# Melphalan and Prednisolone

## Indication
First line or relapsed multiple myeloma in patients who are not eligible for stem cell transplantation.

## ICD-10 codes
Codes with a pre-fix C90

## Regimen details

| Day | Drug | Dose | Route |
|---|---|---|---|
| 1-4 | Melphalan | 7mg/$m^2$ | PO |
| 1-4 | Prednisolone | 40-60mg/$m^2$ OM* | PO |

* Dose may be reduced in elderly and/or frail patients.

## Cycle frequency
28 days

## Number of cycles
Maximum of 6-9 cycles

## Administration
Melphalan is available as 2mg tablets. Melphalan tablets are cytotoxic. Tablets should be swallowed whole with a glass of water and should not be broken, crushed or chewed.

Prednisolone is available as 5mg and 25mg tablets. The dose should be taken once a day in the morning, with or after food.

## Pre-medication
Nil

## Emetogenicity
This regimen has low emetogenic potential.

## Additional supportive medication
$H_2$ antagonist or proton pump inhibitor
Allopurinol 300mg OD (100mg OD if CrCl< 20mL/min) for patients with a high tumour burden, for the first cycle only
Bisphosphonates as per local policy
Antifungal, antiviral and PCP prophylaxis as per local policy

## Extravasation
N/A

## Investigations – pre first cycle

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

Serum electrophoresis (or alternative biological measure of response if M protein not measurable)
Bone marrow aspirate and trephine, including FISH.

## Investigations – pre subsequent cycles

| Investigation | Validity period |
|---|---|
| FBC | 96 hours |
| U+Es (including creatinine) | 7 days |
| LFTs | 7 days |
| Calcium | 7 days |

Serum electrophoresis (or alternative biological measure of response if M protein not measurable)

## Standard limits for administration to go ahead

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

| Investigation | Limit |
|---|---|
| Neutrophils | ≥ 1.0 x $10^9$/L |
| Platelets | ≥ 75 x $10^9$/L |
| Creatinine clearance | ≥ 50mL/min |

## Dose modifications

- **Haematological toxicity**

Treatment on day 1 should only be initiated if neutrophils ≥ 1.0 x $10^9$/L and platelets ≥ 75 x $10^9$/L.

If prolonged grade 4 neutropenia or thrombocytopenia, or thrombocytopenia with bleeding, reduce melphalan dose to 75% for subsequent cycles.

- **Renal impairment**

**Melphalan:**

| **CrCl** (mL/min) | **Melphalan dose** |
|---|---|
| > 50 | 100% |
| 10-50 | 75% |
| < 10 | 50% |

- **Hepatic impairment**

There are no dose modification recommendations for melphalan in hepatic impairment, however, if excess toxicity experienced, consider dose reduction for subsequent cycles.

- **Other toxicities**

## Adverse effects - for full details consult product literature/ reference texts

- **Serious side effects**

Myelosuppression
Tumour lysis syndrome
Cardiac failure
Pulmonary fibrosis

- **Frequently occurring side effects**

Myelosuppression
Constipation, diarrhoea
Nausea and vomiting
Fatigue
Headache
Rash

- **Other side effects**

Confusion
Depression

## Significant drug interactions – for full details consult product literature/ reference texts

**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.

## Additional comments

## References


- Summary of Product Characteristics: Melphalan (Aspen) accessed 3 August 2016 via www.medicines.org.uk
- Palumbo A, Bringhen S, Caravita T, et al; Italian Multiple Myeloma Network, GIMEMA. Oral melphalan and prednisone chemotherapy plus thalidomide compared with melphalan and prednisone alone in elderly patients with multiple myeloma: randomised controlled trial. Lancet. 2006 Mar 11;367(9513):825-31



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