POMALIDOMIDE AND LOW DOSE DEXAMETHASONE

INDICATION

Multiple myeloma at third or subsequent relapse, i.e. after 3 previous treatments including both lenalidomide, bortezomib, as well as alkylators. [NICE TA427]

Requires Bluteq approval

TREATMENT INTENT

Disease modification

GENERAL PRE-ASSESSMENT

1. Ensure all the following staging investigations are done:
   - FBC & film
   - Clotting screen
   - U&Es
   - LFTs
   - Calcium
   - Albumin
   - Uric acid
   - CRP
   - Baseline random blood glucose level
   - Virology: HIV, Hepatitis B (including core antibody), and Hepatitis C
   - Calculated creatinine clearance (CrCl), urine protein/creatinine ratio
   - Electrophoresis and immunofixation for quantitation of serum paraprotein and immunoglobulins.
   - Serum free light chain assay (Freelite)
   - β2 microglobulin
   - LDH
   - Myeloma FISH should be performed in all patients at diagnosis, and in selected patients at relapse/progression to help guide treatment decisions. Samples should be sent to Wessex Regional Genetics Laboratory (address below)
   - Urine pregnancy testing for pre-menopausal women younger than 55 before each cycle.
   - Group and save
   - Imaging as per NICE/network guidance and clinical presentation
   - Bone marrow aspirate and trephine (with immunophenotyping for kappa/lambda if appropriate)
   - Formal assessment of performance status (WHO score)
Myeloma group

Wessex Regional Genetic Laboratory
Salisbury NHS Foundation Trust
Salisbury District Hospital
Salisbury
Wiltshire
SP2 8BJ

Additional Investigations
- Plasma viscosity if hyperviscosity suspected
- Fertility - all patients should be offered fertility advice, as appropriate.
- Hydration - fluid intake of at least 3 litres/day should be attempted.
- Document patient's performance status.
- Treatment must be agreed at the relevant MDT.
- Counselling - all patients should receive verbal and written information on oral chemotherapy.
  Ensure pre-chemotherapy counselling in line with NPSA recommendation and chemotherapy measures.
- Consent - ensure patient has received adequate verbal and written information regarding their disease, treatment and potential side effects. Document in medical notes all information that has been given. Obtain written consent for the treatment including signing Celgene Pregnancy Prevention Programme forms.

REGIMEN SPECIFIC PRE-ASSESSMENT
1. The conditions of the Pomalidomide Celgene Pregnancy Prevention Programme must be fulfilled for all male and female patients. Prescribing and dispensing of lenalidomide must be in line with the Celgene Pregnancy Prevention Programme.
2. Clinical Assessment of thrombo-embolic risk.
3. Consider baseline cardiac and respiratory assessment as per MHRA alert on risk of cardiac failure and interstitial lung disease.

DRUG REGIMEN / CYCLE FREQUENCY

<table>
<thead>
<tr>
<th>Pomalidomide</th>
<th>4mg PO daily on days 1-21</th>
<th>Nocte</th>
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<tbody>
<tr>
<td></td>
<td>WITH</td>
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<tr>
<td>Dexamethasone</td>
<td>40 mg PO daily for ≤ 75 yrs</td>
<td>D1, 8, 15, 22</td>
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<tr>
<td>OR</td>
<td></td>
<td></td>
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<tr>
<td>Dexamethasone</td>
<td>20 mg PO daily for &gt; 75 yrs</td>
<td>D1, 8, 15, 22</td>
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</table>

Consider adding clarithromycin 500 mg bd (250mg bd if not tolerating)
Dexamethasone should not be stopped (Unlike lenalidomide based therapy)

CYCLE FREQUENCY

This is a controlled document and therefore must not be changed

MM.22
Pomalidomide IMNOVID
Authorised by Myeloma lead Dr. Karthik Ramasamy
June 2019
V.1.6
Cycle repeats every 28 days and therapy can continue until progression or toxicity.

Consider reviewing response after 4 cycles of therapy.

DOSE MODIFICATIONS

Haematological
To initiate a new cycle of Pomalidomide, ANC ≥ 1.0 x 10⁹/L and Platelets ≥ 50 x 10⁹/L

<table>
<thead>
<tr>
<th>Toxicity</th>
<th>Dose Modification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neutropenia:</td>
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<tr>
<td>ANC &lt; 0.5 x 10⁹/L OR Febrile Neutropenia and ANC &lt; 1.0 x 10⁹/L. When ANC return to ≥1 x 10⁹/L</td>
<td>Interrupt Pomalidomide, monitor FBC weekly</td>
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<tr>
<td></td>
<td>Resume Pomalidomide at 3 mg OD</td>
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<tr>
<td>For each subsequent drop ANC &lt; 0.5 x 10⁹/L</td>
<td>Interrupt Pomalidomide</td>
</tr>
<tr>
<td>When ANC ≥ 1.0 x 10⁹/L</td>
<td>Resume Pomalidomide at 1 mg less than previous dose</td>
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<tr>
<td>Thrombocytopenia:</td>
<td></td>
</tr>
<tr>
<td>Platelets &lt; 25 x 10⁹/L</td>
<td>Interrupt Pomalidomide, monitor FBC weekly</td>
</tr>
<tr>
<td>When Platelets ≥ 50 x 10⁹/L</td>
<td>Resume Pomalidomide at 3 mg OD</td>
</tr>
<tr>
<td>For each subsequent drop Platelets &lt; 25 x 10⁹/L</td>
<td>Interrupt Pomalidomide</td>
</tr>
<tr>
<td>When Platelets ≥ 50 x 10⁹/L</td>
<td>Resume Pomalidomide at 1 mg less than previous dose</td>
</tr>
</tbody>
</table>

If toxicities occur after dose reductions to 1 mg, then discontinue Pomalidomide.

Weekly injections of G-CSF can be administered to keep maintain dose intensity (aim to keep neutrophil counts >1.0)

Non-Haematological

<table>
<thead>
<tr>
<th>Toxicity</th>
<th>Dose Modification</th>
</tr>
</thead>
<tbody>
<tr>
<td>-Grade 3 or 4</td>
<td>-Interrupt Pomalidomide</td>
</tr>
<tr>
<td>-When resolved to Grade ≤ 2</td>
<td>-Resume Pomalidomide at 1mg less than previous dose</td>
</tr>
</tbody>
</table>

If toxicities occur after dose reductions to 1 mg, then discontinue Pomalidomide.

Renal / Hepatic Impairment

<table>
<thead>
<tr>
<th>Renal</th>
<th>Hepatic</th>
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<tbody>
<tr>
<td>- No dose adjustment required in renal impairment</td>
<td>Avoid if serum bilirubin &gt; 34 umol/L</td>
</tr>
<tr>
<td>-On haemodialysis days, patients should take pomalidomide following haemodialysis</td>
<td>Careful monitoring is required in hepatic impairment</td>
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</tbody>
</table>
INVESTIGATIONS - Pre-treatment and during

- Urine pregnancy testing for pre-menopausal women younger than 55 before each cycle.
- FBC – consider weekly for first cycle then monthly.
- U&E, Ca++, LFTs - monthly.
- Ig’s, paraprotein, urinary BJP and serum free light chain levels in patients with light chain disease or non-secretory myeloma.
- Consider bone marrow assessment after four cycles for non-secretory Myeloma.
- Consider blood glucose monitoring in patients with diabetes and those with signs of glucose intolerance.

CONCURRENT MEDICATIONS

- Allopurinol 300 mg daily for 7 days for cycle 1 only
- Aim to start day before chemotherapy.
- Prophylactic aciclovir 200 mg TDS (consider reducing to 200mg BD if CrCl<10ml/min)
- Consider prophylactic fluconazole 50mg OD if appropriate
- Consider prophylactic co-trimoxazole 960mg OD on M/W/F if heavily pre-treated or previous autograft.
- Proton pump inhibitor or H₂ antagonist at clinician’s discretion.
- Thromboprophylaxis/anticoagulation see VTE section below.
- Bone protection as per NSSG Bone Protection protocol MM.3

Note: If a strong inhibitors of CYP1A2 (e.g. ciprofloxacin, enoxacin and fluvoxamine) is co-administered with pomalidomide, reduce the dose of pomalidomide by 50%.

EMETIC RISK

Minimal.

ADVERSE EFFECTS/REGIMEN SPECIFIC COMPLICATIONS

- **Teratogenic**: The Celgene Pregnancy Prevention Programme must be observed for all male and female patients. Prescribing and dispensing of lenalidomide must be in line with the pregnancy prevention programme.

- **Myelosuppression**: Very common, including neutropenia and thrombocytopenia which may require dose interruptions and reductions. Check bloods at least monthly. Monitor patients with neutropenia for signs of infection. Patients should be advised to monitor themselves for bleeding or bruising, especially if prophylactic VTE treatments are concomitantly administered. Follow dose modifications for haematological toxicity as per section above.
• **Venous thromboembolism (VTE):** There is an increased risk of thrombosis with lenalidomide. Unless the patient is thought to be at particularly low-risk of thrombosis or high-risk of bleeding, some form of VTE prophylaxis is recommended as follows:

1. Prophylactic low-molecular weight heparin OR
2. Prophylactic NOAC e.g. apixaban 2.5mg bd (check product specific information)

Aspirin can be appropriate for patients with no additional risk factors for thrombosis. It is generally not preferred for higher-risk patients with additional risk factors.

If VTE occurs, lenalidomide can be continued and the patient should be fully anticoagulated according to standard guidelines.

• Fatigue, dizziness and confusion
• Peripheral neuropathy, diarrhea/constipation, pneumonia, peripheral oedema.

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TREATMENT RELATED MORTALITY

< 5%

REFERENCES


5. Imnovid® (Pomalidomide 4mg) eMC UK Summary of Product Characteristics for, Celgene, 22 May 2019
## REVIEW

<table>
<thead>
<tr>
<th>Name</th>
<th>Revision</th>
<th>Date</th>
<th>Version</th>
<th>Review date</th>
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<tbody>
<tr>
<td>Nadjoua Maouche Pharmacist</td>
<td>Indication, pre assessment, drug interaction, adverse effects, contraindications section removed</td>
<td>May 2016</td>
<td>1.3</td>
<td>May 2018</td>
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<tr>
<td>Faouzi Djebbari (Haematology Pharmacist)</td>
<td>Updated indication, renal/hepatic impairment, concurrent medicines, drug interactions and references</td>
<td>July 2017</td>
<td>1.4</td>
<td>June 2018</td>
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<tr>
<td>Nadjoua Maouche (Haematology Pharmacist)</td>
<td>Standardise VTE information, pre-assessment, investigation, concurrent medication, adverse effects sections.</td>
<td>June 2018</td>
<td>1.5</td>
<td>June 2019</td>
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<tr>
<td>Myeloma Protocol Review 2019</td>
<td>Update of indications, concurrent medication, and references</td>
<td>June 2019</td>
<td>1.6</td>
<td>June 2020</td>
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