

LEAM Autologous Transplant Conditioning Protocol

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	*Reimbursement Status
Autologous conditioning in non-Hodgkins Lymphoma (NHL)	C85	00468a	Hospital
Autologous conditioning in Hodgkins Lymphoma	C81	00468b	Hospital

**If the reimbursement status is not defined¹, the indication has yet to be assessed through the formal HSE reimbursement process.*

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	Lomustine	200mg/m ²	PO	
-6,-5,-4,-3	^a 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	^{b, c} 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 x 10 ⁹ /L for two consecutive days)
^a The etoposide 200mg/m ² dose may need to be split into two 1000ml bags for stability reasons. These should be administered sequentially.				
^b 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)				
^b 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				

NCCP Regimen: LEAM Therapy	Published: 13/08/2018 Review: 13/08/2020	Version number: 1
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ELIGIBILITY:

- Indications as above

EXCLUSIONS:

- Hypersensitivity to lomustine, 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
- Creatinine clearance
- Coagulation Screen
- ECG and echocardiogram
- Pulmonary Function Tests
- Virology screen -Hepatitis B (HBsAg, HBcoreAb), Hepatitis 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

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Renal and Hepatic Impairment:

Table 1: Dose modifications based on renal and hepatic impairment

Drug	Renal impairment		Hepatic impairment			
Lomustine	Creatinine Cl (ml/min)	Dose	Clinical decision			
	>60	100%				
	45-60	75%				
	30-45	50%				
	<30	Not recommended				
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.

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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 toxicity from lomustine appears to be dose-related). Baseline pulmonary function studies should be conducted along with frequent pulmonary function tests during treatment. Patients with a baseline below 70 % of the predicted Forced Vital Capacity (FVC) or Carbon Monoxide Diffusing Capacity (DLco) are particularly at risk.
- **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:

Lomustine	-	L01AD02
Etoposide	-	L01CB01
Cytarabine	-	L01BC01
Melphalan	-	L01AA03

REFERENCES:

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Version	Date	Amendment	Approved By
1	13/08/2018		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/>

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