RITUXIMAB (maintenance)

INDICATIONS

1ST REMISSION

1. Follicular lymphoma patients who achieved a PR or CR to first-line induction therapy with rituximab in combination with chemotherapy to a maximum of 2 years. (NICE TA226)
2. Marginal zone lymphoma, mantle cell lymphoma or lymphoplasmacytic lymphoma patients who achieved a PR or CR with first-line immunochemotherapy to a maximum of 2 years. (NHSE Baseline Commissioning)

NB: NICE NG52 Non-Hodgkin lymphoma: diagnosis and management recommends rituximab maintenance therapy in mantle cell lymphoma as below but - only the initial 2-year treatment is funded by NHS England.

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Rituximab Maintenance Duration</th>
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</thead>
<tbody>
<tr>
<td>Newly diagnosed mantle cell lymphoma who are not fit enough for autologous stem cell transplantation and where there has been a response to R-CHOP-based immunochemotherapy</td>
<td>Until disease progression (only the initial 2-year treatment is funded by NHS England)</td>
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<tr>
<td>Newly diagnosed mantle cell lymphoma who are in remission after cytarabine-based induction and autologous stem cell transplantation</td>
<td>Up to a maximum of 3 years (only the initial 2-year treatment is funded by NHS England)</td>
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</tbody>
</table>

2ND REMISSION

1. Follicular lymphoma patients who achieved a PR or CR to second-line chemotherapy and who have not progressed on 1st line maintenance or relapsed within 6 months of completion, to a maximum of 2 years. (NICE TA137)

TREATMENT INTENT

Disease modification.
PRE-ASSESSMENT

1. Ensure histology is confirmed prior to administration of chemotherapy and document in notes.
2. Record stage of disease - CT scan (neck, chest, abdomen and pelvis), presence or absence of B symptoms, clinical extent of disease, consider bone marrow aspirate and trephine.
3. Blood tests - FBC, U&Es, LDH, urate, calcium, magnesium, creatinine, LFTs, glucose, Igs, β2 microglobulin, hepatitis B core antibody and hepatitis B surface Ag, hepatitis C antibody
4. Urine pregnancy test - before cycle 1 of each new chemotherapy course for women of child-bearing age unless they are post-menopausal, have been sterilised or undergone a hysterectomy.
5. ECG.
6. Record performance status.
7. Record height and weight.
8. Consent - ensure patient has received adequate verbal and written information regarding their disease, treatment and potential side effects. Document in medical notes all information that has been given. Obtain written consent on the day of treatment.
9. Hydration - in patients with bulky disease pre-hydrate with sodium chloride 0.9% 1 litre over 4-6 hours. For patients at high risk of tumour lysis, refer to the tumour lysis protocol.
10. Advise dental check is carried out by patient's own dental practitioner before treatment starts.
11. Treatment should be agreed in the relevant MDT.

DRUG REGIMEN

<table>
<thead>
<tr>
<th></th>
<th>Intravenous</th>
<th>Subcutaneous*</th>
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</thead>
<tbody>
<tr>
<td><strong>Pre-medications</strong></td>
<td></td>
<td></td>
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<tr>
<td>(30 minutes prior to</td>
<td>Chlorphenamine 10mg IV</td>
<td>Loratadine 10mg PO</td>
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<tr>
<td>rituximab infusion):</td>
<td>Hydrocortisone 100mg IV</td>
<td>Prednisolone 25mg PO</td>
</tr>
<tr>
<td></td>
<td>Paracetamol 1g PO</td>
<td>Paracetamol 1g PO</td>
</tr>
<tr>
<td><strong>RITUXIMAB</strong></td>
<td>375 mg/m² IV infusion in 500 mL sodium chloride 0.9%</td>
<td>1400 mg SC injection** over 5 minutes***</td>
</tr>
</tbody>
</table>

* Patients with follicular lymphoma, or mantle cell lymphoma, or marginal zone lymphoma, who have responded to induction chemotherapy and who are scheduled to commence or continue maintenance single agent rituximab therapy are offered the choice of having SC rituximab instead of IV rituximab. NHS England will therefore commission the use of SC rituximab when used as maintenance single agent therapy in FL, mantle cell lymphoma, marginal zone lymphoma.

** Patient must have received a full dose intravenous rituximab over 1 day (which can be part of R-chemo induction before being switched to subcutaneous formulation.

*** Observe patients for at least 15 minutes following rituximab subcutaneous administration (see subcutaneous rituximab protocol). A longer period may be appropriate in patients with an increased risk of hypersensitivity reactions.

CYCLE FREQUENCY

1st Remission: every TWO months until disease progression or for two years maximum. Follow NICE NG52 (see indications) for mantle cell lymphoma patients if alternative funding is available.

2nd Remission (follicular lymphoma only): every THREE months until disease progression or for

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two years maximum.

RESTAGING

Consider CT NCAP after 1 year, to ensure no progression, and at the end of maintenance.

SPECIAL PRECAUTIONS

- Patients with high tumour burden or with a high number of circulating malignant cells are at risk of cytokine release syndrome. This may manifest as severe dyspnoea, bronchospasm and hypoxia in addition to fever, chills, rigors, urticaria and angio-oedema (usually presents after 1 - 2 hours of infusion). For patients who are at risk of tumour lysis syndrome, refer to the tumour lysis protocol.
- Angina pectoris, or cardiac arrhythmias such as atrial flutter and fibrillation, heart failure or myocardial infarction have occurred in patients treated with rituximab. Patients with a history of cardiac disease and/or cardiotoxic chemotherapy should be monitored closely.
- 10% of patients experience hypotension with the first dose of rituximab, therefore consideration should be given to withholding anti-hypertensive medications 12 hours prior to the rituximab infusion.

DOSE MODIFICATIONS

If rituximab induced neutropenia, consider delaying dose and administering GCSF. May re-challenge with rituximab if recovers.

INVESTIGATIONS

FBC, renal and liver profiles within one month prior to administration.

CONCURRENT MEDICATION

None.

EMETIC RISK

Minimal.

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

Rituximab - severe cytokine release syndrome is characterised by severe dyspnoea, often accompanied by bronchospasm and hypoxia, in addition to fever, chills, rigors, urticaria, and angioedema. Hepatitis B reactivation – see pathway for treatment and management of HBV positive patient. Subcutaneous injections may cause local reactions.
Maintenance treatment is associated with an increase in infections most of which are manageable as an outpatient.

**EXTRAVASATION RISK**

Rituximab: neutral

**TREATMENT RELATED MORTALITY**

Approximately 1% with rituximab-maintenance following R-CVP or R-CHOP (induction and maintenance) in follicular lymphoma.

Maintenance rituximab following bendamustine-rituximab (B-R) induction therapy has been associated with a treatment related mortality (TRM) rate of 4-5% (4.4%) in the GALLIUM trial for patients with follicular lymphoma. As such the value of maintenance rituximab following B-R induction should be very carefully considered and patient selection should be restricted to fit patients < 70 years with minimal infectious complications during induction immunochemotherapy.

The treatment related mortality (TRM) in the marginal zone lymphoma arm of the GALLIUM trial in reported in abstract form as 6.5% with R-chemotherapy followed by maintenance rituximab. R-maintenance should therefore be avoided following R-chemotherapy induction in MZL patients.

**REFERENCES**


<table>
<thead>
<tr>
<th>Name</th>
<th>Revision</th>
<th>Date</th>
<th>Version</th>
<th>Review date</th>
</tr>
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<tbody>
<tr>
<td>Cheuk-kie Jackie Cheung</td>
<td>Investigation frequency</td>
<td>Sep 2019</td>
<td>2.1</td>
<td>May 2020</td>
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**RITUXIMAB (maintenance)**

Authorised by Lymphoma lead Dr Graham Collins

Published: May 2018

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Review: May 2022

Version: 2.3
Lymphoma group

| (Haematology Pharmacist) | updated. |  |  |
|--------------------------|----------|  |  |
| Lymphoma protocol review 2020 | General document review | Aug 2020 | 2.2 | May 2022 |
| NSSG Lymphoma Group | Update of indications for SC route of rituximab | Oct | 2.3 | May 2022 |
NURSING CARE PLAN RITUXIMAB (MAINTENANCE)

**Indication:** Lymphoma patients in first or second remission.

**Frequency:** Rituximab is given following R-Chemotherapy every 2 months (first remission) or every 3 months (second remission) for a maximum of 2 years.

**Alopecia:** No

**Emetic risk:** low

**Bloods:** FBC, renal and liver profiles within one month prior to administration.

**RITUXIMAB:** Monoclonal antibody for CD 20.

**Classification of extravasation:** neutral.

**Emetic risk:** low.

**Side effects:** risk of anaphylaxis, severe dyspnoea, bronchospasm and hypoxia, fever, chills, rigors, urticaria, nausea, hypotension, dizziness, cough, chest tightness, back pain, risk of tumour-lysis syndrome, especially with bulky disease, post infusion side effects include flu-like symptoms, fever, diarrhoea

**Subcutaneous Rituximab**

- Record and document baseline observations.
- Oral pre-med required 30 minutes prior to SC Rituximab
- SC injection is administered over 5 minutes via a 22g BD Saf-T-Intima, and flushed afterwards with 1ml 0.9% Sodium Chloride. Injection site to be covered with gauze and tape.
- Patient to be observed for at least 15 minutes after injection.

If patient is having IV maintenance Rituximab, please refer to Rituximab Single Agent protocol L.43 for administration details.