Utilization Review Policy 216

POLICY: Biosimilars - Rituxan

- Rituxan® (rituximab injection for intravenous use – Genentech)

EFFECTIVE DATE: 1/1/2021
LAST REVISION DATE: 09/18/2025, 03/05/2026

COVERAGE CRITERIA FOR: All Aspirus Medicare Plans

OVERVIEW

Rituximab products are CD20-directed cytolytic antibodies. All approved rituximab intravenous products are indicated for treatment of the following conditions:[1-3,22]

1. **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.
2. **Granulomatosis with polyangiitis** (Wegener's granulomatosis) and **microscopic polyangiitis** in adults, in combination with glucocorticoids.
3. **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.
2. **Pemphigus vulgaris**, for adults with moderate to severe disease.
1. **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.

In addition to the above indications, Rituxan intravenous is also indicated for treatment of the following conditions:[1]

1. **Granulomatosis with polyangiitis** (Wegener's granulomatosis) and **microscopic polyangiitis** in patients ≥ 2 years of age, in combination with glucocorticoids.
2. **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 biosimilars 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 the 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 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 (NMOSD):** The Neuromyelitis Optica Study Group (NEMOS) published revised recommendations for the treatment of NMOSD in 2023 and recommend rituximab as a treatment option for aquaporin-4 (AQP4)-immunoglobulin G (IgG) positive NMOSD and double-negative NMOSD.[20]
- **Oncology indications** covered in National Comprehensive Cancer Network (NCCN) guidelines:[6]
  - **Acute Lymphoblastic Leukemia:** Guidelines (version 2.2025 – June 27, 2025) 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 2.2025 – February 10, 2025), rituximab is included in multiple treatment regimens across the spectrum of disease.[8] Guidelines for pediatric aggressive mature B-cell lymphomas (version 2.2025 – April 28, 2025) 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 3.2025 – June 10, 2025), rituximab is a treatment option for patients with primary cutaneous B-cell lymphoma.[10] For Castleman disease, rituximab is broadly recommended in the guidelines (version 2.2025 – January 28, 2025) for unicentric and multicentric Castleman disease as initial therapy and second-line and subsequent therapy either as monotherapy or in combination with other treatments.[28]
  - **CLL/Small Lymphocytic Lymphoma:** Rituximab features prominently in the guidelines (version 3.2025 – April 2, 2025) and is included in multiple treatment regimens across the spectrum of disease.[7]
  - **Graft-Versus-Host Disease (GVHD):** The hematopoietic cell transplantation guidelines (version 2.2025 – June 3, 2025) list rituximab among the agents used for steroid-refractory chronic GVHD.[15] Among the agents FDA-approved for use in chronic GVHD, Jakafi® (ruxolitinib tablets) is the only agent given a category 1 recommendation for chronic GVHD.

Other alternatives with a category 2A recommendation include Niktimvo™ (axatilimab-csfr), Rezurock® (belumosudil), and Imbruvica® (ibrutinib), Orencia® (abatacept), alemtuzumab, calcineurin inhibitors (e.g., tacrolimus, cyclosporine), etanercept, extracorporeal photopheresis, hydroxychloroquine, imatinib, interleukin-2, low-dose methotrexate, mammalian target of rapamycin inhibitors (e.g., sirolimus), mycophenolate mofetil, pentostatin, and rituximab.

- **Hairy Cell Leukemia:** Guidelines (version 1.2025 – September 26, 2024) 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]
- **Hematopoietic Cell Transplant:** Guidelines (version 2.2025 – June 3, 2025) list rituximab in combination with cyclophosphamide and fludarabine as a non-myeloablative regimen for conditioning for allogeneic transplantation.[15]
- **Histiocytic Neoplasms – Rosai-Dorman Disease:** Guidelines (version 1.2025 – June 20, 2025) recommend rituximab as first-line or subsequent therapy, irrespective of mutation, as a single agent.[29]
- **Hodgkin Lymphoma:** Guidelines (version 2.2025 – January 30, 2025) 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 2.2025 – June 9, 2025) 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 1.2025 – June 3, 2025) recommend rituximab in multiple regimens for induction therapy and relapsed or refractory primary central nervous system lymphoma.[24]
- **Waldenstrom Macroglobulinemia/Lymphoplasmacytic Lymphoma:** Guidelines (version 1.2026 – June 24, 2025) 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 1.2025 – December 20, 2024) 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 myasthenia gravis, immune-mediated encephalitis, myositis, and stage 3 acute kidney injury/elevated serum creatinine.[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 the addition of a biologic (which includes rituximab) or a targeted synthetic disease modifying antirheumatic drug (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 recommendations for the management of SLE (2023) mention rituximab as a therapeutic option for patients who are refractory to standard immunosuppressive therapies.[21]

ANALYSIS OF EVIDENCE

The information provided in the summary of evidence is supported by labeled indications, CMS-approved compendia, published clinical literature, clinical practice guidelines, and/or applicable

National Coverage Determinations (NCDs), Local Coverage Determinations (LCDs), and Local Coverage Articles (LCAs). Refer to the Sources of Information section of this policy for additional information.

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 indication(s). 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.

This policy incorporates Medicare coverage guidance as set forth in National Coverage Determinations (NCDs) and Local Coverage Determinations (LCDs), as well as in companion policy articles and other guidance applicable to the relevant service areas. These documents are cited in the Sources of Information section of this policy. In some cases, this guidance includes specific lists of HCPCS and ICD-10 codes to help inform the coverage determination process. The Articles that include specific lists for billing and coding purposes will be included in the Sources of Information section of this policy. However, to the extent that this policy cites such lists of HCPCS and ICD-10 codes, they should be used for reference purposes only. The presence of a specific HCPCS or ICD-10 code in a chart or companion article to an LCD is not by itself sufficient to approve coverage. Similarly, the absence of such a code does not necessarily mean that the applicable condition or diagnosis is excluded from coverage.

Note: Conditions for coverage outlined in this Medicare Advantage Medical Policy may be less restrictive than those found in applicable National Coverage Determinations, Local Coverage Determinations and/or Local Coverage Articles. Examples of situations where this clinical policy may be less restrictive include, but are not limited to, coverage of additional indications supported by CMS-approved compendia and the exclusion from this policy of additional coverage criteria requirements outlined in applicable National Coverage Determinations, Local Coverage Determinations and/or Local Coverage Articles.

Indications with a ^ below are referenced in both the corresponding Standard Medical Utilization Management Internal Policy AND applicable National Coverage Determinations (NCDs), Local Coverage Determinations (LCDs), and/or Local Coverage Articles (LCAs). Coverage criteria for these indications may be internally developed and/or referenced in applicable NCDs, LCDs, and/or LCAs. For these indications, internally developed coverage criteria is denoted throughout the policy in the following manner: 1) IC-L (internal criteria supported by the labeled indication), 2) IC-COMP (internal criteria supported by CMS-approved compendia), 3) IC-ISGP (internal criteria intended to interpret or supplement general provisions outlined in applicable NCDs, LCDs, and/or LCAs), or 4) IC-EC (internal criteria intended to expand coverage beyond the coverage outlined in applicable NCDs, LCDs, and/or LCAs). For these indications, coverage criteria that is NOT denoted with one of the above indicators is referenced in applicable NCDs, LCDs, and/or LCAs. Additional information supporting the rationale for determination of internal coverage criteria can be found via the Sources of Information section.

Indications with a @ below are referenced in the corresponding Standard Medical Utilization Management Internal Policy, but are NOT directly referenced in applicable National Coverage Determinations (NCDs), Local Coverage Determinations (LCDs), and/or Local Coverage Articles (LCAs). Coverage criteria for these

indications is internally developed. These indications and their respective coverage criteria represent expanded coverage beyond the coverage outlined in applicable NCDs, LCDs, and/or LCAs.

Indications with a # below are supported and referenced in applicable National Coverage Determinations (NCDs), Local Coverage Determinations (LCDs), and/or Local Coverage Articles (LCAs), but are NOT directly referenced in the corresponding Standard Medical Utilization Management Internal Policy. Coverage criteria for these indications is referenced in applicable NCDs, LCDs, and/or LCAs.

RECOMMENDED AUTHORIZATION CRITERIA

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

Preferred Product(s): Truxima, Ruxience, Riabni
Non-Preferred Products(s): Rituxan

Step Therapy Requirements:

Authorization for a non-preferred biologic product or biosimilar will be granted if the patient meets any *one* of the items listed below (A, B, C, D or E). Chart notes documenting the issue must be provided at time of request:

A. The patient is *not* considered a new start to the non-preferred product (new start is defined as no use of the requested product in the previous 365 days) OR

B. Allergic reaction to a specific inactive ingredient in all preferred biologic products or biosimilars OR

C. Adverse reaction to a specific inactive ingredient in all preferred biologic products or biosimilars OR

D. Therapeutic success while taking a non-preferred biologic product or biosimilar and therapeutic failure during an adequate trial of all preferred biologic products or biosimilars which allowed sufficient time for a positive treatment outcome documented by medical chart notes OR

E. The patient has a diagnosis not included in the FDA-approved indications of all preferred products, but is included in the FDA-approved indications of the non-preferred product

Please note:

- Factors such as patient or prescriber preference or healthcare facility's or pharmacy's inability or unwillingness to order or stock the preferred product(s) will not be considered
- Common side effects to all products and infusion-related reactions are not considered documented allergic reactions to a preferred product as they would be expected with the innovator and biosimilar products.

- Generally, an adequate trial of a drug is considered to be three months or longer in order to allow time for efficacy to be established

FDA-Approved Indications

1. Antineutrophil Cytoplasmic Antibody (ANCA)-Associated Vasculitis. ^

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

A) Induction Treatment. Approve for 1 month if the patient meets ALL of the following (i and ii):
- **i.** The patient has an ANCA-associated vasculotide; IC-ISGP AND
  Note: Examples of ANCA-associated vasculitis include granulomatosis with polyangiitis [GPA] {Wegener's granulomatosis (WG)} or microscopic polyangiitis [MPA]).
- **ii.** The requested agent is being administered in combination with glucocorticoids. IC-L

B) Follow-Up Treatment of Patients Who Have Received Induction Treatment for ANCA-Associated Vasculitis (Note: This includes patients who received induction treatment using rituximab infusion or other standard of care immunosuppressants). Approve for 1 year if the patient meets BOTH of the following (i and ii):
- **i.** According to the prescriber, the patient achieved disease control with induction treatment; IC-ISGP AND
- **ii.** If the patient previously received a course of therapy, at least 16 weeks will elapse between courses. IC-ISGP

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

A) Initial Therapy: Approve one of the following:
- 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. Chronic Lymphocytic Leukemia or Small Lymphocytic Lymphoma. ^ eviCore

Criteria. Approve for 1 year.

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

3. B-Cell Lymphoma. ^ eviCore

(Note: Examples of B-cell lymphomas include follicular lymphoma, diffuse large B-cell lymphoma, high-grade B-cell lymphoma, human immunodeficiency virus (HIV)-related B-cell lymphoma, Burkitt lymphoma, Castleman 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.)

Criteria. Approve for 1 year.

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.

---

4. Pemphigus Vulgaris. ^

Criteria. Approve for the duration noted if the patient meets ONE of the following (A, B or C):

A) Initial Treatment. Approve for 1 month.

B) Patient is Being Treated for a Relapse of Pemphigus Vulgaris. Approve for 1 month (which is adequate duration to administer one course of therapy) if subsequent infusions will be administered no sooner than 16 weeks following the previous infusion of a rituximab product. IC-ISGP

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.

C) Patient is Being Treated for Maintenance of Pemphigus Vulgaris. Approve for 1 year if subsequent infusions will be administered no sooner than 16 weeks following the previous infusion of a rituximab product. IC-ISGP

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.

Dosing. Approve 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 every 6 months.

---

5. Rheumatoid Arthritis (RA). ^

Criteria. Approve if the patient meets ONE of the following (A, B or C):

A) Initial Therapy. Approve for 1 month (which is adequate duration to administer one course of therapy) if the patient has tried ONE conventional synthetic disease-modifying antirheumatic drug (DMARD) for at least 3 months. IC-EC

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.

B) Patient has already Received One Course of Rituximab for Rheumatoid Arthritis (RA). Approve for 1 month (which is adequate duration to administer one course of therapy) if 16 weeks or greater will elapse between treatment courses. [IC-ISGP]
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.

C) Patient Has Already Received Two 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 the following (i and ii):

i. 16 weeks or greater will elapse between treatment courses; [IC-ISGP] 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. Patient meets at least ONE of the following (a or b):

1. Patient experienced a beneficial clinical response when assessed by at least one objective measure; [IC-ISGP] 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).
2. 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. [IC-ISGP]

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

OTHER USES WITH SUPPORTIVE EVIDENCE

---

6. Acute Lymphoblastic Leukemia. [@ eviCore]

Criteria. Approve for 1 year if the patient has CD20-positive disease.

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

---

7. Autoimmune Hemolytic Anemia.[@]

Criteria. Approve for 1 month.

Dosing. Approve one course of therapy (4 doses), which consists of ONE the following (A or B):

A) 375 mg/m^2 administered intravenously with doses separated by at least 7 days; OR

B) 100 mg administered intravenously with doses separated by at least 7 days.

---

8. Graft Versus Host Disease. @

Criteria. Approve for the duration noted 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 chronic graft-versus-host disease; AND
- **ii.** Patient has tried at least one systemic medication for graft versus host disease; OR
  Note Examples of systemic medications include systemic corticosteroids (methylprednisolone, prednisone), Jakafi (ruxolitinib), Rezurock (belumosudil), Niktimvo (axatilimab-csfr), cyclosporine, tacrolimus, mycophenolate mofetil, Imbruvica (ibrutinib), imatinib, hydroxychloroquine, methotrexate, Nipent (pentostatin), interleukin-2 (e.g., Proleukin [aldesleukin]), sirolimus, or an etanercept product.

B) 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.

9. Hairy Cell Leukemia. @ eviCore

Criteria. Approve for 1 year.

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

10. Hematopoietic Cell Transplantation. @

Criteria. Approve for 1 month (which is adequate duration to administer one course of therapy) if the medication will be used as part of a conditioning regimen for allogeneic transplant.

Dosing. Approve one course of therapy, which consists of one dose of 375 mg/m^2 administered intravenously before transplant and three doses of 1,000 mg/m^2 separated by at least 7 days after transplant.

11. Hodgkin Lymphoma. @ eviCore

Criteria. Approve for 1 year if the patient has nodular lymphocyte-predominant disease.

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

12. Immune Thrombocytopenia (ITP). ^

Criteria. Approve if the patient meets ONE of the following (A or B):

A) Initial Therapy. Approve for 1 month if the patient has tried one other therapy.
Note: Examples of therapies for ITP include intravenous immunoglobulin (IVIG), anti-D (RHO) immunoglobulin, corticosteroids, Alvaiz (eltrombopag), Doptelet (avatrombopag), Nplate (romiplostim), Promacta (eltrombopag), Tavalisse (fostamatinib), and splenectomy.

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; IC-ISGP 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.** According to the prescriber, the patient responded to therapy; AND
  Note: Examples of a response include a platelet count increase from baseline following treatment with a rituximab product.
- **iii.** According to the prescriber, the patient has relapsed. IC-ISGP
  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.

13. Immunotherapy-Related Toxicities Associated with Checkpoint Inhibitors. @

Criteria. 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 ALL of the following (i, ii, and iii):

- **a.** According to the prescriber, patient developed an immunotherapy-related toxicity; AND
- **b.** Patient developed this immunotherapy-related toxicity while receiving a checkpoint inhibitor; AND
- **c.** Patient is symptomatic despite a trial of at least ONE systemic corticosteroid.

Note: Examples of a corticosteroid include methylprednisolone and prednisone.

B) Patient has Already Received a Course of a Rituximab Product. Approve for 1 month.

Dosing. Approve dosing that meets the following (A or B):

A) Approve up to 500 mg/m^2 or up to 1000 mg 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.

---

14. Interstitial Lung Disease Associated with Systemic Autoimmune Rheumatic Disease. @

Criteria. Approve for the duration noted if the patient meets ONE of the following (A or B):
Note: Examples of systemic autoimmune rheumatic diseases include systemic sclerosis, myositis, mixed connective tissue disease, rheumatoid arthritis, and Sjögren's disease.

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

- **i.** Patient is ≥ 18 years of age; AND
- **ii.** Diagnosis is confirmed by high-resolution computed tomography; OR

B) Patient has Already Received a Course of a Rituximab Product for Interstitial Lung Disease Associated with Systemic Autoimmune Rheumatic Disease. Approve for 1 month if the patient meets ALL of the following (i and ii):

- **i.** 24 weeks or greater will elapse between treatment courses; AND
  Note: For example, there will be a minimum of 24 weeks since the first dose of the previous course and the first dose of the next course of a rituximab product.
- **ii.** Patient has experienced a beneficial response to therapy with rituximab; AND
  Note: Examples of a beneficial response include a reduction in the anticipated decline in forced vital capacity, improvement in 6-minute walk distance, and/or reduction in the number or severity of disease-related exacerbations.

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

---

15. Membranous Nephropathy. @

Criteria. Approve for the duration noted if the patient meets ONE of the following (A or B):

A) Initial Therapy. Approve for 1 month if, according to the prescriber, the patient is at moderate risk or high risk for the progressive loss of kidney function; OR

B) Patient has Already Received a Course of a Rituximab Product for Membranous Nephropathy. Approve for 1 month.

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

A) Approve 1,000 mg administered intravenously for 2 doses separated by at least 14 days; OR

B) Approve 375 mg/m^2 administered intravenously for up to 4 doses separated by at least 7 days.

---

17. Myasthenia Gravis. @

Criteria. Approve for 6 months if the patient meets ONE of the following (A or B):

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

i. Patient has confirmed anti-muscle-specific tyrosine kinase antibody-positive myasthenia gravis; AND

ii. Patient meets ONE of the following (a or b):
   a) Patient previously received or is currently receiving pyridostigmine; OR
   b) Patient has had inadequate efficacy, contraindication, or significant intolerance to pyridostigmine; AND

iii. Patient has tried at least one immunosuppressant therapy; AND
   Note: Examples of immunosuppressant therapies include azathioprine, cyclosporine, mycophenolate mofetil, methotrexate, tacrolimus, and cyclophosphamide. A trial of Imaavy (nipocalimab-aahu intravenous infusion) or Rystiggo (rozanolixizumab-noli subcutaneous infusion) also counts.

iv. Patient has evidence of unresolved symptoms of myasthenia gravis; OR
   Note: Evidence of unresolved symptoms of myasthenia gravis includes difficulty swallowing, difficulty breathing, or a functional disability resulting in the discontinuation of physical activity (e.g., double vision, talking, impairment of mobility).

B) Patient has Already Received a Course of a Rituximab Product for Myasthenia Gravis. Approve if, according to the prescriber, patient is continuing to derive benefit from the rituximab product.
Note: Examples of benefit include reductions in exacerbations of myasthenia gravis; improvements in speech, swallowing, mobility, and respiratory function.

Dosing. Approve one course of therapy that meets ONE of the following (A, B, or C):

A) 1,000 mg administered intravenously for 2 doses separated by at least 14 days; OR

B) 375 mg/m^2 administered intravenously for 4 doses separated by at least 7 days with or without an additional 375 mg/m^2 administered monthly for 2 doses (up to 6 doses total); OR

C) 750 mg/m^2 administered intravenously for 2 doses separated by at least 14 days.

---

16. Multiple Sclerosis. ^

Criteria. 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 and ii):

a. According to the prescriber, the patient has experienced inadequate efficacy or significant intolerance to at least ONE other disease-modifying agent 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. IC-ISGP
   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 criteria (i or ii):

a. Patient has been receiving Rituximab for < 1 year. Approve if at least 6 months will elapse between treatment courses; [IC-ISGP] OR
   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 has been receiving Rituximab for 1 year or more. Approve for 1 year if the patient meets ALL of the following (a and b):
   i. At least 6 months will elapse between treatment courses; [IC-ISGP] 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.
   ii. Patient meets ONE of the following [(1) or (2)]:
      1. Patient experienced a beneficial clinical response when assessed by at least one objective measure; [IC-ISGP] 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.
      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. [IC-ISGP]

Dosing. Approve the following (A and B):
A) Each course is up to 2,000 mg (total); AND
B) Each course is administered as one or two intravenous infusions administered over 1 month.

---

17. Neuromyelitis Optica (NMO) Spectrum Disorder. [@]

Criteria. Approve for 1 month.

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.

---

18. Pediatric Nephrotic Syndrome. ^

Criteria. Approve for the duration noted 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 is ≤ 18 years of age; AND
- ii. Patient meets ONE of the following (a or b):
  - a) Patient has tried at least one systemic corticosteroid; [IC-ISGP] OR
    Note: Examples of systemic corticosteroids include prednisone or prednisolone.
  - b) Patient has tried at least one glucocorticoid-sparing agent for nephrotic syndrome; [IC-ISGP] OR
    Note: Examples of glucocorticoid-sparing agents for nephrotic syndrome include oral calcineurin inhibitors (e.g., tacrolimus, cyclosporine), cyclophosphamide, or mycophenolate mofetil.

B) Patient has Already Received a Course of a Rituximab Product for Pediatric Nephrotic Syndrome. Approve for 1 month.

Dosing. Approve 375 mg/m^2 administered intravenously for up to 4 doses separated by at least 7 days.

19. Primary Central Nervous System Lymphoma. @ eviCore

Criteria. Approve for 1 year.

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

20. Rosai-Dorfman Disease. @ eviCore

Criteria. Approve for 1 year if the patient is ≥ 18 years of age.

Dosing. Approve the requested dose.

21. Systemic Lupus Erythematous (SLE) [Lupus]. @

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

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 (i.e., 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.

---

22. Waldenstrom's Macroglobulinemia/Lymphoplasmacytic Lymphoma. @ eviCore

Criteria. Approve for 1 year.

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

---

23. Solid Organ Transplantation. #
Note: This includes Antibody-Mediated Rejection (AMR).

Criteria. Approve for 1 year if the patient meets ONE of the following (A or B):
A) The medication will be used for desensitization therapy prior to or immediately after transplantation; OR
B) The medication will be used for antibody-mediated rejection.

Dosing. Approve if the requested dosage is based on a transplant center's protocol.

---

24. Immune-Mediated Myopathy/Idiopathic Inflammatory Myopathy. # (Note: Examples include dermatomyositis, polymyositis, antisynthetase syndrome, immune-mediated necrotizing myopathy, inclusion body myositis, nonspecific myositis).

Criteria. Approve for the duration noted if the patient meets ONE of the following (A or B):
A) Initial Therapy. Approve for 1 month if the patient has refractory disease and has failed all first-line therapies.
B) Patient has Already Received a Course of a Rituximab Product for Immune-Mediated Myopathy/Idiopathic Inflammatory Myopathy. Approve for 1 month if the patient has had a positive response to a previous course of a rituximab product for immune-mediated myopathy/idiopathic inflammatory myopathy.

Dosing.[30-33] Approve ONE of the following (A or B):
A) Up to 375 mg/m^2 administered intravenously with 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.

25. Hemophilia (Acquired). #

Criteria. Approve for the duration noted if the patient meets ONE of the following (A or B):
A) Initial Therapy. Approve for 1 month if the patient meets ONE of the following (i or ii):
- **i.** The patient has acquired or refractory hemophilia and the requested medication is being used as first-line therapy in combination with corticosteroids; OR
- **ii.** The patient has refractory disease and the requested medication is being used as a second-line agent.

B) Patient has Already Received a Course of a Rituximab Product for Hemophilia (Acquired). Approve for 1 month if the patient has had a positive response to a previous course of a rituximab product for hemophilia (acquired).

Dosing.[34] Approve up to 375 mg/m^2 administered intravenously with doses separated by at least 7 days.

26. Thrombotic Thrombocytopenic Purpura. #

Criteria. Approve for 1 month if the patient meets both of the following (A and B):
A) The medication will be used in combination with systemic corticosteroids; IC-EC AND
Note: Examples of systemic corticosteroids include prednisone and methylprednisolone.
B) The medication will be used in combination with therapeutic plasma exchange. IC-EC

Dosing. Approve up to 375 mg/m^2 administered intravenously for up to 4 doses separated by at least 7 days.

27. Immunoglobulin G4-Related Disease (IgG4-RD). #

Criteria. Approve for the duration noted if the patient meets ONE of the following (A or B):
A) Initial Therapy. Approve for 1 month if the patient meets ONE of the following (i or ii):
- **i.** The patient has refractory or relapsed disease and the requested medication is being used as second-line therapy after failure of all first-line therapies; OR
- **ii.** The patient has an absolute contraindication to glucocorticoid use.

B) Patient has Already Received a Course of a Rituximab Product for Immunoglobulin G4-Related Disease (IgG4-RD). Approve for 1 month if the patient has had a positive response to a previous course of a rituximab product for immunoglobulin G4-related disease (IgG4-RD).

Dosing.[36-37] Approve ONE of the following (A or B):
A) Up to 375 mg/m^2 administered intravenously with 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.

28. Minimal Change Disease. #

Criteria. Approve for the duration noted if the patient meets ONE of the following (A or B)
A) Initial Therapy. Approve for 1 month if the medication is being used for frequently relapsing or steroid-dependent disease; [IC-ISGP] OR
A) Patient has Already Received a Course of a Rituximab Product for Minimal Change Disease. Approve for 1 month.

Dosing. Approve dosing that meets ONE of the following (A or B):
A) Approve 1,000 mg administered intravenously for up to 2 doses separated by at least 14 days; OR
B) Approve 375 mg/m^2 administered intravenously for up to 4 doses separated by at least 7 days.

---

29. Chronic Inflammatory Demyelinating Polyneuropathy (CIDP). #

Criteria. Approve for the duration noted if the patient meets ONE of the following (A or B):
A) Initial Therapy. Approve for 1 month if the patient has failed intravenous immune globulin (IVIG), glucocorticoids, and plasma exchange.
B) Patient has Already Received a Course of a Rituximab Product for Chronic **Inflammatory Demyelinating Polyneuropathy (CIDP)**. Approve for 1 month if the patient has had a positive response to a previous course of a rituximab product for chronic **inflammatory demyelinating polyneuropathy (CIDP)**.

Dosing.[39] Approve up to 375 mg/m^2 administered intravenously with doses separated by at least 7 days.

---

30. Sjogren's Syndrome. #

Criteria. Approve for the duration noted if the patient meets ONE of the following (A or B):
A) Initial Therapy. Approve for 1 month if the patient has tried corticosteroids and other immunosuppressive agents and these agents were ineffective.
B) Patient has Already Received a Course of a Rituximab Product for **Sjogren's Syndrome**. Approve for 1 month if the patient has had a positive response to a previous course of a rituximab product for **Sjogren's syndrome**.

Dosing.[40-41] Approve up to two 1,000-mg doses administered as an intravenous infusion separated by at least 2 weeks.

---

31. Systemic Sclerosis. #

Criteria. Approve for the duration noted if the patient meets ONE of the following (A or B):
A) Initial Therapy. Approve for 1 month if the patient has tried corticosteroids and other immunosuppressive agents and these agents were ineffective.

B) Patient has Already Received a Course of a Rituximab Product for **Systemic Sclerosis**. Approve for 1 month if the patient has had a positive response to a previous course of a rituximab product for **systemic sclerosis**.

Dosing.[40-41] Approve up to two 1,000-mg doses administered as an intravenous infusion separated by at least 2 weeks.

---

32. Susac Syndrome. #

Criteria. Approve for the duration noted 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.** The patient has severe or extremely severe disease presentation; AND
- **ii.** According to the prescriber, initial treatments are inadequate.
  Note: Examples of initial treatments include corticosteroids and intravenous immunoglobulin (IVIG).

B) Patient has Already Received a Course of a Rituximab Product for **Susac Syndrome**. Approve for 1 month if the patient has had a positive response to a previous course of a rituximab product for **Susac Syndrome**.

Dosing.[27] Approve ONE of the following (A or B):

A) Approve up to a single dose of 500 mg given once and then repeated in 6 months; OR

B) Approve up to a dose of 250 mg once then repeated in 2 weeks followed by 500 mg every 6 months.

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.

SOURCES OF INFORMATION

1. Rituxan intravenous infusion [prescribing information]. South San Francisco, CA: Genentech; December 2021.
2. Ruxience intravenous infusion [prescribing information]. New York, NY: Pfizer; June 2025.
3. Truxima intravenous infusion [prescribing information]. North Wales, PA: Teva/Celltrion; June 2025.
4. Chung SA, Langford CA, Maz M, et al. 2021 American College of Rheumatology/Vasculitis Foundation guideline for the management of antineutrophil cytoplasmic antibody-associated vasculitis. *Arthritis Rheumatol*. 2021 Jul 8 [online ahead of print].
5. Tieu J, Smith R, Basu N, et al. Rituximab for maintenance of remission in ANCA-associated vasculitis: expert consensus guidelines. *Rheumatology (Oxford).* 2020;59(4):e24-e32.
6. The NCCN Drugs and Biologics Compendium. © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on August 5-7, 2025. Search term: rituximab.
7. The NCCN Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Clinical Practice Guidelines in Oncology (version 3.2025 – April 2, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on August 7, 2025.

8. The NCCN B-Cell Lymphoma Clinical Practice Guidelines in Oncology (version 2.2025 – February 10, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on August 7, 2025.
9. The NCCN Pediatric Aggressive Mature B-cell Lymphomas Clinical Practice Guidelines in Oncology (version 2.2025 – April 28, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on August 7, 2025.
10. The NCCN Primary Cutaneous Lymphomas Clinical Practice Guidelines in Oncology (version 3.2025 – June 10, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on August 7, 2025.
11. The NCCN Acute Lymphoblastic Leukemia Clinical Practice Guidelines in Oncology (version 2.2025 –June 27, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on August 7, 2025.
12. The NCCN Hairy Cell Leukemia Clinical Practice Guidelines in Oncology (version 1.2025 – September 22, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on August 6, 2025.
13. The NCCN Hodgkin Lymphoma Clinical Practice Guidelines in Oncology (version 2.2025 – January 30, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on August 7, 2025.
14. The NCCN Waldenstrom's Macroglobulinemia/Lymphoplasmacytic Lymphoma Clinical Practice Guidelines in Oncology (version 1.2026 – June 24, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on August 7, 2025.
15. The NCCN Hematopoietic Cell Transplantation Clinical Practice Guidelines in Oncology (version 2.2025 – June 3, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on August 7, 2025.
16. Fraenkel L, Bathon JM, England BR, et al. 2021 American College of Rheumatology guideline for the treatment of rheumatoid arthritis. *Arthritis Rheumatol*. 2021;73(7):1108-1123.
17. Neunert C, Terrell DR, Arnold DM, et al. American Society of Hematology 2019 guidelines for immune thrombocytopenia. *Blood Adv*. 2019;3(23):3829-3866.
18. A Consensus Paper by the Multiple Sclerosis Coalition. The use of disease-modifying therapies in multiple sclerosis. Updated June 2019. Available at: http://ms-coalition.org/wp-content/uploads/2019/06/MSC_DMTPaper_062019.pdf. Accessed on August 8, 2025.
19. Rae-Grant A, Day GS, Marrie RA, et al. Practice guideline recommendations summary: disease-modifying therapies for adults with multiple sclerosis. Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. *Neurology*. 2018;90:777-788.
20. Kűmpfel T, Giglhuber K, Aktas O, et al. Update on the diagnosis and treatment of neuromyelitis optica spectrum disorders (NMOSD) – revised recommendations of the Neuromyelitis Optica Study Group (NEMOS). Part II: Attack therapy and long-term management. *J Neurol*. 2024;271:141-176.
21. Fanouriakis A, Kostopoulou M, Andersen J, et al. EULAR recommendations for the management of systemic lupus erythematosus: 2023 update. *Ann Rheum Dis.* 2024 Jan 2;83(1):15-29.
22. Riabni intravenous infusion [prescribing information]. Thousand Oaks, CA: Amgen; June 2025.
23. Harman KE, Brown D, Exton LS, et al. British Association of Dermatologists' guidelines for the management of pemphigus vulgaris 2017. *Br J Dermatol*. 2017;177(5):1170-1201.
24. The NCCN Central Nervous System Cancers Clinical Practice Guidelines in Oncology (version 1.2025 – June 3, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on August 7, 2025.
25. The NCCN Pediatric Hodgkin Lymphoma Clinical Practice Guidelines in Oncology (version 2.2025 – June 9, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on August 7, 2025.
26. The NCCN Management of Immunotherapy-Related Toxicities (version 1.2025 – December 20, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on August 7, 2025.
27. Schneider B, Naidoo J, Santomasso B, et al. Management of Immune-Related Adverse Events in Patients Treated With Immune Checkpoint Inhibitor Therapy: ASCO Guideline Update. *J Clin Oncol.* 2021:39(36):4073-4126.
28. The NCCN Castleman Disease Clinical Practice Guidelines in Oncology (version 2.2025 – January 28, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on August 5, 2025.
29. The NCCN Histiocytic Neoplasms Clinical Practice Guidelines in Oncology (version 1.2025 – June 20, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on August 7, 2025.
30. Centers for Medicare and Medicaid Services, National Government Services, Inc, Local Coverage Article: Billing and Coding: Off-label Use of Rituximab and Rituximab Biosimilars (A59101) (Original effective date 11/1/2022; Revision effective date 9/7/25). Accessed on September 16, 2025.
31. Centers for Medicare and Medicaid Services, National Government Services, Inc, Local Coverage Determination (LCD): Off-label Use of Rituximab and Rituximab Biosimilars (L39297) [original date 11/1/2022; Revision effective date 9/7/25]. Accessed on September 16, 2025.
32. Colvin MM, Cook JL, Chang P, et al. Antibody-mediated rejection in cardiac transplantation: emerging knowledge in diagnosis and management: a scientific statement from the American Heart Association. Circulation. 2015;131(18):1608-1639.

33. Vo AA, Lukovsky M, Toyoda M, et al. RITUXIMAB and intravenous immune globulin for desensitization during renal transplantation. N Engl J Med. 2008;359(3):242-251.
34. Levine TD. RITUXIMAB in the treatment of dermatomyositis: an open-label pilot study. Arthritis Rheum. 2005;52(2):601-607.
35. Unger L, Kampf S, Luthke K, Aringer M. RITUXIMAB therapy in patients with refractory dermatomyositis or polymyositis: differential effects in a real-life population. Rheumatology (Oxford). 2014;53(9):1630-1638.
36. de Souza FHC, Miossi R, de Moraes JCB, Bonfa E, Shinjo SK. Favorable RITUXIMAB response in patients with refractory idiopathic inflammatory myopathies. Adv Rheumatol. 2018;58(1):31.
37. Barsotti S, Cioffi E, Tripoli A, et al. The use of RITUXIMAB in idiopathic inflammatory myopathies: description of a monocentric cohort and review of the literature. Reumatismo. 2018;70(2):78-84.
38. Clinical Pharmacology [database online]. Tampa, FL: Elsevier, Inc.; 2022. Available at: https://www.clinicalkey.com/pharmacology/. Accessed on October 10, 2022. Search terms: Rituximab.
39. Zwicker JI, Muia J, Dolatshahi L, et al. Adjuvant low-dose rituximab and plasma exchange for acquired TTP. *Blood*. 2019; 134(13): 1106–1109.
40. Ebbo M, Grados A, Samson M, et al. Long-term efficacy and safety of RITUXIMAB in IgG4-related disease: Data from a French nationwide study of thirty-three patients. PLoS One. 2017;12(9):e0183844.
41. Khosroshahi A, Carruthers MN, Deshpande V, Unizony S, Bloch DB, Stone JH. RITUXIMAB for the treatment of IgG4-related disease: lessons from 10 consecutive patients. Medicine (Baltimore). 2012;91(1):57-66.
42. KDIGO 2021 Clinical Practice Guideline for the Management of Glomerular Diseases. Kidney Int . 2021 Oct;100(4S):S1-S276.
43. Mahdi-Rogers M, Swan AV, van Doorn PA, Hughes RA. Immunomodulatory treatment other than corticosteroids, immunoglobulin and plasma exchange for chronic inflammatory demyelinating polyradiculoneuropathy. *Cochrane Database Syst Rev*. 2010;(11):CD003280.
44. Carubbi F, Cipriani P, Marrelli A, et al. Efficacy and safety of rituximab treatment in early primary Sjögren's syndrome: A prospective, multi-center, follow-up study. Arthritis Res Ther. 2013;15(5):R172.
45. Ramos-Casals M, Tzioufas AG, Stone JH, et al. Treatment of primary Sjögren syndrome: A systematic review. JAMA. 2010;304(4):452-460.
46. The NCCN Management of Immunotherapy-Related Toxicities (version 1.2024 – December 7, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on August 6, 2024.
47. Schneider B, Naidoo J, Santomasso B, et al. Management of Immune-Related Adverse Events in Patients Treated With Immune Checkpoint Inhibitor Therapy: ASCO Guideline Update. *J Clin Oncol.* 2021:39(36):4073-4126.

HISTORY

Type of Revision	Summary of Changes	Date
Policy created	New Medicare Advantage Medical Policy	07/11/2018
Policy revision	Reviewed and revised original policy created 07/11/2018 in accordance with Local Coverage Article A52452 and Rituximab Intravenous Products Utilization Review Policy	08/28/2019
Policy revision	Completion of 2019 monthly monitoring process in accordance with Local Coverage Determination L33394, Local Coverage Article A52452, and Rituximab Intravenous Products Utilization Review Policy.	12/11/2019
Policy revision	Non-clinical update to policy to add the statement "This policy incorporates Medicare coverage guidance as set forth in National Coverage Determinations (NCDs) and Local Coverage Determinations (LCDs), as well as in companion policy articles and other guidance applicable to the relevant service areas. These documents are cited in the References section of this policy. In some cases, this guidance includes specific lists of HCPCS and ICD-10 codes to help inform the coverage determination process. The Articles that include specific lists for billing and coding purposes will be included in the Reference section of this policy. However, to the extent that this policy cites such lists of HCPCS and ICD-10 codes, they should be used for reference purposes only. The presence of a specific HCPCS or ICD-10 code in a chart or companion article to an LCD is not by itself sufficient to approve coverage. Similarly,	1/30/2020

	the absence of such a code does not necessarily mean that the applicable condition or diagnosis is excluded from coverage."	
Policy revision	*Multiple indications – changed "prescribing physician" to "prescriber" * **B-Cell Lymphoma:** Pediatric Aggressive Mature B-cell Lymphoma was added as an example of a B-cell lymphoma * **Antineutrophil Cytoplasmic Antibody (ANCA)-Associated Vasculitis:** For follow-up treatment of patients who have received induction treatment for ANCA-associated vasculitis, the maintenance dose was changed to be up to 1,000 mg per dose (previously was up to 500 mg). * **Acute Lymphoblastic Leukemia (ALL):** To align with updated NCCN guidelines, the requirement that patients who are Philadelphia-chromosome-positive try a tyrosine kinase inhibitor prior to rituximab was removed from the policy. * **Graft Versus Host Disease (GVHD):** To align with updated NCCN guidelines and other policies, criteria were changed to require at least one conventional systemic treatment prior to a rituximab product. Previously, criteria required that the patient had tried at least one other immunosuprressant or be concurrently receiveing an immunosuppressant in combination with rituximab	06/12/2020
Policy revision	**Riabni:** This newly approved biosimilar was added to the policy. There are no changes to the criteria, which apply to all rituximab products included in this policy.	01/12/2021
Policy revision	**Antineutrophil Cytoplasmic Antibody-Associated Vasculitis:** An alternative dosing regimen (up to 250 mg/m^2 for two doses, then up to 250 mg/m^2 not more frequently than once every 6 months) was added. **Acute Lymphoblastic Leukemia:** The Dosing was updated to require a minimum of 7 days between doses (previously was 14 days). **Hairy Cell Leukemia:** The requirement of relapsed or refractory disease was removed. **Primary Central Nervous System Lymphoma:** This condition of approval was added to the policy. **Systemic Lupus Erythematous (SLE) [Lupus]:** A note was added to clarify this includes nephrotic syndrome in a patient with SLE.	07/07/2021
Policy revision	**Antineutrophil Cytoplasmic Antibody-Associated Vasculitis:** The minimum amount of time required between doses was removed from the **Dosing** (not needed since addressed in clinical criteria). For initial therapy, up to two 1,000-mg intravenous doses separated by at least 2 weeks was added as an alternative induction dose. For follow-up treatment of a patient who has received induction treatment, the dosing was separated by age (≥ 18 or < 18 years of age); previously, dosing applied to all patients regardless of age. For a patient ≥ 18 years of age, the dose is up to 1,000 mg intravenously, whereas the dose is based on body surface area (250 mg/m^2) if < 18 years of age. Alternative induction doses were removed from the criteria (not needed).	7/21/2021
Policy 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	08/04/2022

	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.	
Policy revision	**Removed the following indications:** Pre-transplant to suppress panel reactive anti-HLA antibodies in patients with high Panel Reactive Antibody (PRA) Levels to Human Leukocyte Antigens (HLA); Dermatomyositis or Polymyositis; and Grave's Disease/Ophthalmopathy. **Added the following indications:** Antibody-Mediated Rejection (AMR); Immune-Mediated Myopathy/Idiopathic Inflammatory Myopathy; Hemophilia (Acquired); Thrombotic Thrombocytopenic Purpura (Acquired); Immunoglobulin G4-Related Disease (IgG4-RD); Minimal Change Disease; Chronic Inflammatory Demyelinating Polyneuropathy (CIDP); Sjogren's Syndrome and Systemic Sclerosis.	03/01/2023
Policy 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 ≥ 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. **Neuromyelitis Optica Spectrum Disorder:** A total of four weekly doses for a regimen of 375 mg/m^2 intravenous was specified.	09/26/2023
Policy review	**No criteria changes.** Review based on commercial policy annual review	09/04/2024
Aspirus P&T Review	Policy reviewed and approved by Aspirus P&T committee. Annual review process	09/16/2024
Aspirus Update	Moved Riabni to preferred product status effective 1/1/25. Riabni will no longer be targeted by the policy.	12/3/2024
Aspirus Update	Updated step therapy criteria to require clinical need for non-preferred product over the preferred products including chart note documentation to support the need for a non-preferred product.	05/07/2025
Aspirus P&T Review	Policy reviewed and approved by Aspirus P&T committee. Annual review process	09/15/2025
Policy revision	B-Cell Lymphoma: The nomenclature acquired immune deficiency (AIDS)-related B-cell lymphoma was updated to human immunodeficiency virus (HIV)-related B-cell lymphoma. Rheumatoid Arthritis: The requirements for a patient who has already received one or more courses of therapy were modified to a patient has already received one course of a rituximab product and a patient has already received two or more courses of a rituximab product. For patients already receiving one course, the requirements are 16 weeks or greater will lapse between treatment courses and the medication will not be used concurrently with another biologic or with a targeted synthetic DMARD. In addition to these requirements, a patient who has already received two	09/18/2025

	or more courses will either experience a beneficial clinical response when assessed by at least one objective measure or experience an improvement in at least one symptom. Graft-Versus-Host-Disease (GVHD): A requirement was added that patient has chronic GVHD. The requirement patient has tried at least one conventional systemic treatment was modified to at least one systemic medication. Jakafi (ruxolitinib), Rezurock (belumosudil), Niktimvo (axatilimab-csfr), hydroxychloroquine, methotrexate, interleukin-2, sirolimus, and etanercept were added, and antithymocyte globulin and infliximab were removed from the Note of examples of systemic medications. Hematopoietic Cell Transplantation: This was added as a new condition of approval. Immune Thrombocytopenia (ITP): Alvaiz (eltrombopag), Doptelet (avatrombopag), Nplate (romiplostim), Promacta (eltrombopag), Tavalisse (fostamatinib) were added to the Note of examples of therapies for ITP. Immunotherapy-Related Toxicities Associated with Checkpoint Inhibitors: Requirements were added that, according to the prescriber, the patient developed an immunotherapy-related toxicity and developed this immunotherapy-related toxicity while receiving a checkpoint inhibitor. An additional dosing regimen of up to 1,000 mg administered intravenously for 2 doses separated by at least 14 days was added. Rosai-Dorfman Disease: This was added as a new condition of approval. Pemphigus Vulgaris: For a patient being treated for a relapse, the approval duration was changed from 1 year to 1 month. For maintenance therapy dosing, added a frequency of every 6 months.	
Selected revision	**Autoimmune Hemolytic Anemia:** This was added as a new condition of approval. **Immune Thrombocytopenia (ITP):** For a patient that has already received a course of a rituximab product for ITP, the requirements that the patient has responded to therapy and that the patient has relapsed were modified from "as determined by the prescriber" to "according to the prescriber". **Thrombotic Thrombocytopenic Purpura:** Removed “Acquired” from the indication itself, to align with commercial policy. Removed requirement that patient have severe, relapsed, or refractory disease. Changed requirement that patient has failed first line therapy (i.e., plasma exchange and glucocorticoids) to the medication will be used in combination with systemic corticosteroids and therapeutic plasma exchange. Removed continuation criteria. Updated dosing. **Membranous Nephropathy:** This was added as a new condition of approval. **Myasthenia Gravis:** This was added as a new condition of approval. **Minimal Change Disease:** Removed criteria for pediatric nephrotic syndrome and separated that indication out from Minimal Change Disease to align with commercial policy structure. Updated criteria from "The patient has frequently relapsing or glucocorticoid-dependent minimal change disease AND The patient has failed to attain a durable remission with cyclophosphamide or calcineurin inhibitors" to "medication is being used for frequently relapsing or steroid-dependent	03/05/2026

	disease." Removed requirement that patient has had a postive response from continuation criteria. Updated dosing. **Solid Organ Transplantation: Indication wording was updated from** Antibody-Mediated Rejection (AMR) to as listed. Note was added to clarify that this includes Antibody-Mediated Rejection (AMR) (per LCD). Criteria wording was updated from "The requested medication is being used as second-line treatment or as part of a combination treatment for AMR in a kidney, lung, or cardiac transplant patient; OR The requested medication is being used as part of a desensitization protocol in a highly sensitized patient awaiting donor transplant" to "The medication will be used for desensitization therapy prior to or immediately after transplantation; OR The medication will be used for antibody-mediated rejection." Continuation criteria was removed. Updated dosing. **Hematopoietic Stem Cell Transplant:** Dosing was updated to include "administered intravenously." **Pediatric Nephrotic Syndrome:** New indication that was split out from Minimal Change Diseaese. Criteria requires that patient is 18 years of age or younger and has tried at least one systemic corticosteroid or tried at least one glucocorticoid-sparing agent for nephrotic syndrome. Patients who have already received a course of rituximab for this indication do not have to meet these requirements. **Interstitial Lung Disease Associated with Systemic Autoimmune Rheumatic Disease:** This was added as a new condition of approval.	

APPENDIX A

Medication	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)
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)
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