BEAM Autologous Transplant Conditioning Protocol

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	*Reimbursement Indicator
Autologous conditioning in non-Hodgkins Lymphoma (NHL)	C85	00408a	
Autologous conditioning in Hodgkins Lymphoma	C81	00408b	

**If a reimbursement indicator (e.g. ODMS, CDS[i]) is not defined, the drug and its detailed indication have not gone through the formal reimbursement process as legislated for in the Health (Pricing and Supply of Medical Goods) Act 2013.*

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 organize 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 hours
-6,-5,-4,-3	[b]Etoposide	200mg/m^2	IV infusion	1000mL 0.9% NaCl over 1 - 2hours
-6,-5,-4,-3	Cytarabine	200mg/m^2 **AM**	IV infusion	100ml 0.9% NaCl over 30mins
-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 30mins
-2	[c, d]Melphalan	140mg/ m^2	IV push	Give as an IV push over 30 minutes 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 s 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/m2/hr for 2 hours pre-melphalan and for 6 hours post-melphalan

ELIGIBILTY:

- 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, U&Es, LFTs, LDH, Urate
- Creatinine clearance
- 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, U&Es, LFTs 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	**Creatinine Cl (ml/min)**	**Dose**	Clinical decision			
	60	80%				
	45	75%				
	<30	Clinical Decision				
Etoposide	**GFR (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	**GFR (ml/min)**	**Dose**	No dose changes recommended.			
	30-50	50%				
	<30	Clinical decision but not recommended				

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL: 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 lamivudine 100 mg/day orally 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.

ATC CODE:

Carmustine	-	L01AD01
Etoposide	-	L01CB01
Cytarabine	-	L01BC01
Melphalan	-	L01AA03

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;13:588-95.
2. Chopra R, McMillan A et al. The Place of High-Dose BEAM Therapy and Autologous Bone Marrow Transplantation in Poor-Risk Hodgkin's Disease. A Single-Center Eight-Year Study of 155 Patients. Blood 1993; 81(5): 1137-1145
3. Carmustine Summary of Product Characteristics Accessed Feb 2017. Available at http://www.mhra.gov.uk/home/groups/spcpil/documents/spcpil/con1484285627271.pdf
4. Etoposide Summary of Product Characteristics Accessed Feb 2017. Available at: http://www.hpra.ie/img/uploaded/swedocuments/LicenseSPC_PA1422-012-001_19052014154253.pdf

5. Cytarabine Summary of Product Characteristics Accessed Feb 2017. Available at: http://www.hpra.ie/img/uploaded/swedocuments/LicenseSPC_PA1457-007-003_09102014142053.pdf
6. Alkeran Summary of Product Characteristics Accessed Feb 2017. Available at: http://www.hpra.ie/img/uploaded/swedocuments/LicenseSPC_PA1691-004-001_01042015160126.pdf

Version	Date	Amendment	Approved By
1	28/07/2017		Prof Elizabeth Vandenberghe Prof Maccon Keane

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.

[i] ODMS – Oncology Drug Management System
CDS – Community Drug Schemes (CDS) including the High Tech arrangements of the PCRS community drug schemes
Further details on the Cancer Drug Management Programme is available at;
http://www.hse.ie/eng/services/list/5/cancer/profinfo/medonc/cdmp/