

Regimen Monograph

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A - Regimen Name

RITU(MNT-SC) Regimen

riTUXimab (Subcut) (Maintenance)

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 Single agent maintenance therapy of patients with indolent histology, CD20 positive B-cell lymphomas (excluding small lymphocytic lymphoma, CLL), who have responded to induction treatment with combination chemotherapy and/or rituximab. To be considered for NDFP funding, patients must be rituximab naïve prior to induction therapy for indolent histology lymphoma.

Supplementary Public Funding [riTUXimab \(subcut\)](#)
New Drug Funding Program (Rituximab (Biosimilar IV) and Rituximab SC - Maintenance Treatment - Lymphoma)

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B - Drug Regimen

Note: Different rituximab products are **not interchangeable**.

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

Rituximab (subcutaneous) can only be given if the patient has previously received at least one full rituximab IV dose.

riTUXimab (subcut)	1400 mg	Subcut	Day 1
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Maintenance rituximab should be started within 8 weeks of completion of the induction regimen (2015 Hematology disease site group guidelines). Funded by NDFP if maintenance rituximab is started within 6 months of the last dose of induction therapy.

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C - Cycle Frequency

If patient responds to induction therapy:

EVERY 3 MONTHS*

For maximum two years (8 doses total, including any maintenance doses given as IV), unless disease progression or unacceptable toxicity

*Refer to Hematology disease site group guideline

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D - Premedication and Supportive Measures

Antiemetic Regimen: Minimal

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

Pre-medication (prophylaxis for administration reactions)

Administer at least 30 minutes prior to subcut 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.
- In patients who experienced adverse effects with pre-medications, the omission of pre-medications can be considered.

Also refer to the CCO guideline for detailed description of [Management of Cancer Medication-Related Infusion Reactions](#).

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E - Dose Modifications

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

Dosage with toxicity

Toxicity	Rituximab Dose* / Rate
Myelosuppression	No adjustment required.
Severe administration-related or pulmonary	<ul style="list-style-type: none"> • Hold administration if possible. Discontinue if hypersensitivity, pulmonary-related or based on physician discretion. • Manage appropriately; monitor patient until complete resolution.
Other grade 3 toxicity	Delay treatment until \leq grade 2
<ul style="list-style-type: none"> • 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.	

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 were more likely to experience serious adverse events (including cardiac, pulmonary, or other grade 3/4 toxicity) in some clinical trials.

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F - Adverse Effects

Refer to [riTUXimab \(subcut\)](#) drug monograph(s) for additional details of adverse effects.

The incidences below were those reported for rituximab IV, unless the subcutaneous formulation (marked with an asterisk, *) was associated with a relevant difference in incidence.

Common (25-49%)	Less common (10-24%)	Uncommon (< 10%), but may be severe or life-threatening
<ul style="list-style-type: none"> • Myelosuppression +/- infection (including atypical, viral reactivation), bleeding (may be severe)* • Administration-related reactions (includes cutaneous, hypersensitivity and other acute reactions may occur)* 	<ul style="list-style-type: none"> • Fatigue • Nausea, vomiting • Paresthesia • Headache • Rash (may be severe) • Hypotension • Flu-like symptoms 	<ul style="list-style-type: none"> • 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 malignancies (with chemotherapy)

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G - Interactions

Refer to [riTUXimab \(subcut\)](#) drug monograph(s) for additional details. Interactions with subcutaneous rituximab have not been formally studied. The following are based on interactions with rituximab IV.

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

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H - Drug Administration and Special Precautions

Refer to [riTUXimab \(subcut\)](#) drug monograph(s) for additional details.

Note: Different rituximab products are NOT INTERCHANGEABLE.

Rituximab IV and subcutaneous formulations are **not interchangeable**. The dosing and concentrations of these products are different. Refer to [Safety Considerations for the Implementation of Subcutaneous Rituximab Formulation](#).

Administration:

- Do not self-administer rituximab subcut.
- Rituximab subcut is given subcutaneously into the abdominal wall only. Do not give in areas where the skin is red, tender, hard, bruised, or where there are moles or scars.
- Give subcutaneously over approximately 5 minutes
- Observe for at least 15 minutes after administration.
- If there are other subcutaneous medications, they should be given at separate sites.
- Compatible with polypropylene or polycarbonate syringes.
- Keep vials refrigerated in the outer carton; do not freeze. Protect from light.

Also refer to the CCO guideline for detailed description of [Management of Cancer Medication-Related Infusion Reactions](#).

Contraindications:

- Patients with known hypersensitivity to this drug, any of its components, murine proteins, or Chinese Hamster Ovary (CHO) cell proteins
- 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).

Other Warnings / 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 an increased risk of infection following rituximab treatment.
- Exercise caution in patients with neutrophil counts $< 1.5 \times 10^9/L$ and/or platelets $< 75 \times 10^9/L$ 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 \pm slow IIV infusions or infusions split over 2 days for patients with bulky disease or $> 25 \times 10^9/L$ circulating malignant cells.
- Use with caution in patients with pulmonary insufficiency or lung tumour infiltration, and in patients with myelosuppression.
- Avoid the use of live vaccines. Reduced immunogenicity may occur with 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

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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
- Liver function tests; baseline and at each visit
- Renal function tests; baseline and at each visit
- Administration-related and hypersensitivity reactions; according to institutional guidelines; (product monograph: during and for at least 15 minutes after each injection, longer in patients at higher risk of hypersensitivity reactions)
- Clinical assessment of tumour lysis syndrome, hypotension, infection (including viral, opportunistic), bleeding, GI, pulmonary, skin, CNS, cardiovascular side effects; at each visit
- Grade toxicity using the current [NCI-CTCAE \(Common Terminology Criteria for Adverse Events\) version](#)

Suggested Clinical Monitoring

- Cardiovascular symptoms for patients who have cardiac conditions or recurrent cardiac events with rituximab; at each visit

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J - Administrative Information

Approximate Patient Visit	0.75 hour
Pharmacy Workload (average time per visit)	20.946 minutes
Nursing Workload (average time per visit)	35 minutes

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K - References

Davies A, Merli F, Mihaljević B, et al. Efficacy and safety of subcutaneous rituximab versus intravenous rituximab for first-line treatment of follicular lymphoma (SABRINA): a randomised, open-label, phase 3 trial. *Lancet Haematol* 2017 Jun;4(6):e272-e282.

Forstpointner R, Unterhalt M, Dreyling M, et al. Maintenance therapy with rituximab leads to a significant prolongation of response duration after salvage therapy with a combination of rituximab, fludarabine, cyclophosphamide, and mitoxantrone (R-FCM) in patients with recurring and refractory follicular and mantle cell lymphomas: results of a prospective randomized study of the German Low Grade Lymphoma Study Group (GLSG). *Blood*. 2006;108:4003-8.

Panizo C, Bekadja MA, Meddeb B, et al. Safety of subcutaneous administration of rituximab during the first-line treatment of patients with non-Hodgkin lymphoma: the MabRella study. *Haematologica*. 2017;102(s2):1–882. (P640)

Rituximab (subcut) drug monograph, Ontario Health (Cancer Care Ontario).

Salles G, Seymour JF, Offner F, et al. Rituximab maintenance for 2 years in patients with high tumour burden follicular lymphoma responding to rituximab plus chemotherapy (PRIMA): a phase 3, randomised controlled trial. *Lancet* 2011;377(9759):42-51.

van Oers MH, Van Glabbeke M, Giurgea L, et al. Rituximab maintenance treatment of relapsed/resistant follicular non-Hodgkin's lymphoma: long-term outcome of the EORTC 20981 phase III randomized intergroup study. *J Clin Oncol* 2010;28(17):2853-8.

PEBC Advice Documents or Guidelines

- [Rituximab in Lymphoma and Chronic Lymphocytic Leukemia](#)

June 2025 Updated Drug Administration/Special Precautions and Monitoring sections

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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.

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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.

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