Rituximab (Rituxan®)

Biosimilars:

- **Rituximab-abbs (Truxima)**
- **Rituximab-arrx (Riabni)**
- **Rituximab-pvvr (Ruxience)**

Formulation of rituximab is generally insurance driven based on patient's coverage and plan.

Rituximab (and biosimilars) is a genetically engineered chimeric murine/human monoclonal IgG, kappa antibody directed against the CD20 antigen. CD20 is expressed on the majority of B-cells, but the antigen is not found on hematopoietic stem cells, pro-B-cells, normal plasma cells or other normal tissue. B cells are believed to play a role in the pathogenesis of RA and associated chronic synovitis. Administration of rituximab results in a rapid and sustained depletion of circulating and tissue-based B cells. Rituximab is a sterile, clear, colorless, preservative-free liquid concentrate for intravenous administration.

Resources from Manufacturer

Rituxan
Patient Medication Guide
Full Prescribing Information
Rituxan Co-pay Program
Genentech Patient Assistance

Truxima
Patient Medication Guide
Full Prescribing Information
Teva Enrollment Form

Riabni
Patient Medication Guide
Full Prescribing Information
Amgen Copay Program
Financial Assistance through Amgen

Ruxience
Patient Medication Guide
Full Prescribing Information
Pfizer Co-pay card

continued

ACR/ARP Medication Guide

American College of Rheumatology
Empowering Rheumatology Professionals

Association of Rheumatology Professionals
The Interprofessional Division of the American College of Rheumatology

FDA-Approved Indications and Dosing in Rheumatology

Rituximab is indicated for:

- Rheumatoid Arthritis
- Granulomatosis with Polyangiitis (GPS) (Wegener's Granulomatosis)
- Microscopic Polyangiitis (MPA) in pediatric patients over 2 years old
- Pemphigus vulgaris (Rituxan only)
- *Dermatomyositis and polymyositis, refractory disease
- *Lupus nephritis

**Off-label indication*

Intravenous Dosing

- Rheumatoid Arthritis: 1000 mg IV once every 2 weeks for 2 doses; subsequent courses of 1000 mg once every 2 weeks for 2 doses may be administered every 24 weeks or as indicated based on clinical evaluation, but no sooner than every 16 weeks.
- Granulomatosis with Polyangiitis (GPS) (Wegener's Granulomatosis): 375 mg/m2 IV once weekly for 4 doses (manufacturer's labeling) or 1 g once every 2 weeks for 2 doses
- Microscopic Polyangiitis (MPA): 375 mg/m2 IV once weekly for 4 doses, then 50 mg/m2 every 2 weeks for 2 doses, followed by 250 mg/m2 every 6 months based upon clinical response
- Pemphigus vulgaris (Rituxan only): 1 g IV once every 2 weeks for 2 doses, followed by 500 mg once 12 months after initial therapy, then every 6 months thereafter or based on clinical evaluation, but no sooner than every 16 weeks
- Dermatomyositis and polymyositis: 1 g once every 2 weeks for 2 doses
- Lupus nephritis: 1 g on days 0 and 15 or 375 mg/m2 once weekly for 4 doses

Contraindications

Hypersensitivity to any component, murine proteins.

Warnings and Precautions

1. Serious infections–do not administer if active infection is present. Patient greater than 65 years of age, those with comorbid conditions or on concomitant immunosuppressant or corticosteroids may be at greater risk for infection.
2. Reactivation of hepatitis B virus- test HBV infection before starting infliximab and monitor for HBV carriers.
3. Bowel obstruction/perforation: evaluate for abdominal pain, vomiting or related symptoms
4. Cytopenias
5. Renal toxicity
6. Tumor lysis syndrome
7. Cardiac arrhythmias and angina
8. Lupus-like syndrome
9. Live vaccines or therapeutic infectious agents should not be given with concurrent rituximab use
10. For patient with rheumatoid arthritis, there is limited safety data in combination of other biologics with rituximab (other than methotrexate)

Adverse Reactions (≥10%)

- RA (≥10%): upper respiratory tract infection, nasopharyngitis, urinary tract infection, and bronchitis (other important
- GPA and MPA (≥15 %): infections, nausea, diarrhea, headache, muscle spasms, anemia, peripheral edema, infusion-related reactions
- PV (≥15%): infusion-related reactions, depression, upper respiratory tract infection/ nasopharyngitis, headache

Medication Strength and Preparations

Supplied at a concentration of 10 mg/ml in either 100 mg (10 ml) or 500 mg (50 ml) single-use vials

Medication Administration and Storage

- Medication Administration and Storage
- Diluted rituximab solutions for infusion may be stored refrigerated at 2°C to 8°C (36°F to 46°F) for 24 hours

DO NOT ADMINISTER AS AN INTRAVENOUS PUSH OR BOLUS.

1. **First Infusion (day 1):** Initiate infusion at a rate of 50 mg/hr. In the absence of infusion reaction, increase infusion rate by 50 mg/hr increments every 30 minutes, to a maximum of 400 mg/hr.
2. **Subsequent Infusions:** If the patient did not tolerate the first infusion well, start at the same rate as the first infusion (50 mg/hr) and follow directions noted above.
3. If the patient tolerated the first infusion, initiate subsequent infusions at a rate of 100 mg/hr. In the absence of infusion reaction, increase rate by 100 mg/hr increments at 30-minute intervals, to a maximum of 400 mg/hr.
4. Interrupt the infusion or slow the infusion rate for infusion reactions. Continue the infusion rate at one-half the previous rate upon improvement of symptoms.
5. Push 20cc NS flush into bag once bag is nearly empty to clear all medication in the IV tubing.
6. Total minimum infusion time for the first infusion is 4 hours and 15 minutes, plus 15 minutes for the flush.
7. Total minimum infusion time for subsequent infusions is 3 hours and 15 minutes, plus 15 minutes for the flush.

continued

Intravenous Administration Pre-infusion Checklist

1. Tuberculosis Screening

- ■ Verify that latent tuberculosis infection screening has been performed
- ■ Detailed history of patient tuberculosis exposure risk factors
- ■ Confirm the following:
  - ❑ Negative tuberculin skin test/PPD and/or Negative Interferon Gamma Release Assay (Quantiferon or TSpot TB test). Consider chest x-ray in patients with TB risk factors but negative screening tests.
  - ❑ Positive tuberculin skin test/PPD or positive Quantiferon/TSpot TB test with negative chest x-ray.
  - ❑ Patient is at least 4 weeks post initiation of INH or other TB therapy.
  - ❑ Consider repeating screening tests if a patient has subsequently traveled to TB endemic countries or there has been a change in risk factors for TB exposure.

2. Confirm that the patient is hepatitis B negative (particularly HepB Surface Antigen).

3. Ask patient if he/she:

- ■ Is taking any antibiotics
- ■ Has any upcoming surgeries.
- ■ Has a history of asthma? If yes, have inhaler instructions been given?
- ■ Is taking anti-hypertensive medications. If yes, has the patient been given instructions to hold their anti-hypertensive before rituximab infusions?
- ■ Is pregnant or breastfeeding.
- ■ Has recently received vaccines / live vaccines prior to initiating rituximab.

If the answer is yes to any of these questions, review with ordering provider.

continued

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Intravenous Medication Preparation

1. Use appropriate aseptic technique.

- Clean the port of the 250-mL IV bag of 0.9% sodium chloride, USP, or 5% dextrose in water, USP, with an alcohol wipe. Remove 100 mL of 0.9% sodium chloride, USP, or 5% dextrose in water, USP, and discard, leaving 150 mL in the IV bag.
- Remove cap from rituximab vial and clean rubber stopper with alcohol wipe.

2. Carefully withdraw 50 mL (500 mg) from 2 vials of rituximab, for a total of 100 mL. Gentle air injection or push-pull method can be used to ease the withdrawal of rituximab. Discard any unused portion of rituximab.
3. Dilute the 100 mL (1000 mg) of rituximab into the 150-mL IV solution, yielding a final total volume of 250 mL and a final concentration of 4 mg/mL. Remove and dispose of needle and syringe in compliance with hospital and/or office protocol.
4. Gently invert IV bag to mix. Do not shake. Inspect for particulate matter and/or discoloration. Label IV bag with patient's name, drug, dose, and date, and then initial it.
5. Diluted rituximab solution may be stored at 35-46 degrees Fahrenheit for up to 24 hours. Protect solution from direct sunlight.
6. Connect an infusion set to the IV bag containing rituximab. Prime the line. Piggyback the set with rituximab into the port closest to the patient in the primary infusion line. Stop the primary infusion line. Rituximab should not be infused concomitantly in the same line with other medications. Though not mandatory for IV infusion, use of an infusion pump can help regulate the administration and dosage of the drug.

Managing Infusion Reactions

- Acute infusion reaction or anaphylaxis can occur at any time during the administration of this agent and include flu-like symptoms, headache, dyspnea, hypotension, transient fever, chills, gastrointestinal symptoms, and skin rashes.
- If patient reports mild reactions (such as flushing, chills, etc.)
  - ❑ Stop the infusion and assess patient.
- For more severe reactions (such as hives, difficulty breathing, chest pain, high or low blood pressure, swelling of face and hands, fever, chills or anaphylaxis) or where mild reactions persist
  - ❑ Stop the infusion and treat the acute reaction. Then notify the supervising provider immediately to coordinate next plan of action. For mild reactions, consider adding additional pre-medications for subsequent doses.
- Vital Sign Monitoring: Obtain vital signs (patient temperature, blood pressure and pulse) upon arrival, after start of medication, every 15 minutes for the first hour of the infusion, every 30 minutes thereafter, upon discontinuing infusion and before the patient departs the facility. However, if prior history of an acute infusion reaction, monitor vitals every 10 minutes for 30 minutes then every 30 minutes and for 30 minutes after infusion.

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