# LEAM Autologous Transplant Conditioning Regimen

## 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 |

## 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 | | | | |

## 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

**Renal and Hepatic Impairment:**

**Table 1: Dose modifications based on renal and hepatic impairment**

| Drug | Renal impairment | | Hepatic impairment | | | |
|---|---|---|---|---|---|---|
| **Lomustine** | **CrCl (ml/min)** | **Dose** | Clinical decision | | | |
| | >60 | 100% | | | | |
| | 45-60 | 75% | | | | |
| | 30-45 | 50% | | | | |
| | <30 | Not recommended | | | | |
| **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:

**Lomustine:** Moderate to 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.
- **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, such patients should be treated with anti-viral therapy. **(Refer to local infectious disease policy**). These patients should be considered for assessment by hepatology.

  **Lomustine**
- **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.

  **Cytarabine**
- **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:


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.
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3. Sharma A, Kayal S, Iqbal S, Malik P, Raina V. Comparison of BEAM vs LEAM regimen in autologous transplant for lymphoma at AIIMS. Springerplus 2013, 2:489.
4. Lomustine Summary of Product Characteristics Accessed July 2020. Available at https://www.medicines.org.uk/emc/medicine/6252

5. Etoposide Summary of Product Characteristics Accessed July 2020. Available at: http://www.hpra.ie/img/uploaded/swedocuments/LicenseSPC_PA1809-020-001_02022016153110.pdf
6. Cytarabine Summary of Product Characteristics Accessed July 2020. Available at: https://www.medicines.org.uk/emc/product/3802/smpc/history
7. Alkeran Summary of Product Characteristics Accessed July 2020. Available at: https://www.hpra.ie/img/uploaded/swedocuments/Licence_PA1691-004-001_14112019130102.pd
8. NCCP Classification Document for Systemic Anti-Cancer Therapy (SACT) Induced Nausea and Vomiting. V2 2019. Available at: https://www.hse.ie/eng/services/list/5/cancer/profinfo/chemoprotocols/nccp-classification-document-for-systemic-anti-cancer-therapy-sact-induced-nausea-and-vomiting.pdf

| Version | Date | Amendment | Approved By |
|---|---|---|---|
| 1 | 13/08/2018 | | Prof Maccon Keane |
| 2 | 15/07/2020 | Regimen review<br>Updated emetogenic potential section<br>Updated recommended management of hepatitis B reactivation | Prof Maccon Keane |

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.