Indication: First line multiple myeloma, suitable for intensive treatment
For relapsed multiple myeloma after standard therapies have failed / not tolerated.

Regimen details:
- Cyclophosphamide 500 mg orally D1, D8, D15
- Thalidomide 100mg od orally
  After 2 to 4 weeks, increase as tolerated, up to a maximum dose of 200mg od per day.
- Dexamethasone 20mg orally D1, D8, D15 and D22
  Dexamethasone may be initiated at a dose of 40mg if rapid response if required e.g. for patients with renal failure or with cord compression.

Administration: Orally
Thalidomide should be taken 2 hours before bedtime.

Premedication: Not applicable

Frequency: 28 day cycle.
Reassess every cycle. Continue to plateau.
Consider continuing thalidomide maintenance following achievement of plateau.

Extravasation: Not applicable

Anti-emetics: Mild emetogenicity, e.g. metoclopramide 20mg tds prn

Supportive medication:
- Thromboprophylaxis: All patients should receive thromboprophylaxis with aspirin 75mg od unless contraindicated. Patients with a previous VTE or who are at high risk of VTE (one other risk factor in addition to multiple myeloma) should receive LMWH e.g. enoxaparin 40mg sc od as per local protocol.
- Prophylactic laxatives as per local protocol
- Allopurinol 100mg - 300mg od (dependent on renal function) until plateau
- Antifungal prophylaxis as per local protocol
- In addition for patients receiving dexamethasone: PPI or H2-receptor antagonist e.g. omeprazole 20mg od or ranitidine 150mg bd
Cyclophosphamide, Thalidomide, Dexamethasone (CTD) first line for Multiple Myeloma and for relapsed Multiple Myeloma

Regular investigations: 
- FBC: D1 of each cycle
- LFTs: D1 of each cycle
- U&Es: D1 of each cycle
- Bone profile: D1 of each cycle
- Serum paraprotein / serum free light chains at the start of each cycle

Blood pregnancy test for women of child bearing potential within 3 days of the prescription date for every cycle.

Dose Modifications

Haematological Toxicity

Prior to every cycle of CTD:

<table>
<thead>
<tr>
<th>Neutrophils (x 10⁹/L)</th>
<th>Platelets (x 10⁹/L)</th>
<th>CTD</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥1.0 x 10⁹/L</td>
<td>≥ 50 x 10⁹/L</td>
<td>100% dose</td>
</tr>
<tr>
<td>&lt;1.0 x 10⁹/L</td>
<td>&lt; 50 x 10⁹/L</td>
<td>Delay cyclophosphamide 1 week (continue thalidomide and dexamethasone). Restart at same dose when neutrophils and platelets recovered as above. If recurrent, i.e., if neutrophils &lt; 1.0 x 10⁹/L and platelets &lt; 50 x 10⁹/L on day 1 of subsequent cycles (when previously &gt; than these levels), delay cyclophosphamide and consider dose reduction of cyclophosphamide. If the patient was receiving 500mg weekly, reduce to 400mg, if 400mg reduce to 300mg, if 300mg reduce to 200mg.</td>
</tr>
</tbody>
</table>

NB. In the presence of cytopenias due to marrow involvement with myeloma, it is possible that the first cycle will go ahead even if neutrophils <1.0 x 10⁹/L and platelets < 50 x 10⁹/L. This should be confirmed with a Consultant. Consider withholding cyclophosphamide until platelets ≥ 50 x 10⁹/L.

Renal Impairment

If GFR <50ml/min consider 25% reduction in cyclophosphamide dose, if <10ml/min consider 50% reduction in cyclophosphamide dose. Dose reduction should be a clinical decision depending on inter-patient variation

Hepatic Impairment

No dose modification required

Non-Haematological toxicities

Consider reducing thalidomide dose depending on patient tolerability.

Doses reduced for toxicity should not be re-escalated

Reason for Update: Dex 20mg schedule
Approved by Consultant: Matthew Streetly
Version: 4
Approved by Chair Haem TWG: Maj Kazmi
Supersedes: Version 3
Date: 25/02/2011
Prepared by: Laura Cameron
Checked by (Network Pharmacist): Jacky Turner
Cyclophosphamide, Thalidomide, Dexamethasone (CTD) first line for Multiple Myeloma and for relapsed Multiple Myeloma

Toxicities: Thrombosis, somnolence, skin dryness, constipation, sensory peripheral neuropathy, uncommonly motor neuropathy, haematological. Steroid related toxicities including mood changes, restlessness, withdrawal effects, glucose intolerance.

Drug interactions: Not applicable

Comments: Thalidomide must only be prescribed according to the Thalidomide Pregnancy Prevention Programme. All patients receiving thalidomide are required to sign a form to confirm that they understand the requirements of the programme.

References:
Garcia-Sanz R, et al. The combination of thalidomide, cyclophosphamide and dexamethasone (ThaCyDex) is feasible and can be an option for relapsed/refractory multiple myeloma. Hematol J. 2002;3(1):43-8
