

RITUXIMAB

CLASS: Antineoplastic Agent, Monoclonal Antibody; Antirheumatic, Miscellaneous; Immunosuppressant Agent; Monoclonal Antibody

INDICATIONS:

Treatment of CD20-positive non-Hodgkin lymphomas (NHL):

- Relapsed or refractory, low-grade or follicular B-cell NHL (as a single agent)
- Follicular B-cell NHL, previously untreated (in combination with first-line chemotherapy, and as single-agent maintenance therapy if response to first-line rituximab with chemotherapy)
- Nonprogressing, low-grade B-cell NHL (as a single agent after first-line CVP treatment)
- Diffuse large B-cell NHL, previously untreated (in combination with CHOP chemotherapy [or other anthracycline-based regimen])
- Treatment of CD20-positive chronic lymphocytic leukemia (CLL) (in combination with fludarabine and cyclophosphamide)
- Treatment of moderately- to severely-active rheumatoid arthritis (in combination with methotrexate) in adult patients with inadequate response to one or more TNF antagonists
- Treatment of granulomatosis with polyangiitis (GPA; Wegener's granulomatosis) (in combination with glucocorticoids)
- Treatment of microscopic polyangiitis (MPA) (in combination with glucocorticoids)

AVAILABLE DOSAGE FROM THE HOSPITAL:

RITUXIMAB 100MG/10ML VIAL, RITUXIMAB 500MG/50ML VIAL

DOSAGE:**Note:** Details concerning dosing in combination regimens should also be consulted. Pretreatment with acetaminophen and an antihistamine is recommended for all indications. For oncology uses, a uricostatic agent (eg, allopurinol) and aggressive hydration is recommended for patients at risk for tumor lysis syndrome (high tumor burden or lymphocytes $>25,000/\text{mm}^3$). In patients with CLL, *Pneumocystis jirovecii* pneumonia (PCP) and antiherpetic viral prophylaxis is recommended during treatment (and for up to 12 months following treatment). In patients with granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA), PCP prophylaxis is recommended during and for 6 months after rituximab treatment. For patients with RA, premedication with methylprednisolone 100 mg I.V. (or equivalent) is recommended 30 minutes prior to each dose.

-Chronic lymphocytic leukemia (CLL): I.V. infusion: 375 mg/m² on the day prior to fludarabine/cyclophosphamide in cycle 1, then 500 mg/m² on day 1 (every 28 days) of cycles 2-6

-Granulomatosis with polyangiitis (GPA; Wegener's granulomatosis): I.V. infusion: 375 mg/m² once weekly for 4 doses (in combination with methylprednisolone I.V. for 1-3 days followed by daily prednisone)

-Non-Hodgkin lymphoma (NHL; relapsed/refractory, low-grade or follicular CD20-positive, B-cell): I.V. infusion: 375 mg/m² once weekly for 4 or 8 doses

Retreatment following disease progression: 375 mg/m² once weekly for 4 doses

-NHL (diffuse large B-cell): I.V. infusion: 375 mg/m² given on day 1 of each chemotherapy cycle for up to 8 doses

-NHL (follicular, CD20-positive, B-cell, previously untreated): I.V. infusion: 375 mg/m² given on day 1 of each chemotherapy cycle for up to 8 doses

-Maintenance therapy (as a single agent, in patients with partial or complete response to rituximab plus chemotherapy; begin 8 weeks after completion of combination chemotherapy): I.V. infusion: 375 mg/m² every 8 weeks for 12 doses

-NHL (nonprogressing, low-grade, CD20-positive, B-cell, after 6-8 cycles of first line CVP are completed): I.V. infusion: 375 mg/m² once weekly for 4 doses every 6 months for a maximum of 16 doses

-NHL: Combination therapy with ibritumomab: I.V. infusion: 250 mg/m² I.V. day 1; repeat in 7-9 days with ibritumomab (also see Ibritumomab monograph)

-Canadian labeling: NHL, low grade or follicular: I.V. infusion:

- Initial: 375 mg/m² once weekly for 4 doses (as a single agent) **or** 375 mg/m² on day 1 of each 21-day cycle for 8 cycles (in combination with CVP chemotherapy)
- Maintenance (responding to induction therapy): 375 mg/m² every 3 months until disease progression or up to a maximum of 2 years

-Rheumatoid arthritis: I.V. infusion: 1000 mg on days 1 and 15 in combination with methotrexate; subsequent courses may be administered every 24 weeks (based on clinical evaluation), if necessary may be repeated no sooner than every 16 weeks

-Microscopic polyangiitis (MPA): I.V. infusion: 375 mg/m² once weekly for 4 doses (in combination with methylprednisolone I.V. for 1-3 days followed by daily prednisone)

-Chronic graft-versus-host disease (GVHD), refractory (unlabeled use): I.V. infusion: 375 mg/m² once weekly for 4 doses (Cutler, 2006)

-Chronic immune thrombocytopenia (ITP; unlabeled use): I.V. infusion: 375 mg/m² once weekly for 4 doses (Arnold, 2007; Godeau, 2008)

-Hodgkin's lymphoma (unlabeled use): I.V. infusion: 375 mg/m² once weekly for 4 weeks (Ekstrand, 2003; Schulz, 2008)

-Idiopathic membranous nephropathy (IMN), resistant (unlabeled use): I.V. infusion: 375 mg/m² once weekly for 4 doses with retreatment at 6 months (Fervenza, 2010) **or** 1000 mg on days 1 and 15 (Fervenza, 2008) **or** 375 mg/m² single doses titrated to B cell response (Cravedi, 2007)

-Lupus nephritis, refractory (unlabeled use): I.V. infusion: 375 mg/m² once weekly for 4 doses (Melander, 2009) **or** 500-1000 mg on days 1 and 15 (Vigna-Perez, 2006)

-Pemphigus vulgaris, refractory (unlabeled use): I.V. infusion: 375 mg/m² once weekly of weeks 1, 2, and 3 of a 4-week cycle, repeat for 1 additional cycle, then 1 dose per month for 4 months (total of 10 doses in 6 months) (Ahmed, 2006)

-Post-transplant lymphoproliferative disorder (unlabeled use): I.V. infusion: 375 mg/m² once weekly for 4 doses (Choquet, 2006)

-Thrombotic thrombocytopenic purpura (TTP), relapsed/refractory (unlabeled use): I.V. infusion: 375 mg/m² once weekly for 4 doses (Scully, 2007; Scully, 2011)

-Waldenström's macroglobulinemia (unlabeled use): I.V. infusion: 375 mg/m² once weekly for 4 weeks (Dimopoulos, 2002)

Geriatric:

Refer to adult dosing.

COMMON SIDE EFFECT:

- Cardiovascular: Peripheral edema (8% to 16%), hypertension (6% to 12%)
- Central nervous system: Fever (5% to 53%), fatigue (13% to 39%), chills (3% to 33%), headache (17% to 19%), insomnia (≤14%), pain (12%)
- Dermatologic: Rash (10% to 17%; grades 3/4: 1%), pruritus (5% to 17%), angioedema (11%; grades 3/4: 1%)
- Gastrointestinal: Nausea (8% to 23%), diarrhea (10% to 17%), abdominal pain (2% to 14%), weight gain (11%)
- Hematologic: Cytopenias (grades 3/4: ≤48%; may be prolonged), lymphopenia (48%; grades 3/4: 40%; median duration 14 days), anemia (8% to 35%; grades 3/4: 3%), leukopenia (NHL: 14%; grades 3/4: 4%; CLL: grades 3/4: 23%; GPA/MPA: 10%), neutropenia (NHL: 14%; grades 3/4: 4% to 6%; median duration 13 days; CLL: grades 3/4: 30% to 49%), neutropenic fever (CLL: grades 3/4: 9% to 15%), thrombocytopenia (12%; grades 3/4: 2% to 11%)
- Hepatic: ALT increased (≤13%)
- Neuromuscular & skeletal: Neuropathy (≤30%), weakness (2% to 26%), muscle spasm (≤17%), arthralgia (6% to 13%)
- Respiratory: Cough (13%), rhinitis (3% to 12%), epistaxis (≤11%)
- Miscellaneous: Infusion-related reactions (lymphoma: first dose 77%; decreases with subsequent infusions; may include angioedema, bronchospasm, chills, dizziness, fever, headache, hyper-/hypotension, myalgia, nausea, pruritus, rash, rigors, urticaria, and vomiting; reactions reported are lower [first infusion: 32%] in RA; CLL: 59%; grades 3/4: 7% to 9%; GPA/MPA: 12%); infection (19% to 62%; grades 3/4: 4%; bacterial: 19%; viral 10%; fungal: 1%), human antichimeric antibody (HACA) positive (1% to 23%), night sweats (15%)

PREGNANCY RISK FACTORS: C