# High dose Melphalan

## 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

| Day | Drug | Dose | Route |
|---|---|---|---|
| -2* | Melphalan | 200mg/m$^2$** | IV infusion |
| 0 | Thaw and reinfuse stem cells | | |

* 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/m$^2$ 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

$H_2$ 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.

| **Investigation** | **Validity period** |
|---|---|
| FBC and film | 72 hours |
| Clotting screen | 7 days |
| U+Es (including creatinine) | 7 days |
| LFTs | 7 days |
| Calcium | 7 days |
| Magnesium | 7 days |

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

| **Investigation** | **Limit** |
|---|---|
| Creatinine clearance | ≥ 50mL/min |

## Dose modifications

- **Haematological toxicity**

No modifications needed.

- **Renal impairment**

| **CrCl** (mL/min) | **Melphalan dose** |
|---|---|
| > 50 | 100% |
| 30-50 | Reduce dose to 140mg/$m^2$ |
| < 30 | Clinical decision – dose may be split over 2 days |

- **Hepatic impairment**

There are no dose recommendations for melphalan in hepatic impairment.

- **Dosing in obesity (defined as Body Mass Index >30kg/$m^2$)**

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 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

**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


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- Melphalan 50mg Powder and solvent for injection Summary of Product Characteristics. Aspen. Last updated 09.12.2014. Accessed via www.medicines.org.uk on 13.06.17
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Date: August 2017