RITUXIMAB

**Therapeutics**

**Brands**
- Rituxan, MabThera

**Generic?**
No

**Class**
- Immunosuppressant, immunomodulator, monoclonal antibody

**Commonly Prescribed for**
(FDA approved in bold)
- B-cell non-Hodgkin lymphoma (NHL)
- Rheumatoid arthritis
- Myasthenia gravis (MG)
- Multiple sclerosis (MS) (relapsing-remitting)
- Multifocal motor neuropathy
- Anti-myelin-associated glycoprotein (MAG) neuropathy
- Chronic inflammatory demyelinating polyneuropathy (CIDP)
- Neuromyelitis optica
- Dermatomyositis
- Opsoclonus myoclonus
- Sarcoïdosis
- Chronic lymphocytic leukemia
- Waldenstrom macroglobulinemia
- Thrombocytopenic purpura

**How the Drug Works**
- Binds to the CD 20 antigen on pre-B and mature B lymphocytes, inducing apoptosis. The antigen is expressed in greater than 90% of B-cell NHL but not on stem cells, pro-B-cells, plasma cells or normal tissues. B-cells are felt to be important in the pathogenesis of rheumatoid arthritis, MS, MG, and many other autoimmune diseases
- Rituximab may also decrease other biologic markers of inflammation, such as c-reactive protein, serum amyloid protein, and rheumatoid factor

**How Long Until It Works**
- By 2 weeks, but effect on disease may take months

**If It Works**
- May allow reduction in dose or discontinuation of steroids or other agents in the treatment of MG, MS, or other neurological conditions

**If It Doesn’t Work**
- Usually used as an adjunctive agent in conjunction with steroids or other agents in MG, but other agents such as azathioprine, mycophenolate mofetil, and cyclosporine are often used instead. In MS, used as an alternative to other agents for refractory relapsing-remitting patients

**Best Augmenting Combos for Partial Response or Treatment-Resistance**
- Often combined with prednisone or other steroids for treatment of MG, allowing eventual decrease in dose. Occasionally combined with other immunosuppressive agents for many autoimmune diseases, but AEs may increase

**Tests**
- Obtain complete blood counts before beginning and during therapy, more frequently if patient develops cytopenia

**Adverse Effects (AEs)**

**How Drug Causes AEs**
- Serious AEs are related to infusion reactions, immunosuppression, and lymphopenia

**Notable AEs**
- Infusion reactions in 32% usually take place with the first infusion and may include fever, chills, angioedema, bronchospasm, or blood pressure changes. Infection (mostly respiratory tract infections) fever, chills, weakness, itching, headache, and dyspepsia

**Life-Threatening or Dangerous AEs**
- Not uncommon: Severe lymphopenia lasting a few weeks, occurs in about 40% of patients. Neutropenia, leukopenia, and anemia are less common. Reactivation of hepatitis B. Severe mucocutaneous reactions, including Stevens-Johnson syndrome. Severe infection or sepsis. Tumor lysis syndrome
- Rare: JC virus infection leading to progressive multifocal leukoencephalopathy. Bowel obstruction and perforation
DOSING AND USE

Usual Dosage Range
• 375 mg/m² once weekly for 4–8 doses

Dosage Forms
• Injection: 10 mg/mL

How to Dose
• In most cases, given once weekly for 4–8 weeks. Start infusion at a lower rate 50 mg/h and increase by rate of 50 mg/h every 30 minutes to a maximum of 400 mg/h. If tolerated, start at 100 mg/h during subsequent treatments

Dosing Tips
• Do not mix with other drugs. Infusion should be given by staff familiar with potential AEs

Overdose
• Unknown

Long-Term Use
• Usually used on a short-term basis for refractory disorders

Habit Forming
• No

SPECIAL POPULATIONS

Renal Impairment
• No contraindications, but rituximab can cause renal toxicity. Use with caution in patients with preexisting renal disease

Hepatic Impairment
• No known effects

Cardiac Impairment
• No known effects

Elderly
• Older patients with B-cell lymphomas were more likely to experience supraventricular arrhythmias and pulmonary reactions on rituximab

Children and Adolescents
• Effectiveness and safety are unknown

Pregnancy
• Category C. Do not use in individuals considering pregnancy. Use contraception during and 12 months after treatment

Drug Interactions
• Combining with cisplatin causes renal toxicity
• Use with immunosuppressant agents requires close monitoring for infection or other AEs

Do Not Use
• Known hypersensitivity to the drug or its components

Weight Gain
• Unusual

Sedation
• Unusual

What to Do About AEs
• Give slowly or stop infusion for serious AEs. Treat infections appropriately

Best Augmenting Agents for AEs
• For infusion reactions, pretreat with acetaminophen and antihistamines. Pretreatment with IV glucocorticoids may also help

How to Stop
• No need to taper, but monitor for recurrence of neurological disorder

Pharmacokinetics
• B-cells rapidly decrease after administration and peripheral B-lymphocytes are nearly depleted by 2 weeks. Most patients continue to have B-cell depletion for 6 months, but most have normal B-cell levels 1 year after treatment

RITUXIMAB
Breast Feeding

- Discontinue until drug levels are not detectable

The Art of Neuropharmacology

Potential Advantages

- Mechanism of action different than most immunosuppressive agents for neurological disorders

Potential Disadvantages

- Not a first-line agent in any neurological disorder due to lack of proven efficacy and serious AEs

Primary Target Symptoms

- Preventive treatment of complications from diseases such as MG or MS

Pearls

- There are several case reports describing the use of rituximab in refractory MG, including those with MuSK antibodies. Its actions on B cells distinguish rituximab from other agents that act on the cell cycle inhibiting production of B and T lymphocytes (azathioprine, cyclophosphamide, methotrexate, and mycophenolate mofetil)

- or immunosuppression of T-cells (cyclosporine and tacrolimus). The relative efficacy of rituximab compared to other agents is unknown
- Less proven in MS as compared to natalizumab, another monoclonal antibody. It is unknown if other monoclonal antibodies, such as alemtuzumab and daclizumab, are effective. There is an active clinical trial underway looking into the efficacy of rituximab in MS
- In a small study of 16 children with opsoclonus myoclonus and an increased percentage of CD20 B-cells in CSF, 4 infusions of rituximab 375 mg/m² were given in combination with ACTH or immunoglobulins. Treatment allowed reduction in ACTH dose with few relapses
- Open-label studies demonstrate effectiveness in the treatment of immune-mediated neuropathies, such as multifocal motor and vasculitic neuropathies. In anti-MAG neuropathy, treatment improved clinical symptoms, electrophysiological findings, and anti-MAG antibody titers
- Studies of rituximab for the treatment of chronic inflammatory demyelinating polyneuropathy show mixed results
- Case reports indicate usefulness in the treatment of anti-N-methyl-D-aspartate (NMDA) encephalitis, a rare autoimmune, usually paraneoplastic, disease

Suggested Reading


