riTUXimab (S/C 1400mg) Maintenance Therapy- 56 day

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	Reimbursement Status
Maintenance therapy for the treatment of previously untreated follicular CD20 positive, B-cell Non Hodgkin Lymphoma patients responding to induction therapy	C82	00600a	Hospital

TREATMENT:

The starting dose of the drugs detailed below may be adjusted downward by the prescribing clinician, using their independent medical judgement, to consider each patient's individual clinical circumstances.

riTUXimab is administered once every 56 days (starting 2 months after the last dose of induction therapy) for a maximum of two years (12 doses) or until disease progression or toxicity occurs.

Facilities to treat anaphylaxis MUST be present when therapy is administered

Day	Drug	Dose	Route	Cycle
1	**riTUXimab**	1400mg (fixed dose in 11.7 mL)	Subcutaneous injection (SC) over 5 minutes into abdominal wall[1,2,3]	Every 56 days for up to 12 cycles
[1]**Patient must have previously received a full dose intravenous rituximab before being switched to subcutaneous formulation**.				
[2]During treatment with subcutaneous riTUXimab, administer other subcutaneous drugs at alternative injection sites whenever possible				
[3]Patients should be observed for at least 15 minutes following riTUXimab subcutaneous administration. A longer period may be appropriate in patients with an increased risk of hypersensitivity reactions.				

ELIGIBILITY:

- Indications as above
- ECOG 0-2

EXCLUSIONS:

- Hypersensitivity to riTUXimab or any of the excipients or to murine proteins.
- Active, severe infections (e.g. tuberculosis, sepsis and opportunistic infections)
- Patients in a severely immunocompromised state

PRESCRIPTIVE AUTHORITY:

The treatment plan must be initiated by a Consultant medical oncologist or a consultant Haematologist working in the area of haematological malignancies

TESTS:

Baseline tests:

- FBC, renal and liver profile
- Uric acid, SPEP, DAT
- Cardiac function if clinically indicated
- Virology screen -Hepatitis B (HBsAg, HBcoreAb) & C, HIV

*See Adverse Effects/Regimen Specific Complications re Hepatitis B Reactivation

Regular tests:

- FBC, renal and liver profile
- LDH
- Cardiac function if clinically indicated

Disease monitoring:
Disease monitoring should be in line with the patient's treatment plan and any other test/s as directed by the supervising Consultant.

DOSE MODIFICATIONS:

- Any dose modification should be discussed with a Consultant.
- No dose modifications of riTUXimab are recommended

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL: Minimal (**Refer to local policy)**

PREMEDICATIONS:

- Premedication consisting of an anti-pyretic and an anti-histamine should always be administered before each infusion of riTUXimab. Consider the inclusion of a glucocorticoid in patients not receiving glucocorticoid containing chemotherapy.

Table 2: Suggested pre-medications prior to riTUXimab infusion:

Drugs	Dose	Route
Paracetamol	1g	PO 30 minutes prior to riTUXimab administration
Chlorphenamine	4mg	PO 30 minutes prior to riTUXimab administration
PrednisoLONE	25mg	PO 30 minutes prior to riTUXimab administration

OTHER SUPPORTIVE CARE: No specific recommendations

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

The adverse effects listed are not exhaustive. Please refer to the relevant Summary of Product Characteristics for full details.

- **Hypersensitivity/Infusion Reactions/Severe Cytokine Release syndrome**: Before starting riTUXimab subcutaneous injections, all patients must always have received at least one full dose of riTUXimab by intravenous infusion, using riTUXimab intravenous formulation. The highest risk of experiencing an administration related reaction is generally observed at cycle one. Beginning the therapy with riTUXimab intravenous infusion would allow a better handling of the administration reactions by slowing or stopping the intravenous infusion.
  If patients were not able to receive one full riTUXimab intravenous infusion dose prior to the switch, they should continue the subsequent cycles with riTUXimab intravenous formulation until a full intravenous dose is successfully administered. Therefore, the switch to riTUXimab subcutaneous formulation can only occur at the second or subsequent cycles of treatment.
  Administration related reactions have been observed in up to 50% of patients treated with riTUXimab subcutaneous formulation in clinical trials but the majority of reactions where mild or moderate and resolved without any specific treatment.
- **Cardiac Disorders**: Patients with a history of cardiac disease and/or cardiotoxic chemotherapy should be monitored closely.
- **Infections:** riTUXimab should not be administered to patients with an active, severe infection. Caution should be exercised when considering the use of rituximab in patients with a history of recurring or chronic infections or with underlying conditions that may further predispose patients to serious infections. Consideration should be given to the use of antimicrobial prophylaxis.
- **Neutropenia**: If riTUXimab induced neutropenia occurs, consideration can be given to delaying dose and administering GCSF. May rechallenge with rituximab if recovers
- **Hepatitis B Reactivation:** Patients should be tested for both HBsAg and HBcoreAb as per local policy. If either test is positive, such patients should be treated with anti-viral therapy. **(Refer to local infectious disease policy).** These patients should be considered for assessment by hepatology
- **Severe Mucocutaneous Reactions**: These include Steven Johnson syndrome and toxic epidermal necrolysis. Discontinue in patients who develop a severe mucocutaneous reaction. The safety of readministration has not been determined.
- **Progressive multifocal leukoencephalopathy (PML)**: Use of riTUXimab may be associated with an increased risk of PML. If a patient develops PML, the dosing of riTUXimab must be permanently discontinued.
- **Immunisations**:
  - The safety of immunisation with live viral vaccines following riTUXimab therapy has not been studied. Therefore vaccination with live virus vaccines is not recommended whilst on riTUXimab.
  - Patients treated with riTUXimab may receive non-live vaccinations

DRUG INTERACTIONS:

- Antihypertensives: Additive effect of hypotension during riTUXimab infusion. Consider withholding antihypertensives 12 hours before and during riTUXimab infusion.
- Patients with human anti-mouse antibody or human anti-chimeric antibody (HAMA/HACA) titres may have allergic or hypersensitivity reactions when treated with other diagnostic or therapeutic monoclonal antibodies.
- Drug interaction databases should be consulted for more information.

REFERENCES:

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2. Ghielmini M et al. Prolonged treatment with rituximab in patients with follicular lymphoma significantly increases event-free survival and response duration compared with the standard weekly x 4 schedule. Blood. 2004; 103 (12): 4416-4423.
3. McLaughlin P, Grillo-Lopez AJ, Link BK et al. Rituximab chimeric anti-CD20 monoclonal antibody therapy for relapsed indolent lymphoma: half of patients respond to a four-dose treatment program. J Clin Oncol.1998; 16(8):2825-2833.
4. Davis TA, Grillo-Lopez AJ, White CA et al. Rituximab anti-CD20 monoclonal antibody therapy in non-Hodgkin's lymphoma: safety and efficacy of re-treatment. J. Clin Oncol. 2000;18(17):3135-3143.
5. NCCP Classification Document for Systemic Anti-Cancer Therapy (SACT) Induced Nausea and Vomiting. V4 2022. Available at: https://www.hse.ie/eng/services/list/5/cancer/profinfo/chemoprotocols/nccp-classification-document-for-systemic-anti-cancer-therapy-sact-induced-nausea-and-vomiting.pdf
6. MabThera®Summary of Product Characteristics Accessed October 2022 Available at: https://www.ema.europa.eu/en/documents/product-information/mabthera-epar-product-information_en.pdf

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1	09/03/2021		NCCP Lymphoid Clinical Advisory Group
2	12/10/2022	Reviewed.	Prof Maccon Keane

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.