

Chemotherapy Protocol

LYMPHOMA

CISPLATIN-DEXAMETHASONE-GEMCITABINE

(GDP)

Regimen

- Lymphoma – GDP-Cisplatin-Dexamethasone-Gemcitabine

Indication

- Hodgkin's Lymphoma

Toxicity

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

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 and U&Es prior to day one and eight of treatment
- LFTs prior to day one of treatment
- EDTA or calculated creatinine clearance before day one
- 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

Neutrophils ($\times 10^9/L$)		Platelets ($\times 10^9/L$)	Dose Modifications (cisplatin and gemcitabine)
greater than or equal to 1	AND	greater than or equal to 75	100%
greater than or equal to 1	AND	less than 75	Delay 1 week, if platelets are greater than or equal to 50 then give 100% with platelet transfusions as necessary.
less than 1	AND	greater than or equal to 75	Delay 1 week, if neutrophils are greater than or equal to 0.5 then give 100% with G-CSF support
less than 1	AND	less than 75	Delay 1 week: If neutrophils are greater than or equal to 0.5 AND platelets are greater than or equal to 50 then give 100% with G-CSF and platelet transfusions as necessary. If neutrophils are less than 0.5 AND/OR platelets are less than 50 hold treatment, re-check blood counts every 3 days, resume treatment once neutrophils and platelets are greater or equal to 0.5 and 50 respectively

Day 8

Neutrophils (x10 ⁹ /L)		Platelets (x10 ⁹ /L)	Dose Modifications (gemcitabine)
greater than or equal to 1	AND	greater than or equal to 75	100%
0.5 - 0.9	AND	greater than or equal to 75	Give 100% and support with G-CSF OR Give 75% of original dose
greater than or equal to 0.5	AND	50-75	Give 75% of original dose
less than 0.5	OR	less than 50	Omit

Hepatic Impairment

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

Drug	Bilirubin μ mol/L		AST/ALT units	Dose (% of original dose)
Cisplatin	N/A		N/A	No dose adjustment needed
Gemcitabine	greater than 30*		N/A	Initiate treatment with a dose of 800mg/m ²

* Limit reflects local practice and may vary from published sources

Renal Impairment

Drug	Creatinine Clearance (ml/min)	Dose (% of original dose)
Cisplatin	more than 60	100%
	40-59	75%
	less than 40	Consider alternative
Gemcitabine	greater than or equal to 30	100%
	less than 30	Consider dose reduction

Cisplatin

Ototoxicity of grade 2 or above, discuss with consultant – dose may need to be reduced.

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 clinically significant grade 3 non-haematological toxicities reduce gemcitabine and cisplatin doses to 75%.

For all other clinically significant grade 4 non-haematological toxicities reduce gemcitabine and cisplatin doses to 50%.

Regimen

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

Drug	Dose	Days	Administration
Dexamethasone	40mg	1,2,3,4	Oral
Cisplatin	75mg/m ²	1	Intravenous infusion in 1000ml sodium chloride 0.9% with 20mmol potassium chloride over 120 minutes (max rate is 1mg cisplatin/minute)
Gemcitabine	1000mg/m ²	1, 8	Intravenous infusion in 250ml sodium chloride 0.9% over 30 minutes
G-CSF	1 dose	9-15	Subcutaneous

Dose Information

- Cisplatin will be dose banded in accordance with the national dose bands (1mg/ml)
- Gemcitabine will be dose banded in accordance with the national dose bands (100mg/ml)

Administration Information

Extravasation

- Cisplatin – exfoliant
- Gemcitabine – neutral

Other

- Dexamethasone tablets to be taken in the morning with or after food

Additional Therapy

- Antiemetics

15-30 minutes prior to chemotherapy on **day 1**

- aprepitant 125mg oral
- ondansetron 8mg oral or intravenous

As take home medication on day 1

- aprepitant 80mg once a day oral for 2 days starting on day two of treatment
- metoclopramide 10mg three times a day oral as necessary
- ondansetron 8mg twice a day oral for 3 days starting on the evening of day one of treatment

15-30 minutes prior to chemotherapy on **day 8**

- metoclopramide 10mg oral or intravenous

- 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 for 7 days oral for the first cycle only
- Anti-infective prophylaxis including:
 - aciclovir 400mg twice a day oral
 - co-trimoxazole 960mg once a day on Monday, Wednesday and Friday only oral
- Growth factor on days 9 to 15. For example:
 - filgrastim or bioequivalent 30 million units once a day for 7 days from day 9 subcutaneous
 - lenograstim or bioequivalent 33.6 million units once a day for 7 days from day 9 subcutaneous
- 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](#)

- Procurement – X70.4
- Delivery – X72.1 Day 1, X72.4 Day 8

References

1. Crump M, Kuruvilla J, Couban S, et al. Randomized comparison of gemcitabine, dexamethasone, and cisplatin versus dexamethasone, cytarabine, and cisplatin chemotherapy before autologous stem-cell transplantation for relapsed and refractory aggressive lymphomas: NCIC-CTG LY.12. J Clin Oncol. 2014 Nov 1;32(31):3490-6

REGIMEN SUMMARY

GDP-Cisplatin-Dexamethasone-Gemcitabine

Cycle 1 Day 1

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. Dexamethasone 40mg oral
3. Aprepitant 125mg oral
4. Ondansetron 8mg oral or intravenous
5. Gemcitabine 1000mg/m² intravenous infusion in 250ml sodium chloride 0.9% over 30 minutes
6. Furosemide 40mg oral or intravenous
7. Sodium chloride 0.9% 1000ml with 20mmol potassium chloride and 16mmol magnesium sulphate intravenous infusion over 60 minutes
8. Cisplatin 75mg/m² intravenous infusion in 1000ml sodium chloride 0.9% with 20mmol potassium chloride intravenous infusion over 120 minutes (maximum rate 1mg cisplatin/minute)
9. Sodium chloride 0.9% 1000ml with 20mmol potassium chloride and 16mmol magnesium sulphate intravenous infusion over 60 minutes

Take home medicines (day 1 only)

10. Dexamethasone 40mg once a day oral for 3 days starting on day two of treatment
11. Aprepitant 80mg once a day oral for 2 days starting on day two of treatment
12. Metoclopramide 10mg three times a day oral as necessary
13. Ondansetron 8mg twice a day oral for 3 days starting on the evening of day one of treatment
14. Aciclovir 400mg twice a day oral for 21 days
15. Co-trimoxazole 960mg once a day oral on Mondays, Wednesdays and Fridays for 21 days
16. **Growth Factor**
Administration Instructions
Growth factor as per local formulary choice:
 - filgrastim or bioequivalent 30 million units once a day for 7 days starting on day 9 of the cycle subcutaneous
 - lenograstim or bioequivalent 33.6 million units once a day for 7 days starting on day 9 of the cycle subcutaneous

17. Allopurinol 300mg once a day oral for 7 days

Cycle 1 Day 8

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

Cycle 2 & 3 Day 1

20. Dexamethasone 40mg oral
21. Aprepitant 125mg oral
22. Ondansetron 8mg oral or intravenous
23. Gemcitabine 1000mg/m² intravenous infusion in 250ml sodium chloride 0.9% over 30 minutes
24. Furosemide 40mg oral or intravenous
25. Sodium chloride 0.9% 1000ml with 20mmol potassium chloride and 16mmol magnesium sulphate intravenous infusion over 60 minutes
26. Cisplatin 75mg/m² intravenous infusion in 1000ml sodium chloride 0.9% with 20mmol potassium chloride intravenous infusion over 120 minutes (maximum rate 1mg cisplatin/minute)
27. Sodium chloride 0.9% 1000ml with 20mmol potassium chloride and 16mmol magnesium sulphate intravenous infusion over 60 minutes

Take home medicines (day 1 only)

28. Dexamethasone 40mg once a day oral for 3 days starting on day two of treatment
29. Aprepitant 80mg once a day oral for 2 days starting on day two of treatment
30. Metoclopramide 10mg three times a day oral as necessary
31. Ondansetron 8mg twice a day oral for 3 days starting on the evening of day one of treatment
32. Aciclovir 400mg twice a day oral for 21 days
33. Co-trimoxazole 960mg once a day oral on Mondays, Wednesdays and Fridays for 21 days
34. Growth Factor
- Administration Instructions
- Growth factor as per local formulary choice:
- filgrastim or bioequivalent 30 million units once a day for 7 days starting on day 9 of the cycle subcutaneous
 - lenograstim or bioequivalent 33.6 million units once a day for 7 days starting on day 9 of the cycle subcutaneous

Cycle 2 & 3 Day 8

35. Metoclopramide 10mg oral or intravenous

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

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
2	June 2019	Header changed Toxicities removed NHL diagnosis removed Haematology, hepatic and renal tables updated Cisplatin dose changed from 100mg/m ² to 75mg/m ² Duration of allopurinol changed to 7 days Aciclovir, co-trimoxazole & G-CSF added Metoclopramide dose changed to 10mg Bolus removed from intravenous bolus throughout text OPCS and dose banding updated "Warning – Check blood transfusion status" added to cycle 1 Disclaimer added	Rebecca Wills Pharmacist Dr Deborah Wright Pharmacist	Dr Robert Lown Consultant Medical Oncologist
1	July 2012	None	Rebecca Wills Pharmacist Dr Deborah Wright Pharmacist	Dr Andrew Davies Consultant Medical Oncologist Dr Alison 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 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.