1.1 Z-DEX

- **Indication**

  First line treatment of multiple myeloma patients suitable for intensive therapy or resistant to alkylator therapy. For more detail of this regimen and other treatment options in multiple myeloma, please consult UKMF/BCSH Guidelines on the diagnosis and management of multiple myeloma (www.ukmf.org.uk/guidelines).

- **Pre-treatment Evaluation**
  
  - Document FBC (with film), plasma viscosity, U&E, creatinine, LFTs, calcium, glucose, serum protein electrophoresis and paraprotein quantitation, CRP, $\beta_2$-microglobulin and immunoglobulin levels.
  
  - Urine for BJP (and formal evaluation of 24 hour urinary BJP excretion if light chain only myeloma).
  
  - Baseline serum free light chain profile if BJP or non-secretory myeloma.
  
  - Bone marrow aspirate ± trephine (and cytogenetics if part of local protocol).
  
  - Skeletal survey.
  
  
  - Document height and weight and surface area.
  
  - Consider ECG ± echocardiogram if clinical suspicion of cardiac dysfunction.
  
  - Give adequate verbal and written information for patients and relatives concerning patient’s disease, treatment strategy and side effects.
  
  - Obtain written consent from patient or guardian.
  
  - Discuss issues relating to contraception and potential risk of infertility with patient and relatives (if applicable).

- **Drug Regimen**

<table>
<thead>
<tr>
<th>Days</th>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Comments</th>
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<tbody>
<tr>
<td>1-4</td>
<td>Idarubicin</td>
<td>10 mg/m²/day</td>
<td>PO</td>
<td>Comes in 5mg and 10mg capsules</td>
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<tr>
<td>1-4</td>
<td>Dexamethasone</td>
<td>40mg daily</td>
<td>PO</td>
<td>Take in the mornings; swallow whole with food</td>
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NB: Dexamethasone may be given in addition on days 8-11 and days 15-18 for the first course only (dose as above)

- **Cycle Frequency**
• Repeat every 21 days.
• Continue to maximal response, usually 4-6 cycles.

- **Dose Modification**

**Renal Impairment**

The SPC states that renal impairment can affect the clearance of idarubicin. However, there is no dosing advice according to creatinine clearance. The advice is as follows:

- Serum Creatinine <100µmol/l: 100% idarubicin dose
- Serum Creatinine 100-175µmol/l: 50% idarubicin dose
- Serum Creatinine >175µmol/l: Clinical Decision

**NB** A serum creatinine >100µmol/l may not correspond to significant renal impairment, especially in younger patients. However, if there is evidence of impaired renal function, e.g., reduced creatinine clearance or according to Cockcroft and Gault calculation, then it is reasonable to use serum creatinine to guide dosing of idarubicin.

**Hepatic Impairment**

- Serum Bilirubin <40µmol/l: 100% idarubicin dose
- Serum Bilirubin 40-85µmol/l: 50% idarubicin dose
- Serum Bilirubin >85µmol/l: Omit

**Haematological dose reductions**

- The neutrophil count should be ≥ 1.0 x 10^9/l and platelet count ≥ 50 x 10^9/l before giving treatment at any stage. If necessary, treatment should be delayed until these levels are achieved unless they are considered to be due to bone marrow infiltration.
- Dose reductions of idarubicin should be made in subsequent courses depending on the ANC nadir (day 14):
  - ANC nadir <0.2 x 10^9/l: 75% dose reduction
  - ANC nadir <0.5 x 10^9/l: 50% dose reduction
- Dose reductions should be continued throughout the remainder of the treatment
- Consider G-CSF if treatment delays are prolonged or frequent

• **Investigations prior to subsequent cycles**
• FBC, U&E, creatinine, LFTs, calcium, paraprotein level or urinary protein/BJP excretion/serum free light chains, plasma viscosity
• Reassess disease response after each cycle of Z-DEX and then 6 weekly during plateau phase.

• **Concurrent Medication**

• Encourage 3l/24 hours oral fluid intake
• Allopurinol 300mg (or 100mg if creatinine clearance <20mls/min) od po during the first two treatment cycles.
• Nystatin and Chlorhexidine mouthcare.
• Oral systemic PCP prophylaxis is recommended until 2 weeks after the end of treatment - refer to local protocol.
• Consider oral systemic anti-bacterial, anti-viral and/or anti-fungal prophylaxis if patient is neutropenic - refer to local protocol.
• H2–antagonist or PPI is recommended throughout the first cycle if 3 blocks of Dexamethasone are given and for at least the first 7 days of each subsequent cycle.
  **NB:** Standard antacids should not be given as these reduce the absorption of Idarubicin.
• Bisphosphonates (Sodium Clodronate PO or Pamidronate IV).

• **Anti-emetics**

This regimen has moderate emetic potential - refer to local protocol.

• **References**

Cook G, Sharp RA, Tansey P, Franklin IM. A phase I/II trial of Z-Dex (oral Idarubicin and Dexamethasone), an oral equivalent of VAD, as initial therapy at diagnosis or progression in multiple myeloma. British Journal of Haematology 1996; 93: 931-4.

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**Written by:** ASWCS Haematology Site Specific Group  
**Authorised by:**

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**Date for review by Haematology SSG:** October 2009