MADISON NEUROLOGY LLC

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*Neurology Care 7 days a Week. Because Your Brain Matters.*

# Rituxan® / biosimilars

Rituximab

COMPLETE CLINICAL PROTOCOL: PRE-TREATMENT CHECKLIST • ORDER SET • FOLLOW-UP • HOLD/DISCONTINUE CRITERIA

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| **GENERIC NAME** | rituximab |
| **BRAND** | RITUXAN® / biosimilars |
| **MEDICATION CLASS** | Anti-CD20 monoclonal antibody (OFF-LABEL for neurologic indications) |
| **PRESENTATION** | 100 mg/10 mL and 500 mg/50 mL vials; multiple biosimilars (rituximab-abbs, -pvvr, -arrx) — confirm the exact product on the order |
| **ROUTE** | IV infusion only; never IV push or bolus |
| **US INDICATION (FDA)** | OFF-LABEL in neurology: relapsing MS, NMOSD, myasthenia gravis (especially MuSK-antibody positive), autoimmune encephalitis, and other antibody-mediated neurologic disease. FDA-labeled uses are hematologic, rheumatologic, and vasculitic. |

**Class context.**
Off-label status shapes the workflow: payer prior authorization usually requires documented failure/contraindication of labeled alternatives, and informed consent should name the off-label use explicitly. Boxed warnings: fatal infusion reactions, severe mucocutaneous reactions, HBV reactivation, PML.

## Section 1 — Pre-Treatment Checklist

### A. Required screening labs

☐ HBV panel: HBsAg and anti-HBc — REQUIRED before the first dose (boxed warning: reactivation, including fulminant hepatitis). Positive/carrier: hepatology consult and antiviral prophylaxis per specialist before dosing.

☐ Quantitative immunoglobulins (IgG, IgA, IgM) at baseline and periodically — hypogammaglobulinemia accumulates with repeated courses and is the main long-term toxicity of chronic anti-CD20 maintenance.

☐ CBC with differential — baseline; late-onset neutropenia (weeks to months post-dose) is a labeled phenomenon.

- ☐ Baseline CD19/CD20 B-cell count — enables repletion-guided redosing strategies.
- ☐ Pregnancy test for females of reproductive potential.
- ☐ Cardiac history review — infusion reactions can be cardiorespiratory; severe active cardiac disease needs cardiology input first.

### B. Vaccinations

- ☐ Live vaccines: NOT recommended during treatment or until B-cell recovery; complete ≥4 weeks before the first dose.
- ☐ Non-live vaccines: complete ≥2–4 weeks before the first dose when possible; responses under depletion are blunted.
- ☐ Infants exposed in utero: defer live vaccines until the infant's B-cell recovery is confirmed.

### C. Clinical assessments & counseling

- ☐ Document the neurologic indication, prior therapies, and the off-label rationale; obtain explicit informed consent.
- ☐ Baseline disease-specific severity measure (EDSS, MG-ADL, mRS, cognitive/behavioral scale).
- ☐ Active-infection screen before every dose.

### D. Exclusion / hold criteria — do not start

| CRITERION | RATIONALE / REQUIRED ACTION |
|---|---|
| Active HBV or other serious active infection | Do not dose; treat/refer first. |
| Severe (grade 3–4) prior infusion reaction to rituximab | Rechallenge only under a specialist desensitization protocol. |
| Severe active heart failure or unstable arrhythmia | Cardiology clearance before dosing. |
| Live vaccine within 4 weeks | Defer. |

## Section 2 — Order Set

### Premedication

- ☐ Methylprednisolone 100 mg IV (or equivalent) ~30 minutes before each infusion — standard for neuro dosing regimens.
- ☐ Diphenhydramine 25–50 mg PO/IV ~30–60 minutes before each infusion.
- ☐ Acetaminophen 650 mg PO ~30 minutes before each infusion.

### Dosing schedule

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| **Induction (common neuro practice)** | 1,000 mg IV on day 1 and day 15. Alternative: 375 mg/m² weekly × 4 weeks. |
| **Maintenance** | 1,000 mg IV every 6 months, OR redose on CD19+ B-cell repletion + clinical course (repletion-guided maintenance reduces cumulative exposure). |
| **Rate — first infusion** | Start 50 mg/hr; increase 50 mg/hr every 30 minutes to a maximum 400 mg/hr as tolerated. |

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| **Rate — subsequent infusions** | Start 100 mg/hr; increase 100 mg/hr every 30 minutes to a maximum 400 mg/hr if prior doses were tolerated. |
| **Infusion-reaction management** | Interrupt for mild–moderate reactions; resume at half rate when resolved. Grade 4: discontinue permanently. |

### Standing orders — every infusion

- ☐ Infection screen and vital signs (baseline, each rate change, completion) every dose.
- ☐ Pregnancy test before each course for females of reproductive potential.
- ☐ Confirm product/biosimilar identity matches the order before compounding.

### Missed or delayed dose

Redose as soon as feasible after a delayed cycle; reconfirm the infection screen and (if used) the CD19+ count before dosing.

### Contraception & pregnancy

Effective contraception during treatment and for 12 months after the last dose (labeled interval for on-label uses; apply the same for off-label neuro use).

## Section 3 — Follow-Up Protocol

| ITEM | FREQUENCY / TIMING | ACTION / THRESHOLD |
|---|---|---|
| Quantitative immunoglobulins | Every 6–12 months during repeated courses | Falling IgG with recurrent/serious infections → immunology; consider extending interval, switching mechanism, or IVIG supplementation (specialist decision). |
| CD19+ B-cell count | Before each redose if using repletion-guided maintenance | Undetectable B cells + clinically stable → may defer redose; repletion → dose. |
| CBC with differential | Periodically; include a check ~1–3 months post-course | Late-onset neutropenia → hold further dosing until recovered. |
| Infection screen | Before every dose | Hold for active infection. |
| MRI / disease-specific surveillance | Per underlying condition | New progressive deficit in an MS/NMOSD patient → urgent PML-protocol MRI before further dosing. |

## Section 4 — Pause vs. Stop Criteria

### A. Pause or delay (resume when resolved)

| CRITERION | REQUIRED ACTION |
|---|---|
| Active infection | Hold until resolved. |

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| Significant hypogammaglobulinemia with recurrent infections | Delay redosing; immunology review. |
| Recent live vaccine (<4 weeks) | Defer. |
| Late-onset neutropenia | Hold until count recovery. |

### B. Discontinue permanently

| CRITERION | REQUIRED ACTION |
|---|---|
| PML — suspected or confirmed | Discontinue permanently (boxed-warning class event). |
| HBV reactivation | Discontinue; hepatology treatment. |
| Severe mucocutaneous reaction (SJS/TEN) or grade 4 infusion reaction | Discontinue permanently. |
| Sustained severe hypogammaglobulinemia with serious infections | Transition off anti-CD20 maintenance (specialist decision). |

## Section 5 — Notes & Practical Points

- ☐ Long-term rituximab in neurology is usually well tolerated, but the two slow-burn problems are hypogammaglobulinemia and blunted vaccine responses — both need calendar-based monitoring, not symptom-based monitoring.
- ☐ Repletion-guided (CD19+) maintenance is the emerging standard for reducing cumulative exposure in stable patients; document whichever strategy the prescriber has chosen.

**Prepared November 2026 by Madison Neurology LLC.**

This document is an educational compilation and does not reproduce the complete prescribing information. Verify every element against the current FDA label and applicable REMS requirements before clinical use.

- Current U.S. prescribing information via NIH DailyMed — https://dailymed.nlm.nih.gov/dailymed/
- FDA Drugs@FDA database — https://www.accessdata.fda.gov/scripts/cder/daf/
- FDA drug safety and availability updates — https://www.fda.gov/drugs/drug-safety-and-availability

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Questions about infusion referrals: call 608 403 0000. Neurology Care 7 days a Week. Because Your Brain Matters.