Bendamustine & Prednisolone for Multiple Myeloma

Indication:
Relapsed or refractory Multiple Myeloma

Confirm local funding is agreed before commencing therapy. Bendamustine is not licensed for this indication.

Regimen details:
Bendamustine 60mg/m² IV Days 1 and 2
Prednisolone 60mg PO Days 1, 8, 15 and 22

Administration:
Bendamustine IV in 500ml sodium chloride 0.9% over 30 - 60 minutes
Prednisolone Orally

Premedication: None required

Frequency: Every 28 days, for up to 6 cycles

Extravasation: If there is any possibility that extravasation has occurred, contact a senior member of the medical team and follow local protocol for dealing with cytotoxic extravasation of irritant and non-vesicant drugs.

Anti-emetics: Moderate emetogenic potential (30 - 90%)

Supportive medication: Allopurinol 100 - 300 mg od (dependent on renal function) for first cycle. PPI as per local policy.

Regular investigations: FBC D1
U&E D1
LFTs D1

Dose Modifications

Haematological Toxicity due to treatment:

<table>
<thead>
<tr>
<th>Neutrophils (x 10⁹/L)</th>
<th>Platelets (x 10⁹/L)</th>
<th>Bendamustine dose adjustment</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 1.0 x 10⁹/L &amp; ≥ 75 x 10⁹/L</td>
<td>100% dose</td>
<td></td>
</tr>
<tr>
<td>&lt; 1.0 x 10⁹/L &amp; / or &lt; 75 x 10⁹/L</td>
<td>Delay treatment until counts recovered.</td>
<td></td>
</tr>
</tbody>
</table>

Renal Impairment
Creatinine clearance > 10 ml/min give 100% Bendamustine dose.
Creatinine clearance < 10 ml/min; no data available.

Reason for Update: New protocol
Approved by Consultant: Matthew Streetly 20/02/2012
Version: 1
Approved by Chair Haem TWG: Maj Kazmi
Supersedes: All other versions
Date: 20/04/2012
Prepared by: Laura Cameron
Checked by (Network Pharmacist): Jacky Turner
Approved by SELCN DTAC Chair:
Date: 22/03/2012
**Hepatic Impairment**

<table>
<thead>
<tr>
<th>Bilirubin</th>
<th>Bendamustine dose adjustment</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 21umol/L</td>
<td>100% dose</td>
</tr>
<tr>
<td>21 – 52umol/L</td>
<td>70% dose</td>
</tr>
<tr>
<td>&gt; 53umol/L</td>
<td>No information available</td>
</tr>
</tbody>
</table>

**Toxicities:**
Tumour lysis syndrome, cardiac dysfunction, hypotension, hypertension, diarrhoea, constipation.

**Drug interactions:**
Bendamustine metabolism involves the CYP P450 1A2 pathway. There is potential for interaction with CYP1A2 inhibitors such as ciprofloxacin, aciclovir and cimetidine.

**Comments:**
Patients with cardiac disorders: Ensure K+ remains > 3.5mmol/L during treatment with Bendamustine.

Patients may develop infusion related reactions; symptoms include fever, chills, pruritis and rash.

Rarely, anaphylactic reactions can occur. Patients must be asked about symptoms suggestive of infusion reactions after their first cycles of therapy. Measures to prevent severe reactions, including antihistamines, antipyretics and corticosteroids must be considered in subsequent cycles. Patients who have experienced Grade 3 or worse allergic-type reactions should not be re-challenged.

Blood and platelet transfusion according to unit guidelines. Products must be irradiated as patients are at risk of transfusion-associated graft versus host disease - ensure blood transfusion is notified and patient has received a PIL *Information for patients needing irradiated blood* and Alert Card.

**References:**
Ponisch, W et al. Combined bendamustine, prednisolone and thalidomide for refractory or relapsed multiple myeloma after autologous stem-cell transplantation or conventional chemotherapy: results of a Phase I clinical trial. BJH 2008; 143:191-200

Grey-Davies, E. et al. Bendamustine, thalidomide and dexamethasone is an effective salvage regimen for advanced stage multiple myeloma. BJH 2011;153: suppl 1: abstract 47

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