Chemotherapy Protocol

BLADDER

CISPLATIN (35)-GEMCITABINE

Regimen

- Bladder-Cisplatin (35)-Gemcitabine

Indication

- For use in patients unable to tolerate standard cisplatin (70)-gemcitabine due to:
  - poor performance status
  - poor tolerance of cisplatin (70)-gemcitabine
  - impaired renal function

Toxicity

<table>
<thead>
<tr>
<th>Drug</th>
<th>Adverse Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cisplatin</td>
<td>Neuropathy, nephrotoxicity, ototoxicity, highly emetogenic</td>
</tr>
<tr>
<td>Gemcitabine</td>
<td>Peripheral oedema, diarrhoea, constipation, rash, respiratory problems, influenza like symptoms, radiosensitising</td>
</tr>
</tbody>
</table>

The adverse effects listed are not exhaustive. Please refer to the relevant Summary of Product Characteristics for full details.

Monitoring

Drugs

- FBC, LFTs and U&Es prior to day 1 and 8 of treatment

- Calculated or measured creatinine clearance prior to each cycle. EDTA may be considered prior to cycle one or if, during treatment, there are significant changes in renal function.

Dose Modifications

The dose modifications listed are for haematological, liver and renal function and drug specific toxicities only. Dose adjustments may be necessary for other toxicities as well.

In principle all dose reductions due to adverse drug reactions should not be re-escalated in subsequent cycles without consultant approval. It is also a general rule for chemotherapy that if a third dose reduction is necessary treatment should be stopped.

Please discuss all dose reductions / delays with the relevant consultant before prescribing, if appropriate. The approach may be different depending on the clinical circumstances.
Haematological

Consider blood transfusion if patient symptomatic of anaemia or has a haemoglobin of less than 8g/dL.

Day 1

<table>
<thead>
<tr>
<th>Neutrophils (x10^9/L)</th>
<th>Dose Modifications (cisplatin and gemcitabine)</th>
</tr>
</thead>
<tbody>
<tr>
<td>more than or equal to 1</td>
<td>100%</td>
</tr>
<tr>
<td>less than 1</td>
<td>1st Occurrence Delay until recovery. 2nd Occurrence Delay until recovery then give 75% of the original dose.</td>
</tr>
<tr>
<td>Febrile Neutropenia</td>
<td>1st Occurrence Delay until recovery and then re-start treatment using 75% of the original dose.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Platelets (x10^9/L)</th>
<th>Dose Modifications (cisplatin and gemcitabine)</th>
</tr>
</thead>
<tbody>
<tr>
<td>more than or equal to 100</td>
<td>100%</td>
</tr>
<tr>
<td>Less than 100</td>
<td>1st Occurrence Delay until recovery then give 75% of the original dose. 2nd Occurrence Delay until recovery then give 50% of the original dose.</td>
</tr>
</tbody>
</table>

Day 8

<table>
<thead>
<tr>
<th>Neutrophils (x10^9/L)</th>
<th>Dose Modifications (cisplatin and gemcitabine)</th>
</tr>
</thead>
<tbody>
<tr>
<td>more than or equal to 1</td>
<td>100%</td>
</tr>
<tr>
<td>0.5 - 1</td>
<td>75%</td>
</tr>
<tr>
<td>less than 0.5</td>
<td>Omit</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Platelets (x10^9/L)</th>
<th>Dose Modifications (cisplatin and gemcitabine)</th>
</tr>
</thead>
<tbody>
<tr>
<td>more than or equal to 100</td>
<td>100%</td>
</tr>
<tr>
<td>50 - 100</td>
<td>75%</td>
</tr>
<tr>
<td>less than 50</td>
<td>Omit</td>
</tr>
</tbody>
</table>
**Hepatic Impairment**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Bilirubin μmol/L</th>
<th>AST/ALT units/L</th>
<th>Dose (% of original dose)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cisplatin</td>
<td>N/A</td>
<td>N/A</td>
<td>No dose adjustment needed</td>
</tr>
<tr>
<td>Gemcitabine</td>
<td>greater than 30*</td>
<td>N/A</td>
<td>Initiate treatment with a dose of 800mg/m²</td>
</tr>
</tbody>
</table>

*Limit reflects local practice and may vary from published sources

**Renal Impairment**

This regimen has been tolerated in patients with creatinine clearances as low as 40ml/min

<table>
<thead>
<tr>
<th>Drug</th>
<th>Creatinine Clearance (ml/min)</th>
<th>Dose (% of original dose)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cisplatin</td>
<td>40 or greater</td>
<td>100%</td>
</tr>
<tr>
<td></td>
<td>less than 40</td>
<td>Consider alternative</td>
</tr>
<tr>
<td>Gemcitabine</td>
<td>30 or greater</td>
<td>100%</td>
</tr>
<tr>
<td></td>
<td>less than 30</td>
<td>Consider dose reduction</td>
</tr>
</tbody>
</table>

**Other**

Dose reductions or interruptions in therapy are not necessary for those toxicities that are considered unlikely to be serious or life threatening. For example, alopecia, altered taste or nail changes.

For all other non-haematological NCI-CTC grade 3 and above toxicities delay treatment until the adverse effect has resolved to NCI-CTC grade 1 or below. The dose of the causative agent should then be reduced to 75% of the original dose or discontinued as appropriate.

**Regimen**

**21 day cycle for 3 - 6 cycles (3 cycles will be set in Aria)**

First line treatment – 6 cycles

Adjuvant – 4 cycles

Neoadjuvant – 3 cycles

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Days</th>
<th>Administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cisplatin</td>
<td>35mg/m²</td>
<td>1 and 8</td>
<td>Intravenous infusion in 1000ml sodium chloride 0.9% plus 20mmol potassium chloride at a rate of cisplatin of 1mg/min (minimum 60 minutes)</td>
</tr>
<tr>
<td>Gemcitabine</td>
<td>1000mg/m²</td>
<td>1 and 8</td>
<td>Intravenous infusion in 250ml sodium chloride 0.9% over 30 minutes</td>
</tr>
</tbody>
</table>
**Dose Information**

- Cisplatin will be dose banded according to the CSCCN agreed bands
- Gemcitabine will be dose banded according to the CSCCN agreed bands

**Administration Information**

**Extravasation**

- Cisplatin – exfoliant
- Gemcitabine – neutral

**Additional Therapy**

- **Antiemetics**
  15-30 minutes prior to chemotherapy
  - dexamethasone 8mg oral or intravenous
  - ondansetron 8mg oral or intravenous

  As take home medication
  - dexamethasone 4mg oral twice a day for 3 days
  - metoclopramide 10mg oral three times a day as required
  - ondansetron 8mg oral twice a day for 3 days

- **Cisplatin pre and post hydration as follows**
  
  **Pre**
  Furosemide 40mg when required oral or intravenous
  500ml sodium chloride 0.9% with 8mmol magnesium sulphate over 30 minutes

  **Post**
  500ml sodium chloride 0.9% over 30 minutes
  Patients should be advised to drink at least 3 litres of fluid in the 24 hours after administration of cisplatin.

- **Mouthwashes according to local or national policy on the treatment of mucositis**

- **Gastric protection with a proton pump inhibitor or a H₂ antagonist may be considered in patients considered at high risk of GI ulceration or bleed.**
Coding (OPCS)

- Procurement – X70.5
- Delivery – X72.1 & X72.4

References
REGIMEN SUMMARY

Cisplatin (35)-Gemcitabine

Cycles One and Two

Day 1 and 8

1. Dexamethasone 8mg oral or intravenous
2. Ondansetron 8mg oral or intravenous
3. Furosemide 40mg when required oral or intravenous
4. Sodium chloride 0.9% 500ml with magnesium sulphate 8mmol over 30 minutes
5. Gemcitabine 1000mg/m² intravenous infusion in 250ml sodium chloride 0.9% over 30 minutes
6. Cisplatin 35mg/m² in 1000ml sodium chloride 0.9% with 20mmol potassium chloride intravenous infusion at a rate of cisplatin 1mg/minute (minimum 60 minutes).
7. Sodium chloride 0.9% 500ml over 30 minutes

Take Home Medicines – Day 1

8. Dexamethasone 4mg oral twice a day for 3 days starting the day after chemotherapy

Administration Instructions
Dispense a supply for both day 1 and 8 of the cycle.

9. Metoclopramide 10mg oral three times a day when required for nausea

Administration Instructions
Dispense 10 days or an original pack if appropriate to cover day 1 and 8 of the cycle.

10. Ondansetron 8mg oral twice a day for 3 days starting on the evening of chemotherapy treatment

Administration Instructions
Dispense a supply for both day 1 and 8 of the cycle.

Cycle Three

Day 1 and 8

11. Warning – check number of cycles*

12. Dexamethasone 8mg oral or intravenous

13. Ondansetron 8mg oral or intravenous

14. Furosemide 40mg when required oral or intravenous

15. Sodium chloride 0.9% 500ml with magnesium sulphate 8mmol over 30 minutes

16. Gemcitabine 1000mg/m² intravenous infusion in 250ml sodium chloride 0.9% over 30 minutes
17. Cisplatin 35mg/m² in 1000ml sodium chloride 0.9% with 20mmol potassium chloride intravenous infusion at a rate of cisplatin 1mg/minute (minimum 60 minutes)

18. Sodium chloride 0.9% 500ml over 30 minutes

**Take Home Medicines – Day 1**

19. Dexamethasone 4mg oral twice a day for 3 days starting the day after chemotherapy
   Administration Instructions
   Dispense a supply for both day 1 and 8 of the cycle.

20. Metoclopramide 10mg oral three times a day when required for nausea
    Administration Instructions
    Dispense 10 days or an original pack if appropriate to cover day 1 and 8 of the cycle.

21. Ondansetron 8mg oral twice a day for 3 days starting on the evening of chemotherapy treatment
    Administration Instructions
    Dispense a supply for both day 1 and 8 of the cycle.

*Warning to appear on Cycle 3 Day 1 only.*
## DOCUMENT CONTROL

<table>
<thead>
<tr>
<th>Version</th>
<th>Date</th>
<th>Amendment</th>
<th>Written By</th>
<th>Approved By</th>
</tr>
</thead>
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<tr>
<td>1.1</td>
<td>May 2015</td>
<td>Header changed&lt;br&gt;Comment re local bilirubin limit added&lt;br&gt;Metoclopramide dose changed to 10mg&lt;br&gt;Bolus removed from intravenous bolus throughout text&lt;br&gt;Mucositis recommendation changed&lt;br&gt;Dexamethasone TTO clarified&lt;br&gt;Metoclopramide TTO clarified&lt;br&gt;Ondansetron TTO clarified&lt;br&gt;Warning on C3 D1 only clarified&lt;br&gt;Disclaimer added</td>
<td>Donna Kimber Pharmacy Technician</td>
<td>Rebecca Wills Pharmacist</td>
</tr>
<tr>
<td>1</td>
<td>Dec 2012</td>
<td>None</td>
<td>Rebecca Wills Pharmacist</td>
<td>Dr Joanna Gale Consultant Medical Oncologist</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Dr Deborah Wright Pharmacist</td>
<td>Dr Mathew Wheater Consultant Medical Oncologist</td>
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This chemotherapy protocol has been developed as part of the chemotherapy electronic prescribing project. This was and remains a collaborative project that originated from the former CSCCN. These documents have been approved on behalf of the following Trusts:

- Hampshire Hospitals NHS Foundation Trust
- NHS Isle of Wight
- Portsmouth Hospitals NHS Trust
- Salisbury Hospitals NHS Foundation Trust
- University Hospital Southampton NHS Foundation Trust
- Western Sussex Hospitals NHS Foundation Trust

All actions have been taken to ensure these protocols are correct. However, no responsibility can be taken for errors which occur as a result of following these guidelines.