DOSING AND ADMINISTRATION

Rituxan®
Rituximab

DOSING
SCHEDULE OVERVIEW

Administering Rituxan

Rituxan should only be administered by a healthcare professional.

Review the dosing schedule and administration of Rituxan with your patient prior to the start of treatment.

Premedicate with antihistamine and acetaminophen. It is also recommended that glucocorticoids be administered 30 minutes prior to each infusion of Rituxan. Rituxan is administered in combination with methotrexate (MTX). Rituxan is administered by IV infusion at a dose of 1000 mg. Patients receive 2 infusions, one on Day 1 and one on Day 15.

- Retreat every 6 months (24 weeks) or based on clinical evaluation, but no sooner than every 4 months (16 weeks)[1]

Consider scheduling your patient's next infusion immediately following each course of treatment.

Select Important Safety Information: Infections

- Serious, including fatal, bacterial, fungal, and new or reactivated viral infections can occur during and following the completion of Rituxan-based therapy
- Infections have been reported in some patients with prolonged hypogammaglobulinemia (defined as hypogammaglobulinemia >11 months after Rituxan exposure)
- Discontinue Rituxan for serious infections and institute appropriate anti-infective therapy
- Rituxan is not recommended for use in patients with severe, active infections

Attention Healthcare Provider: Provide Medication Guide to patient prior to Rituxan infusion.

For healthcare professional use only. Not to be distributed to patients.

Please see additional Important Safety Information throughout and the Rituxan full Prescribing Information, including **BOXED WARNINGS**.

Rituxan®
Rituximab

INFUSION STEPS

Rituxan should only be administered by a healthcare professional with appropriate medical support to manage serious infusion-related reactions (IRRs) that can be fatal if they occur.

Step 1:

Obtain supplies

Recommended infusion supplies are listed below. Please follow your office protocol. These items must be purchased separately and may be ordered through your distributor of choice. Please note that vials of Rituxan* must be purchased separately.

Standard IV setups including:

- IV tubing (with roller clamps and a Y-access port)
- Tourniquet
- Normal saline or 5% dextrose in water (D5W)
- Adhesive tape
- Syringes and needles
- IV start supplies
- Clamps
- Catheter
- Alcohol wipes

Optional equipment:

- IV pump

IRRs 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
- Epinephrine
- Glucocorticoids
- Bronchodilators
- Antihistamines
- Oxygen
- Acetaminophen

Infusion training and support is available. Contact your Rheumatology Clinical Coordinator to learn more.

*Rituxan vials are stable at 2°C to 8°C (36°F to 46°F). Do not use beyond expiration date stamped on carton. Rituxan vials should be protected from direct sunlight.
Do not freeze or shake.
Note: One additional item appropriate for Rituxan is a medicine-storage refrigerator. Rituxan solutions for infusion may be stored at 2°C to 8°C (36°F to 46°F) for 24 hours. Rituxan solutions for infusion have been shown to be stable for an additional 24 hours at room temperature; however, since Rituxan solutions do not contain a preservative, diluted solutions should be refrigerated at 2°C to 8°C.

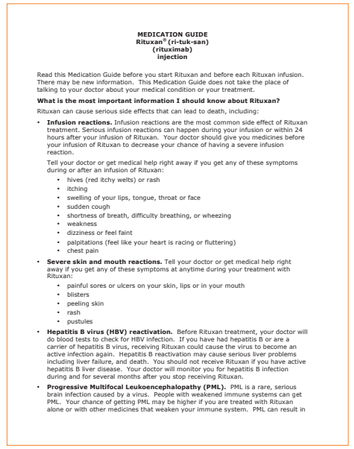
Select Important Safety Information: Cardiovascular Adverse Reactions

- Discontinue infusions for serious or life-threatening cardiac arrhythmias
- Perform cardiac monitoring during and after all infusions of Rituxan for patients who develop clinically significant arrhythmias, or who have a history of arrhythmia or angina

Please see additional Important Safety Information throughout and the Rituxan full Prescribing Information, including **BOXED WARNINGS**.

Step 2:

Provide Medication Guide and review with patient



MEDICATION GUIDE
Rituxan® (ri-tuk-san)
(rituximab)
injection

Read this Medication Guide before you start Rituxan and before each Rituxan infusion. There may be new information. This Medication Guide does not take the place of talking to your doctor about your medical condition or your treatment.

What is the most important information I should know about Rituxan?

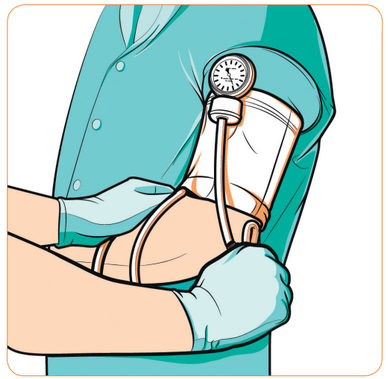
Rituxan can cause serious side effects that can lead to death, including:

- **Infusion reactions.** Infusion reactions are the most common side effect of Rituxan treatment. Serious infusion reactions can happen during your infusion or within 24 hours after your infusion of Rituxan. Your doctor should give you medicines before your infusion of Rituxan to decrease your chance of having a severe infusion reaction.

  Tell your doctor or get medical help right away if you get any of these symptoms during or after an infusion of Rituxan:
  - hives (red itchy welts) or rash
  - itching
  - swelling of your lips, tongue, throat or face
  - sudden cough
  - shortness of breath, difficulty breathing, or wheezing
  - weakness
  - dizziness or feel faint
  - palpitations (feel like your heart is racing or fluttering)
  - chest pain
- **Severe skin and mouth reactions.** Tell your doctor or get medical help right away if you get any of these symptoms at anytime during your treatment with Rituxan:
  - painful sores or ulcers on your skin, lips or in your mouth
  - blisters
  - peeling skin
  - rash
  - pustules
- **Hepatitis B virus (HBV) reactivation.** Before Rituxan treatment, your doctor will do blood tests to check for HBV infection. If you have had hepatitis B or are a carrier of hepatitis B virus, receiving Rituxan could cause the virus to become an active infection again. Hepatitis B reactivation may cause serious liver problems including liver failure, and death. You should not receive Rituxan if you have active hepatitis B liver disease. Your doctor will monitor you for hepatitis B infection during and for several months after you stop receiving Rituxan.
- **Progressive Multifocal Leukoencephalopathy (PML).** PML is a rare, serious brain infection caused by a virus. People with weakened immune systems can get PML. Your chance of getting PML may be higher if you are treated with Rituxan alone or with other medicines that weaken your immune system. PML can result in

Step 3:

Perform Baseline assessment



Check patient's vitals and record patient Baseline assessment.

Attention Healthcare Provider: Provide Medication Guide to patient prior to Rituxan infusion.

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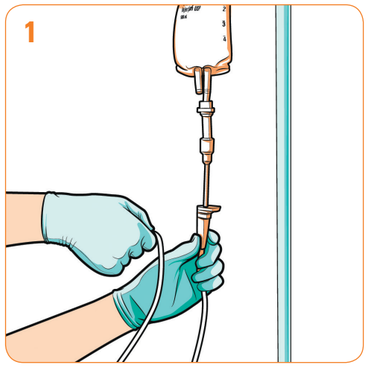
Rituxan®
Rituximab

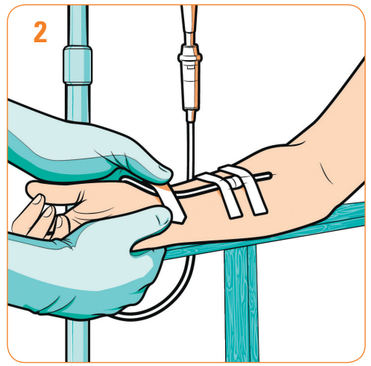
INFUSION STEPS

Step 4:

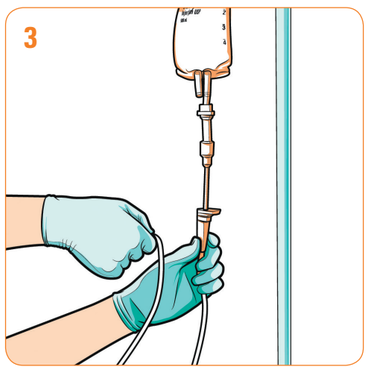
Prepare primary saline line



Connect and prime a primary IV infusion set with an IV bag 0.9% normal saline, USP, or D5W, USP.



Prepare IV site and insert IV catheter. Attach the IV tubing to IV catheter.



Begin IV infusion of 0.9% normal saline, USP, or D5W, USP.

Step 5:

Premedication

Review the prescribing provider's order to determine whether he or she recommended administration of glucocorticoids prior to Rituxan infusion:

- Premedicate with antihistamine and acetaminophen
- In addition, glucocorticoids administered through IV as methylprednisolone 100 mg or its equivalent 30 minutes prior to each infusion are recommended to reduce the incidence and severity of IRRs[1]

Step 6:

Confirm the Rituxan dose needed

Rituxan is administered by IV infusion at a dose of 1000 mg. Patients receive 2 infusions, one on Day 1 and one on Day 15.

Retreat every 6 months (24 weeks) or based on clinical evaluation, but no sooner than every 4 months (16 weeks).

Select Important Safety Information: Renal Toxicity

- Monitor closely for signs of renal failure and discontinue Rituxan in patients with a rising serum creatinine or oliguria

Please see the Rituxan full Prescribing Information and pages 45-47 for **BOXED WARNINGS** and additional Important Safety Information.

Attention Healthcare Provider: Provide Medication Guide to patient prior to Rituxan infusion.

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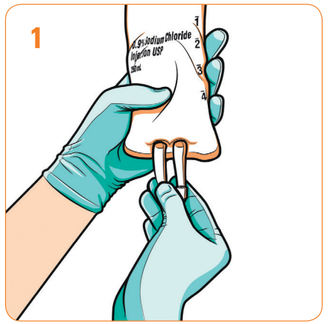
Rituxan®
Rituximab

INFUSION STEPS

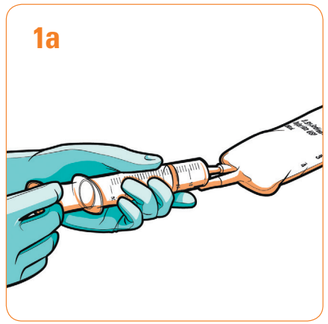
Step 7:

Prepare Rituxan solution

The following steps outline a 4-mg/mL final concentration of Rituxan infusion solution using 250 mL 0.9% normal saline, USP, or D5W, USP. For other concentrations, see the drip-rate chart that follows these administration steps.



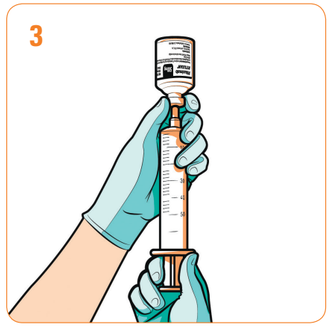
Clean the port of the 250-mL IV bag of normal saline or D5W with an alcohol wipe.



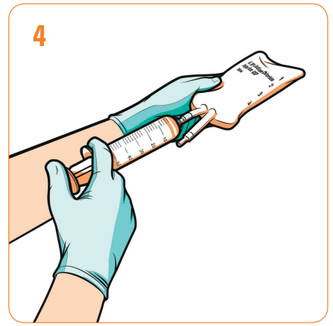
Remove 100 mL of normal saline or D5W and discard, leaving 150 mL in the IV bag.

Remove caps and clean rubber stoppers with alcohol wipes.

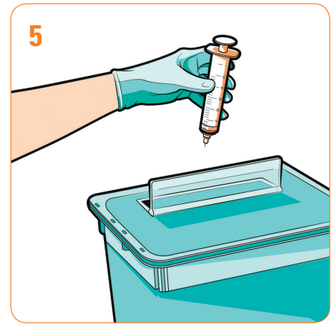
Administration tip | **Always use aseptic technique. Follow your institution's protocol for preparing medications for IV infusions.**



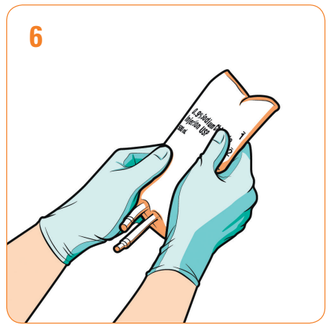
Withdraw the necessary amount of Rituxan and dilute to a final concentration of 1 mg/mL to 4 mg/mL in an infusion bag containing either normal saline or D5W.



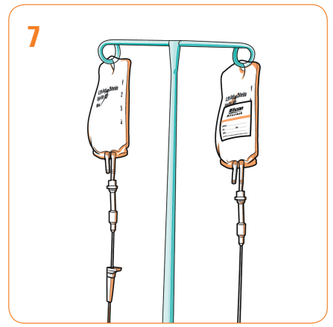
Dilute the 100 mL (1000 mg) of Rituxan into the 150-mL IV solution, yielding a final total volume of 250 mL and a final concentration of 4 mg/mL.



Remove and dispose of needle and syringe in compliance with hospital and/or office protocol.



Gently invert IV bag to mix. Do not shake. Do not add other medications to the bag. Label IV bag with patient's name, drug, dose, and date, and then initial it.



Connect an infusion set to the IV bag containing Rituxan. Infuse total volume of bag. See Step 8 for full administration instructions.

Select Important Safety Information: Bowel Obstruction and Perforation

- Abdominal pain, bowel obstruction and perforation, in some cases leading to death, can occur in patients receiving Rituxan in combination with chemotherapy

Please see additional Important Safety Information throughout and the Rituxan full Prescribing Information, including **BOXED WARNINGS**.

Attention Healthcare Provider: Provide Medication Guide to patient prior to Rituxan infusion.

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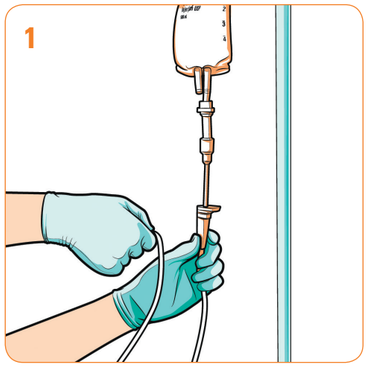
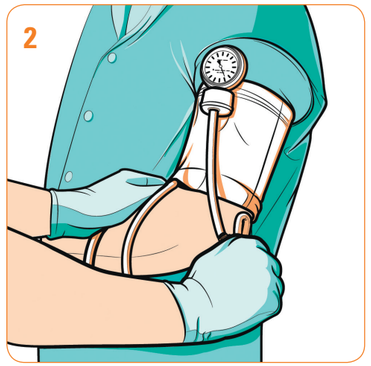
Rituxan®
Rituximab

INFUSION STEPS

Step 8:

Administer Rituxan to patient, and monitor him or her during infusion





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

- Rituxan should not be infused concomitantly in the same line with other medications
- Though not mandatory for IV infusion, use of an infusion pump may help regulate the administration and dose of the drug
- **Optional 2-bag method:** Administer Rituxan using 2 lines as follows:
  - Establish an IV saline line, without medication, to keep patient's vein open. This line can also serve as a means of administering additional medications should an IRR occur
  - Prime Rituxan into a second primary IV line and connect to the lowest port **(closest to the patient)** of the saline line
  - Stop the primary infusion line

Select Important Safety Information: Immunization

- The safety of immunization with live viral vaccines following Rituxan therapy has not been studied, and vaccination with live vaccines is not recommended before or during treatment
- For RA patients, physicians should follow current immunization guidelines and administer non-live vaccines at least 4 weeks prior to a course of Rituxan

Please see additional Important Safety Information throughout and the Rituxan full Prescribing Information, including **BOXED WARNINGS**.

Infusion schedule

- Premedicate with antihistamine and acetaminophen
- In addition, premedication with methylprednisolone 100 mg (30 minutes prior; do not administer as IV push) is recommended

Note: The infusion times listed below do not include premedication.

First infusion (Day 1)

BEGIN AT	EVERY	INCREASE INFUSION RATE	UNTIL MAX INFUSION RATE OF
50 mg/h	30 minutes	50 mg/h*	400 mg/h

TOTAL RITUXAN INFUSION TIME: 4.25 HOURS*

*Only if an IRR does not occur.

Second infusion (Day 15) and subsequent infusions

- If the patient did not experience an IRR with the previous infusion:

BEGIN AT	EVERY	INCREASE INFUSION RATE	UNTIL MAX INFUSION RATE OF
100 mg/h	30 minutes	100 mg/h*	400 mg/h

TOTAL RITUXAN INFUSION TIME: 3.25 HOURS*

*Only if an IRR does not occur.

Attention Healthcare Provider: Provide Medication Guide to patient prior to Rituxan infusion.

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Rituxan® Rituximab

DURING AND AFTER THE INFUSION

Managing IRRs

- Rituxan can cause serious, including fatal, IRRs
- In the event of an IRR, slow or stop the infusion
- Give the patient infusion reaction medications and supportive care as necessary
- Make sure to follow your office protocol
- Depending on the severity of the IRR and the required interventions, temporarily or permanently discontinue Rituxan; resume infusion at a minimum 50% reduction in rate after symptoms have resolved

After the infusion

Instruct patients and family members or attendants about symptoms to watch for and what actions to take in the event of post-infusion complications such as:

- Hives (red itchy welts) or rash
- Itching
- Swelling of your lips, tongue, throat, or face
- Sudden cough
- Shortness of breath, difficulty breathing, or wheezing
- Weakness
- Dizziness or feel faint
- Palpitations (feel like your heart is racing or fluttering)
- Chest pain

If these reactions occur, they typically do so within 24 hours of each infusion.

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

Provide the Medication Guide to patients.

Select Important Safety Information: Embryo-Fetal Toxicity

- Rituxan can cause fetal harm due to B-cell lymphocytopenia in infants exposed to Rituxan in-utero
- Advise pregnant women of the risk to a fetus
- Females of childbearing potential should use effective contraception while receiving Rituxan and for 12 months following the last dose of Rituxan

Please see additional Important Safety Information throughout and the Rituxan full Prescribing Information, including **BOXED WARNINGS**.

Rituxan infusion drip rates*

IF YOUR DESIRED mg/h IS:	DROPS PER MINUTE BASED ON A TUBE WITH A DELIVERY RATE OF:				USING AN INFUSION PUMP, YOUR mL/h SHOULD BE:
	10 DROPS/mL	15 DROPS/mL	20 DROPS/mL	60 DROPS/mL	
FINAL DESIRED RITUXAN CONCENTRATION 4 mg/mL					
50	2	3	4	13	13
100	4	6	8	25	25
150	6	9	13	38	38
200	8	13	17	50	50
250	10	16	21	63	63
300	13	19	25	75	75
350	15	22	29	88	88
400	17	25	33	100	100
FINAL DESIRED RITUXAN CONCENTRATION 2 mg/mL					
50	4	6	8	25	25
100	8	13	17	50	50
150	13	19	25	75	75
200	17	25	33	100	100
250	21	31	42	125	125
300	25	38	50	150	150
350	29	44	58	175	175
400	33	50	67	200	200
FINAL DESIRED RITUXAN CONCENTRATION 1 mg/mL					
50	8	13	17	50	50
100	17	25	33	100	100
150	25	38	50	150	150
200	33	50	67	200	200
250	42	63	83	250	250
300	50	75	100	300	300
350	58	88	117	350	350
400	67	100	133	400	400

*Updated 11/2010.

Attention Healthcare Provider: Provide Medication Guide to patient prior to Rituxan infusion.

For healthcare professional use only. Not to be distributed to patients.

Rituxan®
Rituximab

RA AND GPA & MPA

Administration Checklist

PATIENT NAME _____

DATE OF INFUSION _____

RITUXAN LOTS/VIAL NUMBERS _____

_____

For complete preparation and dosing information, please see the Rituxan Prescribing Information.

Preparing the Rituxan Solution

- Always use aseptic technique
- Withdraw and discard the appropriate amount of 0.9% sodium chloride, USP, or 5% dextrose in water, USP, leaving the appropriate remainder of solution in the intravenous (IV) bag
- Before use, remove caps on Rituxan vials and clean rubber stoppers with alcohol wipes*
- Rituxan should not be mixed or diluted with other drugs

Administering Rituxan

- Review the physician's orders regarding premedications:
  - Premedicate with antihistamine and acetaminophen
- For patients with GPA or MPA, *Pneumocystis carinii* pneumonia prophylaxis is also recommended during treatment and for at least 6 months following the last Rituxan infusion
- Rituxan should only be administered by a healthcare professional with appropriate medical support to manage serious infusion reactions that can be fatal if they occur
- Use standard IV setups
- Infuse the total volume of the IV bag
- Rituxan solutions for infusion may be stored at 2°C to 8°C (36°F to 46°F) for up to 24 hours, and have been shown to be stable for an additional 24 hours at room temperature. Protect from direct sunlight. Do not freeze
- Do not administer Rituxan as an IV push or bolus

First Infusion (Day 1)

BEGIN AT	EVERY	INCREASE INFUSION RATE	UNTIL MAX INFUSION RATE OF
50 mg/h	30 min	50 mg/h†	400 mg/h

Second Infusion and Subsequent Infusions

- If the patient did not experience an infusion reaction with the previous infusion:

BEGIN AT	EVERY	INCREASE INFUSION RATE	UNTIL MAX INFUSION RATE OF
100 mg/h	30 min	100 mg/h†	400 mg/h

*Rituxan vials are stable at 2°C to 8°C (36°F to 46°F). Do not use beyond expiration date stamped on carton. Rituxan vials should be protected from direct sunlight. Do not freeze or shake.

†Only if an infusion reaction does not occur.

Rituxan Dosing for RA

- Administer Rituxan as two 1000 mg IV infusions separated by 2 weeks
- Glucocorticoids administered as methylprednisolone 100 mg IV or its equivalent 30 min prior to each infusion are recommended to reduce the incidence and severity of infusion reactions
- Withdraw 100 mL (1000 mg) of Rituxan from each of 2 vials (50 mL per vial)
- Dilute Rituxan into the infusion bag containing 0.9% sodium chloride, USP, or 5% dextrose in water, USP, to yield the desired concentration of between 1 mg/mL and 4 mg/mL when mixed
- Gently invert bag to mix. **Do not shake**

Rituxan Dosing for GPA & MPA

Induction

- Customize Rituxan dose to the specific patient by using body surface area
  - Administer Rituxan by IV infusion at a dose of 375 mg/m^2 (ie, body surface area dosing) once weekly for 4 weeks for patients with active GPA or MPA
- Methylprednisolone 1000 mg IV per day for 1-3 days followed by oral prednisone 1 mg/kg/day (not exceeding 80 mg/day and tapered per clinical need) is 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
- Gently invert bag to mix. **Do not shake**

Follow-up Treatment

- Administer Rituxan as two 500-mg IV infusions separated by 2 weeks, followed by a 500-mg IV infusion every 6 months or based on clinical assessment
  - Following induction with Rituxan, follow-up treatment should be initiated within 24 weeks or based on clinical evaluation, but no sooner than 16 weeks after the last Rituxan induction infusion
  - Following induction treatment with other immunosuppressants, follow-up treatment should be initiated during the 4-week period that follows disease control
- Patients should receive 100-mg IV methylprednisolone to be completed 30 minutes prior to each Rituxan infusion
- Gently invert bag to mix. **Do not shake**

Indications

- Rituxan® (rituximab), in combination with methotrexate, is indicated for the treatment of adult patients with moderately to severely active rheumatoid arthritis (RA) who have had an inadequate response to one or more TNF antagonist therapies
- Rituxan® (rituximab), in combination with glucocorticoids, is indicated for the treatment of adult patients with Granulomatosis with Polyangiitis (GPA) (Wegener's Granulomatosis) and Microscopic Polyangiitis (MPA)

For additional Important Safety Information, please see throughout and the Rituxan full Prescribing Information, including **BOXED WARNINGS**.

Attention Healthcare Provider: Provide Medication Guide to patient prior to Rituxan infusion.

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Rituxan®
Rituximab

Administration Checklist (cont'd)

Managing Infusion Reactions and Serious Infusion Reactions

- If an infusion reaction develops, stop or slow the infusion and give the patient infusion-reaction medication and supportive care as necessary. Depending on the severity of the infusion reaction and the required interventions, temporarily or permanently discontinue Rituxan
- Resume infusion at a minimum 50% reduction in rate after symptoms have resolved
- Rituxan can cause serious, including fatal, infusion reactions. Serious reactions typically occurred during the first infusion with time to onset of 30 to 120 min. Rituxan-induced infusion reactions and sequelae include urticaria, hypotension, angioedema, hypoxia, bronchospasm, pulmonary infiltrates, acute respiratory distress syndrome, myocardial infarction, ventricular fibrillation, cardiogenic shock, anaphylactoid events, or death
- Medications and supportive care measures should be available and instituted as medically indicated for use in the event of a reaction during administration. These may include, but are not limited to: IV fluids, Epinephrine, Glucocorticoids, Bronchodilators, Antihistamines, Oxygen, and Acetaminophen
- Make sure to follow your office protocol

After the Infusion

- Instruct patients and family members or attendants about symptoms to watch for and what actions to take in the event of any or a combination of the following post-infusion complications:

  Reactions that may occur after the infusion, typically within 24 hours:

  - Hives (red, itchy welts) or rash
  - Itching
  - Swelling of lips, tongue, throat, or face
  - Sudden cough
  - Shortness of breath, difficulty breathing, or wheezing
  - Weakness
  - Dizziness or feel faint
  - Palpitations (feel like your heart is racing or fluttering)
  - Chest pain
- Instruct patients and family members or attendants to seek immediate medical attention if they notice any of the above symptoms or any new symptoms
- Provide patients and caregivers with a copy of the Medication Guide

Reference: Rituxan [package insert]. South San Francisco, CA: Biogen and Genentech USA, Inc.; 2018.

BOXED WARNINGS

Infusion Reactions: **Rituxan administration can result in serious, including fatal infusion reactions. Deaths within 24 hours of Rituxan infusion have occurred. Approximately 80% of fatal infusion reactions occurred in association with the first infusion. Monitor patients closely. Discontinue Rituxan infusion for severe reactions and provide medical treatment for Grade 3 or 4 infusion reactions.**

Severe Mucocutaneous Reactions: **Severe, including fatal, mucocutaneous reactions can occur in patients receiving Rituxan.** Discontinue Rituxan in patients who experience a severe mucocutaneous reaction. The safety of readministration of Rituxan to patients with severe mucocutaneous reactions has not been determined.

Hepatitis B Virus (HBV) Reactivation: **HBV reactivation can occur in patients treated with Rituxan, in some cases resulting in fulminant hepatitis, hepatic failure, and death. Screen all patients for HBV infection before treatment initiation, and monitor patients during and after treatment with Rituxan. Discontinue Rituxan and concomitant medications in the event of HBV reactivation.**

Progressive Multifocal Leukoencephalopathy (PML), **including fatal PML, can occur in patients receiving Rituxan.** Discontinue Rituxan and consider discontinuation or reduction of any concomitant chemotherapy or immunosuppressive therapy in patients who develop PML.

For additional Important Safety Information, please see throughout and the Rituxan full Prescribing Information, including **BOXED WARNINGS**.

Attention Healthcare Provider: Provide Medication Guide to patient prior to Rituxan infusion.

Administration Checklist (cont'd)

Warnings and Precautions

Tumor Lysis Syndrome (TLS): Acute renal failure, hyperkalemia, hypocalcemia, hyperuricemia, or hyperphosphatemia from tumor lysis, sometimes fatal, can occur within 12-24 hours after the first infusion of Rituxan in patients with Non–Hodgkin's Lymphoma (NHL). Administer aggressive intravenous hydration and anti-hyperuricemic therapy in patients at high risk for TLS. Correct electrolyte abnormalities, monitor renal function and fluid balance, and administer supportive care, including dialysis, as indicated.

Infections: Serious, including fatal, bacterial, fungal, and new or reactivated viral infections can occur during and following the completion of Rituxan-based therapy. Discontinue Rituxan for serious infections and institute appropriate anti-infective therapy. Rituxan is not recommended for use in patients with severe, active infections.

Cardiovascular Adverse Reactions: Discontinue infusions for serious or life-threatening cardiac arrhythmias. Perform cardiac monitoring during and after all infusions of Rituxan for patients who develop clinically significant arrhythmias or who have a history of arrhythmia or angina.

Renal Toxicity: Severe, including fatal, renal toxicity can occur after Rituxan administration in patients with Non–Hodgkin's Lymphoma (NHL). Monitor closely for signs of renal failure and discontinue Rituxan in patients with a rising serum creatinine or oliguria.

Bowel Obstruction and Perforation: Abdominal pain, bowel obstruction and perforation, in some cases leading to death, can occur in patients receiving Rituxan in combination with chemotherapy. Evaluate if symptoms of obstruction such as abdominal pain or repeated vomiting occur.

Immunization: The safety of immunization with live viral vaccines following Rituxan therapy has not been studied, and vaccination with live vaccines is not recommended before or during treatment. For RA patients, physicians should follow current immunization guidelines and administer non-live vaccines at least 4 weeks prior to a course of Rituxan.

Embryo-Fetal Toxicity: Rituxan can cause fetal harm due to B-cell lymphocytopenia in infants exposed to Rituxan in-utero. Advise pregnant women of the risk to a fetus. Females of childbearing potential should use effective contraception while receiving Rituxan and for 12 months following the last dose of Rituxan.

Concomitant Use With Biologic Agents and DMARDs Other Than Methotrexate: Limited data are available on the safety of the use of biologic agents or DMARDs other than methotrexate in RA patients exhibiting peripheral B-cell depletion following treatment with Rituxan. Observe patients closely for signs of infection if biologic agents and/or DMARDs are used concomitantly. Use of concomitant immunosuppressants other than corticosteroids has not been studied in GPA or MPA patients exhibiting peripheral B-cell depletion following treatment with Rituxan.

Use in Patients With RA Who Had No Prior Inadequate Response to TNF Antagonists: The use of Rituxan in patients with RA who have not had prior inadequate response to one or more TNF antagonists is not recommended.

Adverse Reactions

Clinical Trials Experience in RA

Among all exposed patients, most common adverse reactions (≥10%) were upper respiratory tract infection, nasopharyngitis, urinary tract infection, and bronchitis. Other important adverse reactions include infusion reactions, serious infections, and cardiovascular events.

Clinical Trials Experience in GPA and MPA

Adverse reactions reported in ≥15% of Rituxan-treated patients were infections, nausea, diarrhea, headache, muscle spasms, anemia, peripheral edema (other important adverse reactions include infusion reactions).

You may report side effects to the FDA at (800) FDA-1088 or www.fda.gov/medwatch. You may also report side effects to Genentech at (888) 835-2555.

For additional Important Safety Information, please see the Rituxan full Prescribing Information, including **BOXED WARNINGS**.

Attention Healthcare Provider: Provide Medication Guide to patient prior to Rituxan infusion.