Gemcitabine (1000mg/m²) and RT therapy

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>Non-metastatic, locally advanced pancreatic cancer</td>
<td>C11</td>
<td>00521a</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 in 3 cycles over ten weeks as described in the treatment table below.

The summary table for the administration of gemcitabine and radiotherapy describes the three cycles as below:

1. Cycle 1 consists of Gemcitabine administered on days 1 and 8 of a 21 day cycle.
2. Cycle 2 (chemoradiotherapy phase) consists of gemcitabine administered on days 1, 8, and 15 of a 28-day cycle concurrent with radiotherapy on days 1 through 5, 8 through 12, and 15 through 19.
3. Cycle 3 consists of Gemcitabine administered on days 1 and 8 of a 21 day cycle.

Facilities to treat anaphylaxis MUST be present when Gemcitabine is administered.

Treatment table for Gemcitabine:

<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 and 8</td>
<td>Gemcitabine</td>
<td>1000mg/m²</td>
<td>IV infusion</td>
<td>250ml NaCl 0.9% over 30mins</td>
<td>1 (21 day cycle)</td>
</tr>
<tr>
<td>1, 8, 15</td>
<td>Gemcitabine</td>
<td>1000mg/m²</td>
<td>IV infusion</td>
<td>250ml NaCl 0.9% over 30mins</td>
<td>2 (concurrently with radiation on day 1-5 and 8-12 and 15-19) (28 day cycle)</td>
</tr>
<tr>
<td>1 and 8</td>
<td>Gemcitabine</td>
<td>1000mg/m²</td>
<td>IV infusion</td>
<td>250ml NaCl 0.9% over 30mins</td>
<td>3 (21 day cycle)</td>
</tr>
</tbody>
</table>

Summary table for administration of gemcitabine and radiotherapy:

<table>
<thead>
<tr>
<th>Cycle number</th>
<th>1 (21 day)</th>
<th>2 (28 day)</th>
<th>3 (21 day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day number</td>
<td>1 8 15</td>
<td>1 8 15 22</td>
<td>1 8 15</td>
</tr>
<tr>
<td>Treatment with gemcitabine</td>
<td>✓ ✓ x ✓ ✓ ✓ x ✓ ✓ x</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Radiotherapy</td>
<td>No radiotherapy</td>
<td>Radiotherapy on days 1-5 and 8-12 and 15-19</td>
<td>No radiotherapy</td>
</tr>
</tbody>
</table>
ELIGIBILITY:
- Indications as above
- ECOG 0-2

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 $\geq 1 \times 10^9/L$ and platelets $\geq 100 \times 10^9/L$.

Table 1: Dose modifications for gemcitabine within a cycle (i.e day 8 and 15)

<table>
<thead>
<tr>
<th>ANC ($\times 10^9$/L)</th>
<th>Platelet count ($\times 10^9$/L)</th>
<th>Other toxicity</th>
<th>Recommended dose of Gemcitabine</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\geq 1$</td>
<td>$\geq 100$</td>
<td></td>
<td>100 %</td>
</tr>
<tr>
<td>0.5 - 1</td>
<td>50 - 100</td>
<td></td>
<td>75%</td>
</tr>
<tr>
<td>&lt; 0.5</td>
<td>&lt; 50</td>
<td></td>
<td>Omit. Do not restart treatment until ANC $\geq 0.5$ and platelets $\geq 50$</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>&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>
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.</td>
</tr>
<tr>
<td>≥30</td>
<td>100%</td>
<td>If bilirubin &gt; 27 micromol/L, initiate treatment with dose of 800 mg/m².</td>
</tr>
<tr>
<td>&lt;30</td>
<td>Consider dose reduction Clinical decision</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 ≥ 2 Pneumonitis</td>
<td>Discontinue gemcitabine</td>
</tr>
<tr>
<td>Grade &gt; 3 Non-haematological toxicity (except nausea/vomiting)</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>Grade &gt; 4 Non-haematological toxicity</td>
<td>Discontinue treatment</td>
</tr>
</tbody>
</table>

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.
NCCP Chemotherapy Regimen

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

ATC CODE:
Gemcitabine L01BC05

REFERENCES:

Version | Date | Amendment | Approved By
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1 | 07/11/2018 | | Prof Maccon Keane

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/

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