

Chemotherapy Protocol

LYMPHOMA

CISPLATIN-GEMCITABINE-METHYLPREDNISOLONE

(GemP)

Regimen

- Lymphoma – GemP-Cisplatin-Gemcitabine-Methylprednisolone

Indication

- Non-Hodgkin's Lymphoma
- Hodgkin's Lymphoma

Toxicity

Drug	Adverse Effect
Cisplatin	Neuropathy, nephrotoxicity, ototoxicity
Gemcitabine	Peripheral oedema, diarrhoea, constipation, rash, respiratory problems, influenza-like symptoms, radiosensitising
Methylprednisolone	Weight gain, GI disturbances, hyperglycaemia, CNS disturbances, cushingoid changes, glucose intolerance

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

Neutrophils (x10⁹/L)	Dose Modifications (gemcitabine)
more than or equal to 1	100%
0.5 - 0.9	Administer 75% of the original dose with prophylactic growth factors
less than 0.5 or febrile neutropenia	Omit
Platelets (x10⁹/L)	Dose Modifications (gemcitabine)
more than 75	100%
50–74	Administer 75% of the original dose
less than 50 or bleeding	Omit

Day 15

Neutrophils ($\times 10^9/L$)	Dose Modifications (cisplatin and gemcitabine)
more than 1	100%
0.5-0.9	Administer 75% of the original dose with prophylactic growth factors
less than 0.5 or febrile neutropenia	1 st Occurrence Delay until greater than or equal to 1 and administer 75% of the original dose with prophylactic growth factors 2 nd Occurrence Delay until greater than or equal to 1 and give 50% of the original dose with prophylactic growth factors
Platelets ($\times 10^9/L$)	Dose Modifications (cisplatin and gemcitabine)
more than or equal to 75	100%
50–74	Administer 75% of the original dose
Less than 50 or bleeding	1 st Occurrence Delay until more than or equal to 75 then administer 75% of the original dose 2 nd 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.

Drug	Bilirubin $\mu\text{mol}/L$		AST/ALT units/L	Dose (% of original dose)
Cisplatin	N/A		N/A	No dose adjustment needed
Gemcitabine	more than 30*		N/A	Initiate treatment with a dose of $800\text{mg}/\text{m}^2$

*Limit reflects local practice and may differ from published sources

Renal Impairment

Drug	Creatinine Clearance (ml/min)	Dose (% of original dose)
Cisplatin	more than 60	100
	40-59	see below*
	less than 40	Consider alternative
Gemcitabine	more than or equal to 30	100%
	less than 30	Consider dose reduction

* 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

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

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

- 1.Chau I, Harries M, Cunningham D et al. Gemcitabine, cisplatin and methylprednisolone chemotherapy (GEM-P) is an effective regimen in patients with poor prognostic primary progressive or multiple relapsed Hodgkins and non-Hodgkins lymphoma. Br J Haematol 2003; 120 (6): 970-977.
- 2.Sirohi B, Cunningham D, Norman A, Last K, Chau I, Horwich A, Oates J, Chong G, Wotherspoon A. Gemcitabine, cisplatin and methylprednisolone (GEM-P) with or without Rituximab in relapsed and refractory patients with diffuse large B cell lymphoma (DLBCL). Hematology 2007; 12(2): 149-53.
- 3.Ng M, Waters J, Cunningham D et al. Gemcitabine, cisplatin and methylprednisolone (GEM-P) is an effective salvage regimen in patients with relapsed and refractory lymphoma. Br J Cancer 2005; 92(8): 1352-7.

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.

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1.3	Jan 2015	Header changed Toxicities removed Hepatic impairment tables updated Metoclopramide dose changed to 10mg Bolus removed from intravenous bolus throughout text Mucositis recommendation changed “Warning-Check blood transfusion status” added to cycle 1 Document control reordered Disclaimer added	Donna Kimber Pharmacy Technician	Rebecca Wills Pharmacist
1.2	Aug 2012	Regimen summary - dexamethasone changed from 2mg twice a day to 4mg once a day (also on page 6). Aprepitant take home instruction changed to starting the day after cisplatin and ondansetron take home changed to starting on the evening of chemotherapy.	Dr Debbie Wright Pharmacist	Donna Kimber System Manager
1.1	July 2012	Regimen summary - number of days of allopurinol supply changed from 21 to 28.	Rebecca Wills Pharmacist	Dr Debbie Wright Pharmacist
1	May 2012	None	Rebecca Wills Pharmacist Dr Debbie Wright Pharmacist	Dr A Davies Consultant Medical Oncologist Dr A Milne Consultant Haematologist

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.