Chemotherapy Protocol

LYMPHOMA

CISPLATIN-GEMCITABINE-METHYLPREDNISOLONE

GemP

Regimen

- Lymphoma – GemP-Cisplatin-Gemcitabine-Methylprednisolone

Indication

- Non-Hodgkin’s Lymphoma
- Hodgkin’s Lymphoma

Toxicity

<table>
<thead>
<tr>
<th>Drug</th>
<th>Adverse Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cisplatin</td>
<td>Neuropathy, nephrotoxicity, ototoxicity</td>
</tr>
<tr>
<td>Gemcitabine</td>
<td>Peripheral oedema, diarrhoea, constipation, rash, respiratory problems, influenza-like symptoms, radiosensitising</td>
</tr>
<tr>
<td>Methylprednisolone</td>
<td>Weight gain, GI disturbances, hyperglycaemia, CNS disturbances, cushingoid changes, glucose intolerance</td>
</tr>
</tbody>
</table>

Patients diagnosed with Hodgkin’s Lymphoma carry a lifelong risk of transfusion associated graft versus host disease (TA-GVHD). Where blood products are required these patients must receive only irradiated blood products for life. Local blood transfusion departments must be notified as soon as a diagnosis is made and the patient must be issued with an alert card to carry with them at all times.

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

Monitoring

Drugs

- FBC prior to day one, eight and fifteen
- LFTs and U&Es prior to first cycle and prior to day fifteen of each cycle
- EDTA or calculated creatinine clearance before each cycle
- Regular monitoring of blood glucose
- Consider formal audiology testing
**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**

Dose modifications for haematological toxicity in the table below are for general guidance only. Always refer to the responsible consultant as any dose reductions or delays will be dependent on clinical circumstances and treatment intent. Low counts can be a consequence of bone marrow infiltration as well as drug toxicity.

Consider blood transfusion if patient symptomatic of anaemia or has a haemoglobin of less than 8g/dL. **Irradiated blood products must be used in Hodgkin’s Lymphoma patients.**

**Day 1 and 8**

<table>
<thead>
<tr>
<th>Neutrophils (x10⁹/L)</th>
<th>Dose Modifications (gemcitabine)</th>
</tr>
</thead>
<tbody>
<tr>
<td>more than or equal to 1</td>
<td>100%</td>
</tr>
<tr>
<td>0.5 - 0.9</td>
<td>Administer 75% of the original dose with prophylactic growth factors</td>
</tr>
<tr>
<td>less than 0.5 or febrile neutropenia</td>
<td>Omit</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Platelets (x10⁹/L)</th>
<th>Dose Modifications (gemcitabine)</th>
</tr>
</thead>
<tbody>
<tr>
<td>more than 75</td>
<td>100%</td>
</tr>
<tr>
<td>50–74</td>
<td>Administer 75% of the original dose</td>
</tr>
<tr>
<td>less than 50 or bleeding</td>
<td>Omit</td>
</tr>
</tbody>
</table>
Day 15

<table>
<thead>
<tr>
<th>Neutrophils (x10^9/L)</th>
<th>Dose Modifications (cisplatin and gemcitabine)</th>
</tr>
</thead>
<tbody>
<tr>
<td>more than 1</td>
<td>100%</td>
</tr>
<tr>
<td>0.5-0.9</td>
<td>Administer 75% of the original dose with prophylactic growth factors</td>
</tr>
</tbody>
</table>
| less than 0.5 or febrile neutropenia | 1st Occurrence  
Delay until greater than or equal to 1 and administer 75% of the original dose with prophylactic growth factors  
2nd Occurrence  
Delay until greater than or equal to 1 and give 50% of the original dose with prophylactic growth factors |

<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 75</td>
<td>100%</td>
</tr>
<tr>
<td>50–74</td>
<td>Administer 75% of the original dose</td>
</tr>
</tbody>
</table>
| Less than 50 or bleeding | 1st Occurrence  
Delay until more than or equal to 75 then administer 75% of the original dose  
2nd Occurrence  
Delay until more than or equal to 75 then administer 50% of the original dose |

Hepatic Impairment

Please note that the approach may be different where abnormal liver function tests are due to disease involvement.

<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>more 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 differ from published sources
Renal Impairment

<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>more than 60</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>40-59</td>
<td>see below*</td>
</tr>
<tr>
<td></td>
<td>less than 40</td>
<td>Consider alternative</td>
</tr>
<tr>
<td>Gemcitabine</td>
<td>more than or equal to 30</td>
<td>100%</td>
</tr>
<tr>
<td></td>
<td>less than 30</td>
<td>Consider dose reduction</td>
</tr>
</tbody>
</table>

* when the creatinine clearance is between 40 and 59 modify the cisplatin dose such that the number used to calculate the dose/m² is the same as the creatinine clearance value. For example a patient with a creatinine clearance of 45ml/min will receive a cisplatin dose of 45mg/m².

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.

Cisplatin

Neurotoxicity occurring at a NCI-CTC grade 2 or above or a new functional deterioration in hearing and/or tinnitus that does not resolve between cycles consider a dose reduction to 75mg/m² in the first instance.

Regimen

28 day cycle for up to 6 cycles

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Days</th>
<th>Administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methylprednisolone</td>
<td>1000mg</td>
<td>1,2,3,4,5</td>
<td>Oral or as an intravenous infusion in 100ml sodium chloride 0.9% over 30 minutes</td>
</tr>
<tr>
<td>Gemcitabine</td>
<td>1000mg/m²</td>
<td>1,8,15</td>
<td>Intravenous infusion in 250ml sodium chloride 0.9% over 30 minutes</td>
</tr>
<tr>
<td>Cisplatin</td>
<td>100mg/m²</td>
<td>15</td>
<td>Intravenous infusion in 1000ml sodium chloride 0.9% with 20mmol potassium chloride over 120 minutes (max rate is 1mg cisplatin/minute)</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
- Methylprednisolone - neutral

Other
- Methylprednisolone when prescribed orally should be taken in the morning with or after food.

Additional Therapy

- Antiemetics
  15-30 minutes prior to chemotherapy on **day 1 and 8** only
  - metoclopramide 10mg oral or intravenous
  
  As take home medication on **day 1** only
  - metoclopramide 10mg three times a day oral as necessary

  15-30 minutes prior to chemotherapy on **day 15** only
  - aprepitant 125mg oral
  - dexamethasone 4mg oral or intravenous
  - ondansetron 8mg oral or intravenous
  
  As take home medication on **day 15** only
  - aprepitant 80mg once a day oral for 2 days
  - dexamethasone 4mg once a day oral for 3 days
  - metoclopramide 10mg three times a day oral as necessary
  - ondansetron 8mg twice a day oral for 3 days

- Cisplatin pre and post hydration as follows;
  
  Pre
  
  Furosemide 40mg oral or intravenous
  
  1000ml sodium chloride 0.9% with 20mmol potassium chloride and 16mmol magnesium sulphate over 60 minutes
  
  Post
  
  1000ml sodium chloride 0.9% with 20mmol potassium chloride and 16mmol magnesium sulphate over 60 minutes
Patients should be advised to drink at least 3 litres of fluid in the 24 hours after administration of cisplatin.

- Allopurinol 300mg once a day oral for the first cycle only
- Consider anti-infective prophylaxis in high risk patients, including:
  - aciclovir 400mg twice a day oral
  - co-trimoxazole 960mg once a day oral on Monday, Wednesday and Friday only
- 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 4.6)**

- Procurement – X71.2
- Delivery – X72.1 Day 1, X72.4 Day 8 & 15

**References**

REGIMEN SUMMARY

GemP-Cisplatin-Gemcitabine-Methylprednisolone

Cycle 1 Day One

1. Warning – Check blood transfusion status
   Administration Instructions
   Patients with HODGKIN’s lymphoma carry a lifelong risk of transfusion associated graft versus host disease. Where blood products are required these patients must receive ONLY IRRADIATED BLOOD PRODUCTS for life. Ensure transfusion departments are notified and the patient has been issued with an alert card to carry with them at all times.

2. Metoclopramide 10mg oral or intravenous

3. Methylprednisolone 1000mg oral or intravenous infusion in 250ml sodium chloride 0.9% over 30 minutes

4. Gemcitabine 1000mg/m² intravenous infusion in 250ml sodium chloride 0.9% over 30 minutes

Take home medicines

5. Allopurinol 300mg once a day oral for 28 days

6. Methylprednisolone 1000mg once a day oral for 4 days starting on day two of treatment

7. Metoclopramide 10mg three times a day oral when required *

Cycle 1 Day Eight

1. Metoclopramide 10mg oral or intravenous

2. Gemcitabine 1000mg/m² intravenous infusion in 250ml sodium chloride 0.9% over 30 minutes

Cycle 1 Day Fifteen

1. Aprepitant 125mg oral

2. Dexamethasone 4mg oral or intravenous

3. Ondansetron 8mg oral or intravenous

4. Gemcitabine 1000mg/m² intravenous infusion in 250ml sodium chloride 0.9% over 30 minutes

5. Furosemide 40mg oral or intravenous

6. Sodium Chloride 0.9% 1000ml with 20mmol potassium chloride and 16mmol magnesium sulphate intravenous infusion over 60 minutes

7. Cisplatin 100mg/m² intravenous infusion in 1000ml sodium chloride 0.9% with 20mmol potassium chloride over 180 minutes
8. Sodium Chloride 0.9% 1000ml with 20mmol potassium chloride and 16mmol magnesium sulphate intravenous infusion over 60 minutes

**Take home medicines**

9. Aprepitant 80mg once a day oral for 2 days starting the day after cisplatin
10. Dexamethasone 4mg once a day oral for 3 days starting the day after cisplatin
11. Metoclopramide 10mg three times a day oral when required
12. Ondansetron 8mg twice a day oral for 3 days starting on the evening of chemotherapy administration

**Cycles 2, 3, 4, 5 & 6 Day One**

8. Metoclopramide 10mg oral or intravenous
9. Methylprednisolone 1000mg oral or intravenous infusion in 250ml sodium chloride 0.9% over 30 minutes
10. Gemcitabine 1000mg/m² intravenous infusion in 250ml sodium chloride 0.9% over 30 minutes

**Take home medicines**

11. Methylprednisolone 1000mg once a day oral for 4 days starting on day two of treatment
12. Metoclopramide 10mg three times a day oral when required *

**Cycles 2, 3, 4, 5 & 6 Day Eight**

1. Metoclopramide 10mg oral or intravenous
2. Gemcitabine 1000mg/m² intravenous infusion in 250ml sodium chloride 0.9% over 30 minutes

**Cycles 2, 3, 4, 5 & 6 Day Fifteen**

1. Aprepitant 125mg oral
2. Dexamethasone 4mg oral or intravenous
3. Ondansetron 8mg oral or intravenous
4. Gemcitabine 1000mg/m² intravenous infusion in 250ml sodium chloride 0.9% over 30 minutes
5. Furosemide 40mg oral or intravenous
6. Sodium Chloride 0.9% 1000ml with 20mmol potassium chloride and 16mmol magnesium sulphate intravenous infusion over 60 minutes
7. Cisplatin 100mg/m² intravenous infusion in 1000ml sodium chloride 0.9% with 20mmol potassium chloride over 180 minutes

8. Sodium Chloride 0.9% 1000ml with 20mmol potassium chloride and 16mmol magnesium sulphate intravenous infusion over 60 minutes

**Take home medicines**

9. Aprepitant 80mg once a day oral for 2 days starting the day after cisplatin

10. Dexamethasone 4mg once a day oral for 3 days starting the day after cisplatin

11. Metoclopramide 10mg three times a day oral when required

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

*On day 8 no metoclopramide will be dispensed as take home medicine. The patient should be counselled that the supply on day one is for both dates.
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.