary</td>
<td>AST elevations do not seem to cause dose limiting toxicities. If bilirubin &gt; 27 μmol/L, initiate treatment with dose of 800 mg/m².</td>
</tr>
<tr>
<td>CISplatin</td>
<td>&gt;60</td>
<td>100%</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>45-59</td>
<td>50%</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>&lt;45</td>
<td>Delay*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gemcitabine</td>
<td>&gt;30</td>
<td>100%</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>&lt;30</td>
<td>Consider dose reduction clinical decision</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Delay if day 1; if day 8, omit CISplatin
Management of adverse events:

Table 3: Dose Modification schedule 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 CISplatin 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>Omit CISplatin or consider substituting CISplatin with CARBOplatin 100% dose of gemcitabine</td>
</tr>
</tbody>
</table>

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL: Moderate-High (Refer to local policy).

PREMEDICATIONS: Pre Hydration therapy required for CISplatin 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 CISplatin 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 CISplatin. Encourage oral hydration. Avoid nephrotoxic drugs such as aminoglycoside antibiotics. Irreversible renal failure associated with hemolytic uremic syndrome may occur (rare) with gemcitabine. Use caution with pre-existing renal dysfunction.
- **Pulmonary Toxicity:** Acute shortness of breath may occur. Discontinue treatment with gemcitabine 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:

Gemcitabine L01BC05

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CISplatin L01XA01

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></td>
<td></td>
<td>Prof Maccon Keane</td>
</tr>
<tr>
<td>2</td>
<td>15/11/2017</td>
<td>Updated title, CISplatin hydration and dosing in renal and hepatic impairment. Applied new NCCP regimen template</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/profinfo/medonc/cdmp/