Rituximab (weekly) for Primary Cutaneous B cell Lymphoma

Indication: Palliative therapy for Low grade Primary Cutaneous B cell Lymphoma (Primary cutaneous Follicle centre cell Lymphoma and Primary cutaneous Marginal Zone Lymphoma)

- multifocal skin disease not treatable with radiotherapy
- Systemic Nodal Disease
- Systemic Visceral Disease

Patients with a high tumour burden, or transformed disease should be considered for combination regimens such as CVP R or CHOP R.

Regimen details: Rituximab 375mg/m² IV D1

Premedication: 30 minutes prior to Rituximab:

- Paracetamol 1000mg orally
- Hydrocortisone 100mg IV
- Chlorphenamine 10mg IV

Administration: Rituximab, as an IV infusion in 250-500ml of 0.9% Sodium Chloride after Premedication, following the next instructions:

First infusion Start at 50mg/hr; escalate in 50mg/hr increments every 30 minutes to a maximum rate of 400mg/hr

Monitor general appearance, blood pressure, pulse, respiratory rate and temperature, every 15 minutes for the first hour. If stable after the first hour, monitor the same parameters but hourly until the infusion is complete. Check infusion rate regularly. Post infusion, patients should be monitored for one hour

If the first infusion is tolerated well (no grade 2 or above infusion-related reactions), the patient is eligible for second and subsequent 90 minute Rituximab infusions

In the event of Grade 2 or above infusion-related reactions, treatment should be temporarily suspended to allow the resolution of these reactions. If symptoms improve, restart at 50% infusion rate and titrate as tolerated.

Such patients are not eligible to follow the 90 minute infusion protocol (see Comments, on page 2)
Subsequent infusions: If no infusion related problems (less than Grade 2) were encountered with first infusion, the second and subsequent infusions of Rituximab can be administered over 90 minutes.

90 minute Rituximab infusion is administered as follows:
The first 100ml of the total volume in the bag is administered over 30 minutes
The remainder of the volume is administered over 60 minutes

Monitor general appearance, blood pressure, pulse, respiratory rate and temperature, every 15 minutes for the first half hour or until stable, then half-hourly, until the end of the infusion

If infusion-related reactions occurred (≥ grade 2) with first infusion, subsequent infusions MUST be infused at an initial rate of 100mg/hour, and increased by 100mg/hour increments at 30 minutes intervals, to a maximum of 400mg/hour
Rapid infusions of Rituximab MUST NOT be administered to these patients, for future infusions

In the event of infusion reactions, treatment should be temporarily suspended to allow the resolution of these reactions. If symptoms improve, restart at 50% infusion rate and accelerate as tolerated (see Comments, on page 3)

Frequency: Every 7 days, for 4 doses

Extravasation: Non-vesicant

Anti-emetics: Minimal emetogenic. Follow Local Anti-emetic Policy

Regular investigations:
- FBC  No more than 7 days prior before treatment (to exclude active infection)
- U&E's, No more than 7 days prior before treatment (to detect abnormalities)
- LFTs  Baseline
- LDH  Baseline

Consider further repeats prior to each weekly infusion if baseline abnormal or clinical concerns

Comments: Hypersensitivity reactions
Anaphylactic and other hypersensitivity reactions have been reported rarely following the IV administration of Rituximab. Typically occur within minutes of starting infusion. Full resuscitation facilities and an anaphylaxis kit must be available at all times
Infusion related adverse events
Infusion reactions predominantly occur during the first 1 – 2 hour of the first infusion. The occurrence is less frequent with subsequent infusions. Premedication with Methylprednisolone significantly reduces the incidence and severity of these reactions.

Mild to moderate infusion related reactions
Mild to moderate infusion related reactions usually respond to a reduction in the rate of infusion, by 50%, and administration of paracetamol, chlorphenamine and if required, hydrocortisone, bronchodilators, oxygen and intravenous fluids (Sodium Chloride 0.9%). Doses of paracetamol and chlorphenamine may be repeated during infusion as necessary up to the maximum BNF dose.

Severe infusion related reactions: cytokine release syndrome (Rare)
Patients who develop evidence of severe reactions, especially severe dyspnoea, bronchospasm or hypoxia (cytokine release syndrome) should have the infusion stopped immediately. Give aggressive symptomatic treatment with paracetamol, chlorphenamine, hydrocortisone, bronchodilators, adrenaline, intravebous fluids (sodium chloride 0.9%) or oxygen.
Patients should be evaluated for evidence of tumour lysis syndrome, including appropriate laboratory tests and, for pulmonary infiltration, with a chest X-ray. The infusion should not be restarted until complete resolution of all symptoms, normalisation of laboratory values and chest X-ray findings and a Consultant Dermatologist approval. If the patient is stable and the infusion is restarted, it should be commenced at half the rate of the previous infusion. If the same adverse reaction occurs for a second time, treatment should be stopped and not recommenced.

Cardiovascular Disease
There is no data on the safety of Rituximab in patients with moderate heart failure (NYHA class III) or severe uncontrolled cardiovascular disease. Therefore, in patients with a known cardiac history, the risk of cardiovascular complications resulting from infusion reactions should be considered before treatment with Rituximab and patients closely monitored during administration. Since hypotension may occur, consideration should be given to withholding anti-hypertensive medications 12 hours prior to the Rituximab infusion.

Infections
Rituximab should not be administered to patients with an active and/or severe infection (e.g. tuberculosis, sepsis and opportunistic infections) or severely immunocompromised patients (e.g. in hypogammaglobulinaemia or where levels of CD4 or CD8 are very low). Caution should be exercised when considering the use of Rituximab in patients with a history of recurring or chronic infections or with underlying conditions which may further predispose patients to serious infection.
### DOSE MODIFICATIONS

**Haematological Toxicity**

<table>
<thead>
<tr>
<th>White Cell Count and Neutrophils and Platelets</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 3.5 x 10⁹/L and ≥ 1.5 x 10⁹/L and ≥ 50 x 10⁹/L</td>
<td>Continue with treatment</td>
</tr>
<tr>
<td>But ≤ 11 x 10⁹/L (**)</td>
<td></td>
</tr>
<tr>
<td>&lt; 3.5 x 10⁹/L &lt; 1.5 x 10⁹/L &lt; 50 x 10⁹/L</td>
<td>Discuss with Consultant</td>
</tr>
</tbody>
</table>

(**) Unless high WBC is due to corticosteroids NOT infection

If counts become low during treatment, this may be due to marrow infiltration and should be discussed with Consultant before any treatment is given.

Use with caution if WBC > 25 x 10⁹/L. Patients with a high tumour burden or with a high number of circulating malignant cells may be at higher risk of especially severe cytokine release syndrome. Consider giving with a reduced infusion rate and monitor very closely. Discuss with Consultant.

**Renal impairment:** No dosage adjustment is necessary

**Hepatic impairment:** No dosage adjustment is necessary

**Toxicities:** Myelosuppression (minor); hypersensitivity reactions; infusion related adverse events (severe dyspnoea, bronchospasm, hypoxia); cardiovascular complications; infections

**Drug interactions:** The concomitant use of Rituximab and immunomodulatory therapies other than Methotrexate, glucocorticoids, salicylates, NSAIDs or analgesics is not recommended

Vaccination should be completed at least four weeks prior to first administration of Rituximab

**References:**

- www.medicines.org.uk
- GSTT protocol for the use of Rituximab for the treatment of AIBD in adult patients. April'08
- SWSCCN- Approved Network regimen. Rituximab. May'08
- Practical Chemotherapy: a multidisciplinary guide. Summerhayes M et al. 2003
- GSTT Guidelines for treating nausea and vomiting in adult patients. September 2007