BEAM

Schedule of treatment

TREATMENT	DAY								
	-7	**-6**	**-5**	**-4**	**-3**	**-2**	**-1**	**0**	**+1**
Planned dates:									
Admission	*								
Carmustine (BCNU) *Chemotherapy*		*							
Etoposide *Chemotherapy*			*	*	*	*			
Cytarabine (Ara-C) *Chemotherapy*			**	**	**	**			
Melphalan *Chemotherapy*							*		
Stem cell infusion								*	
Pentamidine IV *Prevention for a specific pneumonia called PCP*									*
Dexamethasone (D) Ondansetron (O) Aprepitant (A) Olanzapine (Z) *Types of anti-sickness*		D O A Z	D O A Z	D O A Z	O A Z	O A Z	D O A Z	O A Z	O Z
Oral Cryotherapy *To prevent mucositis*							*		

Indication

Chemotherapy-sensitive Hodgkin and non-Hodgkin lymphoma

Treatment intent

Curative

Pre-assessment

- Ensure pre-transplant investigations are carried out as per protocol B3.10a
- Ensure patient has double lumen central line inserted and that this is working.
- Ensure results of pre-transplant investigations are checked by a Haematology SpR or trained and competent Physician Associate and recorded in patient record.
- Haematology SpR or trained and competent Physician Associate to complete electronic BMT front sheet B.2.16g and email to BMT Administrator to distribute and file in patient record.
- Treating Consultant to prescribe chemotherapy and stem cells at least 5 days before admission.
- Supportive treatment to be prescribed on the electronic inpatient chart by Haematology SPR at least 5 days before admission.
- Send Stem cells and Immunotherapies final report of donation and processing form v4.3.3 SCI at least 7 working days before the planned collection date and ensure a copy is placed in the medical notes.
- Please ensure the patient receives irradiated blood products from the start of conditioning. See ‘Guidelines for the use of blood components in adult haematology' for details and individual requirements / duration post-autograft. Ensure irradiation card is attached to the patient's notes and copy given to the patient.
- Ensure pregnancy test is carried out day -7 on all women of child-bearing potential unless they have been sterilized or have undergone a hysterectomy.
- Treatment should be agreed in the relevant MDT.
- **Ambulatory delivery:** Ensure the patients meets the criteria in line with the Ambulatory Care Operational Policy

Chemotherapy and Fluids

Encourage 3L oral fluids daily, give IV if oral intake insufficient.

Day -6		**Carmustine (BCNU)**	**300 mg/m^2** IV infusion in 500 ml glucose 5% over 2 hours
Days -5 to -2 (4 days)		**Etoposide** (4 doses x 200mg/m^2)	**200 mg/m^2 –** give as two consecutive bags of 100 mg/m^2 IV infusion in 1000 ml sodium chloride 0.9% over 1 hour each
		Cytarabine (8 doses)	**200 mg/m^2 every 12 hours** IV infusion in 250ml sodium chloride 0.9% over 30 minutes **Ambulatory delivery:** Administer concurrent sodium chloride 0.9% as continuous infusion via Y-sited multi-day infusor at 0.5mL/hour to maintain line patency.
Day -1	08:00	**Pre-hydration**	Commence 1L oral fluids or administer 1000 ml sodium chloride 0.9% IV infusion over 2 hours.
	09:45	**Oral cryotherapy**	Place the ice cubes/chips/lollies in the mouth prior to melphalan. Continue throughout infusion and for 75 minutes after (2 hours total). Replenish with a new portion of ice before it melts to keep the mouth constantly cool for the whole duration.
	10:00	**Melphalan**	**140 mg/m^2** IV infusion in 100 ml sodium chloride 0.9% over 30 minutes
	10:30	**Post-hydration**	1000 ml sodium chloride 0.9% with 20 mmol potassium chloride IV infusion over 4 hours
Day 0	06:00	**Pre-hydration**	1000 ml sodium chloride 0.9% IV infusion over 4 hours
		Stem cell re-infusion **Min 24hr post melphalan**	Give hydrocortisone 100 mg IV, chlorphenamine 10 mg IV 15 minutes before infusion
Day +1		**Pentamidine***	4 mg/kg (max 300 mg) IV infusion in 100ml sodium chloride 0.9% over 1 hour.
Day +5		**Filgrastim (GCSF)**	Daily subcutaneous injection. Dosing as per local policy until stable engraftment. Substitutions for long-acting granulocyte stimulating colony factors such as peg-filgrastim **are not permitted.**

* Day +1 is a convenient and logical administration time. If this falls at a weekend defer to the next working day.

For **overweight/obese** patients refer to protocol B.56 Guidelines on Chemotherapy Dosing in Obese Adult Patients Undergoing Stem-cell / Bone Marrow transplant.

Dose Modifications

All dose modifications must agreed by a consultant - if patient is on clinical trial, modify as per trial protocol.

Etoposide

Renal Impairment

Creatinine clearance (mL/min)	Etoposide dose
More than 50	100%
15 - 50	75%
Less than 15	50%

Hepatic impairment – significant hypoalbuminemia (less than 25 g/dL) may increase circulating free etoposide and associated toxicities (through increased AUC).

Parameters	Etoposide dose
Bilirubin 26 - 51 micromol/L and/or ALT/AST 60-180 u/L	50% dose
Bilirubin more than 51 micromol/L and/or ALT/AST more than 180 u/L	Clinical decision

Melphalan

Renal impairment

Creatinine clearance (mL/min)	Melphalan dose
More than 50	100%
30 - 50	75%
Less than 30	Clinical decision

Hepatic impairment - no dose adjustment required.

Carmustine

Carmustine can be associated with induced interstitial pneumonitis in the transplant setting. **Consider omitting BCNU if lung function tests < 75% predicted or heavy smoker**. Exercise caution in patients with prior mediastinal irradiation or bleomycin use.

Renal Impairment – limited data available, clinical decision guided by table below.

Creatinine clearance (mL/min)	Carmustine dose
45 - 60	80%
30 - 45	75%
<30	Clinical decision

Hepatic impairment – dose modification not recommended.

Investigations

Daily	FBC, creatinine, urea & electrolytes (U&Es), weight, urinalysis
Alternate days	Liver function tests (LFTs)
Mon/Thurs	Coagulation screen, calcium, magnesium, phosphate
Mon/Fri	Group and save (G&S)
Other	Chest X-ray on admission then weekly and as clinically indicated. Other specimens for virology as clinically indicated

Concurrent medication

Norethisterone	5-10 mg PO/TDS from day 0 until platelets >50 x 10^9/L (menstruating women only)
Fluconazole	50 mg PO/OD from day 0 until neutrophils >1.0 x 10^9/L (or longer if patient on steroids). Refer to Antifungal protocol H.94. http://nssg.oxford-haematology.org.uk/general-clinicalmanagement/H-94-antifungal-therapy-guidelines.pdf
PPI	Omeprazole 20mg OD from start of conditioning until platelet count >50 x 10^9/L (or PPI as per local formulary)
Aciclovir	200 mg PO/TDS (or 250 mg IV/TDS) from day 0 until day +90
Filgrastim (G-CSF)	SC Daily from Day +5 as per local policy until stable engraftment
Pentamidine	4mg/kg/day (max 300mg) IV on day+1 and day +30 (prescribed on ARIA). Unless started on co-trimoxazole at day 30.
Difflam 0.15% MW	Use 15ml as mouthwash QDS when required for sore mouth
AS Saliva Orthana spray	Use 2-3 sprays when required for dry mouth
Oral cryotherapy	**On Day -1**: Place the ice cubes/chips/lollies in the mouth, starting from approximately 15 minutes before melphalan infusion, during melphalan infusion and for 75 minutes after (2 hours total). Replenish with a new portion of ice before it melts to keep the mouth constantly cool for the whole duration (prescribed on ARIA).

Anti-emetics

Regular antiemetics*	
5HT3 antagonist	Ondansetron 8mg BD PO/IV from Day -6 for 10 days
Dexamethasone	8mg OM PO/IV on Day -6 for 1 day 4mg OM PO from Day -5 for 2 days 8mg OM PO/IV on Day -1 for 1 day
NK1 inhibitor	Aprepitant 125mg OM PO on Day -6 for 1 day Aprepitant 80mg OM PO from Day -5 for 6 days
Olanzapine	5mg ON PO from Day -6 for 9 days

When required antiemetics* from the start of conditioning for rescue	
5HT3 antagonist	Ondansetron 8mg BD PO/IV PRN, maximum 32mg in 24 hours
Cyclizine	50mg TDS PO PRN

* Review antiemetic control and optimise in case of breakthrough N&V

Extravasation risk

Carmustine - Vesicant
Etoposide - Irritant
Cytarabine - Neutral
Melphalan – Neutral (irritant in some references)

Medication on discharge (TTOs)

Norethisterone	5-10 mg PO/TDS. Stop when platelets consistently more than 50 x 10^9/L (menstruating women only)
Fluconazole	50 mg PO/OD. Stop when neutrophils consistently more than 1.0 x 10^9/L (or longer if patient on steroids)
Co-trimoxazole	Start when neutrophils consistently more than 1.0 x 10^9/L, 480 mg PO OD on Mon, Wed, Fri until day +120. If allergic to co-trimoxazole, pentamidine 4 mg/kg (max 300 mg) monthly
Aciclovir	200 mg PO/TDS until day +90
PPI	Omeprazole 20mg PO/OD (or as per local formulary). Stop when platelet consistently count more than 50 x 10^9/L unless clinically indicated

Adverse effects / Regimen specific complications

For full exhaustive detailed descriptions, visit https://www.medicines.org.uk/emc/.

Generalised transplant effects such as pancytopenia, fatigue, nausea and vomiting, weight changes, taste disturbance, infections, risk of bleeding and photosensitivity are expected as typical in transplantation. More information available: https://www.cancerresearchuk.org/about-cancer/treatment/bone-marrow-stem-cell-transplants/side-effects

Carmustine Pulmonary fibrosis, lung infiltration, deranged LFTs, renal injury, nausea and vomiting. Infusion reactions – flushing, hypotension, tachycardia, facial pain and headache.

Etoposide Abdominal pain, constipation, arrhythmia, myocardial infraction, rash, extravasation. Hypotension on rapid infusion.

Cytarabine Abdominal pain, diarrhoea, conjunctivitis (less common with low doses), rash, respiratory toxicity (interstitial pneumonitis).

"Cytarabine syndrome" characterised by flu-like symptoms, skin rash and occasionally chest pain - can occur 6 to 12 hours after cytarabine administration. Symptoms generally resolve within 24 hours of completing therapy.

Melphalan Renal injury, alopecia, diarrhea, stomatitis/mucositis, nausea and vomiting

Treatment Related Mortality

1-2%, may be increased in selected patients.

References

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

2) Salar A, Sierra J, Gandarillas M et al. 2001"Autologous stem cell transplantation for clinically aggressive non-Hodgkin's lymphoma: the role of preparative regimens" Bone Marrow Transplant. Feb;27(4):405-12.

3) Schmitz, N., B. Pfistner, M. Sextro, et al. 2002. "Aggressive conventional chemotherapy compared with high-dose chemotherapy with autologous haemopoietic stem-cell transplantation for relapsed chemosensitive Hodgkin's disease: a randomised trial." Lancet 359(9323):2065-2071.

4) UCLH - Dosage Adjustment for Cytotoxics in Hepatic Impairment (Version 3 - updated January 2009).

5) UCLH - Dosage Adjustment for Cytotoxics in Renal Impairment (Version 3 - updated January 2009).

Author(s) clinical protocol: Dr Chris Hatton, Lymphoma Lead

Authorised by: Dr Andy Peniket

Audit: These processes are subject to the OxBMT audit programme

Circulation: NSSG Haematology Website, patient medical notes

Review

Name	Revision	Date	Version	Next review
Dr Andy Peniket	Auto Protocol Day	June 2017	4.1	June 2019
Dr Andy Peniket, Consultant Nadjoua Maouche, Lead Haematology Pharmacist Cristina Ovas, Quality & Data Manager	No changes Revised anti-emetic regime Reformatting to BMT programme document format	June 2019	4.2	June 2021
Cristina Ovas, Quality and Data Manager	Amended anti-emetic regime.	June 2019	4.3	June 2021
Natalia Czub & Donna Constantine, Advanced Cancer Pharmacists Nadjoua Maouche, Lead Haematology Pharmacist	Extended carmustine infusion to 2 hours. Added olanzapine, oral cryotherapy, Difflam MW. Split etoposide OD dose into 2 bags to manage stability.	Feb 2021	4.4	June 2021
Natalia Czub, Advanced Cancer Pharmacist Nadjoua Maouche, Lead Haematology Pharmacist	Extended aprepitant and olanzapine duration. Added saliva spray. Removed Baxter saline infusor volume and product code.	May 2021	4.5	June 2023
	Addition of care plan as an integrated part of the clinical protocol **Clinical protocol not reviewed**	June 2021	4.6	June 2023
	Minor amendment to nursing care plan **Clinical protocol not reviewed**	Nov 2021	4.7	June 2023
Graham Collins, Haematology Consultant Donna Constantine, Advanced Cancer Pharmacist	Format adjustments and minor wording amendments for readability and clarity. Carmustine renal guidance. Reasoning behind respiratory caution.	April 2024	4.8	April 2026
Alexandra Scott BMT Specialist Nurse	Addition of PA role	Nov 2024	4.9	Nov 2025

CARE PLAN ON NEXT PAGE

Nursing Care Plan

Ensure flush volumes are included in rate and volume calculations, i.e. drug and flush should be completed within prescribed administration time.

Carmustine (BCNU) – a cell-cycle phase nonspecific antineoplastic alkylating agent which prevents DNA replication and DNA transcription of the cancer cells.
Side effects: headache, facial flushing (during infusion), dizziness, nausea & vomiting, bone marrow depression

Day -6

- Prime giving set with 5% glucose as Carmustine is manufactured in glucose for stability
- Administer over 2 hour as prescribed
- Flush with 5% glucose when infusion complete

Etoposide – a topoisomerase inhibitor, causing errors in DNA synthesis and promoting apoptosis of the cancer cell
Side effects: mild nausea and vomiting, alopecia, diarrhoea, bone marrow depression
For stability reasons.

Day -5 to – 2

- Check ARIA prescription carefully: etoposide may be manufactured in two separate bags for stability and in this instance, it will be prescribed on ARIA as two separate doses
- Administer bag(s) each over 1 hour as prescribed

Cytarabine – an antimetabolite agent which interferes with the synthesis of DNA, thus causing damage to the cancel cell.
Side effects: mild nausea and vomiting, 'flu-like' symptoms, stomatitis, diarrhoea, bone marrow depression

Day -5 to -2

- **For inpatients administer BD over 30 minutes as prescribed**
- Patient's having their treatment via the Ambulatory Care Unit (ACU) will have the evening dose administered via a CADD pump.

Melphalan - is a cell-cycle non-specific alkylating chemotherapy agent given to suppress bone marrow production. The drug is unstable in solution so the infusion must be established as soon as the drug arrives on the ward.
Side effects: nausea and vomiting, bone marrow suppression, alopecia, mucositis and diarrhea

Day –1
With patient consent, oral cryotherapy should be implemented on day -1 with the aim of preventing/reducing occurrence of oral mucositis.

- 08.00: Infuse IV pre hydration or advise patient to drink 1L oral fluids
- 09.00: Contact Baxters to confirm delivery time
- 09.45: offer patient ice chips/lollies to suck for approximately 15 minutes pre melphalan and throughout the infusion
- 10.00: Administer melphalan infusion over 30 minutes
- 10.30: Administer IV post hydration
- Continue cryotherapy for 75 minutes after completion of Melphalan
- Ensure daily mucositis assessment is carried out and WHO score is documented on EPR in

patient nursing notes.
Refer to Oral Mucositis care plan for additional information: NSSG>BMT>Nursing Care Plan>N.26

Stem Cell Infusion of Frozen Cells Potential complications: Allergic reaction, fluid overload, hyperosmolarity, infusion of micro-aggregates, pulmonary oedema, nausea, vomiting, diarrhoea, abdominal pain, and facial flushing, headache, blurred vision, altered taste and smell due to DMSO.

Day 0

- **0800**: Cells arrive to Laboratory Medicine. Cells to arrive on the ward by the porter as per Physician Associate Thawing SOP (must be >24 hours post-Melphalan)
- **0900**: Administer sodium chloride 0.9% 1 litre over 4 hours.
- **1245**: Administer pre-medications: chlorphenamine, hydrocortisone + antiemetics as prescribed a minimum of 15 minutes prior to stem cell reinfusion
- Ensure O2, suction, and call bell are checked, and anaphylaxis kit is in patient room
- **1300**: Peripheral Blood Stem Cell Infusion:
- Record baseline observations
- Positively identify the patient ID, against each bag of cells and on NHSBT Form 5071 (EPR under 'BMT Coordination')
- Check cells to ensure no clumping, or bag damage
- Take great care when spiking each bag, to prevent inappropriate puncturing. See Cell Management policy NSSG>BMT>Clinical Management> B.2.30 if bag is accidentally punctured
- Each bag of cells must be infused within 15 mins of thawing. The cells may be infused using gravity or an **appropriate** infusion pump, but always through a blood administration giving set and side-armed with Sodium Chloride 0.9%
- Monitor patient closely and observe for any signs of reaction, fluid overload and/or respiratory compromise.
- Record lot numbers of giving sets and saline on NHSBT forms
- Document volume of cells and cell count on NHSBT form, including start and completion time for each bag
- On completion of cells, continue flushing the IV line with saline until it runs clear
- Ensure a copy of the NHSBT form 'Record of issue and infusion' is scanned/ into patient EPR notes
- Ensure completion of NHSBT adverse event form is completed and returned to Haematology Ward Clerk who will forward to NHSBT/SCI

Day +1

Pentamidine isethionate is an antimicrobial medication primarily given for prevention and treatment of Pneumocystis pneumonia (PCP), a severe interstitial pneumonia often seen in patients that are immunocompromised.
Side Effects: can cause hypotension and arrhythmias if electrolytes have not been corrected; dizziness; hypoglycaemia, nausea + vomiting

- Bloods pre administration; U& E's, creatinine, and FBC.
- Administer any replacements necessary prior to infusion.
- (Refer to guidelines for management of hypomagnesaemia in adult clinical haematology on NSSG>Clinical Haematology OUH>Haematology Day Treatment Unit).
- Ensure anti-emetic cover as per protocol

- Perform ECG pre, during and immediately after first dose. Check with the SHO or Registrar to ensure they are happy for you to commence infusion.
- Check blood sugar is within normal range
- Check baseline observations, then 30 minutes into infusion and 5 minutes after completion of infusion. (This only needs to be done on the first dose)
- Ensure the patient is lying down or sitting in a chair whilst the Pentamidine is being infused
- Wear gloves, and apron whilst hanging the bag
- Check blood sugar 60 minutes post-infusion

NB. If the patient has experienced a previous reaction, you may need to consider slowing subsequent infusions. The patient may also require a pre-med of Paracetamol or anti-emetic. In these cases you may advise the patient to eat or drink something sweet during the infusion.

Author(s) Nursing Care Plan: Kirsten Rendall, Autologous Coordinator

Authorised by: Denise Wareham, BMT Senior Specialist Nurse

Audit: These processes are subject to OxBMT audit programme

Circulation: NSSG Haematology Website, patient notes

Review

	Revision	**Date**	**Version**	**Review date**
Kirsten Rendall Auto BMT Coordinator, Denise Wareham BMT Senior Specialist Nurse	Revised nursing care plan and added as an integrated part of the clinical protocol	Jun 2021	1.0	Align with clinical protocol
Denise Wareham, BMT Senior Specialist Nurse	Revision of stem cell infusion time and other minor amendments	Nov 2021	1.1	Align with clinical protocol
Denise Wareham, BMT Senior Specialist Nurse	Formatting	Dec 2021	1.2	Align with clinical protocol
Alexandra Scott BMT Specialist Nurse	Addition of PA role and change from NHSBT defrosting cells.	Nov 2024	1.1	Align with clinical protocol