Indication: Treatment of Multiple Myeloma, having received two or more prior therapies.

Regimen details: Lenalidomide 25 mg od orally D1 to 21
Dexamethasone 20mg od orally Days 1, 8, 15, 22

Administration: Orally

Premedication: Not required

Frequency: 28 day cycle

Extravasation: Not applicable

Anti-emetics: Not required

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.

Allopurinol 100 - 300mg od (dependent on renal function) until plateau

If dexamethasone prescribed:
Antifungal prophylaxis as per local protocol
PPI or H2-receptor antagonist e.g omeprazole 20mg od or ranitidine 150mg bd

Regular investigations: FBC D1
LFTs D1
U&Es D1
Bone profile D1
M-protein / free light chains at the start of each cycle
For women of child bearing potential, pregnancy test within 3 days prior to D1
Dose Modifications

Haematological Toxicity

(NB Recommendations below are different to those stated in the SPC)

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 / or platelets < 75 x 10⁹/L. This should be confirmed with a Consultant

For Day 1, all cycles:

<table>
<thead>
<tr>
<th>Platelets (x 10⁹/L)</th>
<th>Neutrophils (x 10⁹/L)</th>
<th>Lenalidomide</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 30 x 10⁹/L</td>
<td>&amp; ≥ 1.0 x 10⁹/L</td>
<td>100% dose</td>
</tr>
<tr>
<td>&lt; 30 x 10⁹/L</td>
<td>or &lt; 1.0 x 10⁹/L</td>
<td>Delay until platelets ≥ 30 x 10⁹/L and neutrophils ≥ 1.0 x 10⁹/L. Reduce the dose as below.</td>
</tr>
</tbody>
</table>

Thrombocytopenia (platelet < 30 x 10⁹/L)
If the treatment is delayed, due to platelets < 30 x 10⁹/L interrupt treatment and restart at 15mg od when platelets >30 x 10⁹/L.
If the treatment is delayed for a second time due to platelets < 30 x 10⁹/L interrupt treatment and restart at 10mg od when platelets >30 x 10⁹/L.
If the treatment is delayed for a third time due to platelets < 30 x 10⁹/L interrupt treatment and restart at 5mg od when platelets >30 x 10⁹/L.
Do not dose below 5mg once daily.

Neutropenia (neutrophils < 1.0 x 10⁹/L)
If the treatment is delayed for the first time due to neutrophils < 1.0 x 10⁹/L only, interrupt treatment and restart when neutrophils > 1.0 x 10⁹/L at 25mg od.
If other haematological toxicities are observed, i.e thrombocytopenia, restart when neutrophils > 1.0 x 10⁹/L at 15mg od.
If the treatment is delayed for the second time due to neutrophils < 1.0 x 10⁹/L only, interrupt treatment and restart when neutrophils > 1.0 x 10⁹/L at 15mg od.
If the treatment is delayed for the third time due to neutrophils < 1.0 x 10⁹/L only, interrupt treatment and restart when neutrophils > 1.0 x 10⁹/L at 10mg od.
If the treatment is delayed for the fourth time due to neutrophils < 1.0 x 10⁹/L only, interrupt treatment and restart when neutrophils > 1.0 x 10⁹/L at 5mg od.
Do not dose below 5mg once daily.

In cases of neutropenia, consider GCSF support on days 22, 23, 24. This must be on the recommendation of a Consultant Haematologist.
Renal Impairment

Lenalidomide should be used with caution in patients with renal impairment. The following dose reductions are recommended by Celgene:

<table>
<thead>
<tr>
<th>Renal function (CrCl ml/min)</th>
<th>Dose of lenalidomide</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 50 ml/min</td>
<td>100% dose</td>
</tr>
<tr>
<td>&lt; 50 ml/min</td>
<td>10mg once daily. The dose may be increased to 15mg once daily after 2 cycles if the patient is not responding and is tolerating treatment.</td>
</tr>
<tr>
<td>&lt; 30 ml/min, not requiring dialysis</td>
<td>15mg alternate days. The dose may be increased to 10mg once daily if the patient is tolerating treatment.</td>
</tr>
<tr>
<td>End stage renal disease, &lt; 30 ml/min, requiring dialysis</td>
<td>5mg once daily. On dialysis days, the dose should be administered following dialysis.</td>
</tr>
</tbody>
</table>

Hepatic Impairment

There is very limited information available regarding the use of lenalidomide in patients with hepatic insufficiency and it should therefore be used with caution.

Non-Haematological toxicities

Hypothyroidism has been described and should be considered.

Due to the potential for teratogenicity all women of child bearing potential are required to ensure adequate contraception including a barrier method is used. Additionally a negative pregnancy test is required prior to commencing each cycle of therapy. Men are required to undertake to use a barrier method of contraception.

An increased incidence of venous thrombosis has been reported for patients receiving lenalidomide in combination with dexamethasone and erythropoietin and/or anthracycline chemotherapy regimens

Doses reduced for toxicity should not be re-escalated

Drug interactions: None described

Toxicities: Thrombosis, neutropenia, thrombocytopenia, neuropathy, dry skin.
Steroid related toxicities including mood changes, restlessness, withdrawal effects, glucose intolerance

Lenalidomide plus Dexamethasone for Relapsed or Refractory Multiple Myeloma. Dimopoulos M et al NEJM 2007; 357: 2123-32
NICE Technology Appraisal 171 June 2009