REGIMEN TITLE: Z-DEX for Multiple Myeloma

Indication: Treatment of Multiple Myeloma (MM) in patients with newly diagnosed, relapsed or refractory disease

Regimen details:

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Idarubicin</td>
<td>10mg/m² OD</td>
<td>po</td>
<td>1 to 4 only</td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>40mg OM</td>
<td>po</td>
<td>1 to 4 only</td>
</tr>
</tbody>
</table>

Administration: Idarubicin is available as 5mg and 10mg capsules. Different doses may be given on different days to ensure that the total idarubicin dose given over 4 days is close to the desired total of 40mg/m². Dexamethasone should be taken in the morning, with or after food. It can be divided into two daily doses of 20mg BD. The second dose should be taken before 3pm.

Premedication: N/A

Frequency: 21 day cycle for 4 - 8 cycles

Extravasation: N/A

Emetogenicity: Low to Moderate

Supportive medication: Allopurinol 100 - 300mg od (dependant on renal function), starting the day before chemotherapy. H₂ antagonist/PPI cover is recommended while on steroid treatment. Anti-emetic for PRN use e.g. metoclopramide or domperidone. Refer to local policy for guidelines on the following: Mouthcare, Bisphosphonates, PCP prophylaxis. Consider oral systemic anti-bacterial, anti-viral and/or anti-fungal prophylaxis if patient is neutropenic.

Pre-treatment Evaluation:

Height, Weight & BSA
FBC (with film), plasma viscosity, U&Es, Se Cr, LFTs, calcium, glucose, serum protein electrophoresis and paraprotein quantification, B2- 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
Skeletal survey
Consider ECG +/- Echocardiogram if clinical suspicion of cardiac dysfunction.
Discuss issues relating to contraception and potential risk of infertility with patient and relatives (if applicable).
Regular investigations:  
- FBC Monthly
- Se Cr & U&Es Monthly
- LFTs Monthly
Reassess disease response after each cycle of Z-Dex and then every three months during plateau phase.

Dose Modifications

Haematological Toxicity

Neutrophil count must be ≥1.5 x10⁹/L and platelet count must be ≥100 x10⁹/L before giving treatment. Treatment should be delayed until these levels are achieved unless they are considered to be due to bone marrow infiltration.

If ANC nadir <0.2 x 10⁹/L Reduce idarubicin dose by 50%
If ANC nadir 0.2 – 0.5 x 10⁹/L Reduce idarubicin dose by 25%

Renal Impairment

Idarubicin is contra-indicated in severe renal impairment (GFR <10ml/min)

Hepatic Impairment

<table>
<thead>
<tr>
<th>Bilirubin (µmol/l)</th>
<th>Idarubicin Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>20 – 50</td>
<td>Give 50%</td>
</tr>
<tr>
<td>&gt;50</td>
<td>Clinical Decision</td>
</tr>
</tbody>
</table>

Dose modifications for other toxicities as appropriate

Toxicities: Haematological toxicity; commonly neutropenia and thrombocytopenia.
Nausea and vomiting – see Anti-Emetic Guidelines for advice on management
Idarubicin can cause delayed cardiotoxicity.
Steroid side effects e.g. impaired glucose tolerance, altered mood

Drug interactions: None significant

Comments:

Maximum cumulative dose Idarubicin = 400mg/m²
A baseline Echo should be performed where the patient is considered at risk of having impaired cardiac function e.g. significant cardiac history, hypertension, obese, smoker, elderly, previous exposure to anthracyclines, previous thoracic radiotherapy. Echo should be repeated if there is suspicion of cardiac toxicity at any point during treatment, or if cumulative anthracycline dose approaches maximum.

Ensure patients are aware that idarubicin capsules should not be handled by anyone else (e.g. carers). Patients should be advised to wash hands immediately after handling idarubicin capsules. Ensure they have seen a copy of the patient information leaflet for advice about oral chemotherapy.
Patients should be aware that they must return any unused idarubicin capsules to the hospital pharmacy department for special disposal as cytotoxic waste.

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 multiplemyeloma. British Journal of Haematology 1996; 93: 931-4.

