

Chemotherapy Protocol
HAEMATOLOGY – HSCT AUTOGRAFT

MELPHALAN (200mg/m²)

Multiple Myeloma

This regimen will only be available to prescribe at units which carry out autograft transplantation

Regimen

- HSCT – Melphalan (200mg/m²)

Indication

- Conditioning for haematopoietic stem cell transplant in patients with multiple myeloma

Toxicity

Drug	Adverse Effect
Melphalan	Nausea, vomiting, diarrhoea, stomatitis, alopecia and myelosuppression

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 initiating treatment
- GFR measurement done by Nuclear Medicine or creatinine clearance calculation prior to first day of treatment.

Dose Modifications

The dose modifications listed are for liver and renal function. Dose adjustments may be necessary for other co-morbidities as well which will involve discussions with the Transplant Director, Senior Transplant Clinician or patient's consultant.

Haematological

Confirm with transplant consultant before proceeding if there are signs of disease relapse.

Hepatic Impairment

No information is available on melphalan in hepatic impairment. No dose changes recommended.

Renal Impairment

Drug	Creatinine Clearance (ml/min)	Dose
Melphalan	greater than 50ml/min	200mg/m ²
	30 – 50ml/min	140 mg/m ²
	less than 30 ml/min	Clinical decision, high dose melphalan is not recommended

Regimen

Drug	Dose	Days	Administration
Melphalan	200mg/m ²	-1	Intravenous infusion in 500ml sodium chloride 0.9% over 30 minutes

Dose Information

- The melphalan dose is rounded to the nearest 10mg. The National Dose Banding Team have advised not to use dose banding tables for this product in view of the 90 minute expiry (must be made locally for individual patient), the 50mg vial size and frequent stock shortages.

Administration Information

Extravasation

- Melphalan – non-vesicant

Additional Therapy

- Antiemetics
 - aprepitant 125mg once a day prior to melphalan followed by 80mg once a day for the two days afterwards
 - dexamethasone 4mg each morning, on the same days as aprepitant
 - metoclopramide 10mg three times a day oral or intravenous until nausea subsides
 - ondansetron 8mg twice a day oral or intravenous for ten days then review
- Antimicrobials should be prescribed according to the institution guideline and may include:
 - antibacterials for example ciprofloxacin 250mg twice daily from day +5 to continue whilst neutropenic
 - antifungal for example fluconazole 100mg once daily from admission until recovery from neutropenia
 - antivirals for example aciclovir 400mg twice or three times a day from admission to continue after discharge
- Growth factors according to local formulary choice. For example:
 - filgrastim or bioequivalent 30million units subcutaneous once a day starting from day +7 to continue until neutrophils are more than 0.5.

- lenograstim or bioequivalent 33.6million units subcutaneous once a day starting from day +5 to continue until neutrophils are more than 0.5.

- Gastric protection with a proton pump inhibitor should be prescribed throughout admission
- Mouthwashes including:
 - nystatin 1ml four times a day to continue until count recovery
 - sodium chloride 0.9% 10ml four times a day to continue until count recovery
- Thromboprophylaxis
 - in accordance with individual transplant schedule
- Premedication for stem cell transfusion
 - chlorphenamine 10mg intravenous
 - paracetamol 1000mg oral
- Intravenous hydration before and after melphalan infusion prescribed on inpatient prescribing system or using paper proforma (appendix 1)

The evening before melphalan infusion (to be completed by 0930 on the morning of the infusion)

sodium chloride 0.9% with potassium chloride 27mmol 1000ml

The day of melphalan infusion

0900hrs Start fluid chart and daily weights. Contact pharmacy to make melphalan infusion for delivery to ward at 1045hrs

0930hrs 1000ml sodium chloride 0.9% intravenous infusion over 90 minutes

1010hrs 20mg furosemide intravenous bolus

1045hrs Measure urine output since 0900hrs

- If more than 500ml continue with melphalan infusion
- If less than 500ml give second furosemide 20mg intravenous bolus dose and check urine output since 0900hrs again at **1100hrs**:
 - if more than 500ml go ahead with melphalan
 - if less than 500ml contact the prescriber.

1100hrs – give melphalan intravenous infusion over thirty minutes (this product has a short expiry so adhering to set timing is essential)

1130hrs - 1000ml sodium chloride 0.9% intravenous infusion over 120 minutes

1330hrs - 1000ml sodium chloride 0.9% with potassium chloride 27mmol intravenous infusion over 240 minutes

1730hrs - 1000ml sodium chloride 0.9% intravenous infusion over 360 minutes

2330hrs - 1000ml sodium chloride 0.9% with potassium chloride 27mmol intravenous infusion over 480 minutes

- The day after melphalan infusion:

0730hrs - 1000ml sodium chloride 0.9% intravenous infusion over 480 minutes then restart routine intravenous fluids

Coding

- Procurement – 71.5
- Delivery – Inpatient regimen

References

1. P-P-54 Wessex Blood and Marrow Transplant – Dose adjustments for stem cell transplant conditioning agents policy. Version 1.0
2. P-P-43 Wessex Blood and Marrow Transplant – WESSEX BLOOD AND MARROW TRANSPLANT – Conditioning schedule for High Dose Melphalan Policy. Version 1.4
3. Dosage Adjustments for Cytotoxics in Hepatic Impairment January 2009 University College London Hospitals
6. Summary of Product Characteristics for Melphalan (Aspen) – last updated 09 Dec 2014
7. Handbook of Systemic Treatments for Cancer 7th Edition 2012 Lilly Oncology
8. [National Dose Banding Tables](#)

REGIMEN SUMMARY

Melphalan (200mg/m²)

Other than those listed below, supportive medication for this regimen will not appear in Aria as prescribed agents. The administration instructions for each warning describes the agents which must be prescribed on the in-patient chart or general electronic prescribing system.

Day -1

1. Warning – Check supportive medication prescribed

Administration instructions

Please refer to the individual transplant schedule for full details of the required supportive medicines on inpatient prescribing system

1. Antibacterials in accordance with individual transplant schedule
2. Antifungals in accordance with the individual transplant schedule
3. Antivirals in accordance with the individual transplant schedule
4. Thromboprophylaxis in accordance with individual transplant schedule
5. Growth factors in accordance with the individual transplant schedule
6. Aprepitant 125mg once a day on the day of melphalan administration followed by 80mg once a day for two days afterwards
7. Dexamethasone 4mg in the morning with each dose of aprepitant
8. Metoclopramide 10mg three times a day oral or intravenous
9. Ondansetron 8mg twice a day oral or intravenous
10. Gastric protection in accordance with the individual transplant schedule
11. Nystatin mouthwash 1ml four times a day
12. Sodium chloride 0.9% mouthwash 10ml four times a day
13. Chlorphenamine 10mg intravenous when required as a premedication for stem cells
14. Paracetamol 1000mg oral when required as a premedication for stem cells
15. Furosemide 20mg up four times a day when required for the treatment of fluid overload intravenous
16. Melphalan hydration on paper chart (Appendix 1 of protocol)
17. Heparin line lock in accordance with local central venous access device management procedure
18. Reminders for melphalan and stem cells administration

2. Warning – Check hydration and fluid balance

Administration Instructions

See separate hydration prescription chart for the pre hydration (Appendix 1):

1. Overnight to be completed at 0930hrs on day of melphalan infusion, 1000ml sodium chloride 0.9% with potassium chloride 27mmol intravenous infusion
The day of melphalan infusion:
2. 0900hrs on the day of melphalan start fluid chart and daily weights. Contact pharmacy to make melphalan infusion for delivery to ward at 1045hrs
3. 0930hrs 1000ml sodium chloride 0.9% intravenous infusion over 90 minutes
4. 1010hrs 20mg furosemide intravenous bolus
5. 1045hrs Measure urine output since 0900hrs
If more than 500ml continue with melphalan infusion
If less than 500ml give second furosemide 20mg dose intravenous bolus and recheck urine output since 0900hrs again at 1100hrs:
 - if more than 500ml go ahead with melphalan
 - if less than 500ml contact prescriber.

3. Time– Administer melphalan at 1100hrs

4. Melphalan 200mg mg/m² intravenous infusion in 500ml sodium chloride 0.9% over 30 minutes

Administration Instructions - see separate hydration prescription chart for the post hydration (Appendix 1 of protocol)

1. 1100hrs – give melphalan intravenous infusion over thirty minutes
2. 1130hrs - 1000ml sodium chloride 0.9% intravenous infusion over two hours
3. 1330hrs - 1000ml sodium chloride 0.9% with potassium chloride 27mmol intravenous infusion over four hours
4. 1730hrs - 1000ml sodium chloride 0.9% intravenous infusion over six hours

5. 2330hrs - 1000ml sodium chloride 0.9% with potassium chloride 27mmol intravenous infusion over eight hours
6. The day after melphalan infusion: 0730hrs - 1000ml sodium chloride 0.9% intravenous infusion over eight hours and then restart routine intravenous fluids as clinically indicated.

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1	Nov 2017	None	Harriet Launders Pharmacist Dr Deborah Wright Pharmacist	Dr Deborah Richardson Consultant Haematologist Dr Kate Hill Specialist 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;

University Hospital Southampton NHS Foundation Trust – Wessex Blood and Marrow Transplant

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

Unit no Surname First name Date of Birth Ward Consultant	(affix hospital addressograph)	WARD
Appendix 1: WESSEX BLOOD AND MARROW TRANSPLANT – HYDRATION PRESCRIPTION FOR HIGH DOSE MELPHALAN CHEMOTHERAPY CONDITIONING FOR HSCT		

DAY	DATE & TIME	DRUG	DOSE	INFUSION FLUID & VOLUME	ROUTE	INFUSION RATE	GIVEN/ CHECKED	START TIME	COMMENTS
	No later than midnight	HYDRATION FLUID	1000ml	Sodium chloride 0.9% Potassium chloride 0.2% (27mmol) 1000ml	IV	To be completed at 0930hrs on day -1			Rate is variable and depends on time started
	0845	Contact Pharmacy on ext 5037 to inform them that the patient is present. Confirm that they have the melphalan prescription (on ARIA) <input type="checkbox"/> Request melphalan to be on ward by 1045am <input type="checkbox"/> Name of person you spoke to in pharmacy:..... at:hrs Nurse who phoned pharmacy:..... 0900hrs: start fluid balance sheet and start daily weight measurement							
	0930	HYDRATION FLUID	1000 ml	Sodium chloride 0.9% 1000ml	IV	Infuse over 90 minutes at 667ml/hr			
	1000	Aprepitant Dexamethasone Metoclopramide Ondansetron	Prescribed on inpatient prescribing system		Confirm that all of these have been administered on inpatient prescribing system:				
	1010	FUROSEMIDE	20mg		IV BOLUS	20mg over 5minutes			
	1045	FUROSEMIDE	20mg	Measure urine output since 0900hrs. If less than 500ml give this dose of furosemide and continue to remeasure urine output before starting melphalan.	IV BOLUS	20mg over 5minutes			

Prescribed by :	Date:
-----------------	-------

Unit no Surname First name Date of Birth Ward Consultant	(affix hospital addressograph)	Appendix 1: WESSEX BLOOD AND MARROW TRANSPLANT –HYDRATION PRESCRIPTION FOR HIGH DOSE MELPHALAN CHEMOTHERAPY CONDITIONING FOR HSCT	WARD
---	--------------------------------	--	-------------

DAY	DATE & TIME	DRUG	DOSE	INFUSION FLUID & VOLUME	ADDITIVES	ROUTE	INFUSION RATE	GIVEN/ CHECKED	START/ STOP	COMMENTS
	1100	MELPHALAN - See ARIA prescription				If urine output greater than 500ml since 0900hrs continue with melphalan If urine output less than 500ml since 0900hrs (despite two doses of furosemide 20mg iv) contact prescriber first				
	1130	HYDRATION FLUID	1000 ml	Sodium chloride 0.9% 1000ml		IV	Infuse over 2 hours at 500ml/hr			
	1330	HYDRATION FLUID	1000ml	Sodium chloride 0.9% Potassium chloride 0.2% (27mmol) 1000ml		IV	Infuse over 4 hours at 250ml/hr			
	1730	HYDRATION FLUID	1000ml	Sodium chloride 0.9% 1000ml		IV	Infuse over 6 hours at 166ml/hr			
	2330	HYDRATION FLUID	1000ml	Sodium chloride 0.9%, Potassium chloride 0.2% (27mmol) 1000ml		IV	Infuse over 8 hours at 125ml/hr			
	0730	HYDRATION FLUID	1000ml	Sodium chloride 0.9% 1000ml		IV	Infuse over 8 hours at 125ml/hr			

Prescribed by :	Date:	Pharmacist:	Date:
-----------------	-------	-------------	-------