Gemcitabine (1000mg/m²) and CISplatin (70mg/m²) Therapy- 28 day

INDICATIONS FOR USE:

<table>
<thead>
<tr>
<th>INDICATION</th>
<th>ICD10</th>
<th>Regimen Code</th>
<th>*Reimbursement Indicator</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment of patients with locally advanced or metastatic transitional cell carcinoma (TCC) of the urothelium</td>
<td>C67</td>
<td>00282a</td>
<td></td>
</tr>
</tbody>
</table>

*If a reimbursement indicator (e.g. ODMS, CDS) is not defined, the drug and its detailed indication have not been 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, 8 and 15 and CISplatin is administered on day 1 following gemcitabine or day 2 of each 28 day cycle for 4-6 cycles unless 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>1,8 and 15</td>
<td>Gemcitabine</td>
<td>1000mg/m²</td>
<td>IV infusion</td>
<td>250ml NaCl 0.9% over 30mins</td>
<td>Every 28 days</td>
</tr>
<tr>
<td>2</td>
<td>1</td>
<td>*CISplatin</td>
<td>70mg/m²</td>
<td>IV infusion</td>
<td>1000ml NaCl 0.9% over 120mins</td>
<td>Every 28 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 1000 mL sodium chloride 0.9% over 60 minutes.

Administer CISplatin as described above

Post hydration: Administer 1000 ml 0.9% NaCl over 60mins

Mannitol 10% may be used to 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.

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

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

NCCP Chemotherapy Regimen

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NCCP Chemotherapy Regimen

- 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 >1 x 10^9/L and platelets > 100 x 10^9/L

Dose modifications for gemcitabine within a cycle (i.e day 8)

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

<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>&gt;1</td>
<td>and &gt; 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>Omit. Do not restart treatment until ANC &gt; 0.5 and platelets &gt; 50</td>
</tr>
<tr>
<td>ANC &lt; 0.5 for &gt;5 days or ANC &lt; 0.1 for &gt;3 days or Any incidence of febrile neutropenia</td>
<td>or &lt; 25 or 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>
<td></td>
</tr>
</tbody>
</table>
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>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cr Cl (ml/min)</td>
<td>Dose</td>
</tr>
<tr>
<td>CISplatin</td>
<td>≥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</td>
</tr>
<tr>
<td>Gemcitabine</td>
<td>&gt;30</td>
<td>100%</td>
</tr>
<tr>
<td></td>
<td>&lt;30</td>
<td>Consider dose reduction clinical decision</td>
</tr>
</tbody>
</table>

Management of adverse events:

Table 3: Dose Modification of gemcitabine and CISplatin 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>Substitute CARBOplatin AUC 5 or 50% reduction of CISplatin dose after recovery to grade ≤ 1. 100% dose of gemcitabine</td>
</tr>
</tbody>
</table>

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL:

- CISplatin: High (Refer to local policy)
- Gemcitabine: Low (Refer to local policy).

PREMEDICATIONS:

Pre and Post 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 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.

Please refer to NCCP protocol 00283 Gemcitabine Monotherapy-Locally Advanced or metastatic for detailed information on adverse effects/regimen specific complications relating to gemcitabine

**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
- CISplatin: L01XA01

**REFERENCES:**


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NCCP Chemotherapy Regimen

NCCP Regimen: Gemcitabine (1000mg/m²) and CISplatin (70mg/m²) - 28 day

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

Tumour Group: Genitourinary
NCCP Regimen Code: 00282

Version | Date | Amendment | Approved By
--- | --- | --- | ---
1 | | | Prof Maccon Keane
2 | 15/11/2017 | Updated title and dosing in renal and hepatic impairment. Applied new NCCP regimen template | 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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