POLICY: Biosimilars - Rituxan
- Rituxan® (rituximab injection for intravenous use – Genentech)
- Riabni™ (rituximab-arrx for intravenous use – Amgen)

EFFECTIVE DATE: 1/1/2020
LAST REVISION DATE: 08/16/2023

COVERAGE CRITERIA FOR: UCare Medicaid and Exchange Plans Only (PMAP, Connect, MSC+, MnCare, all Individual and Family Plans)

OVERVIEW

Rituximab products are CD20-directed cytolytic antibodies. All approved rituximab intravenous products are indicated for treatment of the following conditions:

- **Chronic lymphocytic leukemia** (CLL), in combination with fludarabine and cyclophosphamide (FC) for the treatment of patients with previously untreated and previously treated CD20-positive disease.
- **Granulomatosis with polyangiitis** (Wegener's granulomatosis) and **microscopic polyangiitis** in adults, in combination with glucocorticoids.
- **Non-Hodgkin lymphoma** (NHL), for the following uses:
  - previously untreated follicular, CD20-positive disease, in combination with first-line chemotherapy, and in patients achieving a complete or partial response to rituximab in combination with chemotherapy, as a single-agent maintenance therapy.
  - for relapsed or refractory, low-grade or follicular, CD20-positive, B-cell disease.
  - for non-progressing (including stable disease) low-grade, CD20-positive, B-cell disease as a single agent after first-line cyclophosphamide/vincristine/prednisone (CVP) chemotherapy.
  - for previously untreated diffuse large B-cell, CD20-positive disease, in combination with cyclophosphamide/doxorubicin/vincristine/prednisone (CHOP) or other anthracycline-based chemotherapy regimens.
- **Rheumatoid arthritis**, in adult patients with moderately to severely active disease, in combination with methotrexate for patients who have had an inadequate response to one or more tumor necrosis factor inhibitors (TNFis).

In addition to the above indications, Rituxan intravenous is also indicated for treatment of the following conditions:

- **Granulomatosis with polyangiitis** (Wegener's granulomatosis) and **microscopic polyangiitis** in patients ≥ 2 years of age, in combination with glucocorticoids.
- **Pemphigus vulgaris**, for adults with moderate to severe disease.
- **B-cell lymphoma,** in patients ≥ 6 months of age with previously untreated, advanced stage, CD20-positive diffuse large B-cell lymphoma, Burkitt lymphoma, Burkitt-like lymphoma, or mature B-cell acute leukemia in combination with chemotherapy.

Riabni, Ruxience, and Truxima are approved as biosimilar to Rituxan intravenous, indicating no clinically meaningful differences in safety and effectiveness and the same mechanism of action, route of administration, dosage form, and strength as Rituxan intravenous. However, minor differences in clinically

inactive components are allowed. At this time, the biosimilars have only demonstrated biosimilarity, not interchangeability.

Guidelines

The use of rituximab is supported in clinical guidelines in numerous situations, both as first-line therapy and in patients who are refractory or have relapsed following treatment with other therapies.[4-21]

- **Antineutrophil Cytoplasmic Antibody (ANCA)-Associated Vasculitis:** Guidelines from the American College of Rheumatology (ACR) [2021] list rituximab among the alternatives for induction or maintenance of remission. Various regimens are recommended with a typical maximum of 1,000 mg/infusion. For maintenance dosing, at least 4 months should separate doses. The optimal dose of rituximab for remission maintenance remains uncertain. Although scheduled maintenance is conditionally recommended over use of CD19+ B-cell counts and/or ANCA titers to guide retreatment, there are data to support both approaches.
- **Immune Thrombocytopenia (ITP):** Guidelines from the American Society of Hematology (ASH) for ITP (2019) mention rituximab as an alternative for children and adults with ITP who do not respond to first-line treatment, and for adults who are corticosteroid-dependent.[17]
- **Multiple Sclerosis (MS):** In June 2019, a consensus paper was updated by the MS Coalition that discusses the use of disease-modifying therapies in MS.[18] Rituximab is listed among various options, involving different mechanisms of action and modes of administration, which have shown benefits in patients with MS. The American Academy of Neurology has practice guidelines regarding disease-modifying therapies for adults with MS.[19] The guidelines mention rituximab for use in MS.
- **Neuromyelitis Optica Spectrum Disorders:** A review article lists rituximab as an effective treatment for neuromyelitis optica.[20]
- Oncology indications covered in National Comprehensive Cancer Network (NCCN) guidelines:[6]
  - **Acute Lymphoblastic Leukemia (ALL):** Guidelines (version 2.2023 – July 28, 2023) list rituximab in multiple regimens for Philadelphia chromosome (Ph)-negative disease for patients with CD20-positive disease.[11] In those with Ph-positive disease, rituximab should be considered in addition to chemotherapy for those with CD20-positive disease, especially in those < 60 years of age.
  - **B-Cell Lymphomas:** In the guidelines (version 5.2023 – July 07, 2023), rituximab is included in multiple treatment regimens across the spectrum of disease.[8] Guidelines for pediatric aggressive mature B-cell lymphomas (version 1.2023 – April 04, 2023) include rituximab intravenous as a component of treatment regimens for induction therapy/initial treatment and as subsequent therapy for relapsed or refractory disease.[9] For primary cutaneous lymphomas (version 1.2023 – January 5, 2023), rituximab is a treatment option for patients with primary cutaneous B-cell lymphoma.[10]
  - **CLL/Small Lymphocytic Lymphoma:** Rituximab features prominently in the guidelines (version 3.2023 – June 12, 2023) and is included in multiple treatment regimens across the spectrum of disease.[7]
  - **Graft-Versus-Host Disease (GVHD):** The hematopoietic cell transplantation guidelines (version 1.2023 – March 31, 2023) list rituximab among the agents used for steroid-refractory chronic GVHD.[15]
  - **Hairy Cell Leukemia:** Guidelines (version 1.2023 – August 30, 2022) recommend rituximab as a component in a preferred primary regimen, and in multiple regimens for relapsed/refractory disease (including in patients with progressive disease after relapsed/refractory therapy).[12]
  - **Hodgkin Lymphoma:** Guidelines (version 2.2023 – November 8, 2022) recommend rituximab ± chemotherapy and/or radiation (depending on the clinical presentation) in the first-line setting for nodular lymphocyte-predominant disease.[13] Rituximab is also used for

relapsed/refractory disease and for maintenance. Guidelines for pediatric disease (version 2.2023 – March 9, 2023) include rituximab in regimens for primary treatment of nodular lymphocyte-predominant disease.[25]

- **Primary Central Nervous System Lymphoma:** Guidelines for central nervous system cancers (version 1.2023 – March 24, 2023) recommend rituximab in multiple regimens for induction therapy and relapsed or refractory primary central nervous system lymphoma.[24]
- **Waldenstrom Macroglobulinemia/Lymphoplasmacytic Lymphoma:** Guidelines (version 1.2023 – July 6, 2022) include rituximab in regimens across the spectrum of disease (primary therapy, previously treated disease, and maintenance).[14]

- **Immunotherapy-Related Toxicities Associated with Checkpoint Inhibitors:** NCCN (version 2.2023 – May 9, 2023) and the American Society of Clinical Oncology (ASCO) guidelines (2021) recommend rituximab as an option for corticosteroid-refractory dermatologic and hematologic immune mediated adverse events, as well as for immune-mediated encephalitis and myositis.[26,27]
- **Pemphigus Vulgaris:** British guidelines (2017) list rituximab in combination with corticosteroids as a first-line therapy.[23]
- **Rheumatoid Arthritis:** Guidelines from ACR (2021) recommend addition of a biologic or a targeted synthetic DMARD for a patient taking the maximum tolerated dose of methotrexate who is not at target.[16]
- **Systemic Lupus Erythematosus (SLE):** European League Against Rheumatism (EULAR) recommendations for the management of SLE (2019) mention rituximab as a therapeutic option for patients who are refractory to standard immunosuppressive therapies.[21]

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of rituximab IV products. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indications. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. Because of the specialized skills required for evaluation and diagnosis of patients treated with rituximab products as well as the monitoring required for adverse events and long-term efficacy, initial approval requires rituximab to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Rituxan and Riabni is recommended for requests meeting both the biosimilar step therapy requirements and indication requirements.

Biosimilar Step Therapy Requirements (New Starts Only)

Criteria. *The patient must meet the following criteria (A or B):*

A) For patients new to Rituxan or Riabni therapy only, must have a trial of Truxima or Ruxience prior to approval of Rituxan or Riabni. New starts to therapy defined as no use of the requested product within the past 180 days for Medicaid and Commercial patients.

B) Patient has a contraindication or other clinical reason why a preferred biosimilar cannot be tried before Rituxan or Riabni.

Note: Biosimilar step only required for indications FDA-Approved for both Rituxan and the biosimilar(s).

FDA-Approved Indications

1. **Antineutrophil Cytoplasmic Antibody (ANCA)-Associated Vasculitis.** Approve for the duration noted if the patient meets ONE of the following (A or B):
   A) Induction Treatment. Approve for 1 month if the patient meets ALL of the following (i, ii, and iii):
      i. Patient has an ANCA-associated vasculotide; AND
      ii. Note: Examples of ANCA-associated vasculitis include granulomatosis with polyangiitis (GPA) [Wegener's granulomatosis] or microscopic polyangiitis (MPA).
      iii. The medication is being administered in combination with glucocorticoids; AND
      iv. The medication is prescribed by or in consultation with a rheumatologist, nephrologist, or immunologist.
   B) Follow-Up Treatment of Patients Who Have Received Induction Treatment for ANCA-Associated Vasculitis. Approve for 1 year if the patient meets BOTH of the following (i and ii):
   Note: This includes a patient who received induction treatment using a rituximab product or other standard of care immunosuppressants.
      i. According to the prescriber, the patient achieved disease control with induction treatment; AND
      ii. If the patient previously received a course of therapy, at least 16 weeks will elapse between courses.

   Dosing. Approve one of the following (A or B):
   A) Initial Therapy: Approve one of the following (i or ii):
      i. 375 mg/m^2 per dose administered intravenously for 4 doses separated by at least 7 days; OR
      ii. Up to two 1,000 mg intravenous doses separated by at least 2 weeks.
   B) Follow-Up Treatment of a Patient Who Has Received Induction Treatment for ANCA-Associated Vasculitis: Approve one of the following (i or ii):
      i. ≥ 18 years of age: Up to 1,000 mg administered by intravenous infusion for 6 doses; OR
      ii. < 18 Years of age: Up to 250 mg/m^2 administered by intravenous infusion for 2 doses.

2. **B-Cell Lymphoma.** Approve for 1 year if prescribed by or in consultation with an oncologist.
   Note: Examples of B-cell lymphomas include follicular lymphoma, diffuse large B-cell lymphoma, high-grade B-cell lymphoma, 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), primary mediastinal large B-cell lymphoma, mantle cell lymphoma, post-transplant lymphoproliferative disorders, gray zone lymphoma, primary cutaneous B-cell lymphoma, pediatric aggressive mature B-cell lymphomas.

   Dosing. Approve one of the following regimens (A or B):
   A. Approve up to 375 mg/m^2 per dose administered intravenously with doses separated by at least 7 days; OR
   B. Approve up to 375 mg/kg^2 on two days of each cycle.

3. **Chronic Lymphocytic Leukemia or Small Lymphocytic Lymphoma.** Approve for 1 year if prescribed by or in consultation with an oncologist.

   Dosing. Approve up to 500 mg/m^2 administered as an intravenous infusion on 1 day of each cycle.

4. **Pemphigus Vulgaris.** Approve for the duration noted if the patient meets ONE of the following (A or B):
   a. Initial Treatment. Approve for 1 month (which is adequate duration to administer one course of therapy) if the patient meets BOTH of the following (i and ii):
      i. Therapy is initiated in combination with a corticosteroid unless contraindicated; AND
         Note: An example of a corticosteroid is prednisone.
      ii. The medication is prescribed by or in consultation with a dermatologist.
   b. Patient is Being Treated for a Relapse or for Maintenance of Pemphigus Vulgaris. Approve for 1 year if the patient meets BOTH of the following (i and ii):
      i. Subsequent infusions will be administered no sooner than 16 weeks following the previous infusion of a rituximab product; AND
      ii. The medication is prescribed by or in consultation with a dermatologist.

   Dosing. Approve one of the following (A or B):
   A) Initial Treatment or Treatment of a Relapse. Approve one course of therapy, which consists of up to two 1,000 mg doses administered as an intravenous infusion separated by at least 2 weeks; OR
   B) Maintenance Therapy. Approve up to 500 mg per dose administered intravenously.

5. **Rheumatoid Arthritis.** Approve for the duration noted if the patient meets ONE of the following (A or B):
   A) Initial Therapy. Approve for 1 month (which is adequate duration to administer one course of therapy) if the patient meets ALL of the following conditions (i, ii, and iii):
      i. Patient has tried ONE conventional synthetic disease-modifying antirheumatic drug (DMARD) for at least 3 months; AND
         Note: Examples of conventional synthetic DMARDs include methotrexate [oral or injectable], leflunomide, hydroxychloroquine, and sulfasalazine. An exception to the requirement for a trial of one conventional synthetic DMARD can be made if the patient already has a 3-month trial of at least one biologic other than the requested drug. A biosimilar of the requested biologic does not count. Refer to Appendix A for examples of biologics used for rheumatoid arthritis. A patient who has already tried a biologic is not required to "step back" and try a conventional synthetic DMARD.
      ii. The medication will not be used concurrently with another biologic or with a targeted synthetic DMARD; AND
         Note: Refer to Appendix A for examples of biologics and targeted synthetic DMARDs.
      iii. The medication is prescribed by or in consultation with a rheumatologist.
   B) Patient has already Received One or More Courses of a Rituximab Product for Rheumatoid Arthritis. Approve for 1 month (which is adequate duration to administer one course of therapy) if the patient meets ALL of the following conditions (i, ii, and iii):
      i. 16 weeks or greater will elapse between treatment courses; AND
         Note: For example, there will be a minimum of 16 weeks since the first dose of the previous course and the first dose of the next course of a rituximab product.
      ii. The medication will not be used concurrently with another biologic or with a targeted synthetic DMARD; AND
         Note: Refer to Appendix A for examples of biologics and targeted synthetic DMARDs.
      iii. If the patient has already received two or more courses of therapy, the patient meets at least ONE of the following (a or b):
         a. Patient experienced a beneficial clinical response when assessed by at least one objective measure; OR

Note: Examples of standardized and validated measures of disease activity include Clinical Disease Activity Index (CDAI), Disease Activity Score (DAS) 28 using erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP), Patient Activity Scale (PAS)-II, Rapid Assessment of Patient Index Data 3 (RAPID-3), and/or Simplified Disease Activity Index (SDAI).

b) Patient experienced an improvement in at least one symptom, such as decreased joint pain, morning stiffness, or fatigue; improved function or activities of daily living; decreased soft tissue swelling in joints or tendon sheaths.

Dosing. Approve one course of therapy, which consists of up to two 1,000mg intravenous doses separated by at least 2 weeks.

Other Uses with Supportive Evidence

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6. Acute Lymphoblastic Leukemia. Approve for 1 year if the patient meets BOTH of the following (A and B):

A) Patient has CD20-positive disease; AND

B) The medication is prescribed by or in consultation with an oncologist.

Dosing: Approve up to 375 mg/m^2 administered intravenously with doses separated by at least 7 days.

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7. Graft-Versus-Host Disease. Approve for the duration noted if the patient meets ONE of the following (A or B):

i. Initial Therapy. Approve for 1 month if the patient meets the following (i and ii):

i. Patient has tried at least one conventional systemic treatment for graft versus host disease; AND

Note: Examples include systemic corticosteroids (methylprednisolone, prednisone), cyclosporine, tacrolimus, mycophenolate mofetil, Imbruvica (ibrutinib capsules and tablets), imatinib, antithymocyte globulin, Nipent (pentostatin infusion), or an infliximab product.

ii. The medication is prescribed by or in consultation with an oncologist, hematologist, or a physician affiliated with a transplant center.

ii. Patient has Already Received a Course of a Rituximab Product for Graft-Versus-Host Disease. Approve for 1 year if the patient meets at least ONE of the following (i or ii):

i. When assessed by at least one objective measure, patient experienced a beneficial clinical response from baseline (prior to initiating a rituximab product); OR

Note: An example of objective measures is normalization of liver function tests, red blood cell count, or platelet count, or resolution of fever or rash.

ii. Compared with baseline (prior to initiating a rituximab product), patient experienced an improvement in at least one symptom, such as improvement in skin, oral mucosal, ocular, or gastrointestinal symptoms (e.g., nausea, vomiting, anorexia).

Dosing. Approve up to 375 mg/m^2 administered intravenously with doses separated by at least 7 days.

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8. Hairy Cell Leukemia. Approve for 1 year if the medication is prescribed by or in consultation with an oncologist.

Dosing. Approve up to 375 mg/m^2 administered intravenously with doses separated by at least 7 days.

9. Hodgkin Lymphoma. Approve for 1 year if the patient meets BOTH of the following (A and B):
A) Patient has nodular lymphocyte-predominant disease; AND
B) The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve up to 375 mg/m^2 administered intravenously with doses separated by at least 7 days.

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10. Immune Thrombocytopenia (ITP). Approve if the patient meets ONE of the following (A or B):
A) Initial Therapy. Approve for 1 month if the patient meets BOTH of the following (i and ii):
i. Patient has tried one other therapy; AND
Note: Examples of therapies for ITP include intravenous immunoglobulin (IVIG), anti-D (RHO) immunoglobulin, corticosteroids, and splenectomy.
ii. The agent is prescribed by or in consultation with a hematologist.
B) Patient has Already Received a Course of a Rituximab Product for ITP. Approve for 1 month if the patient meets ALL of the following (i, ii, and iii):
i. At least 6 months will elapse between treatment courses; AND
Note: For example, there will be a minimum of 6 months separating the first dose of the previous course and the first dose of the requested course of a rituximab product.
ii. Patient responded to therapy as determined by the prescriber; AND
Note: Examples of a response include a platelet count increase from baseline following treatment with a rituximab product.
iii. The prescriber has determined that the patient has relapsed.
Note: Examples of a relapse include the patient experiences thrombocytopenia after achievement of a remission.

Dosing. Approve up to 375 mg/m^2 administered intravenously with doses separated by at least 7 days.

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11. Immunotherapy-Related Toxicities Associated with Checkpoint Inhibitors. Approve for the duration noted if the patient meets the following (A or B):
Note: Examples of checkpoint inhibitors are Keytruda (pembrolizumab intravenous infusion), Opdivo (nivolumab intravenous infusion), Yervoy (ipilimumab intravenous infusion), Tecentriq (atezolizumab intravenous infusion), Bavencio (avelumab intravenous infusion), Imfinzi (durvalumab intravenous infusion), and Libtayo (cemiplimab-rwlc intravenous infusion).
A) Initial Therapy. Approve for 1 month if the patient meets BOTH of the following (i and ii):
i. Patient is symptomatic despite a trial of at least ONE systemic corticosteroid; AND
Note: Examples of a corticosteroid include methylprednisolone and prednisone.
ii. The medication is prescribed by or in consultation with an oncologist, neurologist, rheumatologist, or dermatologist.
B) Patient has Already Received a Course of a Rituximab Product. Approve for 1 month if prescribed by or in consultation with an oncologist, neurologist, rheumatologist, or dermatologist.

Dosing. Approve dosing that meets the following (A or B):
A) Approve up to 500 mg/m^2 administered intravenously for 2 doses separated by at least 14 days; OR
B) Approve up to 375 mg/m^2 administered intravenously for 4 doses separated by at least 7 days.

12. Multiple Sclerosis. Approve for 1 year if the patient meets ONE of the following (A or B):

A) Initial Therapy. Approve if the patient meets ALL the following (i, ii, iii, and iv):

i. According to the prescriber, the patient has experienced inadequate efficacy or significant intolerance to at least TWO other disease-modifying agent for multiple sclerosis; AND
Note: See Appendix B for examples of disease-modifying agents used for multiple sclerosis.

ii. Medication will not be used concurrently with another disease-modifying agent used for multiple sclerosis; AND
Note: See Appendix B for examples of disease-modifying agents used for multiple sclerosis.

iii. Medication is prescribed by or in consultation with a neurologist or a physician who specializes in the treatment of multiple sclerosis; AND

iv. At least 6 months will elapse between treatment courses.
Note: For example, if the patient has already received a course of therapy there will be a minimum of 6 months separating the first dose of the previous course and the first dose of the requested course of therapy.

B) Patient is Currently Receiving Rituximab. Approve if the patient meets one of the following (i or ii):

i. Patient has been receiving Rituximab for < 1 year. Approve if the patient meets ALL of the following (a, b, and c):

a. Medication will not be used concurrently with another disease-modifying agent used for multiple sclerosis; AND
Note: See Appendix B for examples of disease-modifying agents used for multiple sclerosis.

b. At least 6 months will elapse between treatment courses; AND
Note: For example, if the patient has already received a course of therapy there will be a minimum of 6 months separating the first dose of the previous course and the first dose of the requested course of therapy.

c. Medication is prescribed by or in consultation with a neurologist or a physician who specializes in the treatment of multiple sclerosis; OR

ii. Patient has been receiving Rituximab for 1 year or more. Approve for 1 year if the patient meets ALL of the following (a, b, c, and d):

a. Medication will not be used concurrently with another disease-modifying agent used for multiple sclerosis; AND
Note: See Appendix B for examples of disease-modifying agents used for multiple sclerosis.

b. At least 6 months will elapse between treatment courses; AND
Note: For example, if the patient has already received a course of therapy there will be a minimum of 6 months separating the first dose of the previous course and the first dose of the requested course of therapy.

c. Patient meets ONE of the following [(1) or (2)]:

1. Patient experienced a beneficial clinical response when assessed by at least one objective measure; OR
Note: Examples include stabilization or reduced worsening in disease activity as evaluated by magnetic resonance imaging (MRI) [absence or a decrease in gadolinium enhancing lesions, decrease in the number of new or enlarging T2 lesions]; stabilization or reduced worsening on the Expanded Disability Status Scale (EDSS) score; achievement in criteria for No Evidence of Disease Activity-3 (NEDA-3) or NEDA-4; improvement on the fatigue symptom and impact questionnaire-relapsing multiple sclerosis (FSIQ-RMS) scale; reduction or absence of relapses; improvement or maintenance on the six-minute walk test or 12-Items Multiple Sclerosis Walking Scale; improvement on the Multiple Sclerosis Functional Composite (MSFC) score; and or attenuation of brain volume loss; OR

2. Patient experienced stabilization, slow progression, or improvement in at least one symptoms such as motor function, fatigue, vision, bowel/bladder function, spasticity, walking/gait, or pain/numbness/tingling sensation; AND

d. Medication is prescribed by or in consultation with a neurologist or a physician who specializes in the treatment of multiple sclerosis.

Dosing. Approve up to 2,000 mg (total) administered as one or two intravenous infusions administered over 1 month.

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13. Neuromyelitis Optica Spectrum Disorder. Approve for 1 month if prescribed by or in consultation with a neurologist.

Dosing. Approve ONE of the following (A or B):

A) Up to 375 mg/m^2 administered intravenously for 4 doses separated by at least 7 days; OR

B) Up to two 1,000 mg doses administered as an intravenous infusion separated by at least 2 weeks.

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14. Primary Central Nervous System Lymphoma. Approve for 1 year if prescribed by or in consultation with an oncologist.

Dosing: Approve up to 375 mg/m^2 administered intravenously with doses separated by at least 7 days.

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15. Systemic Lupus Erythematosus (SLE) [Lupus]. Approve for the duration noted if the patient meets ONE of the following (A or B):

Note: This includes nephrotic syndrome in a patient with SLE.

A) Initial Therapy. Approve for 1 month (adequate duration to receive one course) if the patient meets BOTH of the following (i and ii):

i. Patient has tried at least ONE standard immunomodulating or immunosuppressant agent; AND
Note: Examples of standard immunomodulating or immunosuppressant agents include hydroxychloroquine, corticosteroids (e.g., prednisone, methylprednisolone), methotrexate, azathioprine, mycophenolate, and cyclophosphamide.

ii. The medication is prescribed by or in consultation with a rheumatologist, nephrologist, or neurologist.

B) Patient has Already Received a Course of a Rituximab Product for SLE. Approve for 1 month (adequate duration to receive one course) if 6 months or greater will elapse between treatment courses

Note: There will be a minimum of 6 months separating the first dose of the previous rituximab course and the first dose of the requested course of rituximab.

Dosing. Approve the requested dose.

16. Waldenstrom's Macroglobulinemia/Lymphoplasmacytic Lymphoma. Approve for 1 year if prescribed by or in consultation with an oncologist.

Dosing. Approve up to 375 mg/m^2 administered intravenously with doses separated by at least 7 days.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of rituximab intravenous products is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

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HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	**B-Cell Lymphoma:** High-grade B-cell lymphoma was added as an example of a B-Cell Lymphoma. To align with guidelines, dosing was updated to approve up to two doses per cycle. **Rheumatoid Arthritis:** Note was clarified to state that a previous trial of a biologic applies to one biologic other than the requested drug. A biosimilar of the requested biologic does not count. A requirement was added for a patient who has already received two or more courses of a rituximab product to have at least one objective or subjective response to therapy. Previously, response was more general and according to the prescriber. **Graft-Versus-Host Disease:** For initial therapy, the initial approval was changed to be for 1 month (previously was for 1 year). A requirement was added for a patient who has already received a course of a rituximab product to have at least one objective or subjective response to therapy. **Multiple Sclerosis:** For the required previous trial of at least one other disease-modifying agent for multiple sclerosis, it was clarified that inadequate efficacy or significant intolerance was according to the prescriber. Examples of disease-modifying agents used for multiple sclerosis were moved to an appendix (previously listed as examples in a note within the criteria). For a patient who has been receiving a rituximab product for 1 year or longer, response criteria were developed for reauthorization in which the patient either experienced a beneficial clinical response when assessed by at least one objective measure (with examples provided in a Note), or the patient experienced stabilization, slowed progression, or improvement in at least one symptom such as motor function, fatigue, vision, bowel/bladder function, spasticity, walking/gait, or pain/numbness/tingling sensation.	07/20/2022
Annual Revision	**Antineutrophil Cytoplasmic Antibody (ANCA)-Associated Vasculitis:** Dosing was updated to specify a total of four doses for initial therapy. For follow up treatment, a total of six doses was specified for patients $\geq$ 18 years of age and two doses for patients < 18 years of age. **Immunotherapy-Related Toxicities Associated with Checkpoint Inhibitors:** This condition of approval was added. **Multiple Sclerosis:** For initial therapy, trial of at least one other disease-modifying agent was changed to require a trial of at least two other disease-modifying agents. **Neuromyelitis Optica Spectrum Disorder:** A total of four weekly doses for a regimen of 375 mg/m^2 intravenous was specified.	08/16/2023

APPENDIX A

	Mechanism of Action	Examples of Inflammatory Indications*
Biologics		
Adalimumab SC Products (Humira®, biosimilars)	Inhibition of TNF	AS, CD, JIA, PsO, PsA, RA, UC
Cimzia® (certolizumab pegol SC injection)	Inhibition of TNF	AS, CD, nr-axSpA, PsO, PsA, RA
Etanercept SC Products (Enbrel®, biosimilars)	Inhibition of TNF	AS, JIA, PsO, PsA
Infliximab IV Products (Remicade®, biosimilars)	Inhibition of TNF	AS, CD, PsO, PsA, RA, UC
Simponi®, Simponi® Aria™ (golimumab SC injection, golimumab IV infusion)	Inhibition of TNF	SC formulation: AS, PsA, RA, UC
		IV formulation: AS, PJIA, PsA, RA
Actemra® (tocilizumab IV infusion, tocilizumab SC injection)	Inhibition of IL-6	SC formulation: PJIA, RA, SJIA
		IV formulation: PJIA, RA, SJIA
Kevzara® (sarilumab SC injection)	Inhibition of IL-6	RA
Orencia® (abatacept IV infusion, abatacept SC injection)	T-cell costimulation modulator	SC formulation: JIA, PSA, RA
		IV formulation: JIA, PsA, RA
Rituximab IV Products (Rituxan®, biosimilars)	CD20-directed cytolytic antibody	RA
Kineret® (anakinra SC injection)	Inhibition of IL-1	JIA^, RA
Stelara® (ustekinumab SC injection, ustekinumab IV infusion)	Inhibition of IL-12/23	SC formulation: CD, PsO, PsA, UC
		IV formulation: CD, UC
Siliq™ (brodalumab SC injection)	Inhibition of IL-17	PsO
Cosentyx™ (secukinumab SC injection)	Inhibition of IL-17A	AS, nr-axSpA, PsO, PsA
Taltz® (ixekizumab SC injection)	Inhibition of IL-17A	AS, nr-axSpA, PsO, PsA
Ilumya™ (tildrakizumab-asmn SC injection)	Inhibition of IL-23	PsO
Skyrizi™ (risankizumab-rzaa SC injection)	Inhibition of IL-23	PsO
Tremfya™ (guselkumab SC injection)	Inhibition of IL-23	PsO
Entyvio™ (vedolizumab IV infusion)	Integrin receptor antagonist	CD, UC
Targeted Synthetic DMARDs		
Otezla® (apremilast tablets)	Inhibition of PDE4	PsO, PsA
Olumiant® (baricitinib tablets)	Inhibition of JAK pathways	RA
Rinvoq® (upadacitinib extended-release tablets)	Inhibition of JAK pathways	RA
Xeljanz® (tofacitinib tablets)	Inhibition of JAK pathways	RA, PJIA, PsA, UC
Xeljanz® XR (tofacitinib extended-release tablets)	Inhibition of JAK pathways	RA, PsA, UC

* Not an all-inclusive list of indication (e.g., oncology indications and rare inflammatory conditions are not listed). Refer to the prescribing information for the respective agent for FDA-approved indications; SC – Subcutaneous; TNF – Tumor necrosis factor; IV – Intravenous, IL – Interleukin; PDE4 – Phosphodiesterase 4; JAK – Janus kinase; AS – Ankylosing spondylitis; CD – Crohn's disease; JIA – Juvenile idiopathic arthritis; PsO – Plaque psoriasis; PsA – Psoriatic arthritis; RA – Rheumatoid arthritis; UC – Ulcerative colitis; nr-axSpA – Non-radiographic axial spondyloarthritis; ^ Off-label use of Kineret in JIA supported in guidelines; DMARDs – Disease-modifying antirheumatic drug.

APPENDIX B

Medication	Mode of Administration
Aubagio® (teriflunomide tablets)	Oral
Avonex® (interferon beta-1a intramuscular injection)	Injection (self-administered)
Bafiertam® (monomethyl fumarate delayed-release capsules)	Oral
Betaseron® (interferon beta-1b subcutaneous injection)	Injection (self-administered)
Briumvi™ (ublituximab-xiij intravenous infusion)	Injection
Copaxone® (glatiramer acetate subcutaneous injection, generic)	Injection (self-administered)
Extavia® (interferon beta-1b subcutaneous injection)	Injection (self-administered)
Gilenya® (fingolimod capsules)	Oral
Glatopa® (glatiramer acetate subcutaneous injection)	Injection (self-administered)
Kesimpta® (ofatumumab subcutaneous injection)	Injection (self-administered)
Lemtrada® (alemtuzumab intravenous infusion)	Intravenous infusion
Mavenclad® (cladribine tablets)	Oral
Mayzent® (siponimod tablets)	Oral
Ocrevus® (ocrelizumab intravenous infusion)	Intravenous infusion
Plegridy® (peginterferon beta-1a subcutaneous or intramuscular injection)	Injection (self-administered)
Ponvory™ (ponesimod tablets)	Oral
Rebif® (interferon beta-1a subcutaneous injection)	Injection (self-administered)
Tascenso ODT™ (fingolimod orally disintegrating tablets)	Oral
Tecfidera® (dimethyl fumarate delayed-release capsules, generic)	Oral
Tysabri® (natalizumab intravenous infusion)	Intravenous infusion
Vumerity® (diroximel fumarate delayed-release capsules)	Oral
Zeposia® (ozanimod capsules)	Oral