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	Melphalan: Hospital
Conditioning Therapy in patients with other plasma cell dyscrasia such as AL amyloidosis	E85	00454b	Melphalan: Hospital

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				

ELIGIBILITY:

- 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

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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: 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

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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.

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

REFERENCES:

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9. NCCP Classification Document for Systemic Anti-Cancer Therapy (SACT) Induced Nausea and Vomiting. V3 2021. 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	31/08/2018		Dr Kamal Fadalla
2	16/09/2021	Regimen review Updated emetogenic potential Updated wording regarding management of hepatitis B reactivation	Dr Kamal Fadalla

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.

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