OVERVIEW
Rituxan is a chimeric murine/human monoclonal antibody directed specifically against the CD20 antigen found on the surface of normal and malignant B lymphocytes.

Rituxan is indicated for the following uses:
1. in combination with methotrexate (MTX), for the treatment of adult patients with moderately to severely active RA who have had an inadequate response to one or more tumor necrosis factor (TNF) antagonist therapies; AND
2. treatment of relapsed or refractory, low-grade or follicular, CD20-positive, B-cell, NHL\(^1\); AND
3. for previously untreated follicular, CD20-positive, B-cell NHL in combination with first-line chemotherapy, and in patients achieving a complete or partial response to Rituxan in combination with chemotherapy, as a single-agent maintenance therapy; AND
4. treatment of non-progressing (including stable disease) low-grade, CD20-positive, B-cell NHL as a single agent after first-line cyclophosphamide/vincristine/prednisone (CVP) chemotherapy; AND
5. treatment of previously untreated diffuse large B-cell, CD20-positive NHL in combination with cyclophosphamide/doxorubicin/vincristine/prednisone (CHOP) or other anthracycline-based chemotherapy regimens; AND
6. in combination with fludarabine and cyclophosphamide (FC) for the treatment of patients with previously untreated and previously treated CD20-positive chronic lymphocytic leukemia (CLL); AND
7. treatment of adults with Wegener’s Granulomatosis and Microscopic Polyangiitis in combination with glucocorticoids.

POLICY STATEMENT
Drug(s) in this policy also follow the Inflammatory Conditions preferred step therapy requirements for Rheumatoid Arthritis.

RECOMMENDED AUTHORIZATION CRITERIA
Coverage of rituximab is recommended in those who meet the following criteria:

1. **Autobodies to Neutrophil Cytoplasmic Antigens (ANCA)-Associated Vasculitis.**

   **Criteria.** *Patient must meet the following criteria (a, b, and c):*
   a) Rituxan is prescribed by or in consultation with an rheumatologist, nephrologist, or immunologist; AND
   b) The patient has an ANCA-associated vasculotide (e.g., granulomatosis with polyangiitis [GPA] {Wegener’s granulomatosis (WG)}, or microscopic polyangiitis [MPA]); AND
   c) Rituxan is being administered in combination with glucocorticoids.
Dosing in ANCA-Associated Vasculitis. Dosing must meet the following: 375 mg/m² IV once weekly.

Initial Approval/Extended Approval.
Initial Approval. Approve for 1 month.
Extended Approval. Approve for an additional 1 month of therapy if 6 months or greater have elapsed since the first dose of the previous Rituxan regimen; and the patient is experiencing a beneficial response as stated by the prescriber.

2. Chronic Lymphocytic Leukemia (CLL) or Small Lymphocytic Lymphoma (SLL).

Criteria. The patient must meet the following criteria:
a) Rituxan is prescribed by or in consultation with an oncologist or hematologist.

Dosing in CLL/SLL.
a) Dose must meet ONE of the following:
i. 375 mg/m² as an IV infusion, then 500 mg/m² on Day 1 of Cycles 2 through 6; OR
ii. 375 mg/m² as an IV infusion on Day 1 of each chemotherapy cycle.

Approval. Approve 1 year.

3. B-Cell Lymphoma (e.g., Follicular Lymphoma, Diffuse Large B-Cell Lymphoma [DLBCL], Acquired Immune Deficiency [AIDS]-Related B-Cell Lymphoma, Burkitt Lymphoma, Castleman’s Disease, Marginal Zone Lymphoma [e.g., extranodal or MALT {gastric or nongastric}, nodal, or splenic marginal zone lymphoma], Mantle Cell Lymphoma, Post-Transplant Lymphoproliferative Disorders, Gray Zone Lymphoma).

Criteria. The patient must meet the following criterion: Rituxan is prescribed by or in consultation with an oncologist or hematologist.

Dosing in B-Cell Lymphoma. Dosing must meet ONE of the following (a OR b):
a) Initial Treatment or Retreatment: Dose must meet ONE of the following:
i. 375 mg/m² as an intravenous infusion given once weekly; OR
ii. 375 mg/m² as an IV infusion on Day 1 of each chemotherapy cycle; OR
iii. If administered with Zevalin: 250 mg/m² as an IV infusion on Day 1 and then repeat the dose on Day 7, 8, or 9.
b) Maintenance Treatment: Patient must meet ONE of the following:
i. 375 mg/m² as an IV infusion every 8 weeks; OR
ii. 375 mg/m² as an IV infusion every 12 weeks;
iii. 375 mg/m² as an IV infusion once weekly for 4 weeks (repeated at 6-month intervals); OR
iv. 375 mg/m² as an IV infusion once weekly repeated monthly.

Approval: Approve 1 year.

4. Rheumatoid Arthritis (RA) in an Adult.

Criteria. Patient must meet the following criteria (A AND B):
A) The patient has tried ONE conventional synthetic disease-modifying antirheumatic drug (DMARD) for at least 3 months (e.g., methotrexate [oral or injectable], leflunomide, hydroxychloroquine, and sulfasalazine).

(NOTE: An exception to the requirement for a trial of one conventional synthetic DMARD can be made if the patient has already has a 3-month trial at least one biologic disease-modifying antirheumatic drug (DMARD) [e.g., Cimzia, Humira, Remicade, Simponi {Aria or SC}, Actemra {IV or SC}, Kineret, Orencia {IV or SC}, and Rituxan]. These patients who have already tried a biologic for RA are not required to “step back” and try a conventional synthetic DMARD); AND

B) Rituxan is prescribed by or in consultation with a rheumatologist.

**Dosing in RA in an Adult.** Dosing must meet ONE of the following (a OR b):

a) Two 1,000-mg IV infusions separated by 2 weeks; OR

b) Two 500-mg IV infusions separated by 2 weeks.

**Initial Approval:** Approve 4 months.

**Extended Approval:** Approve for an additional 4 months if at least 16 weeks since the last dose has occurred.

5. **Graft-Versus-Host Disease (GVHD).**

**Criteria.** Patient must meet the following criteria (A AND B):

A) Rituxan is prescribed by or in consultation with an oncologist, hematologist, or a physician affiliated with a transplant center; AND

B) The patient meets ONE of the following conditions (i or ii):

i. The patient has tried one immunosuppressant for graft-versus-host disease (GVHD) [e.g., one corticosteroid such as methylprednisolone, antithymocyte globulin, cyclosporine, Thalomid®, [thalidomide tablets], tacrolimus, mycophenolate mofetil, sirolimus {Rapamune®, generic}, Nipent® {pentostatin infusion], imatinib {Gleevec®, generic}, methotrexate, or Remicade® {infliximab infusion}]; OR

ii. The patient is concurrently receiving at least one of these medications (e.g., one corticosteroid such as methylprednisolone, antithymocyte globulin, cyclosporine, Thalomid, tacrolimus, mycophenolate mofetil, sirolimus, Nipent, imatinib, methotrexate, or Remicade) in combination with Rituxan.

**Dosing in GVHD.** Dosing must meet the following (A, B, OR C):

A) 375 mg/m² IV once weekly; OR

B) 375 mg/m² IV once weekly for 4 doses followed by a similar infusion once monthly or once every 3 months; OR

C) 50 mg/m² once weekly.

**Initial Approval/Extended Approval.**

**Initial Approval.** Approve for 1 month.

**Extended Approval.** Approve for 6 months if the patient is experiencing a beneficial response as stated by the prescriber.

6. **Immune Thrombocytopenia (ITP).**

**Criteria.** Patient must meet the following criteria (a AND b):

a) Rituxan is prescribed by or in consultation with a hematologist; AND
b) The patient has tried one other therapy (e.g., intravenous immunoglobulin [IVIG], anti-D [RHO] immunoglobulin, corticosteroids, splenectomy).

**Dosing in ITP.** *Dosing must meet the following:* 375 mg/m² IV once weekly.

**Initial Approval/Extended Approval.**
*Initial Approval:* Approve 1 month.
*Extended Approval:* Approve for an additional 1 month of therapy if 6 months or greater have elapsed since the first dose of the previous Rituxan regimen; and the patient is experiencing a beneficial response as stated by the prescriber.

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### 7. Multiple Sclerosis.

**Criteria.** *Patient must meet the following criterion (A AND B):*

A) The patient has tried at least ONE other disease-modifying agent for MS (e.g., Ocrevus® [ocrelizumab IV infusion], Avonex [interferon beta-1a for intramuscular [IM] injection], Rebif [interferon beta-1a SC injection], Betaseron [interferon beta-1b SC injection], Extavia [interferon beta-1b SC injection], Copaxone [glatiramer acetate SC injection], Glatopa [glatiramer acetate SC injection], Plegidry [peginterferon beta-1a SC injection], Gilenya [fingolimod capsules], Aubagio [teriflunomide tablets], Tecfidera [dimethyl fumarate delayed-release capsules], Lemtrada [alemtuzumab IV injection], or Zinbryta [daclizumab SC injection]); AND

B) Rituxan IV is prescribed by or in consultation with a physician who specializes in the treatment of MS and/or a neurologist.

**Dosing in MS.** *Dosing must meet the following (A OR B):*

A) Initial dose of 500 mg to 2,000 mg (may be divided into two infusions within 1 month).

B) Repeat doses of 500 mg or 2,000 mg IV (may be divided into two infusions within 1 month) if at least 6 months has elapsed since the previous dose.

**Initial Approval/Extended Approval.**
*Initial Approval/Extended Approval.* Approve for 1 year.

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### 8. Neuromyelitis Optica (NMO).

**Criteria.** *Patient must meet the following criterion (A):*

A) *Induction*
   i. 375 mg/m² IV once weekly for induction; OR
   ii. 1,000 mg infused twice within 2 weeks for induction; OR

A) *Maintenance.*
   i. 375 mg/m² as a single dose; OR
   ii. 1,000 mg infused twice within 2 weeks.
9. Systemic Lupus Erythematous (SLE) [Lupus].

Criteria. Patient must meet the following criteria (a AND b):

a) Rituxan is prescribed by or in consultation with a rheumatologist, nephrologist, or neurologist; AND

b) The patient meets ONE of the following conditions (i or ii)

i. The patient has neuropsychiatric manifestations of SLE AND has tried at least ONE other therapy (e.g., at least one antidepressant, antipsychotic, corticosteroid, immunosuppressant, or plasma exchange); OR

ii. The patient has lupus nephritis AND has tried at least ONE immunosuppressant (e.g., mycophenolate mofetil, cyclophosphamide, azathioprine.).

Dosing in SLE. Approve the requested dose.

Initial Approval/Extended Approval.
Initial Approval. Approve for 1 month.

Extended Approval: Approve for an additional 1 month of therapy if 6 months or greater have elapsed since the first dose of the previous Rituxan regimen; and the patient is experiencing a beneficial response as stated by the prescriber.

10. Patients with another indication that is not listed but is cited in the National Comprehensive Cancer Network (NCCN) guidelines as a category 1, 2A, or 2B recommendation. Prescriber will provide specific diagnosis for documentation. Approve.

Initial Approval/Extended Approval.
Approval. Approve for 1 year.

10. Patient has been Established on Rituxan. Approve if the patient meets the conditions for coverage required for dosing and indication AND the patient is experiencing a beneficial response as stated by the prescriber.

Approval Duration: dependent on indication. See above.

CONDITIONS NOT RECOMMENDED FOR APPROVAL
(Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

1. Concurrent Use with a Biologic Disease-Modifying Antirheumatic Drug (DMARD) or Targeted Synthetic DMARD. Rituxan should not be administered in combination with another biologic agent for an inflammatory condition (e.g., Actemra® [tocilizumab for IV infusion], Kineret® [anakinra for SC injection], Orenica, or a TNF antagonist [Cimzia, Enbrel, Humira, Remicade, Simponi, or Simponi Aria]). Combination therapy with two biologic agents is not recommended due to a higher rate of adverse effects with combinations and lack of additive efficacy. Xeljanz should not be used in combination with biologic DMARDs such as Rituxan. Targeted synthetic DMARDs (e.g., Xeljanz, Otezia) do not have data supporting use in combination with biologic DMARDs. Due to similar safety concerns (i.e., increased risk of AEs) plus lack of evidence of additive efficacy, targeted synthetic DMARDs should not be used in combination with biologic DMARDs such as Rituxan.
Note: This does NOT exclude the use of conventional synthetic DMARDs (e.g., MTX, leflunomide, hydroxychloroquine, and sulfasalazine) in combination with Rituxan.

2. **Current Use with Disease-Modifying Agents Used for Multiple Sclerosis (MS).**
   Rituxan has not been evaluated in combination with other disease-modifying agents used for MS (e.g., Ocrevus, Avonex, Betaseron, Extavia, Rebif, Plegridy, Copaxone, Glatopa, Gilenya, Aubagio, Tecfidera, Tysabri, Lemtrada, or Zinbryta); therefore, safety and efficacy have not been adequately established. The concomitant use of Rituxan IV with other immune-modulating or immunosuppressive therapies is anticipated to increase the risk of immunosuppression.

**References**

- Xeljanz® tablets [prescribing information]. New York, NY: Pfizer Inc; May 2014.