Rituximab (monotherapy and maintenance)

**Indication**

Monotherapy in relapsed/refractory stage III or IV CD20 positive follicular Non Hodgkins Lymphoma (NHL) where there is resistance to or intolerance of chemotherapy.

**Maintenance therapy** for:
- previously untreated, or relapsed, Stage III or IV CD20 positive follicular NHL which has responded to rituximab-containing induction chemotherapy.
- relapsed, Stage III or IV CD20 positive follicular NHL which has responded to rituximab-containing induction chemotherapy in patients who have not received rituximab maintenance previously.
- mantle cell lymphoma in patients who respond to standard first line chemotherapy.
- marginal zone lymphoma in patients who respond to standard first line chemotherapy.

(NICE TA226)

**ICD-10 codes**

Codes with a prefix C82

**Regimen details**

**IV dosing**

<table>
<thead>
<tr>
<th>Day (see dose intervals below)</th>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Rituximab</td>
<td>375mg/m²</td>
<td>IV infusion</td>
</tr>
</tbody>
</table>

**SC dosing**

For maintenance therapy rituximab may be given by subcutaneous injection:

<table>
<thead>
<tr>
<th>Day (see dose intervals below)</th>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Rituximab</td>
<td>1400mg</td>
<td>SC injection</td>
</tr>
</tbody>
</table>

**Cycle frequency**

**Monotherapy (IV infusion):**

Weekly for 4 doses (may be repeated if good response)

**Maintenance (IV infusion or SC injection):**

Previously untreated: one dose every 2 months (starting 2 months after last dose of induction chemotherapy) until relapse (maximum 2 years or 12 doses)
(May alternatively be given 3 monthly as below, at the consultants’ discretion. Note – this is unlicensed)

Relapsed: one dose every 3 months (starting 3 months after last dose of induction chemotherapy) until relapse (maximum 2 years or 8 doses)

**Number of cycles**

As above

**Administration**

**Intravenous**

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 by 50mg/hour every 30 minutes to a maximum of 400mg/hour. Subsequent
infusions should be initiated at 100 mg/hour and if tolerated increased by 100mg/hour increments every 30 minutes to a maximum of 400 mg/hour.

**Subcutaneous**

Rituximab subcutaneous should be injected by slow subcutaneous injection over approximately 5 minutes into the abdominal wall (never into areas where the skin is red, bruised, tender or hard, or where there are moles or scars). The needle must only be attached to the syringe immediately prior to administration to avoid potential needle clogging.

If an injection is interrupted it can be resumed at the same site, or another location may be used, as appropriate. Observe for at least 15 minutes after subcutaneous injection.

**Pre-medication**

Rituximab premedication:

- Paracetamol 1g PO 60 minutes prior to rituximab
- Chlorthalamine 10mg IV bolus (or 4mg PO) 15 minutes prior to rituximab
- Dexamethasone 8mg IV bolus or hydrocortisone 100mg IV bolus (or prednisolone 25mg PO) 15 minutes prior to rituximab

**Emetogenicity**

This regimen has low emetic potential

**Additional supportive medication**

Monotherapy: Allopurinol 300mg OD (or 100mg OD if creatinine clearance <20mL/min) to start prior to therapy and continued for the first 2 infusions.

**Extravasation**

Rituximab is neutral (Group 1)

**Investigations – pre first dose**

<table>
<thead>
<tr>
<th>Investigation</th>
<th>Validity period</th>
</tr>
</thead>
<tbody>
<tr>
<td>FBC (with film)</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>LDH</td>
<td>14 days</td>
</tr>
</tbody>
</table>

Additional investigations:

Hepatitis B and C serology – results **must** be reviewed before administration.

Monotherapy: only baseline results required, unless abnormal or clinical reason to repeat.

**Investigations – pre subsequent doses**

<table>
<thead>
<tr>
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<th>Validity period</th>
</tr>
</thead>
<tbody>
<tr>
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<tr>
<td>U+E (including creatinine)</td>
<td>14 days</td>
</tr>
<tr>
<td>LFTs</td>
<td>14 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>$\geq 1.5 \times 10^9$/L</td>
</tr>
<tr>
<td>Platelets</td>
<td>$\geq 75 \times 10^9$/L</td>
</tr>
</tbody>
</table>
Dose modifications
- Haematological toxicity
  If counts low, discuss with consultant, may be due to bone marrow infiltration.

- Renal impairment
  No dose modification required.

- Hepatic impairment
  No dose modification required.

- Other toxicities
  N/A

Adverse effects - for full details consult product literature/ reference texts
- Serious side effects
  Myelosuppression
  Tumour lysis syndrome
  Hypotension and bronchospasm (infusion related and usually transient)
  Cardiac disorders

- Frequently occurring side effects
  Angiodema
  Pruritus, rash
  Headache
  Nausea
  Local site reactions (SC only)

- Other side effects

Significant drug interactions – for full details consult product literature/ reference texts
Nil significant, although data is limited.

Additional comments

References
- Summary of Product Characteristics Rituximab (Roche) Intravenous accessed 8 July 2015 via www.medicines.org.uk
- Summary of Product Characteristics Rituximab (Roche) SC accessed 8 July 2015 via www.medicines.org.uk
- NICE TA266 (Rituximab maintenance) accessed 8 July 2015 via www.nice.org.uk
- Van Oers et al; Rituximab maintenance treatment of relapsed/resistant follicular non-Hodgkin's lymphoma JCO 2010; 28 (17): 2853 - 2858