WG& MPA
DOSING AND ADMINISTRATION
FOR NURSES

Rituxan for Wegener's granulomatosis (WG) and microscopic polyangiitis (MPA)

THE FIRST AND ONLY FDA-APPROVED THERAPY FOR WG AND MPA

Dosing and Administration Guide

INDICATION

Rituxan® (rituximab), in combination with glucocorticoids, is indicated for the treatment of patients with Wegener's granulomatosis (WG) and microscopic polyangiitis (MPA).

Rituxan is not recommended for treatment of patients with severe active infections.

IMPORTANT SAFETY INFORMATION

BOXED WARNINGS

Rituxan administration can result in serious, including fatal, adverse reactions. These include:

- **infusion reactions**
- **tumor lysis syndrome (TLS)**
- **severe mucocutaneous reaction**
- **progressive multifocal leukoencephalopathy (PML)**

Warnings and Precautions

Rituxan administration can also result in additional serious, including fatal, adverse reactions including:

- hepatitis B reactivation
- cardiovascular events
- other infections including bacterial, fungal, new or reactivated viral infections

Use of concomitant immunosuppressants other than corticosteroids has not been studied in WG or MPA patients exhibiting peripheral B-cell depletion following treatment with Rituxan.

Observe patients closely for signs of infection if immunosuppressants other than corticosteroids are used concomitantly.

Common adverse reactions include infections, nausea, diarrhea, headache, muscle spasms, anemia, and peripheral edema.

*For additional safety information, please see the full prescribing information, including **BOXED WARNINGS** and Medication Guide.*

Attention healthcare provider: Provide Medication Guide to patient prior to Rituxan infusion.

PLEASE NOTE THAT THE FOLLOWING DOSING AND ADMINISTRATION INSTRUCTIONS APPLY TO RITUXAN FOR WEGENER'S GRANULOMATOSIS (WG) AND MICROSCOPIC POLYANGIITIS (MPA).

When administering Rituxan for rheumatoid arthritis (RA), refer to the Rituxan for RA Infusion Tool Kit, found in the Rituxan RA Nurse Center Resource Library at www.RituxanRAnursecenter.com

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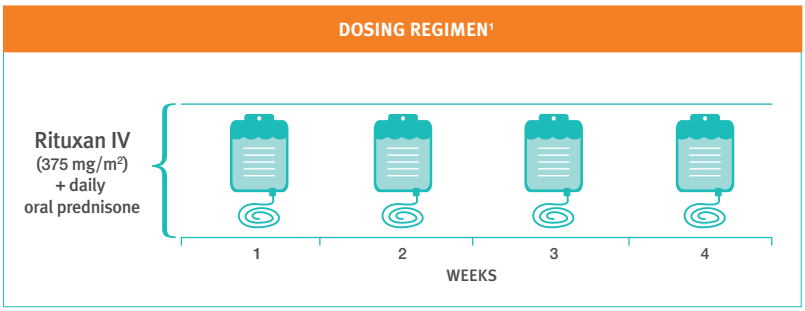
Rituxan for Wegener's granulomatosis (WG) and microscopic polyangiitis (MPA) (continued)

Prior to initiating Rituxan

Glucocorticoids administered as methylprednisolone 1000 mg intravenously per day for 1 to 3 days followed by oral prednisone 1 mg/kg/day (not to exceed 80 mg/day and tapered per clinical need) are recommended to treat severe vasculitis symptoms. This regimen should begin within 14 days prior to or with the initiation of Rituxan and may continue during and after the 4-week course of Rituxan treatment.

Dosing regimen



- **Rituxan is administered by intravenous (IV) infusion at a dose of 375 mg/m² (ie, body surface area dosing) once weekly for 4 weeks.**

Calculating the dose

Because the dosing amount per patient will vary, it's a good idea to calculate the specific dose required for each patient **prior to his or her scheduled date of infusion**. This, in turn, will help you order the correct number of vials needed ahead of time.

STEP 1:

Calculate body surface area (BSA) of the patient using his or her height and weight.[1]

- The calculation requires the patient's actual body weight and height, measured within 14 days of administering Rituxan
- The formula for calculating BSA used in the clinical trial was:

BSA in m^2 = (weight in kg)$^{0.425}$ x (height in cm)$^{0.725}$ x 0.007184

STEP 2:

Using the patient's BSA, calculate the weekly Rituxan dose with the following formula.[2]

Weekly dose = BSA (m^2) x 375 mg

For quick reference, please see the Rituxan Mixing Tables on page 4.

STEP 3:

Rituxan should be administered each week for 4 weeks

Following methylprednisolone infusions, oral prednisone 1 mg/kg/day is recommended (not to exceed 80 mg/day, and tapered per clinical need)

PCP and prophylaxis

PCP prophylaxis is also recommended for patients with WG or MPA during treatment and for at least 6 months following the last Rituxan infusion.

IMPORTANT SAFETY INFORMATION

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Rituxan for Wegener's granulomatosis (WG) and microscopic polyangiitis (MPA) (continued)

Preparing Rituxan

- **DO NOT ADMINISTER AS IV PUSH OR BOLUS**
- Always use aseptic technique. A hood is not required to mix Rituxan
- The length of the infusion depends on the patient's Rituxan dose, which is based on the patient's BSA
- Prepare an IV bag of normal saline or D5W containing the appropriate amount needed to dilute Rituxan to the proper concentration as follows:
  - **Using mixing tables provided below**, refer to the table that corresponds with the desired Rituxan concentration (4 mg/mL, 2 mg/mL, or 1 mg/mL) and locate the row with the patient's BSA
  - Read across to the **diluent volume*** column to identify **the amount of normal saline or D5W that should be left in the IV bag**
  - Withdraw and discard the unneeded normal saline or D5W. (NOTE: This amount will vary according to each patient's BSA, the Rituxan dose, and the desired Rituxan concentration)
  - Read across to the **Rituxan volume to withdraw** column to identify the Rituxan volume needed based on the BSA-calculated dose. Carefully withdraw that amount of Rituxan. Gentle air injection or push-pull method can be used to ease the withdrawal of Rituxan
  - Gently add Rituxan to the IV bag. The final IV bag volume should be equal to the **total infusion volume** column on the Mixing Tables on page 4
  - Gently invert IV bag to mix. **Do not shake**
  - Infuse the total volume of the IV bag

*Normal saline or D5W.

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Rituxan for Wegener's granulomatosis (WG) and microscopic polyangiitis (MPA) (continued)

Rituxan WG and MPA Mixing Tables

4 mg/mL

TO DELIVER 375 MG/M² AT A CONCENTRATION OF 4 MG/ML OF RITUXAN

BSA (m^2)	Rituxan dose (mg)	Rituxan volume to withdraw (mL*)	Diluent volume† (mL)	Total infusion volume (mL)
1.3	488	49	74	123
1.4	525	53	80	133
1.5	563	56	84	140
1.6	600	60	90	150
1.7	638	64	96	160
1.8	675	68	102	170
1.9	713	71	107	178
2.0	750	75	113	188
2.1	788	79	119	198
2.2	825	83	125	208

2 mg/mL

TO DELIVER 375 MG/M² AT A CONCENTRATION OF 2 MG/ML OF RITUXAN

BSA (m^2)	Rituxan dose (mg)	Rituxan volume to withdraw (mL*)	Diluent volume† (mL)	Total infusion volume (mL)
1.3	488	49	196	245
1.4	525	53	212	265
1.5	563	56	224	280
1.6	600	60	240	300
1.7	638	64	256	320
1.8	675	68	272	340
1.9	713	71	284	355
2.0	750	75	300	375
2.1	788	79	316	395
2.2	825	83	332	415

*For ease of reconstitution, some numbers have been rounded.
†Normal saline or D5W.

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Rituxan for Wegener's granulomatosis (WG) and microscopic polyangiitis (MPA) (continued)

Rituxan WG and MPA Mixing Tables (continued)

1 mg/mL

TO DELIVER 375 mg/m² AT A CONCENTRATION OF 1 mg/mL OF RITUXAN				
BSA (m²)	Rituxan dose (mg)	Rituxan volume to withdraw (mL*)	Saline diluent volume (mL)	Total infusion volume (mL)
1.3	488	49	441	490
1.4	525	53	477	530
1.5	563	56	504	560
1.6	600	60	540	600
1.7	638	64	576	640
1.8	675	68	612	680
1.9	713	71	639	710
2.0	750	75	675	750
2.1	788	79	711	790
2.2	825	83	747	830

*For ease of reconstitution, some numbers have been rounded.
†Normal saline or D5W.

Standard equipment for infusion

Standard IV setups include:

- IV tubing (with roller clamps and a Y access port)
- IV pump (optional)
- Normal saline or D5W
- Syringes and needles
- Clamps
- Alcohol wipes
- Tourniquet
- Adhesive tape
- IV start supplies
- Catheter

Infusion reactions are a possibility with the administration of Rituxan. Medications and supportive care measures should always be available during an infusion, including but not limited to:

- IV fluids
- Glucocorticoids
- Antihistamines
- Acetaminophen
- Epinephrine
- Bronchodilators
- Oxygen

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Rituxan for Wegener's granulomatosis (WG) and microscopic polyangiitis (MPA) (continued)

Medication guide

Provide the Rituxan Medication Guide to the patient, review it with him or her prior to each infusion, and answer any questions he or she may have.

Premedication

Review the physician's order to determine if premedications are to be administered prior to Rituxan infusion. Recommended premedications are acetaminophen and an antihistamine.[2]

Administration overview

CAUTION: DO NOT ADMINISTER RITUXAN AS AN IV PUSH OR BOLUS

- Rituxan should not be infused concomitantly in the same line with other medications
- Rituxan can be administered via a drip method or using a pump
- **Optional 2-bag method**: Administer Rituxan using 2 lines as follows:
  - Establish a primary IV line with saline, without medication, to maintain vein patency. This line can also serve as a means of administering additional fluids or medications should it become necessary
  - Piggyback a second, dedicated line, for administration of Rituxan solution through the port closest to the patient in the primary infusion line. Prime the secondary line with Rituxan solution
  - Clamp/interrupt the primary saline line to begin administration of the Rituxan solution

First infusion (Day 1)

- Begin infusion at a rate of 50 mg/h
- If an infusion reaction does not occur, escalate the infusion rate in 50 mg/h increments every 30 minutes, to a maximum of 400 mg/h
- Infusion times will vary from patient to patient depending upon the dose administered, which is based on the patient's body surface area (BSA)

Subsequent infusions (Days 8, 15, and 22)

- If the patient experienced an infusion reaction during the first infusion, start at the same rate as the first infusion (50 mg/h) and follow directions noted above
- If the patient tolerated the infusion well, begin at a rate of 100 mg/h
- If an infusion reaction does not occur, continue to escalate the infusion rate in 100 mg/h increments every 30 minutes, to a maximum of 400 mg/h
- Infusion times will vary from patient to patient depending upon dose the administered, which is based on the patient's body surface area (BSA)

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Rituxan for Wegener's granulomatosis (WG) and microscopic polyangiitis (MPA) (continued)

Managing infusion reactions

- Rituxan can cause severe, including fatal, infusion reactions
- In the event of an infusion reaction, slow or stop the infusion
- Institute medical management (eg, glucocorticoids, epinephrine, bronchodilators, or oxygen) for infusion reactions as stated in office protocol
- Depending on the severity of the infusion reaction and the required interventions, consider resumption of the infusion at a minimum 50% reduction in rate after symptoms have resolved

After the infusion

- Hives or rash
- Itching
- Swelling of the lips, tongue, throat, or face
- Sudden cough
- Shortness of breath, difficulty breathing, or wheezing
- Weakness
- Dizziness or feeling faint
- Palpitations
- Chest pain

Instruct patients and family members or attendants to seek immediate medical attention if they notice any of the above symptoms.

Limited data are available on the safety and efficacy of subsequent courses of Rituxan in patients with WG and MPA. In the active-controlled, double-blind study, subsequent courses of Rituxan were allowed for patients experiencing a relapse of disease. The safety and efficacy of retreatment with Rituxan have not been established.

How supplied

Rituxan vials [100 mg (NDC 50242-051-21) and 500 mg (NDC 50242-053-06)] are stable at 2°C-8°C (36°F-46°F). Do not use beyond expiration date stamped on carton. Rituxan vials should be protected from direct sunlight. Do not freeze or shake.

REQUEST THE RITUXAN WG and MPA Administration Pocket Guide

Contact a Rheumatology Clinical Coordinator (RCC) or your Genentech representative to request your guide. It includes:

- Detailed charts for preparing Rituxan
- Instructions for administering Rituxan for WG and MPA
- An accompanying calculator to determine the BSA-calculated Rituxan dose

RCCs are available to help educate healthcare professionals on the administration of Rituxan for WG and MPA. To schedule an appointment, please contact a Rituxan RCC or Rituxan Representative.

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Reference: 1. Data on file, Genentech USA/Biogen Idec. **2.** Rituxan [package insert]. South San Francisco, CA: Biogen Idec Inc. and Genentech USA, Inc.; February 2010.

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Rituxan® Rituximab