**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 patients with locally advanced or metastatic adenocarcinoma of the pancreas</td>
<td>C25</td>
<td>00283a</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 is administered once weekly for up to 7 weeks followed by a week of rest (1 cycle = 56 days). Subsequent cycles should consist of injections once weekly for 3 consecutive weeks out of every 4 weeks until disease progression or unacceptable toxicity develops.

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

<table>
<thead>
<tr>
<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, 8 15, 22, 29, 36, 43</td>
<td>Gemcitabine</td>
<td>1000mg/m²</td>
<td>IV infusion</td>
<td>250ml NaCl 0.9% over 30mins</td>
<td>Cycle 1 (56 days)</td>
</tr>
<tr>
<td>1, 8 and 15</td>
<td>Gemcitabine</td>
<td>1000mg/m²</td>
<td>IV infusion</td>
<td>250ml NaCl 0.9% over 30mins</td>
<td>Cycle 2 onwards (28 days)</td>
</tr>
</tbody>
</table>

**Eligibility:**

- Indication as above
- ECOG 0-2
- Macroscopic complete resection of tumour
- Adequate marrow reserve (ANC > 1.5 x 10⁹/L, platelets > 100x10⁹/L)
- Adequate renal (creatinine ≤ 1.5xULN) and liver function (bilirubin ≤ 26micromol; AST/ALK ≤ 5xULN)

**Exclusions:**

- Hypersensitivity to gemcitabine or any of the excipients
- Breast feeding

**Prescriptive Authority:**

The treatment plan must be initiated by a Consultant Medical Oncologist.
TESTS:
Baseline tests:
- FBC, renal and liver profile

Regular tests:
- FBC prior to each treatment
- 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:
Prior to commencing a new treatment cycle (i.e. day 1), ANC must be >1 x 10^9/L and platelets > 100 x 10^9/L

Table 1: Dose modifications for gemcitabine for haematological toxicity on treatment day

<table>
<thead>
<tr>
<th>ANC (x 10^9/L)</th>
<th>Platelet count (x 10^9/L)</th>
<th>Recommended dose of Gemcitabine</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;1 and &gt; 100</td>
<td>100 %</td>
<td></td>
</tr>
<tr>
<td>0.5-1 or 50-100</td>
<td>75% or delay based on clinical assessment</td>
<td></td>
</tr>
<tr>
<td>&lt; 0.5 or &lt;50</td>
<td>Delay</td>
<td></td>
</tr>
</tbody>
</table>

Renal and Hepatic Impairment:

Table 2: Dose modification of 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>Gemcitabine</td>
<td>Cr Cl (ml/min)</td>
<td>AST elevations do not seem to cause dose limiting toxicities. If bilirubin &gt; 27 micromol/L, initiate treatment with dose of 800 mg/m².</td>
</tr>
<tr>
<td>&gt;30 100%</td>
<td>Consider dose reduction clinical decision</td>
<td></td>
</tr>
<tr>
<td>&lt;30</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Management of adverse events:

Table 3: Dose Modification of gemcitabine for Adverse Events

<table>
<thead>
<tr>
<th>Adverse reactions</th>
<th>Recommended dose modification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade &gt; 3 Non-haematological toxicity</td>
<td>Therapy with gemcitabine should be withheld (until toxicity has resolved to grade ≤ 1) and may be resumed with 50% dose reduction or treatment discontinued at discretion of prescribing consultant.</td>
</tr>
<tr>
<td>(except nausea/vomiting)</td>
<td></td>
</tr>
<tr>
<td>Grade &gt; 4 Non-haematological toxicity</td>
<td>Discontinue treatment</td>
</tr>
</tbody>
</table>

NCCP Regimen: Gemcitabine (1000mg/m²)
Monotherapy- 56 day

Published: 24/11/2015
Review: 31/08/2020
Version number: 3

Tumour Group: Gastrointestinal
NCCP Regimen Code: 00283
ISMO Contributor: Prof Maccon Keane

This information is valid only on the day of printing, for any updates please check www.hse.ie/NCCP-ChemoRegimens
NCCP Chemotherapy Regimen

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL:
Gemcitabine  Low (Refer to local policy).

PREMEDICATIONS: None usually required

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.
- **Pulmonary Toxicity**: Acute shortness of breath may occur. 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.
- **Irreversible renal failure** associated with haemolytic uraemic syndrome may occur rarely with gemcitabine. Use caution with pre-existing renal impairment.
- **Infusion time**: Infusion time prolonged beyond 60 minutes has been shown to increase volume of distribution and has been associated with an increase in toxicity. However, given in the context of a fixed dose rate (FDR) regimen, prolonged infusions have also been reported to produce a higher response rate than standard regimens in association with a higher intracellular accumulation of its active metabolite (dFdCTP) (3-7).

DRUG INTERACTIONS:
- Current drug interaction databases should be consulted for more information.

ATC CODE:
Gemcitabine  L01BC05

REFERENCES:
3. BCCA Protocol Summary for Palliative Chemotherapy for Pancreatic Adenocarcinoma, Gallbladder Cancer, and Cholangiocarcinoma Using Gemcitabine Protocol Code GIPGEM revised 1 June 2017
4. Veltkamp SA, Beijnen JH, Schellens JHM. Prolonged versus standard gemcitabine infusion: translation of molecular pharmacology to new treatment strategy
5. Pollera CF, Ceribelli A, Crecco M, et al. Prolonged infusion gemcitabine: a clinical phase I study at low- (300 mg/m²) and high-dose (875mg/m²) levels. Invest New Drugs 1997;15(2):115-121.


<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>06/12/2017</td>
<td>Updated title, indications, dosing for haematological toxicity and dosing in renal and hepatic impairment. Applied new NCCP regimen template</td>
<td>Prof Maccon Keane</td>
</tr>
<tr>
<td>3</td>
<td>31/08/2018</td>
<td>Updated treatment table and dosing modifications for haematological toxicity</td>
<td>Prof Maccon Keane</td>
</tr>
</tbody>
</table>

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.

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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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