**Bendamustine 120 (Relapsed/refractory NHL)**

**Indication**
Monotherapy for relapsed/refractory non-Hodgkin’s lymphoma in patients who have progressed during or within 6 months following treatment with rituximab or a rituximab-containing regimen.

Note: funding should be secured prior to commencing treatment.

There are a number of bendamustine protocols – please ensure this is the correct one for your patient. This protocol should NOT be used in combination with rituximab. Refer to alternative protocol.

**ICD-10 codes**
Codes with a prefix C88, C82, C83

**Regimen details**

<table>
<thead>
<tr>
<th>Day</th>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 and 2</td>
<td>Bendamustine</td>
<td>120mg/m²</td>
<td>IV infusion</td>
</tr>
</tbody>
</table>

**Cycle frequency**
21 days

**Number of cycles**
Up to 6 cycles

**Administration**
Bendamustine is administered in 500mL sodium chloride 0.9% over 30-60 minutes.

**Pre-medication**
Pre-hydration may be required if bulky disease (e.g. 1000mL sodium chloride 0.9% over 4-6 hours)
Antiemetics as per local policy.

**Emetogenicity**
This regimen has moderate emetic potential

**Additional supportive medication**
Allopurinol 300mg OD (100mg OD if CrCl < 20mL/min) for the first 2 weeks. Some patients may require for subsequent cycles. (Omit allopurinol on days of bendamustine administration – see interactions section).
Antiviral and PCP prophylaxis as per local policy.

**Extravasation**
Bendamustine is an irritant (Group 3)
Investigations – pre first cycle

<table>
<thead>
<tr>
<th>Investigation</th>
<th>Validity period (or as per local policy)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FBC</td>
<td>14 days</td>
</tr>
<tr>
<td>U+E (including creatinine)</td>
<td>14 days</td>
</tr>
<tr>
<td>LFTs</td>
<td>14 days</td>
</tr>
</tbody>
</table>

Hepatitis B and C serology: HBV serology (aAg and cAb) must be checked before first dose rituximab. Avoid rituximab in active hepatitis B. Consider anti-viral (eg entecavir 500micrograms OD) where there is evidence of past infection.

HIV status.

TP53 mutational status (R-bendamustine has limited efficacy if TP53 mutated)

Investigations – pre subsequent cycles

<table>
<thead>
<tr>
<th>Investigation</th>
<th>Validity period (or as per local policy)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FBC*</td>
<td>72 hours</td>
</tr>
<tr>
<td>U+E (including creatinine)</td>
<td>72 hours</td>
</tr>
<tr>
<td>LFTs</td>
<td>72 hours</td>
</tr>
</tbody>
</table>

*Serum potassium must be monitored in all patients with cardiac disorders. If serum potassium <3.5mmol/L start potassium supplementation and perform an ECG.

Standard limits for administration to go ahead

If blood results not within range, authorisation to administer must be given by prescriber/consultant

<table>
<thead>
<tr>
<th>Investigation</th>
<th>Limit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neutrophils</td>
<td>≥ 1.0 x 10^9/L</td>
</tr>
<tr>
<td>Platelets</td>
<td>≥ 100 x 10^9/L</td>
</tr>
<tr>
<td>Creatinine clearance (CrCl)</td>
<td>≥ 10ml/min</td>
</tr>
<tr>
<td>Bilirubin</td>
<td>≤ ULN</td>
</tr>
</tbody>
</table>

Dose modifications

- **Haematological toxicity**
  If neutrophils < 1.0x 10^9/L and/or platelets < 100 x 10^9/L delay treatment until recovery. Consider bendamustine dose reduction – discuss with consultant.

- **Renal impairment**
  There is no information regarding use of bendamustine if CrCl ≤ 10mL/min. Discuss with consultant.

- **Hepatic impairment**

<table>
<thead>
<tr>
<th>Bilirubin (x ULN)</th>
<th>Bendamustine dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ ULN</td>
<td>100%</td>
</tr>
<tr>
<td>1-3</td>
<td>70%</td>
</tr>
<tr>
<td>&gt; 3</td>
<td>Discuss with consultant (no information)</td>
</tr>
</tbody>
</table>

- **Other toxicities**
  For any grade 3-4 toxicity (except alopecia) delay treatment until toxicity ≤ grade 1 and consider reducing subsequent bendamustine doses to 50% - discuss with consultant.
Adverse effects - for full details consult product literature/ reference texts

- **Serious side effects**
  Myelosuppression  
  Cardiotoxicity including arrhythmia  
  Infertility  
  Stevens-Johnson syndrome and toxic epidermal necrolysis (bendamustine with allopurinol)  
  Possible risk of secondary malignancies

- **Frequently occurring side effects**
  Myelosuppression  
  Nausea and vomiting  
  Mucositis, stomatitis  
  Diarrhoea, constipation  
  Hypokalaemia  
  Renal impairment

- **Other side effects**
  Raised transaminases  
  Alopecia  
  Fatigue  
  Insomnia  
  Rash, urticaria

**Significant drug interactions** – for full details consult product literature/ reference texts

**Warfarin/coumarin anticoagulants**: increased or fluctuating anticoagulant effects. Avoid if possible, consider switching patient to a low molecular weight heparin during treatment or if the patient continues taking an oral anticoagulant monitor the INR at least once a week and adjust dose accordingly.

**Allopurinol**: reports of Stevens-Johnson syndrome and toxic epidermal necrolysis – avoid concurrent administration.

**CYP 1A2 inhibitors**: metabolism of bendamustine by cytochrome P450 (CYP) 1A2 isoenzyme is a significant route of hepatic clearance so interaction with CYP1A2 inhibitors such as fluvoxamine, ciprofloxacin, aciclovir and cimetidine is possible. May increase toxicity – avoid concomitant use.

**Additional comments**

Patients must receive irradiated blood products for all future transfusions.

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**References**
