Indication
High dose chemotherapy consolidation with stem cell support for patients with multiple myeloma.

ICD-10 codes
Codes with a pre-fix C90

Regimen details

<table>
<thead>
<tr>
<th>Day</th>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
</tr>
</thead>
<tbody>
<tr>
<td>-2*</td>
<td>Melphalan</td>
<td>200mg/m²**</td>
<td>IV infusion</td>
</tr>
<tr>
<td>0</td>
<td>Thaw and reinfuse stem cells</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Consider moving to D-1 should scheduling difficulties arise. Ensure agreed with patient’s consultant and transplant team before adjusting and ensure at least 24 hours between melphalan and stem cell return.

**Consider reduced dose of 140mg/m² if poor performance status, over 65 years of age, reduced renal function (GFR <50mL/min) or other co-morbidities.

Cycle frequency
N/A

Number of cycles
Second autologous stem cell transplants are standard of care to consolidate second-line therapy in patients achieving >18 months remission prior to relapse.

Administration
Pre-hydration:
- Sodium Chloride 0.9% 1000mL over 30 minutes
- Sodium Chloride 0.9% 1000mL over 30 minutes
- Furosemide 20mg IV bolus.

Ensure urine output is ≥ 500mL/hour (if insufficient repeat furosemide dose)

Melphalan is then administered in 500mL sodium chloride 0.9% over 30 minutes.

Post hydration:
- Sodium Chloride 0.9% 1000mL over 30 minutes
- Sodium Chloride 0.9% 1000mL over 30 minutes

DO NOT allow patient to get into significantly positive fluid balance – give furosemide as appropriate.

Pre-medication
Pre-hydration and furosemide as above.

Emetogenicity
This regimen has high emetogenic potential. Consider dexamethasone 8mg BD on day of melphalan.
**Additional supportive medication**

- H₂ antagonist or proton pump inhibitor
- Antifungal, antiviral and antibacterial prophylaxis as per local policy
- Anti-emetics as per local policy
- Mouthcare as per local policy
- PCP prophylaxis (co-trimoxazole) to commence once engrafted, weekly folic acid to start with co-trimoxazole.
- Tumour lysis syndrome prophylaxis is only indicated in a BMT setting for patients with a malignancy that is not in complete remission.

**Extravasation**

Melphalan is neutral (Group 1)

**Investigations – pre first cycle**

Please note that weight and surface area calculation should be within 28 days of starting conditioning, U+Es and LFTs within 7 days and FBC within 72 hours. Patient work up and consent must be completed during pre-treatment evaluation.

<table>
<thead>
<tr>
<th>Investigation</th>
<th>Validity period</th>
</tr>
</thead>
<tbody>
<tr>
<td>FBC and film</td>
<td>72 hours</td>
</tr>
<tr>
<td>Clotting screen</td>
<td>7 days</td>
</tr>
<tr>
<td>U+Es (including creatinine)</td>
<td>7 days</td>
</tr>
<tr>
<td>LFTs</td>
<td>7 days</td>
</tr>
<tr>
<td>Calcium</td>
<td>7 days</td>
</tr>
<tr>
<td>Magnesium</td>
<td>7 days</td>
</tr>
</tbody>
</table>

Serum electrophoresis (or alternative biological measure of response if M protein not measurable)
Consider formal measurement of creatinine clearance.
ECG and echocardiogram as clinically indicated.

**Standard limits for administration to go ahead**

If blood results not within range, authorisation to administer must be given by prescriber/ consultant

<table>
<thead>
<tr>
<th>Investigation</th>
<th>Limit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Creatinine clearance</td>
<td>≥ 50mL/min</td>
</tr>
</tbody>
</table>

**Dose modifications**

- **Haematological toxicity**
  
  No modifications needed.

- **Renal impairment**

<table>
<thead>
<tr>
<th>CrCl (mL/min)</th>
<th>Melphalan dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 50</td>
<td>100%</td>
</tr>
<tr>
<td>30-50</td>
<td>Reduce dose to 140mg/m²</td>
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<tr>
<td>&lt; 30</td>
<td>Clinical decision – dose may be split over 2 days</td>
</tr>
</tbody>
</table>

- **Hepatic impairment**

  There are no dose recommendations for melphalan in hepatic impairment.

- **Dosing in obesity (defined as Body Mass Index >30kg/m²)**

  Consider dosing patients using actual body weight. Dose limiting toxicity of mucositis.
**Adverse effects** – Please refer to the ‘Summary of Product Characteristics’ (SPC) for a comprehensive list of side effects and cautions at [http://www.medicines.org.uk](http://www.medicines.org.uk) however the more common side effects to monitor for are:

- Allergic reactions including anaphylaxis (reported rarely)
- Nausea, vomiting
- Diarrhoea
- Mucositis – severe in 20%
- Alopecia
- Pulmonary Fibrosis
- Dermatitis
- Acute leukaemia with long term therapy
- Transient sensation of warmth/tingling
- Pancytopenia
- Infection (potentially life-threatening)
- Transplant related mortality – 1-3%

**Significant drug interactions** – Please refer to the ‘Summary of Product Characteristics’ (SPC) for a comprehensive list of interactions and cautions at [http://www.medicines.org.uk](http://www.medicines.org.uk)

- **Warfarin/coumarin anticoagulants**: increased or fluctuating anticoagulant effects. Avoid if possible, consider switching patient to a low molecular weight heparin during treatment or if the patient continues taking an oral vitamin K antagonist monitor the INR at least once a week and adjust dose accordingly.

- **Nephrotoxic drugs**: Increased risk of nephrotoxicity when melphalan given in combination with nephrotoxic drugs

**Additional comments**

All patients must receive irradiated cellular blood components to prevent the rare occurrence of transfusion associated graft versus host disease. Issue patient with DoH irradiated blood information sheet and card.

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**References**

- Cunningham D, Paz-Ares L, Milan S et al. High dose Melphalan and Autologous bone marrow transplantation as consolidation in previously untreated myeloma. JCO,1994;12:759-63
- Renal Drug handbook, 3rd edition. Ashley C, Currie A. Radcliffe Publishing Ltd