POMALIDOMIDE AND LOW DOSE DEXAMETHASONE

INDICATION

Multiple myeloma at third or subsequent relapse, i.e. after 3 previous treatments including both lenalidomide and bortezomib. (NICE TA427 -BLUETEQ required)

TREATMENT INTENT

Disease modification

GENERAL PRE-ASSESSMENT

1. Ensure all the following staging investigations are done:
   o Consider baseline cardiac and respiratory assessment as per MHRA alert
   o FBC & film
   o Clotting screen
   o U&Es
   o LFTs
   o Calcium
   o Albumin
   o Uric acid
   o CRP
   o Virology: HIV, Hepatitis B (including core antibody), and Hepatitis C
   o Calculated creatinine clearance (CrCl), urine protein/creatinine ratio
   o Electrophoresis and immunofixation for quantitation of serum paraprotein and immunoglobulins.
   o Serum free light chain assay (Freelite)
   o β2 microglobulin
   o 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)
   o Urine pregnancy testing for pre-menopausal women younger than 55 before each cycle.
   o Group and save
   o Imaging as per NICE/network guidance and clinical presentation
   o Bone marrow aspirate and trephine (with immunophenotyping for kappa/lambda if appropriate)
   o Formal assessment of performance status (WHO score)

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

- Plasma viscosity if hyperviscosity suspected

2. Fertility - all patients should be offered fertility advice, as appropriate.
3. Hydration - fluid intake of at least 3 litres /day should be attempted.
5. Counselling - all patients should receive verbal and written information on oral chemotherapy.
6. Ensure pre-chemotherapy counselling in line with NPSA recommendation and chemotherapy measures.
7. 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. The manufacturer's risk management programme should be observed - see special warning below.

8. **Treatment must be agreed at the relevant MDT.**

REGIMEN SPECIFIC PRE ASSESSMENT

The conditions of the Pomalidomide Celgene Pregnancy Prevention Programme must be fulfilled for all male and female patients.

Clinical assessment of thrombo-embolic risk.

<table>
<thead>
<tr>
<th>Drug Regimen / Cycle Frequency</th>
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<tbody>
<tr>
<td><strong>Pomalidomide</strong></td>
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<tr>
<td><strong>Dexamethasone</strong></td>
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<tr>
<td>40 mg PO daily for ≤ 75 yrs</td>
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<tr>
<td>OR</td>
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<tr>
<td><strong>Dexamethasone</strong></td>
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Consider adding clarithromycin 500 mg bd (250mg bd if not tolerating)
Consider low dose cyclophosphamide, depending on local funding
Dexamethasone should not be stopped (Unlike lenalidomide based therapy)

CYCLE FREQUENCY

Cycle repeats every 28 days and therapy can continue until progression or toxicity.
DOSE MODIFICATIONS

Capsule strengths available 1mg, 2mg, 3mg and 4 mg

Haematological
To initiate a new cycle of Pomalidomide, ANC ≥ 1.0 x 10^9/L and Platelets ≥ 50 x 10^9/L

<table>
<thead>
<tr>
<th>Toxicity</th>
<th>Dose Modification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neutropenia:</td>
<td></td>
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<tr>
<td>ANC &lt; 0.5 x 10^9/L or Febrile Neutropenia and ANC &lt; 1.0 x 10^9/L. When ANC return to ≥1 x 10^9/L</td>
<td>Interrupt Pomalidomide, monitor FBC weekly</td>
</tr>
<tr>
<td>For each subsequent drop ANC &lt; 0.5 x 10^9/L When ANC ≥ 1.0 x 10^9/L</td>
<td>Interrupt Pomalidomide</td>
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<tr>
<td></td>
<td>Resume Pomalidomide at 3 mg OD</td>
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<tr>
<td></td>
<td>Resume Pomalidomide at 1 mg less than previous dose</td>
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<tr>
<td>Thrombocytopenia:</td>
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</tr>
<tr>
<td>Platelets &lt; 25 x 10^9/L</td>
<td>Interrupt Pomalidomide, monitor FBC weekly</td>
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<tr>
<td>When Platelets ≥ 50 x 10^9/L</td>
<td>Resume Pomalidomide at 3 mg OD</td>
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<td>For each subsequent drop Platelets &lt; 25 x 10^9/L When Platelets ≥ 50 x 10^9/L</td>
<td>Interrupt Pomalidomide</td>
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<tr>
<td></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>
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<tbody>
<tr>
<td>Grade 3 or 4 -When resolved to Grade ≤ 2 -Interrupt Pomalidomide -Resume Pomalidomide at 1mg less than previous dose</td>
<td></td>
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</table>

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

Renal / Hepatic Impairment

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

- Ensure all staging investigations (as listed under the PRE-ASSESSMENT heading above) are done.
- Urine pregnancy testing for pre-menopausal women younger than 55 before each cycle.
- Consider bone marrow assessment after four cycles for non-secretory Myeloma.
- 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.

RESPONSE ASSESSMENT

Consider reviewing response after 4 cycles of therapy.

CONCURRENT MEDICATIONS

- Consider prophylactic laxatives to be taken if needed.
- Allopurinol 300 mg daily for 7 days for cycle 1 only. Aim to start day before chemotherapy.
- Proton pump inhibitor or H₂ antagonist at clinician’s discretion.
- Consider prophylactic fluconazole.
- Bone protection as per NSSG Bone Protection protocol MM.3
- Thromboprophylaxis/anticoagulation Aspirin or LMWH based on risk profile.
- LMWH/DOAG
- Consider prophylactic co-trimoxazole if heavily pre-treated or previous autograft.
- Prophylactic acyclovir 200 mg bd to tid (depending on renal function).

DRUG INTERACTIONS

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

- **Teratogenicity:** Prescribing and dispensing of Pomalidomide must be in line with the pregnancy prevention programme.

- **Myelosuppression:** very common. Patients may require dose interruption and/or modification due to thrombocytopenia and/or neutropenia as above. Blood counts to be monitored monthly.

- **Venous thromboembolism (VTE):**
  
  There is an increased risk of thrombosis, and some form of prophylaxis is recommended as follows:

  1. Aspirin can be appropriate for patients with no additional risk factors for thrombosis
  2. If additional risk factors consider:
     - Prophylactic low-molecular weight heparin, OR
     - Vitamin K antagonists at a therapeutic dose, to maintain an international normalised ratio (INR) of 2–3, OR
     - Direct oral anticoagulant e.g. apixaban for thromboprophylaxis or treatment dose as indicated.

  Aspirin is generally not preferred for higher risk patients with additional risk factors such as immobility. If VTE occurs, thalidomide 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.

TREATMENT RELATED MORTALITY

< 5%

REFERENCES


5. eMC UK Summary of Product Characteristics for Imnovid 4mg, Celgene, 27 September 2016

## 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>
</tr>
<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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