

Chemotherapy Protocol
MESOTHELIOMA
CISPLATIN-PEMETREXED

Regimen

- Mesothelioma – Cisplatin-Pemetrexed

Indication

- First line therapy of advanced pleural mesothelioma where the disease is not suitable for surgical resection
- WHO Performance Status 0, 1

Toxicity

Drug	Adverse Effect
Cisplatin	Neuropathy, nephrotoxicity, ototoxicity
Pemetrexed	Diarrhoea, skin reactions, neuropathy

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

Monitoring

Disease

- A baseline chest x-ray should be performed before starting treatment and up to date (ideally within 1 month) cross section imaging should also be performed

Regimen

- FBC, LFTs and U&Es before each cycle
- A chest x-ray should be performed before each cycle
- Consider formal audiology test if relevant

Dose Modifications

The dose modifications listed are for haematological, liver and renal function 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. The following is a general guide only.

Haematological

Prior to prescribing the following treatment criteria must be met;

Criteria	Eligible Level
Neutrophil	equal to or more than $1.5 \times 10^9/L$
Platelets	equal to or more than $100 \times 10^9/L$

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

Subsequently if the neutrophils are less than $1.5 \times 10^9/L$, then in the first instance delay treatment for 7 days. If counts recover at this point continue at the initial dose. If counts remain low continue with treatment using a 20% dose reduction. If the myelosuppression recurs despite this dose reduction stop treatment.

If the platelets are less than $100 \times 10^9/L$ then in the first instance delay treatment for 7 days. If the counts recover at this point continue at the initial dose. If the counts still fall within this range continue using a 20% dose reduction. If the platelet level falls below $50 \times 10^9/L$ reduce the dose by 50%.

Liver Impairment

Drug	Adjustment
Cisplatin	No dose adjustment required
Pemetrexed	Clinical decision

Renal Impairment

Drug	Creatinine Clearance (ml/min)	Dose (% of original dose)
Cisplatin	more than 60	100
	50-60	75
	40-50	50
	less than 40	Do not use
Pemetrexed	Do not administer if the creatinine clearance is less than 45ml/min	

Regimen

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

Drug	Dose	Days	Administration
Cisplatin	75mg/m ²	1	Intravenous infusion in 1000ml sodium chloride 0.9% with 20mmol potassium chloride at a maximum rate of 1mg cisplatin/min (minimum time 120 minutes)
Pemetrexed	500mg/m ²	1	Intravenous infusion in 100ml glucose 5% or sodium chloride 0.9% over 10 minutes

[Dose Information](#)

- Cisplatin will be dose banded as per the CSCCN agreed bands
- Pemetrexed will be dose banded as per the CSCCN agreed bands

[Administration Information](#)

- Cisplatin should be administered 30 minutes after the end of the pemetrexed infusion
- Pemetrexed may be administered in 100ml of either glucose 5% or sodium chloride 0.9% over 10 minutes. The choice of fluid will be dependent on the product stocked by pharmacy. The fluid and volume will not appear in the prescription but can be located in the instructions notepad

[Extravasation](#)

- Cisplatin – exfoliant
- Pemetrexed - inflammitant

[Additional Therapy](#)

- Folic acid 5mg once daily starting 1 – 2 weeks prior to and continuing for three weeks after the last dose of pemetrexed.
- Hydroxocobalamin intramuscular injection 1mg every three months starting 1 – 2 weeks prior to pemetrexed.
- Antiemetics

15-30 minutes prior to chemotherapy;

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

Ensure the patient has taken oral dexamethasone starting the day before

pemetrexed. On the occasions where individuals attend for treatment and have forgotten to take the dexamethasone pre-medication administer an intravenous bolus dose of dexamethasone 10mg 15-30 minutes before chemotherapy.

As take home medication;

- aprepitant 80mg once a day for 2 days oral
- dexamethasone 4mg twice a day for 1 day starting the day before chemotherapy is due and dexamethasone 4mg once a day on the day of and the day after chemotherapy oral
- metoclopramide 10mg three times a day when required oral
- ondansetron 8mg twice a day for 3 days oral

- Cisplatin pre and post hydration as follows;

Pre

Furosemide 40mg oral or intravenous bolus

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.

- 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
- Prophylactic antibiotics can be considered if required

[Additional Information](#)

- Consideration should be given to draining pleural or peritoneal effusions prior to pemetrexed administration

[Coding](#)

- Procurement – X71.5
- Delivery – X72.1

References

1. National Institute of Clinical Excellence (2009). TA135 Pemetrexed for the treatment of mesothelioma. London: DOH.
2. Santoro A, O'Brien ME, Stahel RA et al. Pemetrexed plus cisplatin or pemetrexed plus carboplatin for chemo-naïve patients with malignant pleural mesothelioma: results of the International Expanded Access Programme. J Thorac Oncol 2008; 3 (7): 756 – 763.

REGIMEN SUMMARY

Cisplatin-Pemetrexed

Cycle 1, 2, 3, 4, 5

Day Minus One

1. Dexamethasone 4mg twice a day oral*

Day One

2. Aprepitant 125mg oral
3. Dexamethasone 4mg once a day oral (from TTO)*
4. Ondansetron 8mg oral or intravenous bolus
5. Furosemide 40mg oral or intravenous bolus
6. 1000ml sodium chloride 0.9% with 20mmol potassium chloride and 16mmol magnesium sulphate over 60 minutes
7. Pemetrexed 500mg/m² intravenous infusion in 100ml glucose 5% or sodium chloride 0.9% over 10 minutes
8. Cisplatin 75mg/m² intravenous infusion in 1000ml sodium chloride 0.9% with 20mmol potassium chloride at a maximum rate of 1mg cisplatin/minute (minimum time 120 minutes)
9. 1000ml sodium chloride 0.9% with 20mmol potassium chloride and 16mmol magnesium sulphate over 60 minutes

Take Home Medicines

10. Aprepitant 80mg once a day for 2 days starting on day 2 oral
11. Dexamethasone 4mg twice a day oral for 1 day starting the day before the pemetrexed infusion and 4mg once a day on the day of and the day after pemetrexed.
12. Metoclopramide 10mg three times a day when required oral
13. Ondansetron 8mg twice a day for three days starting on the evening of day 1 of the cycle oral
14. Folic acid 5mg once a day oral (continuous)

Hydroxocobalamin will not be included as part of the Aria regime and must be prescribed separately on the cycle for which it is due.

Cycle 6

Day Minus One

1. Dexamethasone 4mg twice a day oral*

Day One

2. Aprepitant 125mg oral
3. Dexamethasone 4mg once a day oral (from TTO)*
4. Ondansetron 8mg oral or intravenous bolus
5. Furosemide 40mg oral or intravenous bolus
6. 1000ml sodium chloride 0.9% with 20mmol potassium chloride and 16mmol magnesium sulphate over 60 minutes
7. Pemetrexed 500mg/m² intravenous infusion in 100ml glucose 5% or sodium chloride 0.9% over 10 minutes
8. Cisplatin 75mg/m² intravenous infusion in 1000ml sodium chloride 0.9% with 20mmol potassium chloride at a maximum rate of 1mg cisplatin/minute (minimum time 120 minutes)
9. 1000ml sodium chloride 0.9% with 20mmol potassium chloride and 16mmol magnesium sulphate over 60 minutes

Take Home Medicines

10. Aprepitant 80mg once a day for 2 days starting on day 2 oral
11. Metoclopramide 10mg three times a day when required oral
12. Ondansetron 8mg twice a day for three days starting on the evening of day 1 of the cycle oral
13. Folic acid 5mg once a day oral (continuous)

Hydroxocobalamin will not be included as part of the Aria regime and must be prescribed separately on the cycle for which it is due.

* In Aria Planner the dexamethasone 4mg twice daily will appear on days 1, and dexamethasone 4mg once a day on days 2 and 3 of treatment. This is the supply for the next cycle. The patient should have been given the supply for cycle one in the pre-assessment or consent clinic. The administration instructions reflect this.

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1.3	Jan 2016	Pemetrexed administration instructions changed throughout the text	Dr Deborah Wright Pharmacist	Donna Kimber Pharmacy Technician
1.2	Dec 2013	Header changed to NHS badge In name "and" replaced with dash Adverse effects put in table and toxicity removed Dose modification tabulated Renal and hepatic function tabulated Clarification added on the number of cycles set in Aria Regimen tabulated Twice daily changed to twice a day Regimen name added to summary Summary re-numbered Metoclopramide dose changed to 10mg Cycle 6 added with no dexamethasone pre-med included Document control tabulated Hospital representation and disclaimer added	Dr Deborah Wright Pharmacist	Liz Harrison Pharmacist
1.1	Sept 2010	Font changed to Arial Header altered to include "Strength through Partnership" Drug names given capitals in regimen Extravasation moved to under Administration Information Footer changed to include regimen name and review date removed Standard paragraph added to introduction in dose modifications Dose modifications format (not information) changed Administration information added Granisetron removed from antiemetics Aprepitant incorporated as per superusers Coding added Summary page added Document control added	Dr Deborah Wright Pharmacist	Donna Kimber Pharmacy Technician
1	Jan 2010	None	Dr Deborah Wright Pharmacist	Dr Andrew Bates Consultant Clinical Oncologist Dr Tim Gulliford Consultant Medical

				Oncologist
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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 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.