High Dose Melphalan Conditioning Therapy for Autologous Stem Cell Transplant

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	*Reimbursement Status
Conditioning Therapy in patients with Multiple Myeloma prior to autologous stem cell transplant	C90	00454a	Hospital
Conditioning Therapy in patients with other plasma cell dyscrasia such as AL amyloidosis	E85	00454b	Hospital

**If the reimbursement status is not defined [i], the indication has yet to be assessed through the formal HSE reimbursement process.*

TREATMENT:

The starting dose of the drugs detailed below may be adjusted downward by the prescribing clinician, using their independent medical judgement, to consider each patients individual clinical circumstances.

Note:

- **Hydration therapy required for safe administration of melphalan (See Table 1 below)**
- **Short expiry time of melphalan, ensure to organize timings with pharmacy**

Table 1: Treatment table

Day	Drug	Dose	Route	Diluent & Rate
-2	[a,b,c]Melphalan	200mg/m^2/day	IV	Give as an IV push over 30 minutes via side-arm of a fast-running NaCl 0.9% infusion
0	Stem cell infusion			(minimum 24 hours post 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]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 6 hours post-melphalan 10mmol K^+ may be added to each 1L of fluid. The patient should also be recommended to drink a minimum of 2L. Consider additional IV fluids if a patient is unable to drink adequate fluids.				
[c]Maintain strict fluid balance during therapy, by (1) monitoring fluid balance and (2) daily weights. If fluid balance becomes positive by >1000mls or weight increases by >1 Kg, the patient should be reviewed and consideration given to diuresing with furosemide				

ELIGIBILTY:

- Indications as above

EXCLUSIONS:

- Hypersensitivity to melphalan or any of the excipients
- Pregnancy

PRESCRIPTIVE AUTHORITY:

The treatment plan must be initiated by a Consultant Haematologist working in the area of haematological malignancies

TESTS:

Baseline tests:

- FBC, renal and liver profile
- Uric acid, LDH
- Creatinine Clearance
- Coagulation screen
- Cardiac Function : ECG, ECHO
- 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 2: Dose modification of melphalan in renal and hepatic impairment

Renal Impairment		Hepatic Impairment
Cr Cl (ml/min)	**Dose**	No dose changes recommended
30-50	140mg/m^2	
<30	Clinical Decision	

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL: Moderate-high (**Refer to local policy).**

PREMEDICATIONS: 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)**
- Mouthcare **(Refer to local policy)**
- Anti-viral prophylaxis **(Refer to local policy)**
- Anti-fungal prophylaxis **(Refer to local policy)**
- Anti-bacterial prophylaxis (**Refer to local policy**)

- All patients must receive irradiated cellular blood components starting one week prior to conditioning and until 3 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.

- **Neutropenia:** Fever or other evidence of infection must be assessed promptly and treated aggressively.
- **Thrombocytopenia:** Support with platelet transfusion may be required.
- **Hepatitis B Reactivation**: All patients for stem cell transplantation 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
- **Mucositis:** Management is usually conservative with pain killer, hydration and treatment of secondary infection

DRUG INTERACTIONS:

- Current drug interaction databases should be consulted for more information.

ATC CODE:

Melphalan - L01AA03

REFERENCES:

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Version	Date	Amendment	Approved By
1	31/08/2018		Dr Kamal Fadalla

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/