# RITUXAN
## DOSING AND ADMINISTRATION

RA GPA & MPA PV

RA

GPA & MPA

PV

### 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 and pediatric patients 2 years of age and older with Granulomatosis with Polyangiitis (GPA) (Wegener's Granulomatosis) and Microscopic Polyangiitis (MPA)
- Rituxan® (rituximab) is indicated for the treatment of adult patients with moderate to severe pemphigus vulgaris (PV)

### BOXED WARNINGS

**Infusion-Related Reactions: Rituxan administration can result in serious, including fatal infusion-related 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-related 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.

Please see the Rituxan full Prescribing Information and pages 24-31 for **BOXED WARNINGS** and additional Important Safety Information.

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

Rituxan®
Rituximab

**Patient Type**

Rituxan, in combination with methotrexate, is indicated for rheumatoid arthritis (RA) in adult patients with moderately to severely active RA who have had an inadequate response to one or more TNF antagonist therapies.

**Dose**

- Administer Rituxan as two 1000-mg intravenous infusions separated by 2 weeks
- Glucocorticoids administered as methylprednisolone 100 mg intravenous or its equivalent 30 min prior to each infusion are recommended to reduce the incidence and severity of infusion-related reactions
- Subsequent courses should be administered every 24 weeks or based on clinical evaluation, but not sooner than every 16 weeks
- Rituxan is given in combination with methotrexate
- Premedicate before each infusion with acetaminophen and an antihistamine
- Gently invert bag to mix. Do not shake

**Prior to First Infusion:**

Screen all patients for HBV infection by measuring HBsAg and anti-HBc before initiating treatment with Rituxan. Obtain complete blood counts (CBC), including platelets, prior to the first dose. For important information about screening labs (prior to first infusion), see Section 5.3 of the PI.

Anti-HBc, hepatitis B core antibody; HBsAg, surface antigen of the hepatitis B virus; HBV, hepatitis B virus; TNF, tumor necrosis factor.



**Time**

- First infusion (Day 1)

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

**TOTAL RITUXAN INFUSION TIME: 4 hrs and 15 min***

*Only if an infusion-related reaction does not occur.

  - Initiate infusion at a rate of 50 mg/h
  - In the absence of an infusion-related reaction, increase infusion rate by 50 mg/h increments every 30 min, to a maximum of 400 mg/h
  - Total infusion time: 4 hrs and 15 min

- Second infusion (Day 15) and subsequent infusions

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

**TOTAL RITUXAN INFUSION TIME: 3 hrs and 15 min†**

†Only if an infusion-related reaction does not occur.

  - Standard infusion: Initiate infusion at a rate of 100 mg/h
  - In the absence of an infusion-related reaction, increase rate by 100 mg/h increments every 30 min, to a maximum of 400 mg/h
  - Total infusion time: 3 hrs and 15 min

Please see the Rituxan full Prescribing Information and pages 24-31 for **BOXED WARNINGS** and additional Important Safety Information.

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

Rituxan®
Rituximab

**Infusion-Related Reactions**

Rituxan can cause severe, including fatal, infusion-related reactions. Severe reactions typically occurred during the first infusion with time to onset of 30-120 min. Depending on the severity of the infusion-related reaction and the required interventions, temporarily or permanently discontinue Rituxan. Institute medical management (eg, glucocorticoids, epinephrine, bronchodilators, or oxygen) for infusion-related reactions as needed.

Resume infusion at a minimum 50% reduction in rate after symptoms have resolved.

**Route**

- **Rituxan is administered only as an intravenous infusion. Do not administer as an intravenous push or bolus**
- Rituxan should only be administered by a healthcare professional with appropriate medical support to manage severe infusion-related reactions, which can be fatal, if they occur
- Use a sterile needle and syringe to prepare Rituxan

**Documentation**

Please remember to complete all documentation and follow all proper procedures for your clinic before and after each infusion. In patients with RA, GPA, or MPA, obtain CBC with differential and platelet counts at 2- to 4-month intervals during Rituxan therapy. Continue to monitor for cytopenias after final dose and until resolution.



## Final desired Rituxan concentration: **4 mg/mL***

### RITUXAN INFUSION DRIP RATES

**For RA:** Dilute 1000 mg (100 mL) of Rituxan in 150 mL of 0.9% sodium chloride, USP, or 5% dextrose in water, USP (final volume once diluted = 250 mL)

| 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 | |
| 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 |

CBC, complete blood count; GPA, granulomatosis with polyangiitis; MPA, microscopic polyangiitis; RA, rheumatoid arthritis; USP, United States Pharmacopeia.
*Updated 11/2010.

Rituxan
Rituximab

## Final desired Rituxan concentration: **2 mg/mL***

### RITUXAN INFUSION DRIP RATES

**For RA:** Dilute 1000 mg (100 mL) of Rituxan in 400 mL of 0.9% sodium chloride, USP, or 5% dextrose in water, USP (final volume once diluted = 500 mL)

| 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 | |
| 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 |

*Updated 11/2010.

Please see the Rituxan full Prescribing Information and pages 24-31 for **BOXED WARNINGS** and additional Important Safety Information.

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



## Final desired Rituxan concentration: **1 mg/mL†**

### RITUXAN INFUSION DRIP RATES

**For RA:** Dilute 1000 mg (100 mL) of Rituxan in 900 mL of 0.9% sodium chloride, USP, or 5% dextrose in water, USP (final volume once diluted = 1000 mL)

| 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 | |
| 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 |

RA, rheumatoid arthritis; USP, United States Pharmacopeia.

†Updated 11/2010.

Rituxan® Rituximab

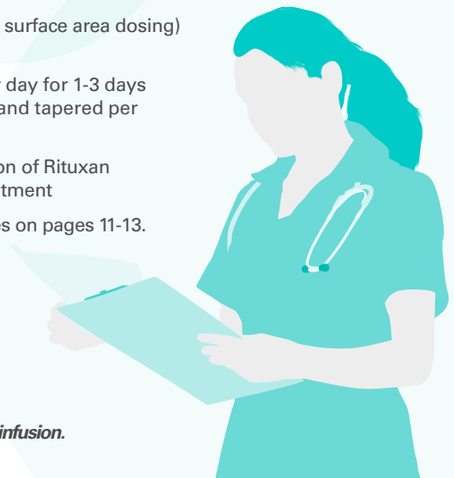
# GPA & MPA

**Patient Type**

- Rituxan, in combination with glucocorticoids, is indicated for the treatment of adult patients with Granulomatosis with Polyangiitis (GPA) (Wegener's Granulomatosis) and Microscopic Polyangiitis (MPA)

**Induction Treatment**

- Dosing of Rituxan for GPA and MPA is based on body surface area (BSA)
  - Calculate BSA of the patient using his or her height and weight:
    - BSA in $m^2$ = (weight in kg)$^{0.425}$ x (height in cm)$^{0.725}$ x 0.007184
    - 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
- Glucocorticoids administered as 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) 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
- Please refer to the Rituxan drip rates on pages 5-7 and the mixing tables on pages 11-13. Gently invert bag to mix. Do not shake



**Follow-up Treatment In Adult Patients Who Have Achieved Disease Control**

- Administer Rituxan as two 500-mg intravenous infusions separated by 2 weeks, followed by a 500-mg intravenous infusion every 24 weeks or based on clinical assessment
  - Follow-up dose (500 mg) infusion bag concentration will change and the infusion drip rate will change accordingly
- If disease control was induced with Rituxan, begin follow-up treatment within 24 weeks, but no sooner than 16 weeks
  - If disease control was induced with other standard of care immunosuppressants, begin follow-up treatment within 4 weeks of achieving disease control
- For GPA and MPA patients, glucocorticoids are given in combination with Rituxan
- *Pneumocystis jirovecii* pneumonia prophylaxis is also recommended for patients with GPA or MPA during treatment and for at least 6 months following the last Rituxan infusion
- Please refer to the Rituxan drip rates on pages 14-15. Gently invert bag to mix. Do not shake

**Prior to First Infusion:**

Screen all patients for HBV infection by measuring HBsAg and anti-HBc before initiating treatment with Rituxan. Obtain complete blood counts (CBC), including platelets, prior to the first dose. For important information about screening labs (prior to first infusion), see Section 5.3 of the PI.

Please see the Rituxan full Prescribing Information and pages 24-31 for **BOXED WARNINGS** and additional Important Safety Information.

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

Anti-HBc, hepatitis B core antibody; HBsAg, surface antigen of the hepatitis B virus; HBV, hepatitis B virus.

Rituxan® Rituximab

**Time**

- First infusion (Day 1)
  - Begin infusion at rate of 50 mg/h
  - If an infusion-related reaction does not occur, escalate the infusion rate in 50-mg/h increments every 30 min, to a maximum of 400 mg/h
- Subsequent infusions (Days 8, 15, and 22)
  - If the patient tolerated the previous infusion, begin at a rate of 100 mg/h
  - If an infusion-related reaction does not occur, continue to escalate the infusion rate in 100-mg/h increments every 30 min, 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 BSA

**Infusion-Related Reactions**

Rituxan can cause severe, including fatal, infusion-related reactions. Severe reactions typically occurred during the first infusion with time to onset of 30-120 min. Depending on the severity of the infusion-related reaction and the required interventions, temporarily or permanently discontinue Rituxan. Institute medical management (eg, glucocorticoids, epinephrine, bronchodilators, or oxygen) for infusion-related reactions as needed.

Resume infusion at a minimum 50% reduction in rate after symptoms have resolved.

**Route**

- **Rituxan is administered only as an intravenous infusion. Do not administer as an intravenous push or bolus**
- Rituxan should only be administered by a healthcare professional with appropriate medical support to manage severe infusion-related reactions, which can be fatal, if they occur
- Use a sterile needle and syringe to prepare Rituxan

**Documentation**

Please remember to complete all documentation and follow all proper procedures for your clinic before and after each infusion. In patients with RA, GPA, or MPA, obtain CBC with differential and platelet counts at 2- to 4-month intervals during Rituxan therapy. Continue to monitor for cytopenias after final dose and until resolution.



**This mixing table applies to induction treatment with Rituxan for Granulomatosis with Polyangiitis (GPA) and Microscopic Polyangiitis (MPA)**

## Mixing table: 4 mg/mL (INDUCTION)

**TO DELIVER 375 mg/m² AT A CONCENTRATION OF 4 mg/mL OF RITUXAN**

| BSA ($m^2$) | Rituxan dose (mg) | Rituxan volume (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 |
| 2.3 | 863 | 86 | 130 | 216 |

| BSA ($m^2$) | Rituxan dose (mg) | Rituxan volume (mL*) | + Diluent volume† (mL) | = Total infusion volume (mL) |
|---|---|---|---|---|
| 2.4 | 900 | 90 | 135 | 225 |
| 2.5 | 938 | 94 | 141 | 235 |
| 2.6 | 975 | 98 | 147 | 245 |
| 2.7 | 1013 | 101 | 152 | 253 |
| 2.8 | 1050 | 105 | 158 | 263 |
| 2.9 | 1088 | 109 | 164 | 273 |
| 3.0 | 1125 | 113 | 169 | 282 |
| 3.1 | 1163 | 116 | 175 | 291 |
| 3.2 | 1200 | 120 | 180 | 300 |
| 3.3 | 1238 | 124 | 186 | 310 |

BSA, body surface area; CBC, complete blood count; GPA, granulomatosis with polyangiitis; MPA, microscopic polyangiitis; RA, rheumatoid arthritis

*For ease of reconstitution, some numbers have been rounded.

†Normal saline or D5W. Dilute the Rituxan dose in either 0.9% Sodium Chloride, USP, or 5% Dextrose Injection, USP.

*FOR APPROPRIATE DRIP RATE, PLEASE SEE PAGE 5.*

Please see the Rituxan full Prescribing Information and pages 24-31 for **BOXED WARNINGS** and additional Important Safety Information.

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

Rituxan®
Rituximab

**This mixing table applies to induction treatment with Rituxan for Granulomatosis with Polyangiitis (GPA) and Microscopic Polyangiitis (MPA)**

## Mixing table: **2 mg/mL (INDUCTION)**

| TO DELIVER 375 mg/m² AT A CONCENTRATION OF 2 mg/mL OF RITUXAN | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| BSA ($m^2$) | Rituxan dose (mg) | Rituxan volume (mL*) | + | Diluent volume† (mL) | = | Total infusion volume (mL) | BSA ($m^2$) | Rituxan dose (mg) | Rituxan volume (mL*) | + | Diluent volume† (mL) | = | Total infusion volume (mL) |
| 1.3 | 488 | 49 | | 196 | | 245 | 2.4 | 900 | 90 | | 360 | | 450 |
| 1.4 | 525 | 53 | | 212 | | 265 | 2.5 | 938 | 94 | | 375 | | 469 |
| 1.5 | 563 | 56 | | 224 | | 280 | 2.6 | 975 | 98 | | 390 | | 488 |
| 1.6 | 600 | 60 | | 240 | | 300 | 2.7 | 1013 | 101 | | 406 | | 507 |
| 1.7 | 638 | 64 | | 256 | | 320 | 2.8 | 1050 | 105 | | 420 | | 525 |
| 1.8 | 675 | 68 | | 272 | | 340 | 2.9 | 1088 | 109 | | 435 | | 544 |
| 1.9 | 713 | 71 | | 284 | | 355 | 3.0 | 1125 | 113 | | 450 | | 563 |
| 2.0 | 750 | 75 | | 300 | | 375 | 3.1 | 1163 | 116 | | 466 | | 582 |
| 2.1 | 788 | 79 | | 316 | | 395 | 3.2 | 1200 | 120 | | 480 | | 600 |
| 2.2 | 825 | 83 | | 332 | | 415 | 3.3 | 1238 | 124 | | 495 | | 619 |
| 2.3 | 863 | 86 | | 346 | | 432 | | | | | | | |

BSA, body surface area.
*For ease of reconstitution, some numbers have been rounded.
†Normal saline or D5W. Dilute the Rituxan dose in either 0.9% Sodium Chloride, USP, or 5% Dextrose Injection, USP.

*FOR APPROPRIATE DRIP RATE, PLEASE SEE PAGE 6.*

Please see the Rituxan full Prescribing Information and pages 24-31 for **BOXED WARNINGS** and additional Important Safety Information.

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



**This mixing table applies to induction treatment with Rituxan for Granulomatosis with Polyangiitis (GPA) and Microscopic Polyangiitis (MPA)**

## Mixing table: **1 mg/mL (INDUCTION)**

| TO DELIVER 375 mg/m² AT A CONCENTRATION OF 1 mg/mL OF RITUXAN | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| BSA ($m^2$) | Rituxan dose (mg) | Rituxan volume (mL‡) | + | Diluent volume§ (mL) | = | Total infusion volume (mL) | BSA ($m^2$) | Rituxan dose (mg) | Rituxan volume (mL‡) | + | Diluent volume§ (mL) | = | Total infusion volume (mL) |
| 1.3 | 488 | 49 | | 441 | | 490 | 2.4 | 900 | 90 | | 810 | | 900 |
| 1.4 | 525 | 53 | | 477 | | 530 | 2.5 | 938 | 94 | | 844 | | 938 |
| 1.5 | 563 | 56 | | 504 | | 560 | 2.6 | 975 | 98 | | 877 | | 975 |
| 1.6 | 600 | 60 | | 540 | | 600 | 2.7 | 1013 | 101 | | 912 | | 1013 |
| 1.7 | 638 | 64 | | 576 | | 640 | 2.8 | 1050 | 105 | | 945 | | 1050 |
| 1.8 | 675 | 68 | | 612 | | 680 | 2.9 | 1088 | 109 | | 979 | | 1088 |
| 1.9 | 713 | 71 | | 639 | | 710 | 3.0 | 1125 | 113 | | 1012 | | 1125 |
| 2.0 | 750 | 75 | | 675 | | 750 | 3.1 | 1163 | 116 | | 1047 | | 1163 |
| 2.1 | 788 | 79 | | 711 | | 790 | 3.2 | 1200 | 120 | | 1080 | | 1200 |
| 2.2 | 825 | 83 | | 747 | | 830 | 3.3 | 1238 | 124 | | 1114 | | 1238 |
| 2.3 | 863 | 86 | | 777 | | 863 | | | | | | | |

BSA, body surface area.
‡For ease of reconstitution, some numbers have been rounded.
§Normal saline or D5W. Dilute the Rituxan dose in either 0.9% Sodium Chloride, USP, or 5% Dextrose Injection, USP.

*FOR APPROPRIATE DRIP RATE, PLEASE SEE PAGE 7.*

Rituxan® Rituximab

## Final desired Rituxan concentration: 2 mg/mL* (FOLLOW-UP)

### RITUXAN INFUSION DRIP RATES

| **For GPA and MPA:** Dilute 500 mg (50 mL) of Rituxan in 200 mL of 0.9% sodium chloride, USP, or 5% dextrose in water, USP (final volume once diluted = 250 mL) | | | | | |
|---|---|---|---|---|---|
| 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 | |
| 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 |

GPA, granulomatosis with polyangiitis; MPA, microscopic polyangiitis; USP, United States Pharmacopeia.

*Updated 02/2019.

Please see the Rituxan full Prescribing Information and pages 24-31 for **BOXED WARNINGS** and additional Important Safety Information.

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



## Final desired Rituxan concentration: 1 mg/mL† (FOLLOW-UP)

### RITUXAN INFUSION DRIP RATES

| **For GPA and MPA:** Dilute 500 mg (50 mL) of Rituxan in 450 mL of 0.9% sodium chloride, USP, or 5% dextrose in water, USP (final volume once diluted = 500 mL) | | | | | |
|---|---|---|---|---|---|
| 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 | |
| 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 |

GPA, granulomatosis with polyangiitis; MPA, microscopic polyangiitis; USP, United States Pharmacopeia.

†Updated 02/2019.

Rituxan®
Rituximab

# PV

**Patient Type**

- Rituxan is indicated for the treatment of adult patients with moderate to severe pemphigus vulgaris (PV)

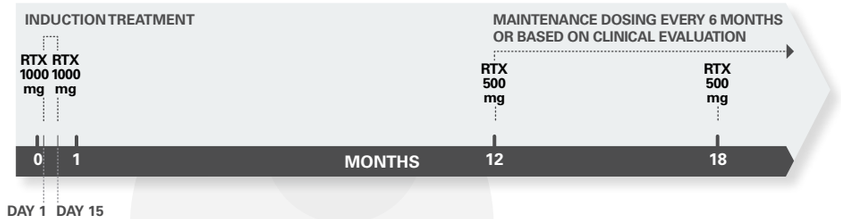
**Dose**

- Prior to each infusion:
  - Administer methylprednisolone 100 mg IV or equivalent glucocorticoid 30 min prior to each infusion to reduce the incidence and severity of infusion-related reactions
  - Premedicate with an antihistamine and acetaminophen
  - Gently invert bag to mix. Do not shake
- *Pneumocystis jirovecii* pneumonia (PCP) prophylaxis should be considered for patients with PV during and following Rituxan treatment
- Induction treatment: Two 1000-mg intravenous infusions separated by 2 weeks, in combination with a tapering course of glucocorticoids
- Maintenance treatment: One 500-mg intravenous infusion at Month 12 and every 6 months thereafter or based on clinical evaluation
- Treatment for relapse: One 1000-mg intravenous infusion upon relapse. Administer no sooner than 16 weeks from previous infusion. Consider resuming or increasing the glucocorticoid dose based on clinical evaluation
- Subsequent courses: Administer no sooner than 16 weeks from previous infusion

**Prior to First Infusion:**

Screen all patients for HBV infection by measuring HBsAg and anti-HBc before initiating treatment with Rituxan. Obtain complete blood counts (CBC), including platelets, prior to the first dose. For important information about screening labs (prior to first infusion), see Section 5.3 of the PI.

**Time**




Anti-HBc, hepatitis B core antibody; HBsAg, surface antigen of the hepatitis B virus; HBV, hepatitis B virus; RTX, Rituxan.



Please see the Rituxan full Prescribing Information and pages 24-31 for **BOXED WARNINGS** and additional Important Safety Information.

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

Rituxan® Rituximab

# PV

**Route**

- **Rituxan is administered only as an intravenous infusion. Do not administer as an intravenous push or bolus**
- Rituxan should only be administered by a healthcare professional with appropriate medical support to manage severe infusion-related reactions, which can be fatal, if they occur
- Use a sterile needle and syringe to prepare Rituxan

**Time**

- First infusion (Day 1)

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

**TOTAL RITUXAN INFUSION TIME: 4 hrs and 15 min***

*Only if an infusion-related reaction does not occur.

  - Initiate infusion at a rate of 50 mg/h
  - In the absence of an infusion-related reaction, increase infusion rate by 50 mg/h increments every 30 min, to a maximum of 400 mg/h
  - Total infusion time: 4 hrs and 15 min

- Second infusion (Day 15) and subsequent infusions

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

**TOTAL RITUXAN INFUSION TIME: 3 hrs and 15 min†**

†Only if an infusion-related reaction does not occur.

  - Initiate infusion at a rate of 100 mg/h
  - In the absence of an infusion-related reaction, increase infusion rate by 100 mg/h increments every 30 min, to a maximum of 400 mg/h
  - Total infusion time: 3 hrs and 15 min



- Maintenance treatment

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

**TOTAL RITUXAN INFUSION TIME: 2 hrs‡**

‡Only if an infusion-related reaction does not occur.

  - Initiate infusion at a rate of 100 mg/h
  - In the absence of an infusion-related reaction, increase infusion rate by 100 mg/h increments every 30 min, to a maximum of 400 mg/h
  - Maintenance dose (500 mg) infusion bag concentration will change and the infusion drip rate will change accordingly
  - Total infusion time: 2 hrs

**Infusion-Related Reactions**

Rituxan can cause severe, including fatal, infusion-related reactions. Severe reactions typically occurred during the first infusion with time to onset of 30-120 min. Depending on the severity of the infusion-related reaction and the required interventions, temporarily or permanently discontinue Rituxan. Institute medical management (eg, glucocorticoids, epinephrine, bronchodilators, or oxygen) for infusion-related reactions as needed.

Resume infusion at a minimum 50% reduction in rate after symptoms have resolved.

**Documentation**

Please remember to complete all documentation and follow all proper procedures for your clinic before and after each infusion.

Please see the Rituxan full Prescribing Information and pages 24-31 for **BOXED WARNINGS** and additional Important Safety Information.

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

Rituxan® Rituximab

## Final desired Rituxan concentration: **4 mg/mL* (INDUCTION OR RELAPSE)**

### RITUXAN INFUSION DRIP RATES

| **For PV:** Dilute 1000 mg (100 mL) of Rituxan in 150 mL of 0.9% sodium chloride, USP, or 5% dextrose in water, USP (final volume once diluted = 250 mL) | | | | | |
|---|---|---|---|---|---|
| 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 | |
| 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 |

*Updated 11/2010.

USP, United States Pharmacopeia.

## Final desired Rituxan concentration: **2 mg/mL† (INDUCTION OR RELAPSE)**

### RITUXAN INFUSION DRIP RATES

| **For PV:** Dilute 1000 mg (100 mL) of Rituxan in 400 mL of 0.9% sodium chloride, USP, or 5% dextrose in water, USP (final volume once diluted = 500 mL) | | | | | |
|---|---|---|---|---|---|
| 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 | |
| 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 |

†Updated 11/2010.

Please see the Rituxan full Prescribing Information and pages 24-31 for **BOXED WARNINGS** and additional Important Safety Information.

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



Rituxan® Rituximab

## Final desired Rituxan concentration: **2 mg/mL* (MAINTENANCE)**

### RITUXAN INFUSION DRIP RATES

| **For PV:** Dilute 500 mg (50 mL) of Rituxan in 200 mL of 0.9% sodium chloride, USP, or 5% dextrose in water, USP (final volume once diluted = 250 mL) | | | | | |
|---|---|---|---|---|---|
| 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 | |
| 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 |

*Updated 02/2019.

USP, United States Pharmacopeia.

## Final desired Rituxan concentration: **1 mg/mL† (MAINTENANCE)**

### RITUXAN INFUSION DRIP RATES

| **For PV:** Dilute 500 mg (50 mL) of Rituxan in 450 mL of 0.9% sodium chloride, USP, or 5% dextrose in water, USP (final volume once diluted = 500 mL) | | | | | |
|---|---|---|---|---|---|
| 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 | |
| 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 02/2019.

USP, United States Pharmacopeia.



Please see the Rituxan full Prescribing Information and pages 24-31 for **BOXED WARNINGS** and additional Important Safety Information.

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

Rituxan®
Rituximab

## BOXED WARNINGS

**Infusion-Related Reactions: Rituxan administration can result in serious, including fatal infusion-related 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-related 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.

## 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 patients treated with Rituxan, physicians should review the patient's vaccination status and patients should, if possible, be brought up to date with all immunizations in agreement with current immunization guidelines prior to initiating Rituxan 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 rituximab in-utero. Advise pregnant women of the potential risk to a fetus. Verify pregnancy status in females of reproductive potential prior to initiating Rituxan. Advise females of reproductive potential to use effective contraception while receiving Rituxan and for 12 months after the last dose.

**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, MPA, or PV 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.

Please see the Rituxan full Prescribing Information and pages 24-31 for **BOXED WARNINGS** and additional Important Safety Information.

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

Rituxan®
Rituximab

## Adverse Reactions

### Clinical Trials Experience in RA

Among all exposed patients, adverse reactions reported in greater than 10% of patients include infusion-related reactions, upper respiratory tract infection, nasopharyngitis, urinary tract infection, and bronchitis.

In placebo-controlled studies, adverse reactions reported in ≥5% of patients were hypertension (8% vs 5%), nausea (8% vs 5%), upper respiratory tract infection (7% vs 6%), arthralgia (6% vs 4%), pyrexia (5% vs 2%), and pruritus (5% vs 1%) in Rituxan-treated vs placebo-treated patients, respectively.

*Infusion-Related Reactions:* In the Rituxan RA pooled, placebo-controlled studies, incidence of any adverse event within 24 hours of an infusion was 32% vs 23% after the first infusion and 11% vs 13% after the second infusion in the Rituxan-treated patients and placebo group, respectively. Incidence of acute infusion-related reactions was 27% vs 19% after the first infusion and 9% vs 11% after the second infusion in the Rituxan-treated patients and placebo group, respectively. Serious acute infusion-related reactions were experienced by <1% of patients in either treatment group. Acute infusion-related reactions required dose modification (stopping, slowing, or interruption of the infusion) in 10% and 2% of patients receiving Rituxan or placebo, respectively, after the first course.

*Infections:* In the pooled, placebo-controlled studies, incidence of any type of infection was 39% vs 34%, Rituxan-treated vs placebo, respectively. The most common infections were nasopharyngitis, upper respiratory tract infections, urinary tract infections, bronchitis, and sinusitis. The incidence of serious infections was 2% vs 1%, Rituxan-treated vs placebo group, respectively.

In the experience with Rituxan in 2578 RA patients, the rate of serious infection was 4.31 per 100 patient-years. The most common serious infections (≥0.5%) were pneumonia or lower respiratory tract infections, cellulitis, and urinary tract infections. Fatal serious infections included pneumonia, sepsis, and colitis. Rates of serious infection remain stable in patients receiving subsequent courses.

In 185 Rituxan-treated RA patients with active disease, subsequent treatment with a biologic DMARD, the majority of which were TNF antagonists, did not appear to increase the rate of serious infection.



*Cardiovascular Adverse Reactions:* In the pooled, placebo-controlled studies, incidence of serious cardiovascular reactions was 1.7% vs 1.3%, Rituxan-treated vs placebo, respectively. Three cardiovascular deaths occurred during the double-blind period of the RA studies including all Rituxan regimens (3/769=0.4%) compared to none in the placebo treatment group (0/389). In the experience with Rituxan in 2578 RA patients, the rate of myocardial infarction (MI) was consistent with MI rates in the general RA population. Rituxan should be discontinued in the event of a serious or life-threatening cardiac event.

*Hypophosphatemia and Hyperuricemia:* In the pooled, placebo-controlled studies, newly occurring hypophosphatemia (<2.0 mg/dL) was 12% vs 10%, Rituxan-treated vs placebo, respectively. Hypophosphatemia was more common in patients who received corticosteroids. Newly occurring hyperuricemia (>10 mg/dL) was observed in 1.5% vs 0.3%, Rituxan-treated vs placebo, respectively.

## Immunogenicity

A total of 273/2578 (11%) patients with RA tested positive for anti-rituximab antibodies at any time after receiving Rituxan. Anti-rituximab antibody positivity was not associated with increased rates of infusion-related reactions or other adverse events. Upon further treatment, the proportions of patients with infusion-related reactions were similar between anti-rituximab antibody positive and negative patients, and most reactions were mild to moderate. Four anti-rituximab antibody positive patients had serious infusion-related reactions, and the temporal relationship between anti-rituximab antibody positivity and infusion-related reaction was variable. The clinical relevance of anti-rituximab antibody formation in Rituxan-treated patients is unclear.

Please see the Rituxan full Prescribing Information and pages 24-31 for **BOXED WARNINGS** and additional Important Safety Information.

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

Rituxan®
Rituximab

## 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, and infusion-related reactions.

***Induction Treatment of Patients with Active GPA/MPA (GPA/MPA Study 1)***

*Infusion-Related Reactions:* In GPA/MPA Study 1, 12% vs 11% (Rituxan-treated vs cyclophosphamide) of patients experienced at least one infusion-related reaction. Infusion-related reactions included cytokine release syndrome, flushing, throat irritation, and tremor. In the Rituxan group, the proportion of patients experiencing an infusion-related reaction was 12%, 5%, 4%, and 1% following the first, second, third, and fourth infusions, respectively. Patients were premedicated with antihistamine and acetaminophen before each Rituxan infusion and were on background oral corticosteroids, which may have mitigated or masked an infusion-related reaction; however, there is insufficient evidence to determine whether premedication diminishes the frequency or severity of infusion-related reactions.

*Infections:* In GPA/MPA Study 1, 62% vs 47% (Rituxan-treated vs cyclophosphamide-treated, respectively) of patients experienced an infection by Month 6. The most common infections in the Rituxan group were upper respiratory tract infections, urinary tract infections, and herpes zoster. The incidence of serious infections was 11% vs 10% (Rituxan-treated vs cyclophosphamide, respectively), with rates of approximately 25 and 28 per 100 patient-years, respectively. The most common serious infection was pneumonia.

*Hypogammaglobulinemia:* Hypogammaglobulinemia (IgA, IgG, or IgM below the lower limit of normal) has been observed in patients with GPA and MPA treated with Rituxan in GPA/MPA Study 1. At 6 months, in the Rituxan group, 27%, 58%, and 51% of patients with normal immunoglobulin levels at baseline had low IgA, IgG, and IgM levels, respectively, compared to 25%, 50%, and 46% in cyclophosphamide group.



***Treatment of Patients with GPA/MPA who have Achieved Disease Control with Induction Treatment (GPA/MPA Study 2)***

In GPA/MPA Study 2, the safety profile was consistent with the known safety profile of Rituxan in immunologic indications.

*Infusion-Related Reactions:* In GPA/MPA Study 2, 7/57 (12%) patients in the EU-approved rituximab arm reported infusion-related reactions. The incidence of IRR symptoms was highest during or after the first infusion (9%) and decreased with subsequent infusions (<4%). One patient had two serious IRRs, two IRRs led to a dose modification, and no IRRs were severe, fatal, or led to withdrawal from the study.

*Infections:* In GPA/MPA Study 2, 30/57 (53%) patients in the EU-approved rituximab arm and 33/58 (57%) in the azathioprine arm reported infections. The incidence of all grade infections was similar between the arms. The incidence of serious infections was similar in both arms (12%). The most commonly reported serious infection in the group was mild or moderate bronchitis.

***Treatment of Pediatric Patients with GPA/MPA (GPA/MPA Study 4)***

The safety profile in pediatric GPA and MPA patients was consistent in type, nature and severity with the known safety profile of Rituxan in adult patients with FDA-approved immunological indications.

*Infusion-Related Reactions*

In GPA/MPA Study 4, the proportion of patients experiencing an IRR was 32%, 20%, 12%, and 8% following the first, second, third, and fourth infusions, respectively. The observed symptoms of IRRs were similar to those in adult GPA and MPA patients treated with Rituxan. *[see Warning and Precautions (5.1)].*

*Serious Infections*

In GPA/MPA Study 4, serious infections were reported in 7 patients (28%), and included influenza (2 patients [8%]) and lower respiratory tract infection (2 patients [8%]) as the most frequently reported events.

*Hypogammaglobulinemia*

Hypogammaglobulinemia (IgG or IgM below the lower limit of normal), including prolonged hypogammaglobulinemia (defined as Ig levels below lower limit of normal for at least 4 months) was observed in GPA/MPA Study 4. During the overall study period, 18/25 patients (72%) had prolonged low IgG levels, including 15 patients who also had prolonged low IgM. Three patients received treatment with intravenous immunoglobulin

## Immunogenicity

A total of 23/99 (23%) Rituxan-treated patients with GPA or MPA tested positive for anti-rituximab antibodies by 18 months in GPA/MPA Study 1. The clinical relevance of anti-rituximab antibody formation in Rituxan-treated patients is unclear. In GPA/MPA Study 4, a total of 4/21 (19%) Rituxan-treated pediatric patients with GPA and MPA developed anti-rituximab antibodies during the overall study period (assessed at Month 18).

## Clinical Trials Experience in Pemphigus Vulgaris (PV)

Adverse reactions reported in ≥10% of patients treated with the Ritux 3 regimen* vs patients treated with prednisone monotherapy were infusion-related reactions (58% vs N/A), depression (18% vs 11%), herpes simplex (13% vs 3%), and alopecia (13% vs 0%).

*Infusion-Related Reactions*

Infusion-related reactions were the most commonly reported adverse drug reactions (58%) with the Ritux 3 regimen. All infusion-related reactions were mild to moderate (Grade 1 or 2) except one Grade 3 serious infusion-related reaction (arthralgia) associated with the Month 12 maintenance infusion. No patients were withdrawn from treatment due to infusion-related reactions.



*Infections*

Fourteen patients (37%) treated with the Ritux 3 regimen experienced treatment-related infections compared to 15 patients (42%) treated with prednisone monotherapy. The most common infections in the patients treated with the Ritux 3 regimen were herpes simplex, herpes zoster, bronchitis, urinary tract infection, fungal infection, and conjunctivitis. Three patients (8%) treated with the Ritux 3 regimen experienced a total of 5 serious infections and 1 patient (3%) treated with prednisone monotherapy experienced 1 serious infection.

## Immunogenicity

Using a new ELISA assay, a total of 19/34 (56%) patients with PV treated with the Ritux 3 regimen tested positive for anti-rituximab antibodies by 18 months. The clinical relevance of anti-rituximab antibody formation in Rituxan treated PV patients is unclear.

## Additional Important Safety Information

## Lactation

Advise women not to breastfeed during treatment with Rituxan and for 6 months after the last dose due to the potential for serious adverse reactions in breastfed children.

**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**.

*Ritux 3 regimen = Roche-manufactured, EU-approved rituximab product
EU = European Union

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

Rituxan®
Rituximab

# Rituxan®

## Rituximab

## BOXED WARNINGS

**Infusion-Related Reactions: Rituxan administration can result in serious, including fatal infusion-related 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-related 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.

Please see the Rituxan full Prescribing Information and pages 24-31 for **BOXED WARNINGS** and additional Important Safety Information.

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