

Chemotherapy Protocol

LYMPHOMA

CARMUSTINE-CYTARABINE-ETOPOSIDE (split)-MELPHALAN

(BEAM)

Inpatient Regimen

[Regimen](#)

Lymphoma – InP-BEAM (split)-Carmustine-Cytarabine-Etoposide-Melphalan

[Indication](#)

- Conditioning for autologous peripheral blood stem cell transplant (PBSCT) / bone marrow transplant in individuals with either Non Hodgkin Lymphoma (NHL) or Hodgkin Lymphoma

[Toxicity](#)

Drug	Adverse Effect
Carmustine	Pulmonary toxicity
Cytarabine	CNS toxicity, conjunctivitis, flu-like syndrome, pulmonary toxicity, gastro-intestinal toxicity
Etoposide	Hypotension on rapid infusion, hyperbilirubinaemia
Melphalan	Gastro-intestinal disturbances, stomatitis

Patients treated with BEAM are at risk of transfusion-associated graft versus host disease (TA-GVHD). Where blood products are required these patients must receive irradiated blood products for the 1 week prior to harvest and for at least 12 weeks after the transplant has taken place. Patients with Hodgkin lymphoma carry a lifelong risk of graft versus host disease and must always receive irradiated blood products. 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, LFTs (including albumin) and U&Es prior to day one of treatment
- EDTA or calculated creatinine clearance prior to each melphalan infusion
- Monitor the fluid balance during the administration of melphalan, including throughout the administration of the pre and post hydration. Ensure the urine output is more than 250ml/hour immediately prior to the administration of melphalan

Dose Modifications

The dose modifications listed are for haematological, liver and renal function and some limited 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

Treatment will be given regardless of blood results.

Consider blood transfusion if patient symptomatic of anaemia or has a haemoglobin of less than 8g/dL. Irradiated blood products must be used.

Hepatic Impairment

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

Drug	Bilirubin μmol/L		AST/ALT units/L	Dose (% of original dose)
Carmustine	N/A		N/A	No dose adjustment necessary
Cytarabine	more than 34			50% The dose may be escalated dependent on toxicity
Etoposide	30-51	or	60-180	Consider dose reducing to 50%
	more than 51	or	more than 180	Clinical decision
Melphalan	N/A		N/A	No dose adjustment necessary

Renal Impairment

Drug	Creatinine Clearance (ml/min)	Dose (% of original dose)
Carmustine	more 60	100%
	46-60	80%
	30-45	75%
	less than 30	Clinical decision
Cytarabine	N/A	No dose adjustment necessary
Etoposide	more than 50	100%
	15-50	75%
	less than 15	50%
Melphalan	more than 50	100%
	30-50	75%
	less than 30	Clinical decision

Other

Carmustine

It may be necessary to reduce the dose of carmustine in patients with reduced pulmonary function. Carmustine dose reductions in this situation are to be made at the discretion of the consultant oncologist/haematologist only.

Etoposide

Where significant reductions in albumin levels occur consider reducing the dose of etoposide.

Regimen

1 cycle will be set in Aria

Drug	Dose	Days	Administration
Carmustine	300mg/m ²	-6	Intravenous infusion in 500ml sodium chloride 0.9% over 60 minutes
Cytarabine	200mg/m ² every 12 hours	-5,-4,-3,-2	Intravenous infusion in 100ml sodium chloride 0.9% over 30 minutes
Etoposide	200mg/m ²	-5,-4,-3,-2	Intravenous infusion in 2000ml sodium chloride 0.9% over 120 minutes (this will be administered as two infusions of 100mg/m ² in 1000ml sodium chloride 0.9% over 60 minutes administered sequentially)
Melphalan	140mg/m ²	-1	Intravenous infusion in 500ml sodium chloride 0.9% over 30 minutes

Dose Information

- Carmustine will be dose rounded to the nearest 10mg (down if halfway)
- Cytarabine will be dose banded in accordance with the national dose bands (20mg/ml)
- Etoposide will be dose banded in accordance with the national dose bands (20mg/ml)
- The melphalan dose will be dose rounded to the nearest 10mg (down if halfway). 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

- Carmustine – irritant
- Cytarabine – non-vesicant
- Etoposide – irritant
- Melphalan – irritant

Other

- Due to the stability of etoposide the total dose of 200mg/m² will be split into two infusions of 100mg/m² in 1000ml sodium chloride 0.9% over 60 minutes. The two infusions are given sequentially, the second is started as soon as the first infusion is complete. The total duration of etoposide administration is 120minutes.
- Ensure the urine output is more than 250ml/hour immediately prior to the administration of melphalan

Additional Therapy

This is an in-patient regimen. Please ensure all supportive and take home medicines are prescribed on the in-patient chart or general electronic prescribing system. Please refer to the transplant schedule for the individual patient.

- Antiemetics

Starting 15-30 minutes prior to chemotherapy

- dexamethasone 2mg twice a day for 10 days oral or intravenous starting on day -6 of the cycle
- metoclopramide 10mg three times a day for 10 days oral or intravenous starting on day -6 of the cycle
- ondansetron 8mg twice a day for 10 days oral or intravenous

- aprepitant 125mg once only orally on the day of the melphalan infusion then 80mg once a day for the subsequent two days
- Anti-infectives
 - aciclovir 400mg oral twice a day until day +90
 - ciprofloxacin 250mg oral twice a day from day+1 (stop when neutrophils are greater than 1)
 - pentamidine 300mg by nebuliser prior to discharge
 - co-trimoxazole 960mg once a day on Monday, Wednesday and Friday (start from 28 days post discharge, if neutrophils are greater than 1 and platelets are greater than 50, and continue until day +120)
 - fluconazole 100mg once a day oral (stop when neutrophils are greater than 1 unless the patient remains on corticosteroids)
 - nystatin suspension 1ml four times a day oral (stop when neutrophils are greater than 1 unless the patient remains on corticosteroids)
- Thromboprophylaxis, continued until platelets are less than $50 \times 10^9/L$, or as directed by the consultant, according to local formulary choices;
 - dalteparin 5000units once a day subcutaneous injection
 - enoxaparin 40mg once a day subcutaneous injection
 - heparin 5000units twice a day subcutaneous injection
- Growth factors such as filgrastim biosimilar 30million units (300mcg) once a day subcutaneous from day +5 (stop when neutrophils are greater than $1 \times 10^9/L$ for at least 24 hours, or greater than 3 on any occasion)
- Intravenous hydration before and after melphalan infusion

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 dose intravenous bolus 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

- Furosemide 20mg oral or intravenous bolus to maintain fluid balance and a urine output of more than 250ml/hour immediately prior to melphalan administration
- In menstruating women consider norethisterone 5mg three times a day oral to prevent menstruation. This may be stopped when the platelets are more than $50 \times 10^9/L$.
- Mouthcare for the prophylaxis or treatment of mucositis in accordance with local or national guidelines
- Gastric protection with a proton pump inhibitor or a H_2 antagonist according to local formulary choice;
 - esomeprazole 20mg once a day oral
 - omeprazole 20mg once a day oral
 - lansoprazole 15mg once a day oral
 - pantoprazole 20mg once a day oral
 - rabeprazole 20mg once a day oral
 - cimetidine 400mg twice a day oral
 - famotidine 20mg once a day oral
 - nizatidine 150mg twice a day oral
 - ranitidine 150mg twice a day oral

[Additional Information](#)

- Irradiated blood products must be used
- Autologous stem cells/ bone marrow will be infused on day 0, at least 24 hours after the melphalan infusion

Coding

- Procurement – X70.5
- Delivery – Not Required

References

1. Mills W, Chopra R, McMillan A et al. BEAM chemotherapy and autologous bone marrow transplantation for patients with relapsed or refractory non-Hodgkin's lymphoma. J Clin Oncol (1995);13(3): 588-95

REGIMEN SUMMARY

InP-BEAM (split)-Carmustine-Cytarabine-Etoposide (split)-Melphalan

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 -6

1. Warning – Check blood transfusion status

Administration Instructions

Patients treated with BEAM 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. Warning – Check supportive medication prescribed

Administration instructions

Please refer to the individual transplant schedule. In general the following is required;

1. Aprepitant 125mg once a day oral on the day of melphalan administration followed by 80mg once a day for two days after melphalan administration
2. Dexamethasone 2mg twice a day, days -6 to +3 oral or intravenous
3. Metoclopramide 10mg three times a day, days -6 to +3 then as required oral or intravenous
4. Ondansetron 8mg twice a day, days -6 to +3 oral or intravenous
5. Growth factors such as biosimilar filgrastim 30million units once a day from day +5 (stop when neutrophils are greater than $1 \times 10^9/L$ for at least 24 hours or are greater than $3 \times 10^9/L$ on any occasion)
6. Aciclovir 400mg oral twice a day until day +90
7. Ciprofloxacin 250mg twice a day from day +1 and continued until neutrophils are greater than $1 \times 10^9/L$.
8. Co-trimoxazole 960mg once a day on Monday, Wednesday and Friday (start from 28 days post discharge if the neutrophils are greater than $1 \times 10^9/L$ and platelets are greater than $50 \times 10^9/L$ and continue until day +120)
9. Fluconazole 100mg once a day (stop when neutrophils are greater than $1 \times 10^9/L$)
10. Pentamidine 300mg nebuliser prior to discharge
11. Thromboprophylaxis with a low molecular weight heparin until platelets are less than $50 \times 10^9/L$
12. Furosemide 20mg when required oral or intravenous bolus
13. Melphalan pre and post hydration
14. Gastric protection
15. Consider mouthwashes
16. Consider norethisterone for menstruating women

3. Carmustine $300\text{mg}/\text{m}^2$ intravenous infusion in 500ml sodium chloride 0.9% over 60 minutes

Day -5, -4, -3, -2

4. Warning – Cytarabine is TWICE a day (12hrs apart)

Administration Instructions

Cytarabine is administered TWICE a day at 12 hour intervals (0900 and 2100)

5. Cytarabine $200\text{mg}/\text{m}^2$ intravenous infusion in 100ml sodium chloride 0.9% over 30 minutes every 12 hours (9am and 9pm)

Administration Instructions

Cytarabine is administered TWICE a day at 12 hour intervals (0900 and 2100)

6. Warning – Etoposide is TWO infusions ()

Administration Instructions

Due to the stability of etoposide the total dose of $200\text{mg}/\text{m}^2$ will be split into two infusions of $100\text{mg}/\text{m}^2$ in 1000ml sodium chloride 0.9% over 60 minutes. The two infusions are given sequentially, the second is started as soon as the first infusion is complete. The total duration of etoposide administration is 120minutes.

7. Etoposide $100\text{mg}/\text{m}^2$ intravenous infusion in 1000ml sodium chloride 0.9% over 60 minutes

Administration Instructions

Due to the stability of etoposide the total dose of $200\text{mg}/\text{m}^2$ will be split into two infusions of $100\text{mg}/\text{m}^2$ in 1000ml sodium chloride 0.9% over 60 minutes. The two infusions are given sequentially, the second is started as soon as the first infusion

is complete. The total duration of etoposide administration is 120minutes.

8. Etoposide 100mg/m² intravenous infusion in 1000ml sodium chloride 0.9% over 60 minutes

Administration Instructions

Due to the stability of etoposide the total dose of 200mg/m² will be split into two infusions of 100mg/m² in 1000ml sodium chloride 0.9% over 60 minutes. The two infusions are given sequentially, the second is started as soon as the first infusion is complete. The total duration of etoposide administration is 120minutes

Day -1

9. Warning – Check hydration and fluid balance

Administration Instructions

See separate fluid prescription for the pre hydration:

1. Overnight to be completed at 0930hrs on day of melphalan infusion, 1000ml sodium chloride 0.9% with potassium chloride 0.2% (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.

10. Time– Administer melphalan at 1100

11. Melphalan 140mg/m² intravenous infusion in 500ml sodium chloride 0.9% over 30 minutes

Administration Instructions - see separate fluid prescription for the post hydration requirements

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 0.2% (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 0.2% (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

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1.1	August 2018	Split added to regimen name. Etoposide changed to two infusions of 100mg/m ² Furosemide dose changed to 20mg Administration instructions updated to describe the two etoposide infusions. Warning added regarding the two infusions Corticosteroid statement removed from fluconazole. Gastricprotection added Thromboprophylaxis change to include formulary choices Disclaimer added	Dr Deborah Wright Pharmacist	Harriet Launders Pharmacist
1	August 2017	None	Rebecca Wills Pharmacist Dr Deborah Wright Pharmacist	Dr Rob Lown 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 that occur as a result of following these guidelines. These protocols should be used in conjunction with other references such as the Summary of Product Characteristics and relevant published papers.