

Drug Monograph

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A - Drug Name

riTUXimab

COMMON TRADE NAME(S): Rituxan®; Truxima™; Riximyo™; Ruxience™; Riabni™

- Different rituxumab products are **not interchangeable**.
- For additional information on biosimilars, refer to:
 - [Position Statements for the Clinical Operational Implementation of Oncology Biosimilars](#) from the pan-Canadian Clinical Operations Working Group
 - [Clinician Fact Sheet](#)

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B - Mechanism of Action and Pharmacokinetics

Rituximab is a chimeric mouse-human monoclonal IgG1κ antibody. It binds to the CD20 antigen (human B-lymphocyte-restricted differentiation antigen, Bp35), a hydrophobic transmembrane protein, which is expressed on B-lymphocytes and on > 90% of B cell non-Hodgkin's lymphomas. CD20 is not shed from the cell surface and does not internalize upon antibody binding. Rituximab is thought to deplete CD20-positive cells via antibody-dependent cell-cytotoxicity and complement-mediated cell lysis.

Distribution

Binds to lymphoid tissues with little or no binding to non-lymphoid tissues. Pharmacokinetics are dose proportional. Circulating B-cells were observed to be depleted within the first 3 doses in most patients and sustained for up to 6-9 months post-treatment; levels started to recover at 6 months after treatment and median B-cell levels returned to normal by 12 months after treatment completion.

Cross blood brain barrier? no information found

PPB no information found

Metabolism

The metabolism of rituximab is not fully understood.

Active metabolites no

Inactive metabolites no

Elimination

Clearance of rituximab decreases markedly with accumulation of the drug which occurs after multiple infusions. Detectable in serum for 3 to 6 months after completion of treatment.

Half-life 60 hours (after 1st infusion)
174 hours (after 4th infusion)

Urine no information found

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C - Indications and Status**Health Canada Approvals:**

- Non-Hodgkin lymphoma (NHL)
- Chronic lymphocytic leukemia (CLL)

Refer to the product monograph for a full list and details of approved indications.

Other Uses:

- Relapsed or refractory hairy cell leukemia
- Acute lymphoblastic leukemia
- Hodgkin lymphoma

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D - Adverse Effects**Emetogenic Potential:** Minimal**Extravasation Potential:** None

The following adverse effects were reported in patients receiving rituximab as monotherapy. It also included severe or life-threatening adverse events from other sources or post-marketing.

ORGAN SITE	SIDE EFFECT* (%)	ONSET**
Cardiovascular	Arrhythmia (1%)	I
	Arterial thromboembolism (1-2%)	E
	Cardiotoxicity (rare)	E
	Hypertension (5%)	I E
	Hypotension (10%)	I
	Venous thromboembolism (3%)	E
Dermatological	Alopecia (1-10%)	E
	Rash (11%) (may be severe)	I E
Gastrointestinal	Abdominal pain (7%)	I E
	Anorexia, weight loss (3%)	E
	Constipation (1%)	I
	Diarrhea (4%)	I
	Dyspepsia (3%)	E
	GI obstruction (<1%)	E D
	GI perforation (<1%)	E D
	Mucositis (1%)	E
	Nausea, vomiting (17%)	I
General	Edema (5%)	E
	Fatigue (18%)	I
	Flu-like symptoms (>10%)	I E
Hematological	Hemolysis (<1%)	E
	Hyperviscosity (Waldenstrom's; rare)	I E
	Immunosuppression (± opportunistic infections, ≥ 10%)	E
	Myelosuppression ± infection, bleeding (11%) (higher incidence with chemotherapy, may be severe)	E
Hypersensitivity	Hypersensitivity (77%) (7% severe; with first infusion)	I

Immune	Antibody response (1%) (antichimeric antibodies)	E
	Other Viral reactivation (including hepatitis B; rare)	D
Metabolic / Endocrine	Abnormal electrolyte(s) (2%)	E
	Hyperglycemia (5%)	E
	Tumour lysis syndrome (<1%)	I
Musculoskeletal	Musculoskeletal pain (8%) (or stiffness)	I E
Neoplastic	Secondary malignancy (5%) (with chemotherapy)	L
Nervous System	Anxiety (2%)	E
	Dizziness (7%)	E
	Headache (13%)	I E
	Leukoencephalopathy (PML - rare)	E
	Neuropathy (rare, peripheral or cranial)	E D
	Paresthesia (16%)	E
	Posterior reversible encephalopathy syndrome (PRES) (rare)	E
	Sleep disorder (2%)	E
Ophthalmic	Conjunctivitis (1%)	E
	Optic nerve disorder (rare)	E
	Watering eyes (3%)	E
Renal	Nephrotoxicity (1-10%)	E
Respiratory	Cough, dyspnea (8%)	I E
	Pneumonitis (rare)	I E
Vascular	Vasculitis (rare)	E D

* "*Incidence*" may refer to an absolute value or the higher value from a reported range.

"*Rare*" may refer to events with < 1% incidence, reported in post-marketing, phase 1 studies, isolated data or anecdotal reports.

** I = *immediate* (onset in hours to days) E = *early* (days to weeks)
D = *delayed* (weeks to months) L = *late* (months to years)

The most common adverse effects are **infusion-related symptoms, fatigue, headache, rash, neutropenia and infections**. Adverse effects are more frequent in older patients, and in patients with high bulk disease. In clinical trials, there was a higher incidence of severe neutropenia in rituximab-containing arms as compared to the chemotherapy-only arms.

Acute reactions:

- **Infusion-related symptoms**, which may be related to cytokine release, include fever and chills/rigors, urticaria, bronchospasm, ARDS, angioedema, hypotension and flushing; they usually occur 30 minutes to 2 hours after the start of the first infusion and may be fatal. The majority of serious infusion reactions were observed with the first infusion, in which approximately 80% of fatal infusion reactions were reported. The incidence decreases with subsequent infusions. Infusion reactions are more common in patients with high tumour burdens and are fatal in up to 0.07% of patients. Autoimmune diseases or other co-morbidities may have contributed to the fatal outcome.
- **Anaphylaxis** (including fatalities) may occur, usually with the second or subsequent infusion. These may not be clinically distinguishable from infusion-related reactions.
- Severe **pulmonary reactions** with dyspnea, bronchospasm, hypoxia, and pulmonary infiltrates or edema have been reported, and are more common in patients with pulmonary involvement or disease. Acute symptoms appear within 1-2 hours of the initiation of the first infusion, while pneumonitis may appear 1-4 weeks after the infusion.
- Signs and symptoms of **tumour lysis syndrome** (TLS) have been reported to occur within 1 to 2 hours after the first infusion. Patients at risk (high tumour burden) should be closely monitored and prophylaxis considered.
- Symptoms of these acute reactions usually resolve with slowing or interruption of the rituximab infusion and aggressive treatment (IV saline, diphenhydramine and acetaminophen ± bronchodilators, IV corticosteroids or epinephrine). However, deterioration may occur after initial improvement of pulmonary or severe infusion-related symptoms and patients should be carefully monitored until complete symptom resolution. TLS should be excluded.
- Patients with pre-existing **cardiac** conditions, including arrhythmias and angina, should be carefully monitored throughout the infusion and in the immediate post-infusion period. Infusions should be discontinued in serious or life-threatening cardio-pulmonary events.

Serious Reactions:

Arterial thromboembolism, such as stroke, has been described in elderly patients who received rituximab especially in combination. Patients with cardiovascular disease or risk factors should be carefully monitored for signs of cerebral ischemia.

Severe **mucocutaneous reactions** (Stevens-Johnson syndrome, toxic epidermal necrolysis, paraneoplastic pemphigus, lichenoid dermatitis or vesiculobullous dermatitis) have been described and may be fatal. The onset of these reactions can vary from days to several months following exposure to rituximab.

Bowel obstruction and perforation (some fatal cases) have been reported. The mean time of onset for these GI symptoms is 6 days.

Infections are common, including opportunistic infections. **Reactivation** of tuberculosis or hepatitis B virus (HBV) infection may occur during treatment, with fulminant hepatitis, hepatic failure and death, including in patients with normal hepatitis B surface antigen but who are seropositive. The risk is increased in patients receiving steroids and/or chemotherapy. Patients should be screened for hepatitis B virus prior to starting treatment. Refer to the [hepatitis B virus screening and management](#) guideline.

Cases of Pneumocystis Jiroveci Pneumonia (PJP) have been reported. Infections have been reported in some patients with prolonged hypogammaglobulinemia (>11 months after rituximab exposure).

There have been isolated reports of JC virus reactivation in NHL patients, resulting in fatal **progressive multifocal leukoencephalopathy** (PML). Rituximab should be held at first signs or symptoms suggestive of PML, which may progress over days to weeks and can include progressive unilateral weakness, clumsiness of limbs, confusion, cognitive or personality changes. Patients suspected of having PML should be investigated with MRI and lumbar puncture to evaluate JC viral DNA.

Posterior reversible leukoencephalopathy syndrome (PRES) has been reported rarely; brain imaging confirms diagnosis. Risk factors include hypertension and concomitant immunosuppressive therapy.

Other **viral infections** (including fatal cases), such as CMV, herpes simplex, varicella, hepatitis C, West Nile, etc. have been reported up to one year following rituximab cessation. Patients who are HIV-positive with Kaposi's sarcoma have been reported to have rapid Kaposi's sarcoma progression.

Patients who develop human anti-murine antibodies (HAMA) or human anti-chimeric antibodies for rituximab (HACA) may have allergic or hypersensitivity reactions when treated with rituximab or other murine or chimeric monoclonal antibodies.

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E - Dosing

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](#).

Refer to protocol by which patient is being treated.

Screen for hepatitis B virus in all cancer patients starting systemic treatment. Refer to the [hepatitis B virus screening and management](#) guideline.

Consider withholding antihypertensive medication 12 hours prior to and during rituximab infusion

Pre-medication:

Administer at least 30 minutes prior to IV rituximab (prophylaxis for infusion reactions):

- 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.

Other supportive care:

- Prophylaxis for tumour lysis (high bulk disease)

Adults:

Various dosing and schedules are used depending on the indication. Refer to the product monograph or related regimen monographs for details.

Setting	Initial treatment (IV)	Maintenance (after response to induction therapy) (IV)	
Low Grade/Follicular			
Single Agent	375 mg/m ² q1w x 4 doses	Previously untreated with advanced high-tumour burden: 375mg/m ² q 2-3 months, for max 12 doses (2 years) ⁽²⁾	Previously treated patients: 375 mg/m ² q 3 months until disease progression (max 2 years)
With CVP ⁽¹⁾	▶ 375 mg/m ² q3w x 8 cycles		
With CHOP ^(1,2)	▶ 375 mg/m ² q3w x 6-8 cycles		
Diffuse Large B Cell			
With CHOP ⁽¹⁾	375 mg/m ² q3w x 6-8 cycles ⁽²⁾	Not applicable	
CLL			
With FC	Cycle 1: 375 mg/m ² day 1 ⁽³⁾ then Cycles 2-6: 500 mg/m ² day 1 ⁽³⁾	Not applicable	
¹ Give on day 1 POST-steroid and PRE-cytotoxic regimen. ² Hematology disease site group guideline recommends q3 month dosing as a reasonable schedule. NDFP funds up to a maximum of 8 doses (over 2 years). ³ Consider methylprednisolone IV ± slower infusion or split dose over 2 days for cycles where bulky disease or lymphocyte counts > 25 x 10 ⁹ /L.			

Dosage with Toxicity:

Toxicity	Rituximab Dose* / Infusion Rate
Myelosuppression	No adjustment required.
Other grade 3 toxicity	Delay infusion until \leq grade 2
<ul style="list-style-type: none"> 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	<ul style="list-style-type: none"> Stop or slow the infusion. Manage the symptoms. <p>Restart:</p> <ul style="list-style-type: none"> Once symptoms have resolved, restart at 50% of the rate at which the IR occurred. 	<ul style="list-style-type: none"> Re-challenge at 50% of the administration rate at which the IR occurred and with pre-medications. Consider adding oral montelukast \pm oral acetylsalicylic acid.
3 or 4	<ul style="list-style-type: none"> Stop the infusion. Aggressively manage symptoms. 	<ul style="list-style-type: none"> 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.

Dosage with Hepatic Impairment:

No dosage adjustment required; stop if evidence of hepatitis.

Dosage with Renal Impairment:

No dosage 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.

Children:

Safety and effectiveness in children have not been established. Hypogammaglobulinemia has been observed in pediatric patients and may be severe, requiring long-term immunoglobulin substitution therapy.

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F - Administration Guidelines

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](#).

For details on rituximab subcut administration, refer to [rituximab \(subcut\)](#) drug monograph.

- 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:**First infusion:**

- Recommended to be administered over a graduated rate: 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:

- If no severe infusion reaction (grade 3 or 4) occurred with the first cycle, a rapid infusion of IV rituximab over a total of 90 minutes can be initiated with cycle 2 (20% of the dose in the first 30 min then the remaining 80% over 60 min).
- OR 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).
- Alternatively, subcutaneous administration of rituximab can be considered starting with cycle 2.

When bulky disease present or WBC > 25-50 x 10⁹/L, consider:

- A slower infusion rate, or
- Split dosing over days 1-2, or
- Delaying rituximab treatment until chemotherapy has reduced the lymphocyte count

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

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G - Special Precautions

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 x 10⁹/L and/or platelets < 75 x 10⁹/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 10⁹/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 the use of inactivated vaccines.

Other Drug Properties:

- Carcinogenicity: Unknown

Pregnancy and Lactation:

- Teratogenicity: Unknown
- Mutagenicity: Unknown
- Fetotoxicity: Unknown
- Pregnancy:
Rituximab is not recommended for use during pregnancy. IgGs are known to pass the placental barrier. There have been reports of infants with transient B-cell depletion and lymphocytopenia. Adequate contraception should be used by patients and their partners during treatment, and for **12 months** after the last dose.
- Breastfeeding:
IgG is excreted into breast milk. Breastfeeding is not recommended during treatment and for **6 months** after the last dose.
- Fertility effects: Unknown

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Formal drug interaction studies have not been performed with rituximab.

AGENT	EFFECT	MECHANISM	MANAGEMENT
Antihypertensive agents	potentiation of hypotension with infusion	Additive effects	consider withholding temporarily (12 hours before and during infusion)
cisplatin	renal failure	Unknown	use with extreme caution; monitor renal function closely

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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

Monitor Type	Monitor Frequency
CBC	Baseline and at each visit
Liver function tests	Baseline and at each visit
Renal function tests	Baseline and at each visit
Infusion-related reactions, tumour lysis syndrome, respiratory toxicities	During and post-infusion according to institution guidelines, especially for the first infusion
Clinical assessment of hypotension, infection, 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

Monitor Type	Monitor Frequency
Cardiovascular symptoms in patients who have cardiac conditions or recurrent cardiac events with rituximab	At each visit

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J - Supplementary Public Funding

New Drug Funding Program ([NDFP Website](#))

- Rituximab (Biosimilar IV) and Rituximab SC in Combination with Chemotherapy - Indolent B-cell Lymphoma
- Rituximab (Biosimilar IV) and Rituximab SC - Second Line - Chronic Lymphocytic Leukemia
- Rituximab (Biosimilar IV) and Rituximab SC - Retreatment - Indolent Lymphoma
- Rituximab (Biosimilar IV) and Rituximab SC - Retreatment - Aggressive Histology Lymphoma
- Rituximab (Biosimilar IV) and Rituximab SC - Previously Untreated Chronic Lymphocytic Leukemia
- Rituximab (Biosimilar IV) and Rituximab SC - Maintenance Treatment - Lymphoma
- Rituximab (Biosimilar IV) and Rituximab SC - In Combination with Venetoclax - Relapsed Chronic Lymphocytic Leukemia
- Rituximab (Biosimilar IV) and Rituximab SC - HIV-Related Aggressive Histology B-cell Lymphoma
- Rituximab (Biosimilar IV) and Rituximab SC - Aggressive Histology Lymphoma
- Rituximab (Biosimilar IV) - Single Agent - Indolent Lymphoma
- Rituximab (Biosimilar IV) - In Combination with Idelalisib - Relapsed Chronic Lymphocytic Leukemia
- Rituximab (Biosimilar IV) - As Part of the MATRix Regimen in Newly Diagnosed Previously Untreated PCNSL
- Polatuzumab Vedotin with Bendamustine and Rituximab (Biosimilar) - Relapsed or Refractory Diffuse Large B-cell Lymphoma
- Rituximab (Biosimilar IV) and Rituximab SC - In Combination with Ibrutinib for Previously Treated Waldenströms Macroglobulinemia

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K - References

McEvoy GK, editor. AHFS Drug Information 2013. Bethesda: American Society of Health-System Pharmacists, p. 1181-9.

Product Monograph: Rituxan® (rituximab). Roche Canada, June 2023.

Sehn LH, Donaldson J, Filewich A, et al. Rapid infusion rituximab in combination with steroid containing chemotherapy can be given safely and substantially reduces resource utilization. Blood 2004; 104(11): A1407.

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.

June 2025 Updated Indications, Special Precautions, and Monitoring sections

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L - Disclaimer

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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