ORAL MELPHALAN +/- PREDNISOLONE

INDICATION

Treatment for patients who are not candidates for autologous stem cell transplantation and who are treated with a palliative intent.

GENERAL PRE-ADMINISTRATION

1. Ensure all the following staging investigations are done:
   - FBC & film
   - Clotting screen
   - U&Es
   - LFTs
   - Calcium
   - Albumin
   - Uric acid
   - CRP
   - Virology: HIV, Hepatitis B (including core antibody), and Hepatitis C
   - Calculated creatinine clearance (CrCl), urine protein/creatinine ratio
   - Electrophoresis and immunofixation for quantitation of serum paraprotein and immunoglobulins.
   - Serum free light chain assay (Freelite)
   - β2 microglobulin
   - Myeloma FISH should be performed in all patients at diagnosis, and in selected patients at relapse/progression to help guide treatment decisions. Samples should be sent to Wessex Regional Genetics Laboratory (address below)
   - Urine pregnancy testing for pre-menopausal women younger than 55 before each cycle.
   - Group and save
   - Imaging as per NICE/network guidance and clinical presentation
   - Bone marrow aspirate and trephine (with immunophenotyping for kappa/lambda if appropriate)

Wessex Regional Genetic Laboratory
Salisbury NHS Foundation Trust
Salisbury District Hospital
Salisbury
Wiltshire
SP2 8BJ

Additional investigation:
   - Plasma viscosity if hyperviscosity suspected

2. Hydration - fluid intake of at least 3 litres /day should be attempted.
4. Counselling - all patients should receive verbal and written information on oral chemotherapy. Ensure pre-chemotherapy counselling in line with NPSA recommendation and chemotherapy measures.
5. Consent - ensure patient has received adequate verbal and written information regarding their disease, treatment and potential side effects. Document in medical notes all the information that has been given and that patient consent has been obtained.

**DRUG REGIMEN**

<table>
<thead>
<tr>
<th>Melphalan</th>
<th>7 mg/m² po daily (tablets are 2 mg in strength)</th>
<th>Days 1 to 4</th>
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<tbody>
<tr>
<td>WITH OR WITHOUT</td>
<td></td>
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<tr>
<td>Prednisolone</td>
<td>20-60 mg po daily Dose reduction may be necessary in the elderly.</td>
<td>For 5 days</td>
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**CYCLE FREQUENCY**

Every 4-6 weeks until plateau phase (paraprotein level stable for 3 months) then stop.

**DOSE MODIFICATIONS**

- Neutrophil count should be > 1.0 x 10⁹/L and platelet count should be > 75 x 10⁹/L before starting treatment unless low counts are thought to be disease related.
- The dose should be reduced if Grade 3 or 4 myelotoxicity occurs, alternatively consider changing to cyclophosphamide.
- If the nadir neutrophil count is > 1.5 and nadir platelets > 100, consideration may be given to a cautious increase in dose for subsequent cycles.

**Melphalan:**

<table>
<thead>
<tr>
<th>Renal</th>
<th>Hepatic</th>
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<tbody>
<tr>
<td>GFR 30 – 50 ml/min 75% dose</td>
<td>No recommendations. If excess toxicity, consider dose reduction on subsequent cycles</td>
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<tr>
<td>GFR &lt; 30 ml/min clinical decision</td>
<td></td>
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</tbody>
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**INVESTIGATIONS - First and Subsequent Cycles**

- FBC.
- U&Es, Creatinine, glucose, Ca⁺⁺.
- Alternate cycles Ig’s, paraprotein.
- 24 hr urine for Bence Jones protein and / or Freelite assay at alternate cycles in light chain myeloma.
- Urine pregnancy testing for pre-menopausal women younger than 55 before each cycle.
- Consider bone marrow assessment after four cycles for non-secretory myeloma.
- Random blood glucose/ blood sugar
CONCURRENT MEDICATIONS

- Allopurinol 300 mg daily for 7 days for cycle 1 only.
- Proton pump inhibitor or H2 antagonist at clinician’s discretion.
- Consider prophylactic fluconazole if steroid related side effects.
- Bone protection as per NSSG Bone Protection protocol MM.3
- Prophylactic acyclovir 200 mg bd-tid (depending on renal function)

EMETIC RISK

Minimal.

REFERENCES


2- eMC UK Summary of Product Characteristics for Melphalan 2mg tabs, Aspen, March 2014

3- eMC UK Summary of Product Characteristics for Prednisolone 1mg and 5 mg tablets, Wockhardt UK Ltd, November 2015

REVIEW

<table>
<thead>
<tr>
<th>Name</th>
<th>Revision</th>
<th>Date</th>
<th>Version</th>
<th>Review date</th>
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</thead>
<tbody>
<tr>
<td>Nadjoua Maouche, Pharmacist</td>
<td>Cycle frequency section updated, dose modifications, reference section</td>
<td>May 2016</td>
<td>4.3</td>
<td>May 2018</td>
</tr>
<tr>
<td>Manuela Sultanova Service Coordinator</td>
<td>Formatting, Standardisation of General pre-assessment section and correction of Wessex lab address</td>
<td>August 2017</td>
<td>4.4</td>
<td>May 2018</td>
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