Indication
Monotherapy for relapsed / refractory Diffuse Large B-cell Lymphoma (DLBL) as 3rd or 4th line treatment for patients who have previously been treated with rituximab.

(NICE TA306)

ICD-10 codes
Codes with a prefix C83.3

Regimen details

<table>
<thead>
<tr>
<th>Day</th>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
</tr>
</thead>
<tbody>
<tr>
<td>Days 1, 8, and 15</td>
<td>Pixantrone</td>
<td>50mg/m²*/day</td>
<td>IV infusion</td>
</tr>
</tbody>
</table>

* (50mg/m² is equivalent to 85mg/m² pixantrone dimaleate)

Cycle frequency
28 days

Number of cycles
Up to 6 cycles

Administration
Pixantrone should be administered as an IV infusion in sodium chloride 0.9% (final volume 250mL) over a minimum of 60 minutes. (Final concentration < 0.58mg/mL).

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

Emetogenicity
This regimen has moderate emetic potential.

Additional supportive medication
Allopurinol 300mg OD (100mg OD if CrCl < 20mL/min) for 7 days (cycle 1 only)
Antiemetics as required
Antiviral and antifungal prophylaxis

Extravasation
Pixantrone is an exfoliant.
Investigations – pre first cycle

<table>
<thead>
<tr>
<th>Investigation</th>
<th>Validity period</th>
</tr>
</thead>
<tbody>
<tr>
<td>FBC</td>
<td>14 days</td>
</tr>
<tr>
<td>U+Es (including creatinine)</td>
<td>14 days</td>
</tr>
<tr>
<td>LFTs</td>
<td>14 days</td>
</tr>
<tr>
<td>LDH</td>
<td>14 days</td>
</tr>
<tr>
<td>Calcium</td>
<td>14 days</td>
</tr>
<tr>
<td>Magnesium</td>
<td>14 days</td>
</tr>
<tr>
<td>Glucose</td>
<td>14 days</td>
</tr>
</tbody>
</table>

ECG +/- echocardiogram
Pregnancy test for women of child bearing potential.

Investigations – pre subsequent cycles

<table>
<thead>
<tr>
<th>Investigation</th>
<th>Validity period</th>
</tr>
</thead>
<tbody>
<tr>
<td>FBC</td>
<td>96 hours</td>
</tr>
<tr>
<td>U+Es (including creatinine)</td>
<td>7 days</td>
</tr>
<tr>
<td>LFTs</td>
<td>7 days</td>
</tr>
</tbody>
</table>

Standard limits for administration to go ahead on day 1
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 10⁹/L</td>
</tr>
<tr>
<td>Platelets</td>
<td>≥ 75 x 10⁹/L</td>
</tr>
<tr>
<td>Creatinine clearance</td>
<td>&gt; 50mL/min</td>
</tr>
<tr>
<td>AST/ALT</td>
<td>See below</td>
</tr>
<tr>
<td>Bilirubin</td>
<td>See below</td>
</tr>
</tbody>
</table>

Dose modifications
• Haematological toxicity
On day 1 if neutrophils < 1.0 x 10⁹/L or platelets < 75 x 10⁹/L treatment should be delayed until recovery.

Doses on day 8 and 15 should be modified as below:

Day 8 and 15:

<table>
<thead>
<tr>
<th>Neutrophils (x 10⁹/L)</th>
<th>Platelets (x 10⁹/L)</th>
<th>Pixantrone dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 1.0</td>
<td>And &gt; 50</td>
<td>100%</td>
</tr>
<tr>
<td>0.5-1.0</td>
<td>Or 25-50</td>
<td>Delay until neutrophils ≥ 1.0 x 10⁹/L and platelets ≥ 50 x 10⁹/L</td>
</tr>
<tr>
<td>&lt; 0.5</td>
<td>Or &lt; 25</td>
<td>Delay until neutrophils ≥ 1.0 x 10⁹/L and platelets ≥ 50 x 10⁹/L Reduce dose to 80%</td>
</tr>
</tbody>
</table>

• Renal impairment
Pixantrone has not been studied in renal impairment, therefore use with caution.

• Hepatic impairment
Pixantrone has not been studied in patients with hepatic impairment. Use with caution in mild-moderate hepatic impairment and not recommended in severe hepatic impairment.
- **Other toxicities**

  **Cardiac toxicity:**
  If any grade 3-4 cardiac toxicity or persistent decline in LVEF: delay treatment until recovery to ≤ grade 1. Consider discontinuing treatment if ≥ 15% decline in LVEF from baseline.

  **Other toxicity:**
  Any grade 3-4 non cardiac toxicity: delay until recovery to ≤ grade 1 and recommence with 80% dose.

**Adverse effects** - for full details consult product literature/ reference texts

- **Serious side effects**
  Myelosuppression
  Cardiotoxicity
  Tumour lysis syndrome

- **Frequently occurring side effects**
  Myelosuppression
  Photosensitivity reactions
  Anorexia
  Taste disturbance
  Headache
  Dyspnoea, cough
  Nausea, vomiting
  Altered LFTs

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

No drug interactions have been reported in human subjects and no drug-drug interaction studies in humans have been performed.

**Additional comments**

This medicinal product contains approximately 1000 mg (43 mmol) sodium per dose after dilution. To be taken into consideration by patients on a controlled sodium diet.

Patients should be advised regarding sun protection due to risk of photosensitivity reactions.

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**References**


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Date: June 2017