High Dose Melphalan Conditioning Therapy for Autologous Stem Cell Transplant

INDICATIONS FOR USE:

<table>
<thead>
<tr>
<th>INDICATION</th>
<th>ICD10</th>
<th>Regimen Code</th>
<th>Reimbursement Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conditioning Therapy in patients with Multiple Myeloma prior to autologous stem cell transplant</td>
<td>C90</td>
<td>00454a</td>
<td>Hospital</td>
</tr>
<tr>
<td>Conditioning Therapy in patients with other plasma cell dyscrasias such as AL amyloidosis</td>
<td>E85</td>
<td>00454b</td>
<td>Hospital</td>
</tr>
</tbody>
</table>

*If the reimbursement status is not defined*, 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 patient's 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

<table>
<thead>
<tr>
<th>Day</th>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Diluent &amp; Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>-2</td>
<td>^x^c Melphalan</td>
<td>200mg/m²/day</td>
<td>IV</td>
<td>Give as an IV push over 30 minutes via side-arm of a fast-running NaCl 0.9% infusion</td>
</tr>
<tr>
<td>0</td>
<td>Stem cell infusion</td>
<td></td>
<td></td>
<td>(minimum 24 hours post melphalan infusion)</td>
</tr>
<tr>
<td>+5</td>
<td>G-CSF</td>
<td>5mcg/kg</td>
<td>sc</td>
<td>Starting +5 (until ANC &gt; 1.0 x 10⁹/L for two consecutive days)</td>
</tr>
</tbody>
</table>

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/m²/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
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

<table>
<thead>
<tr>
<th>Renal Impairment</th>
<th>Hepatic Impairment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cr Cl (ml/min)</td>
<td>Dose</td>
</tr>
<tr>
<td>30-50</td>
<td>140mg/m²</td>
</tr>
<tr>
<td>&lt;30</td>
<td>Clinical Decision</td>
</tr>
</tbody>
</table>

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:


Comments and feedback welcome at oncologydrugs@cancercontrol.ie.

1 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/