BEAM Autologous Transplant Conditioning Protocol

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	Reimbursement Status
Autologous conditioning in Non-Hodgkins Lymphoma (NHL)	C85	00408a	Hospital
Autologous conditioning in Hodgkins Lymphoma	C81	00408b	Hospital

TREATMENT:

Chemotherapy is administered over a 6-day period as described below and autologous stem cells are re-infused on day 0 of the stem cell transplant.

Note:

- **Hydration therapy required for safe administration of melphalan (See Table below)**
- **Short expiry time of melphalan, ensure to organise timings with pharmacy**

Facilities to treat anaphylaxis MUST be present when therapy and stem cells are administered.

Day	Drug	Dose	Route	Diluent & Rate
-7	[a]Carmustine (BCNU)	300mg/m^2	IV infusion	1000ml 5% dextrose over 1 hour
-6,-5,-4,-3	[b]Etoposide	200mg/m^2	IV infusion	1000mL 0.9% NaCl over 60 mins
-6,-5,-4,-3	Cytarabine	200mg/m^2 **AM**	IV infusion	100ml 0.9% NaCl over 30 mins
-6,-5,-4,-3	Cytarabine (Note: There should be a 12 hour interval between cytarabine doses)	200mg/m^2 **PM**	IV infusion	100ml 0.9% NaCl over 30 mins
-2	[c, d]Melphalan	140mg/m^2	IV push	Give as an IV push over 30mins via side-arm of a fast-running NaCl 0.9% infusion
0	Stem cell infusion	Do not re-infuse stem cells within 24 hours of Melphalan infusion.		
+5	G-CSF (Round to nearest whole syringe)	5mcg/kg	SC	Starting +5 (until ANC > 1.0 x 10^9/L for two consecutive days)

[a]Carmustine intravenous solution is unstable in polyvinyl chloride container. The carmustine solution should be administered from PVC free containers only.

[b]The etoposide 200mg/m^2 dose may need to be split into two 1000ml bags for stability reasons. These should be administered sequentially.

[c]When reconstituted, melphalan has a very short expiry time **(Refer to local policy for guidance on stability and shelf life to co-ordinate administration with pharmacy compounding).**

[d]Ensure excretion of melphalan by use of appropriate hydration therapy **(Refer to local policy or see suggested hydration here).** 0.9% NaCl given at a rate of 125ml/m^2/hr for 2 hours pre-melphalan and for 6 hours post-melphalan.

ELIGIBILITY:

- Indications as above

EXCLUSIONS:

- Hypersensitivity to carmustine, etoposide, cytarabine, melphalan or any of the excipients.

PRESCRIPTIVE AUTHORITY:

The treatment plan must be initiated by a Consultant Medical Oncologist or Consultant Haematologist working in the area of autologous stem cell transplantation in a unit suitable for carrying out this treatment.

TESTS:

Baseline tests:

- FBC, renal and liver profile
- LDH, Uric acid
- Coagulation Screen
- ECG and echocardiogram
- Pulmonary Function Tests
- Virology screen - Hepatitis B (HBsAg, HBcoreAb) & C, HIV I and II, CMV and HSV.
  *Hepatitis B reactivation: See Adverse events/ Regimen specific complications

Regular tests:

- FBC, renal and liver profile required daily

Disease monitoring:

Disease monitoring should be in line with the patient's treatment plan and any other test/s as directed by the supervising Consultant.

DOSE MODIFICATIONS:

- Any dose modification should be discussed with a Consultant .

Renal and Hepatic Impairment:

Table 1: Dose modifications based on renal and hepatic impairment

Drug	Renal impairment		Hepatic impairment			
Carmustine	**CrCl (ml/min)**	**Dose**	Clinical decision			
	46-60	80%				
	30-45	75%				
	<30	Clinical Decision				
Etoposide	**CrCl (ml/min)**	**Dose**	**Bilirubin (micromol/L)**		**AST**	**Dose**
	>50	100%	26-51	or	60-180	50%
	15-50	75%	>51	or	>180	Clinical decision
	<15	50%				
Cytarabine	No dose reduction necessary		If bilirubin >34micromol/L, give 50% dose			
Melphalan	**CrCl (ml/min)**	**Dose**	No dose changes recommended			
	30-50	50%				
	<30	Clinical decision but not recommended				

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL:

Carmustine: High **(Refer to local policy)**.
Etoposide: Low **(Refer to local policy)**.
Cytarabine: Low **(Refer to local policy)**.
Melphalan: High **(Refer to local policy)**.

PRE-MEDICATIONS:

- To prevent a chemical induced conjunctivitis developing with cytarabine, artificial tears may be administered (2 drops per eye 4 hourly) starting 1 day before cytarabine treatment and continuing for 48 hours after last dose of cytarabine as prophylaxis. If patient becomes symptomatic treatment may escalate to Prednisolone eye drops (e.g. Pred Mild) 1-2 drops per eye 4 hourly during waking hours prior to cytarabine and continued 5 days post treatment should be considered.
- Prior to stem cell infusion administer pre-medications as per local policy.

OTHER SUPPORTIVE CARE:

- PJP prophylaxis **(Refer to local policy)** *Do not give Co-trimoxazole until engraftment achieved* and continue until day 100 or CD4 count > 200/microlitre.
- Proton Pump Inhibitor **(Refer to local policy)**
- Tumour lysis syndrome prophylaxis **(Refer to local policy)**
- Mouthcare **(Refer to local policy)**
- Anti-viral prophylaxis **(Refer to local policy)**
- Anti-fungal prophylaxis **(Refer to local policy)**
- All patients must receive irradiated cellular blood components starting one week prior to BEAM conditioning and until 12 months after stem cell infusion to prevent transfusion associated graft versus host disease.

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS:

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

- **Myelosuppression:** is profound and will require blood and platelet support. Neutropenic sepsis **must** be assessed promptly and treated acutely with broad spectrum antibiotics as per local policy.
- **Gastrointestinal toxicity:** is common with this regimen. Diarrhoea should be treated appropriately (Refer to local policy) and ensure patients have adequate fluid intake.
- **Pulmonary toxicity**: Pulmonary fibrosis and pulmonary infiltrates can occur with carmustine injection. Pulmonary toxicities are more common with cumulative doses >1,400 mg/m^2; however, pulmonary toxicity can occur at lower doses. Pulmonary function tests are performed prior to therapy and carmustine should not be given if the DLCO is <50%. Patients should be advised to immediately report any signs of respiratory complications, and this should result in discontinuation of therapy.
- **Hepatitis B Reactivation**: All lymphoma patients should be tested for both HBsAg and HBcoreAb as per local policy. If either Hepatitis B test is positive, patients should be treated with anti-viral therapy during transplantation and for six months afterwards and should be monitored with at least monthly liver function tests and hepatitis B virus DNA at least every two months. If the hepatitis B virus DNA level rises during this monitoring, management should be reviewed with an appropriate specialist with experience managing hepatitis.
- **Cytarabine syndrome:** Treatment with cytarabine may cause a 'Cytarabine Syndrome' characterised by flu-like symptoms, skin rash and occasionally chest pain.

DRUG INTERACTIONS:

- Melphalan may reduce the threshold for carmustine-induced pulmonary toxicity.
- Current drug interaction databases should be consulted for more information.

REFERENCES:

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Version	Date	Amendment	Approved By
1	28/07/2017		Prof Elisabeth Vandenberghe Prof Maccon Keane
2	26/07/2019	Standardisation of treatment table Amended recommendation for Hep B reactivation	Prof Elisabeth Vandenberghe
3	12/10/2021	Regimen reviewed Updated emetogenic potential.	Prof Maccon Keane
4	12/09/2022	Updated emetogenic potential	Prof Maccon Keane

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.