**Indication**
First or second line treatment of symptomatic Waldenstrom’s macroglobulinaemia for patients who are unable to tolerate a fludarabine containing regimen.

**ICD-10 codes**
Codes prefixed with D88

**Regimen details**

<table>
<thead>
<tr>
<th>Day</th>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Dexamethasone</td>
<td>20mg STAT</td>
<td>PO or IV</td>
</tr>
<tr>
<td>1</td>
<td>Rituximab</td>
<td>375mg/m²</td>
<td>IV</td>
</tr>
<tr>
<td>1-5</td>
<td>Cyclophosphamide</td>
<td>100mg/m² BD</td>
<td>PO</td>
</tr>
</tbody>
</table>

**Cycle frequency**
21 days

**Number of cycles**
6 cycles

**Administration**
Dexamethasone is available as 500microgram and 2mg tablets. It is taken orally 30 minutes prior to rituximab.

Rituximab is administered in 500mL sodium chloride 0.9%. The first infusion should be initiated at 50mg/hour and if tolerated the rate can be increased at 50mg/hour every 30 minutes to a maximum of 400mg/hour. Subsequent infusions should be initiated at 100 mg/hour and if tolerated increased at 100mg/hour increments every 30 minutes to a maximum of 400 mg/hour.

Cyclophosphamide is available as 50mg tablets, doses should be rounded to the nearest 50mg. Tablets should be swallowed whole on an empty stomach (unless gastric irritation occurs and in that case they may be taken with meals). Patients should be advised to maintain good hydration.

**Pre-medication**
Rituximab premedication:
- Paracetamol 1g PO 60 minutes prior to rituximab infusion
- Chlorphenamine 10mg IV bolus 15 minutes prior to rituximab infusion
- Dexamethasone 20mg PO or IV 30 minutes prior to rituximab (as per dosing table above)

**Emetogenicity**
This regimen has low emetic potential.
Additional supportive medication
Allopurinol 300mg OD (or 100mg OD if creatinine clearance <20mL/min) for the first cycle.
H₂ antagonist or proton-pump inhibitor as per local policy.
Antiemetics as per local policy.
Aciclovir and co-trimoxazole as per local policy.
Consider GCSF support for patient > 70 years or with neutropenia.

Extravasation
Rituximab is neutral (Group 1)

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>
<tr>
<td>Glucose</td>
<td>14 days</td>
</tr>
<tr>
<td>DAT</td>
<td>14 days</td>
</tr>
<tr>
<td>Serum electrophoresis</td>
<td>14 days</td>
</tr>
<tr>
<td>Bone marrow aspirate and trephine biopsy</td>
<td>Within 8 weeks</td>
</tr>
</tbody>
</table>

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>
<tr>
<td>Serum electrophoresis</td>
<td>7 days</td>
</tr>
</tbody>
</table>

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 x10⁹ /L</td>
</tr>
<tr>
<td>Platelets</td>
<td>≥ 100</td>
</tr>
<tr>
<td>CrCl</td>
<td>&gt; 20mL/min</td>
</tr>
</tbody>
</table>

Dose modifications
- Haematological toxicity
If neutrophils < 1.0 x 10⁹/L and/or platelets < 50 x 10⁹/L delay by one week or until resolved.
In the case of febrile neutropenia (neutrophils < 0.5 x 10⁹/L and fever > 38.5°C) during the previous cycle consider GCSF support (as per local policy) or reduce cyclophosphamide dose to 50%.

- Renal impairment

<table>
<thead>
<tr>
<th>Creatinine Clearance (mL/min)</th>
<th>Cyclophosphamide dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 20</td>
<td>100%</td>
</tr>
<tr>
<td>10-20</td>
<td>75%</td>
</tr>
<tr>
<td>&lt;10</td>
<td>50%</td>
</tr>
</tbody>
</table>

- Hepatic impairment
Cyclophosphamide is not recommended if bilirubin > 1.5 x ULN or AST/ALT > 3 x ULN (consultant decision)
• **Other toxicities**
  IgM flare (rise in IgM levels by > 25%) - omit Rituximab if IgM level is > 30g/L at cycle 1.

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

- **Serious side effects**
  IgM flare
  Myelosuppression
  Myocardial toxicity
  Infertility

- **Frequently occurring side effects**
  Myelosuppression
  Nausea, vomiting
  Hypotension
  Alopecia
  Haemorrhagic cystitis

- **Other side effects**
  Headache

**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.

**Cyclophosphamide:**
- **Amiodarone:** increased risk of pulmonary fibrosis – avoid if possible
- **Clozapine:** increased risk of agranulocytosis – avoid concomitant use
- **Digoxin tablets:** reduced absorption – give as liquid form
- **Indapamide:** prolonged leucopenia is possible - avoid
- **Itraconazole:** may increase adverse effects of cyclophosphamide
- **Phenytoin:** reduced absorption - may need to increase dose of phenytoin
- **Grapefruit juice:** decreased or delayed activation of cyclophosphamide. Patients should be advised to avoid grapefruit juice for 48 hours before and on day of cyclophosphamide dose.

**Additional comments**
Patients should be advised of the need for contraception (both male and female patients) prior to commencing treatment.

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**References**
