Regimen Monograph

A - Regimen Name

RITU Regimen

riTUXimab

Disease Site
Hematologic
Lymphoma - Non-Hodgkin's Low Grade

Intent
Palliative

Regimen Category
Evidence-Informed :

Regimen is considered appropriate as part of the standard care of patients; meaningfully improves outcomes (survival, quality of life), tolerability or costs compared to alternatives (recommended by the Disease Site Team and national consensus body e.g. pan-Canadian Oncology Drug Review, pCODR). Recommendation is based on an appropriately conducted phase III clinical trial relevant to the Canadian context OR (where phase III trials are not feasible) an appropriately sized phase II trial. Regimens where one or more drugs are not approved by Health Canada for any indication will be identified under Rationale and Use.

Rationale and Uses
Treatment of relapsed or refractory follicular, mantle cell or other CD20-positive low grade lymphomas, in patients who cannot tolerate further chemotherapy

Supplementary Public Funding
riTUXimab
New Drug Funding Program (Rituximab (Biosimilar IV) - Single Agent - Indolent Lymphoma)

back to top

B - Drug Regimen

Note: Different rituximab products are NOT INTERCHANGEABLE.

riTUXimab	375 mg /m²	IV

back to top

C - Cycle Frequency

Induction: WEEKLY X 4 DOSES

For patients who have responded to induction therapy, and were rituximab-naïve prior to induction, refer to maintenance rituximab regimen - RITU(MNT) or RITU(MNT-SC).

back to top

D - Premedication and Supportive Measures

Antiemetic Regimen: Minimal (infusion-related events)

Other Supportive Care:

- **Screen for hepatitis B virus in all cancer patients starting systemic treatment.** Refer to the hepatitis B virus screening and management guideline.
- If high volume disease, consider steroids and prophylaxis for tumour lysis

Pre-medication (prophylaxis for infusion reactions):

Administer at least 30 minutes prior to IV rituximab:

- Oral antipyretic (e.g. acetaminophen)
- H1-receptor antagonist (e.g. diphenhydramine)
- Corticosteroid (e.g. methylprednisolone 80 mg IV) in patients with high bulk disease or pulmonary involvement if no corticosteroids are already being given as part of the chemotherapy regimen

back to top

E - Dose Modifications

See premedication and monitoring sections for supportive care, screening and monitoring recommendations.

Doses should be modified according to the protocol by which the patient is being treated.

Dosage with toxicity

Toxicity	Rituximab Dose* / Infusion Rate
Myelosuppression	No adjustment required.
Other grade 3 toxicity	Delay infusion until ≤ grade 2
• Any pulmonary toxicity • Other grade 4 toxicity • Severe mucocutaneous toxicity • Serious/life-threatening cardio-pulmonary events • Reactivation of tuberculosis or hepatitis B • Evidence of active hepatitis • PML / PRES	Discontinue
*Missed or delayed doses may be administered at a later time point, based on physician's discretion.	

Management of Infusion-related reactions:

Also refer to the CCO guideline for detailed description of Management of Cancer Medication-Related Infusion Reactions.

Grade	Management	Re-challenge
1 or 2	• Stop or slow the infusion. • Manage the symptoms.	• Re-challenge at 50% of the administration rate at which the IR occurred and with pre-medications. • Consider adding oral montelukast ± oral acetylsalicylic acid.

	Restart: • Once symptoms have resolved, restart at 50% of the rate at which the IR occurred.	
3 or 4	• Stop the infusion. • Aggressively manage symptoms.	• Consider clinical benefit and risks of further treatment. Consider patient factors, severity and nature of the IR and availability of suitable alternative treatment. • Consider desensitization for patients with recurrent reactions despite pre-medications and a slower infusion rate.

Hepatic Impairment

No adjustment required; stop if evidence of hepatitis.

Renal Impairment

No adjustment required.

Dosage in the Elderly

No dose adjustment required. Exercise caution as older patients are more likely to experience serious adverse events (including cardiac, pulmonary, or other grade 3/4 toxicity).

back to top

F - Adverse Effects

Refer to riTUXimab drug monograph(s) for additional details of adverse effects

Very common (≥ 50%)	Common (25-49%)	Less common (10-24%)	Uncommon (< 10%), but may be severe or life-threatening
• Infusion reactions (may be severe and include hypersensitivity)	N/A	• Fatigue • Nausea, vomiting • Paresthesia • Headache • Rash (may be severe) • Myelosuppression +/- infection (including atypical, viral reactivation), bleeding (may be severe) • Hypotension • Flu-like symptoms	• Arrhythmia, cardiotoxicity • Arterial/venous thromboembolism • Bowel obstruction/perforation • Pneumonitis • RPLS / PRES, PML • Optic and cranial nerve disorder • Tumour lysis syndrome • Nephrotoxicity • Vasculitis • Hemolysis • Hyperviscosity • Secondary malignancy (with chemotherapy)

back to top

G - Interactions

Refer to riTUXimab drug monograph(s) for additional details

- Consider withholding antihypertensive medication 12 hours prior to and during rituximab administration.

back to top

H - Drug Administration and Special Precautions

Refer to riTUXimab drug monograph(s) for additional details

Administration

Note: Different rituximab products are NOT INTERCHANGEABLE

Rituximab IV and SC formulations are not interchangeable. The dosing and concentrations of these products are different.

- Rituximab should be administered in a setting where full resuscitation facilities are immediately available, and under the close supervision of someone experienced and capable of dealing with severe infusion-related reactions.
- DO NOT administer as an IV push or bolus.
- Dilute to a final concentration of 1-4 mg/mL in normal saline or D5W.
- To avoid foaming, gently invert the bag to mix the solution.
- Do not admix with other drugs.
- Administer rituximab through a dedicated line.
- Compatible with PVC or polyethylene bags.
- Keep vials refrigerated; do not freeze. Protect from light.
- **Infusion rates:**
    - When bulky disease present or WBC > 25-50 x 10^9/L:
        - Consider a slower infusion rate, or
        - Split dosing over days 1-2, or
        - Consider delaying rituximab treatment until chemotherapy has reduced the lymphocyte count
- First infusion: initial rate of 50 mg/h, then escalate rate in 50 mg/h increments every 30 minutes, to a maximum of 400 mg/h (about 4.25 hours in total).
- **Subsequent infusions:**
- Initial rate of 100 mg/h, then escalate rate in 100 mg/h increments every 30 minutes, to a maximum of 400 mg/h as tolerated (about 3.25 hours in total).
- Published data suggest that a 90 minute infusion (20% of the dose in the first 30 min then the remaining 80% over 60 min) can be used for second and subsequent infusions, if no reaction occurred with the first infusion.

Also refer to the CCO guideline for detailed description of Management of Cancer Medication-Related Infusion Reactions.

Contraindications:

- Patients with known hypersensitivity and anaphylactic reactions to proteins of similar mouse or human origin, to Chinese Hamster Ovary (CHO) cell proteins or to any component of this product.
- Patients who have or have had PML, have active and/or severe infections, active hepatitis B, or severely immunocompromised (e.g. AIDS patients with very low CD4 or CD8 counts).
- Avoid the use of live vaccines.

Precautions:

- Exercise caution in patients with a history of recurring or chronic infections or with underlying conditions which may further predispose patients to serious infection. Patients may have increased risk of infection following rituximab treatment.
- Prior to starting rituximab in HBV seropositive patients, consultation with a liver disease expert is recommended to determine ongoing monitoring of HBV reactivation and its management.
- Exercise caution in patients with neutrophil counts < 1.5 x 10^9/L and/or platelets < 75 x 10^9/L due to limited experience in this patient group.
- Use with *extreme caution* in patients with pre-existing cardiovascular disease or in patients with high tumour burden. Consider steroids ± slow infusions or infusions split over 2 days for patients with bulky disease or > 25 x 10^9/L circulating malignant cells.
- Use with caution in patients with pulmonary insufficiency or lung tumour infiltration, and in patients with myelosuppression.
- Reduced immunogenicity may occur with the use of inactivated vaccines.

Pregnancy/lactation

- This regimen is not recommended for use in pregnancy. Adequate contraception should be used by patients and their partners while on treatment and after the last treatment dose. Recommended methods and duration of contraception may differ depending on the treatment. Refer to the drug monograph(s) for more information.
- Breastfeeding is not recommended during this treatment and after the last treatment dose. Refer to the drug monograph(s) for recommendations after the last treatment dose (if available).
- Fertility effects: Unknown

back to top

I - Recommended Clinical Monitoring

Treating physicians may decide to monitor more or less frequently for individual patients but should always consider recommendations from the product monograph.

Refer to the hepatitis B virus screening and management guideline for monitoring during and after treatment.

Recommended Clinical Monitoring

- CBC; baseline and at each visit
- LFTs; baseline and at each visit
- Renal functions tests; baseline and at each visit
- Monitor patients during and for at least 15 minutes after each rituximab dose, longer in patients at higher risk of infusion-related reactions
- Clinical assessment of infusion-related reactions, tumour lysis syndrome, hypotension, infection, bleeding, GI, pulmonary, skin, CNS, cardiovascular side effects; regular

- Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for Adverse Events) version

Suggested Clinical Monitoring

- Monitor closely for cardiovascular symptoms for patients who have cardiac conditions or recurrent cardiac events with rituximab

back to top

J - Administrative Information

Approximate Patient Visit	3 to 5 hours
Pharmacy Workload (average time per visit)	20.946 minutes
Nursing Workload (average time per visit)	69.167 minutes

back to top

K - References

Davis TA, White CA, Grillo-Lopez AJ, et al. Single-agent monoclonal antibody efficacy in bulky non-Hodgkin's lymphoma: Results of a phase II trial of rituximab. J Clin Oncol 1999;17(6):1851-7.

Maloney DG, Grillo-López AJ, White CA, et al. IDECC2B8 (Rituximab) anti-CD20 monoclonal antibody therapy in patients with relapsed low grade non-Hodgkin's lymphoma. Blood 1997;90(6):2188-95.

McLaughlin P, Grillo-López AJ, Link BK, Levy R, Czuczman MS, Williams ME, 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;16:2825-33.

Rituximab drug monograph, Cancer Care Ontario.

Salar A, Casao D, Cervera M, et al. Rapid infusion of rituximab with or without steroid-containing chemotherapy: 1-yr experience in a single institution. Eur J Haematol 2006: 77: 338–340

Sehn LH, Donaldson J, Filewich A, et al. Rapid infusion rituximab in combination with corticosteroid-containing chemotherapy or as maintenance therapy is well tolerated and can safely be delivered in the community setting. Blood 2007;109(10):4171-3.

PEBC Advice Documents or Guidelines

- Rituximab in Lymphoma and Chronic Lymphocytic Leukemia

November 2023 Modified Pregnancy/lactation section

back to top

M - Disclaimer

Regimen Abstracts

A Regimen Abstract is an abbreviated version of a Regimen Monograph and contains only top level information on usage, dosing, schedule, cycle length and special notes (if available). It is intended for healthcare providers and is to be used for informational purposes only. It is not intended to constitute or be a substitute for medical advice, and all uses of the Regimen Abstract are subject to clinical judgment. Such information is provided on an "as-is" basis, without any representation, warranty, or condition, whether express, or implied, statutory or otherwise, as to the information's quality, accuracy, currency, completeness, or reliability, and Cancer Care Ontario disclaims all liability for the use of this information, and for any claims, actions, demands or suits that arise from such use.

Information in regimen abstracts is accurate to the extent of the ST-QBP regimen master listings, and has not undergone the full review process of a regimen monograph. Full regimen monographs will be published for each ST-QBP regimen as they are developed.

Regimen Monographs

Refer to the New Drug Funding Program or Ontario Public Drug Programs websites for the most up-to-date public funding information.

The information set out in the drug monographs, regimen monographs, appendices and symptom management information (for health professionals) contained in the Drug Formulary (the "Formulary") is intended for healthcare providers and is to be used for informational purposes only. The information is not intended to cover all possible uses, directions, precautions, drug interactions or adverse effects of a particular drug, nor should it be construed to indicate that use of a particular drug is safe, appropriate or effective for a given condition. The information in the Formulary is not intended to constitute or be a substitute for medical advice and should not be relied upon in any such regard. All uses of the Formulary are subject to clinical judgment and actual prescribing patterns may not follow the information provided in the Formulary.

The format and content of the drug monographs, regimen monographs, appendices and symptom management information contained in the Formulary will change as they are reviewed and revised on a periodic basis. The date of last revision will be visible on each page of the monograph and regimen. Since standards of usage are constantly evolving, it is advised that the Formulary not be used as the sole source of information. It is strongly recommended that original references or product monograph be consulted prior to using a chemotherapy regimen for the first time.

Some Formulary documents, such as the medication information sheets, regimen information sheets and symptom management information (for patients), are intended for patients. Patients should always consult with their healthcare provider if they have questions regarding any information set out in the Formulary documents.

While care has been taken in the preparation of the information contained in the Formulary, such information is provided on an "as-is" basis, without any representation, warranty, or condition, whether express, or implied, statutory or otherwise, as to the information's quality, accuracy, currency, completeness, or reliability.

CCO and the Formulary's content providers shall have no liability, whether direct, indirect, consequential, contingent, special, or incidental, related to or arising from the information in the Formulary or its use thereof, whether based on breach of contract or tort (including negligence), and even if advised of the possibility thereof. Anyone using the information in the Formulary does so at his or her own risk, and by using such information, agrees to indemnify CCO and its content providers from any and all liability, loss, damages, costs and expenses (including legal fees and expenses) arising from such person's use of the information in the Formulary.

back to top