MP-T Melphalan, Prednisolone and Thalidomide (Myeloma)

**DRUG ADMINISTRATION SCHEDULE**

<table>
<thead>
<tr>
<th>Day 1 to 28</th>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Schedule</th>
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<tbody>
<tr>
<td></td>
<td><strong>Thalidomide</strong></td>
<td><em>200mg</em></td>
<td>Oral</td>
<td>ONCE Daily for 28 days</td>
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<tr>
<td>Days 1 to 7</td>
<td>Melphalan*</td>
<td><em>4 mg/m²</em></td>
<td>Oral</td>
<td>ONCE Daily for SEVEN days</td>
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<tr>
<td>Days 1 to 7</td>
<td>Prednisolone*</td>
<td><em>40 mg/m²</em></td>
<td>Oral</td>
<td>ONCE Daily for SEVEN days</td>
</tr>
</tbody>
</table>

**CYCLE LENGTH AND NUMBER OF DAYS**

28 day cycle

**APPROVED INDICATIONS**

Multiple Myeloma

**ELIGIBILITY CRITERIA**

Patients unsuitable for allergenic/autologous stem cell transplant

**RECOMMENDED TAKE HOME MEDICATION**

No anti-emetic cover is usually required.
Consider Allopurinol 300mg once daily during the first cycle.
Consider gastro protection (proton pump inhibitor) with steroid.
Thrombo-prophylaxis using standard medical prophylaxis dose of Low Molecular Weight Heparin (LMWH) should be prescribed (unless contra-indicated) with all thalidomide-chemotherapy combinations. Duration of LMWH remains uncertain but should be at least for the first 3 months of treatment when the risk of VTE is greatest. LMWH requires dose reduction in renal impairment.

**INVESTIGATIONS / MONITORING REQUIRED**

**Prior to first cycle:** CT-Scan, Chest X-Ray, LDH, Bone Marrow, FBC, U&E’s, LFT’s, Protein Electrophoresis, Uric Acid, Calcium, β2-MicroGlobulin,

**Prior to each cycle:** U&E’s, LFT’s, FBC, Protein Electrophoresis, Calcium

**ASSESSMENT OF RESPONSE**

Protein Electrophoresis

**REVIEW BY CLINICIAN**

Prior to each cycle

**NURSE / PHARMACIST LED REVIEW**

As per local practice
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ADMINISTRATION NOTES

- Patients **must not** become or attempt to become pregnant during thalidomide treatment. For women of child bearing potential, a negative pregnancy test during the 24 hours prior to each cycle of thalidomide will be required.
- Thalidomide Celgene™ is licensed for the first-line treatment of multiple myeloma in the UK by Celgene, who have developed a risk management programme, ‘Thalidomide Celgene™ Pregnancy Prevention Programme’
- In the Pregnancy Prevention Programme prescribers must:
  - Communicate the risks and benefits of Thalidomide Celgene™ therapy to their patients
  - Prescribers must complete a ‘Treatment Initiation Form’ along with your patient (this only needs to be done once).
  - Provide the patient with a ‘Health Card’
  - Provide pregnancy prevention measures and counselling
  - Perform a pregnancy test (as appropriate) prior to every prescription
  - Supply a ‘Prescription Authorisation Form’ with each prescription to show confirmation that your patient has received counselling and pregnancy test date and result (if appropriate).
  - Remind your patient of the safe use of Thalidomide Celgene™
- In the Pregnancy Prevention Programme pharmacists must:
  - Register the Pharmacy with the Pregnancy Prevention Programme
  - Obtain a copy of the patient’s ‘Treatment Initiation Form’ before the first dispense
  - Dispense Thalidomide Celgene™ only if the prescriber has annotated the ‘Prescription Authorisation Form’ correctly
  - Remind all patients of the safe use of Thalidomide Celgene™, each time a prescription is dispensed
- Blood Glucose Tolerance may be affected by high dose dexamethasone, patients with diabetes should increase frequency of glucose monitoring
- Thalidomide is sedating and so should be taken at night.
- Thalidomide may cause venous thromboembolism – patients should be encouraged to report calf pain early.
- This is a complex regimen: patients will need time and assistance to understand when and how they should take this treatment.
- Melphalan is supplied as 2mg tablets. Doses should be rounded to the nearest 2mg.
- Melphalan interacts with nalidixic acid, ciclosporin, phenytoin, and clozapine.
- Patients should take their prednisolone with meals. They can divide the dose if desired but should avoid taking a dose after 6pm.
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TOXICITIES

**Common:** Moderate Emesis, Myelosuppression, Fatigue, Dyspepsia, Constipation, Rash, Sedation,

**Less Common:** Thromboembolism, Increased blood glucose, Peripheral Neuropathy, Pulmonary fibrosis; Acute Leukaemia following long-term use.

DOSE MODIFICATION / TREATMENT DELAYS

**Haematological Toxicity:**

*(Note: where haematological disease is affecting bone marrow function, lower treatment parameters may be acceptable. This should be clearly documented for the specific patient.)*

Delay treatment on day 1 if ANC <1.0 x 10^9cells/l or PLT <75 x 10^9cells/l.

**Renal Function:**

Melphalan is renally excreted. Explicit dose modifications are not available for melphalan, however, melphalan should not be given if Serum Cr >300 μmol/l. For patients who are frail, or have co-existing medical illness or mild renal impairment dose reduction may be advisable from the outset – adjusted on subsequent cycles to account for toxicity.

**Hepatic Function:**

No dose modification is normally required.

TREATMENT LOCATION

Suitable for self administration in patients own homes, under the supervision of haematology teams from Level 1 to 4 Haematology Services.

REFERENCES:

Falcon et al. Melphalan and prednisone plus thalidomide versus melphalan and prednisone alone or reduced-intensity autologous stem cell transplantation in elderly patients with multiple myeloma (IFM 99–06): a randomised trial Lancet 2007; 370: 1209–18

Palumbo et al: Oral melphalan and prednisone chemotherapy plus thalidomide compared with melphalan and prednisone alone in elderly patients with multiple myeloma: randomised controlled trial Lancet 2006; 367: 825–31
### MP-T Melphalan, Prednisolone and Thalidomide (Myeloma)

#### DOCUMENT CONTROL

<table>
<thead>
<tr>
<th>Document Title:</th>
<th>MP-T NECN protocol CRP08 H029</th>
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<td>Document No:</td>
<td>CRP08 H029</td>
</tr>
<tr>
<td>Current Version:</td>
<td>2.3</td>
</tr>
<tr>
<td>Author:</td>
<td>Steve Williamson / Simon Lyons</td>
</tr>
<tr>
<td>Reviewed by:</td>
<td>Calum Polwart</td>
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<tr>
<td>Approved by:</td>
<td>Calum Polwart</td>
</tr>
<tr>
<td>Date Reviewed:</td>
<td>17 July 2014</td>
</tr>
<tr>
<td>Due for Review:</td>
<td>June 2016</td>
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#### Summary of Changes

<table>
<thead>
<tr>
<th></th>
<th>Amendments to dose modifications</th>
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<tr>
<td>1.1a</td>
<td>Correction to schedule and typos.</td>
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<tr>
<td>2.0a</td>
<td>Expanded LMWH Guidance. References to ThalidomidePharmion replaced with ThalidomideCelgene</td>
</tr>
<tr>
<td>2.1</td>
<td>Protocol reviewed. Typing errors corrected.</td>
</tr>
<tr>
<td>2.2</td>
<td>Formatting updated.</td>
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<tr>
<td>2.3</td>
<td>Nadir dose modification removed as does not reflect clinical trial practice</td>
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