Drug Coverage Policy

Effective Date……02/01/2026
Coverage Policy Number……IP0319
Policy Title……. Rituximab Intravenous Products for Non-Oncology Indications

Rituximab Intravenous Products for Non-Oncology Indications

- Riabni™ (rituximab-arrx intravenous infusion – Amgen)
- Rituxan® (rituximab intravenous infusion – Genentech)
- Ruxience® (rituximab-pvvr intravenous infusion – Pfizer)
- Truxima® (rituximab-abbs intravenous infusion – Celltrion/Teva)

INSTRUCTIONS FOR USE

The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment where appropriate and have discretion in making individual coverage determinations. Where coverage for care or services does not depend on specific circumstances, reimbursement will only be provided if a requested service(s) is submitted in accordance with the relevant criteria outlined in the applicable Coverage Policy, including covered diagnosis and/or procedure code(s). Reimbursement is not allowed for services when billed for conditions or diagnoses that are not covered under this Coverage Policy (see "Coding Information" below). When billing, providers must use the most appropriate codes as of the effective date of the submission. Claims submitted for services that are not accompanied by covered code(s) under the applicable Coverage Policy will be denied as not covered. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

OVERVIEW

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

- **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.
- **Pemphigus vulgaris**, for adults with moderate to severe disease.
- **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]

- **Granulomatosis with polyangiitis** (Wegener's granulomatosis) and **microscopic polyangiitis** in patients ≥ 2 years of age, in combination with glucocorticoids.
- **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, biosimilars have not demonstrated interchangeability.

Guidelines

The use of rituximab is supported in clinical guidelines in numerous situations, both as first-line therapy and in patients who have refractory disease 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.

- **Autoimmune Hemolytic Anemia (AIHA):** AIHA is divided serologically into warm type (65% of cases), cold type (29% of cases are cold hemagglutinin disease [CHAD]), paroxysmal cold hemoglobinuria (1% of cases), or mixed AIHA (5% of cases).[30] For primary warm AIHA, prednisolone is recommended first-line by the British Society for Haematology (BSH) with rituximab as second-line if no response or if patient relapses. Third-line options include azathioprine, cyclosporin, danazol, mycophenolate mofetil, or splenectomy. For CHAD, rituximab is considered a first-line therapy. Mixed AIHA is treated as warm AIHA. Supportive care is recommended for paroxysmal cold hemoglobinuria. The BSH guidelines note that the standard regimen for rituximab IV is 375 mg/m^2 weekly for 4 consecutive weeks; however low dose rituximab (i.e., 100 mg weekly for 4 weeks with prednisolone, first or second line) produced comparable response rates.
- **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]
- **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]
- **Interstitial Lung Disease Associated with Systemic Autoimmune Rheumatic Disease (SARD-ILD):** The American College of Rheumatology (ACR) and the American College of Chest Physicians (CHEST) [2023] conditionally recommend rituximab as a first-line ILD treatment option for adults with SARD-ILD.[48] Other first-line options include mycophenolate, azathioprine, and cyclophosphamide. In addition, rituximab is conditionally recommended for people with SARD-ILD progression despite first ILD treatment. Rituximab is also conditionally recommended for people with SARD and rapidly progressive ILD as a first-line treatment option. Other first-line treatment options include cyclophosphamide, intravenous immune globulin, mycophenolate, a calcineurin inhibitor, and Janus kinases inhibitors. Recommended dosing is 1 gram IV every 2 weeks for 2 doses; treatment may be repeated every 24 weeks as needed.
- **Membranous Nephropathy:** The Kidney Disease: Improving Global Outcomes (KDIGO) Clinical Practice Guideline for the Management of Glomerular Diseases (2021) list rituximab as a therapeutic option for membranous nephropathy in patients at moderate risk or high risk for progressive loss of kidney function.[31] In patients who relapse, initial therapy can be repeated or treatment may be switched to rituximab if the initial treatment was a calcineurin inhibitor or cyclophosphamide. KDIGO recommends a treatment regimen of 1 or 2 infusions of 1 gram of rituximab each administered 2 weeks apart or 375 mg/m^2 give 1-4 times at weekly intervals.
- **Minimal Change Disease (MCD):** The Kidney Disease: Improving Global Outcomes (KDIGO) Clinical Practice Guideline for the Management of Glomerular Diseases (2021) list rituximab as a therapeutic option for adults with frequently relapsing or steroid-dependent MCD.[31] KDIGO recommends one of the following induction regimens: 375 mg/m^2 weekly

for 4 doses; 375 mg/m^2 for a single dose and repeat after one week if CD19 cells > 5/mm^3; or 1 gram/dose for 2 doses, 2 weeks apart. For relapses after induction, either 375 mg/m^2 for one dose or 1 gram for 1 dose is recommended.

- **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.
- **Myasthenia Gravis (MG):** An international consensus guidance for the management of MG was published in 2016.[35] The consensus guidance recommends pyridostigmine for the initial treatment in most patients with MG. The ability to discontinue pyridostigmine can indicate that the patient has met treatment goals and may guide the tapering of other therapies. Corticosteroids or immunosuppressant therapy should be used in all patients with MG who have not met treatment goals after an adequate trial of pyridostigmine. Nonsteroidal immunosuppressant agents used in MG include azathioprine, cyclosporine, mycophenolate mofetil, methotrexate, and tacrolimus. It is usually necessary to maintain some immunosuppression for many years, sometimes for life. Plasma exchange and intravenous immunoglobulin can be used as short-term treatments for certain patients. An update to an international consensus guidance for the management of MG was published in 2020.[36] Rituximab should be considered as an early therapeutic option in patients with muscle specific kinase antibody-positive MG who have an unsatisfactory response to initial immunotherapy. While the efficacy of rituximab in acetylcholine receptor antibody-positive MG is uncertain, it is an option if patients fail or do not tolerate other immunosuppressive agents. Various dosing regimens have been utilized in both prospective trials and retrospective analyses that are referenced in the consensus guidance.
- **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] NCCN provides a specific regimen of 375 mg/m^2 IV for 1 day before transplant and 1,000 mg/m^2 IV on days 1, 8, and 15 after transplant.
- **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]

- **Pediatric Nephrotic Syndrome:** The Kidney Disease: Improving Global Outcomes (KDIGO) 2025 Clinical Practice Guideline for the Management of Nephrotic Syndrome in Children recommends rituximab as a treatment option for steroid-sensitive nephrotic syndrome in children who have frequent relapses despite optimal combinations of prednisone and glucocorticoid-sparing oral agents.[32] For steroid-resistant nephrotic syndrome, KDIGO recommends cyclosporine or tacrolimus as initial second-line therapy. A

potential role was suggested for the use of rituximab in patients with calcineurin inhibitor-resistant, steroid-resistant nephrotic syndrome. KDIGO provides a dosing recommendation for rituximab of 375 mg/m^2 IV for 1 to 4 doses. Supporting references that used more than 1 dose separated infusions by at least 1 week.

- **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]
- **Solid Organ Transplantation:** Various transplant center protocols and clinical practice guidelines discuss the use of rituximab for highly sensitized patients as part of desensitization protocols and for acute antibody-mediated rejection following transplantation.[37-44]
- **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]
- **Thrombotic Thrombocytopenic Purpura (TTP):** The International Society on Thrombosis and Haemostasis (ISTH) [2025] recommends the addition of rituximab to corticosteroids and therapeutic plasma exchange for patients experiencing their first acute event or relapses of immune-mediated TTP.[33-34] This is a conditional recommendation in the context of very low certainty of evidence. A dosing regimen of rituximab IV 375 mg/m^2 administered weekly for 4 doses has been used in a phase II study and observed in retrospective analyses.[45-47]

This coverage policy addresses the use of rituximab for non-oncology indications. The use of rituximab for oncology indications (including post-transplant lymphoproliferative disorder and Castleman's disease) and Rituxan Hycela® (rituximab and hyaluronidase human) are addressed in a separate coverage policy. Please refer to the related coverage policy (Oncology Medications #1403).

Coverage Policy

POLICY STATEMENT

Prior Authorization is required for 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.

Documentation: Documentation is required where noted in the criteria as **[documentation required]**. Documentation may include, but is not limited to, chart notes, laboratory tests, claims records, and/or other information. All documentation must include patient-specific identifying information.

Rituximab intravenous products (Rituxan, Riabni, Ruxience, Truxima) are considered medically necessary when ONE of the following is met:

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, iii and iv):
     - **i.** Patient has an ANCA-associated vasculotide; AND
       Note: Examples of ANCA-associated vasculitis include granulomatosis with polyangiitis (Wegener's granulomatosis), or microscopic polyangiitis.
     - **ii.** The medication is being administered in combination with glucocorticoids; AND
     - **iii.** The medication is prescribed by or in consultation with a rheumatologist, nephrologist, pulmonologist, or immunologist; AND
     - **iv.** Preferred product criteria is met for the product(s) as listed in the below table(s); OR
   - **B.** Follow-Up Treatment of Patients Who Have Received Induction Treatment for ANCA-Associated Vasculitis. Approve for 1 year if the patient meets ALL of the following (i, ii, and iii):
     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; AND.
     - **iii.** Preferred product criteria is met for the product(s) as listed in the below table(s).

   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; OR
   - **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 two doses.

2. **Pemphigus Vulgaris.** Approve for the duration noted if the patient meets ONE of the following (A, B, or C):
   - **A.** Initial Treatment. Approve for 1 month (which is adequate duration to administer one course of therapy) if the patient meets ALL of the following (i ii, and iii):
     - **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; AND
     - **iii.** Preferred product criteria is met for the product(s) as listed in the below table(s); OR

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 the patient meets ALL of the following (i, ii and iii):
- **i.** Subsequent infusions will be administered no sooner than 16 weeks following the previous infusion of a rituximab product; 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 is prescribed by or in consultation with a dermatologist; AND
- **iii.** Preferred product criteria is met for the product(s) as listed in the below table(s)

C. Patient is Being Treated for Maintenance of Pemphigus Vulgaris. Approve for 1 year if the patient meets ALL of the following (i, ii and iii):
- **i.** Subsequent infusions will be administered no sooner than 16 weeks following the previous infusion of a rituximab product; 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 is prescribed by or in consultation with a dermatologist; AND
- **iii.** Preferred product criteria is met for the product(s) as listed in the below table(s)

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 every 6 months.

3. Rheumatoid Arthritis. Approve for the duration noted 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 meets ALL of the following (i, ii, iii and iv):
- **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; AND
- **iv.** Preferred product criteria is met for the product(s) as listed in the below table(s); OR

B. Patient has already received one course 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 (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. Preferred product criteria is met for the product(s) as listed in the below table(s); OR

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

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. 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; AND

iv. Preferred product criteria is met for the product(s) as listed in the below table(s).

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

4. Autoimmune Hemolytic Anemia. Approve for 1 month if the patient meets BOTH of the following (A and B):

A. The medication is prescribed by or in consultation with a hematologist; AND

B. Preferred product criteria is met for the product(s) as listed in the below table(s).

Dosing: Approve one course of therapy (4 doses), which consists of ONE of 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.

5. **Graft-Versus-Host Disease.** 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 ALL of the following (i, ii, iii, and iv)
        - **i.** Patient has chronic graft-versus-host disease; AND
        - **ii.** Patient has tried at least one systemic medication for graft-versus-host disease; AND
          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.
        - **iii.** The medication is prescribed by or in consultation with an oncologist, hematologist, or a physician affiliated with a transplant center; AND
        - **iv.** Preferred product criteria is met for the product(s) as listed in the below table(s); OR
    - **B.** Patient has Already Received a Course of a Rituximab Product for Graft-Versus-Host Disease. Approve for 1 year if the patient meets BOTH of the following (i and ii):
        - **i.** Patient meets ONE of the following (a or b):
            - **a.** When assessed by at least one objective measure, patient experienced a beneficial clinical response from baseline (prior to initiating a rituximab product); OR
              Note: Examples of objective measures include normalization of liver function tests, red blood cell count, or platelet count; or resolution of fever or rash.
            - **b.** 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); AND
        - **ii.** Preferred product criteria is met for the product(s) as listed in the below table(s).

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

6. **Hematopoietic Cell Transplantation.** Approve for 1 month (which is adequate duration to administer one course of therapy) if the patient meets ALL of the following (A, B and C):
    - **A.** The medication will be used as part of a conditioning regimen for allogeneic transplant; AND
    - **B.** The medication is prescribed by or in consultation with an oncologist, hematologist, or a physician affiliated with a transplant center; AND
    - **C.** Preferred product criteria is met for the product(s) as listed in the below table(s).

    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 administered intravenously separated by at least 7 days after transplant.

7. **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 ALL of the following (i, ii, and iii):
        - **i.** Patient has tried one other therapy; AND

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.

ii. The medication is prescribed by or in consultation with a hematologist; AND

iii. Preferred product criteria is met for the product(s) as listed in the below table(s); OR

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, iii, and iv):

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. 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; AND
Note: Examples of relapse include the patient experiences thrombocytopenia after achievement of a remission.

iv. Preferred product criteria is met for the product(s) as listed in the below table(s).

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

8. Immunotherapy-Related Toxicities Associated with Checkpoint Inhibitors. Approve for the duration noted if the patient meets ONE of 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, iii, iv, and v):

i. According to the prescriber, patient developed an immunotherapy-related toxicity; AND

ii. Patient developed this immunotherapy-related toxicity while receiving a checkpoint inhibitor; AND

iii. Patient is symptomatic despite a trial of at least ONE systemic corticosteroid; AND
Note: Examples of a corticosteroid include methylprednisolone and prednisone.

iv. The medication is prescribed by or in consultation with an oncologist, hematologist, nephrologist, neurologist, rheumatologist, or dermatologist; AND

v. Preferred product criteria is met for the product(s) as listed in the below table(s); OR

B. Patient has Already Received a Course of a Rituximab Product. Approve for 1 month if the patient meets BOTH of the following (i and ii):

i. The medication is prescribed by or in consultation with an oncologist, hematologist, nephrologist, neurologist, rheumatologist, or dermatologist; AND

ii. Preferred product criteria is met for the product(s) as listed in the below table(s).

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

A. Approve up to 500 mg/m^2 or up to 1,000 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

9. Interstitial Lung Disease Associated with Systemic Autoimmune Rheumatic Disease. 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, ii, iii, and iv):

i. Patient is ≥ 18 years of age; AND

ii. Diagnosis is confirmed by high-resolution computed tomography; AND

iii. The medication is prescribed by or in consultation with a pulmonologist or a rheumatologist; AND

iv. Preferred product criteria is met for the product(s) as listed in the below table(s); 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, ii, iii, and iv):

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.

iii. The medication is prescribed by or in consultation with a pulmonologist or a rheumatologist; AND

iv. Preferred product criteria is met for the product(s) as listed in the below table(s).

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

10. Membranous Nephropathy. 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 ALL of the following (i, ii and iii):

i. According to the prescriber, the patient is at moderate risk or high risk for the progressive loss of kidney function; AND

ii. The medication is prescribed by or in consultation with a nephrologist; AND

iii. Preferred product criteria is met for the product(s) as listed in the below table(s); OR

B. Patient has Already Received a Course of a Rituximab Product for Membranous Nephropathy. Approve for 1 month if the patient meets BOTH of the following (i and ii):
- **i.** The medication is prescribed by or in consultation with a nephrologist; AND
- **ii.** Preferred product criteria is met for the product(s) as listed in the below table(s).

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.

11. Minimal Change Disease. 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 ALL of the following (i, ii and iii):
  - **i.** The medication is being used for frequently relapsing or steroid-dependent disease; AND
  - **ii.** The medication is prescribed by or in consultation with a nephrologist; AND
  - **iii.** Preferred product criteria is met for the product(s) as listed in the below table(s); OR
- **B.** Patient has Already Received a Course of a Rituximab Product for Minimal Change Disease. Approve for 1 month if patient meets both of the following (i and ii):
  - **i.** The medication is prescribed by or in consultation with a nephrologist; AND
  - **ii.** Preferred product criteria is met for the product(s) as listed in the below table(s).

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.

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, iv and v):
  - **i.** According to the prescriber, the patient has experienced inadequate efficacy or significant intolerance to at least TWO other disease-modifying agents 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.** The 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; 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; AND

v. Preferred product criteria is met for the product(s) as listed in the below table(s); OR

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

d. Preferred product criteria is met for the product(s) as listed in the below table(s); 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, d, and e):

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 of a beneficial clinical response 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 symptom 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; AND
e. Preferred product criteria is met for the product(s) as listed in the below table(s),

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

13. Myasthenia Gravis. 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, iv, v and vi)
  - **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; AND
    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).
  - **v.** The medication is prescribed by or in consultation with a neurologist; AND
  - **vi.** Preferred Product Criteria is met for the product(s) as listed in the below table(s).
- **B.** Patient has Already Received a Course of a Rituximab Product for Myasthenia Gravis. Approve if the patient meets ALL of the following (i, ii and ii):
  - **i.** According to the prescriber, patient is continuing to derive benefit from the rituximab product; AND
    Note: Examples of benefit include reductions in exacerbations of myasthenia gravis; improvements in speech, swallowing, mobility, and respiratory function.
  - **ii.** The medication is prescribed by or in consultation with a neurologist; AND
  - **iii.** Preferred Product Criteria is met for the product(s) as listed in the below table(s).

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.

14. Neuromyelitis Optica Spectrum Disorder. Approve for 1 month if the patient meets BOTH of the following (A and B):
- **A.** Medication is prescribed by or in consultation with a neurologist; AND

B. Preferred Product Criteria is met for the product(s) as listed in the below table(s):

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.

15. Pediatric Nephrotic Syndrome. 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 ALL of the following (i, ii, iii and iv):
  - **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; OR
      Note: Examples of systemic corticosteroids include prednisone or prednisolone.
    - **b.** Patient has tried at least one glucocorticoid-sparing agent for nephrotic syndrome; AND
      Note: Examples of glucocorticoid-sparing agents for nephrotic syndrome include oral calcineurin inhibitors (e.g., tacrolimus, cyclosporine), cyclophosphamide, or mycophenolate mofetil.
  - **iii.** The medication is prescribed by or in consultation with a nephrologist; AND
  - **iv.** Preferred product criteria is met for the product(s) listed in the below table(s); OR
- **B.** Patient has Already Received a Course of a Rituximab Product for Pediatric Nephrotic Syndrome. Approve for 1 month if patient meets BOTH of the following (i and ii):
  - **i.** The medication is prescribed by or in consultation with a nephrologist; AND
  - **ii.** Preferred product criteria is met for the product(s) as listed in the below table(s).

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

16. Solid Organ Transplantation. Approve for 1 year if the patient meets ALL of the following (A, B, and C):
- **A.** Patient meets ONE of the following (i or ii):
  - **i.** The medication will be used for desensitization therapy prior to or immediately after transplantation; OR
  - **ii.** The medication will be used for antibody-mediated rejection; AND
- **B.** The medication will be prescribed by or in consultation with a physician affiliated with a transplant center; AND
- **C.** Preferred product criteria is met for the product(s) as listed in the below table(s).

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

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

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; AND

iii. Preferred product criteria is met for the product(s) as listed in the below table(s); OR

B. Individual has Already Received a Course of a Rituximab Product for SLE. Approve for 1 month (adequate duration to receive one course) if the patient meets both of the following (i and ii)::

i. 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.

ii. Preferred product criteria is met for the product(s) as listed in the below table(s).

Dosing. Approve the requested dose.

18. **Thrombotic Thrombocytopenic Purpura.** Approve for 1 month if the patient meets ALL of the following (A, B, C, and D):

A. The medication will be used in combination with systemic corticosteroids; AND
Note: Examples of systemic corticosteroids include prednisone and methylprednisolone.

B. The medication will be used in combination with therapeutic plasma exchange; AND

C. The medication is prescribed by or in consultation with a hematologist; AND

D. Preferred product criteria is met for the product(s) as listed in the below table(s).

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

Employer Plans:

Product	Criteria
Rituxan (rituximab intravenous infusion)	Patient meets BOTH of the following (A and B): **A.** Patient has tried ALL of the following: Truxima, Riabni, and Ruxience **[documentation required]** **B.** Patient cannot continue to use each formulary alternative due to a formulation difference in the inactive ingredient(s) [e.g., differences in stabilizing agent, buffering agent, and/or surfactant] which, according to the prescriber, would result in a significant allergy or serious adverse reaction **[documentation required]**

Individual and Family Plans:

Product	Criteria
Rituxan (rituximab intravenous infusion)	Patient meets BOTH of the following (A and B): **A.** Patient has tried ALL of the following: Truxima, Riabni, and Ruxience **[documentation required]** **B.** Patient cannot continue to use each formulary alternative due to a formulation difference in the inactive ingredient(s) [e.g., differences

Product	Criteria
	in stabilizing agent, buffering agent, and/or surfactant] which, according to the prescriber, would result in a significant allergy or serious adverse reaction **[documentation required]**

Conditions Not Covered

Rituximab products (Rituxan, Riabni, Ruxience, Truxima) for any other non-oncology use is considered not medically necessary. Criteria will be updated as new published data are available.

Coding Information

Note: 1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

HCPCS Codes	Description
J9312	Injection, rituximab, 10 mg
Q5115	Injection, rituximab-abbs, biosimilar, (truxima), 10 mg
Q5119	Injection, rituximab-pvvr, biosimilar, (ruxience), 10 mg
Q5123	Injection, rituximab-arrx, biosimilar, (Riabni), 10 mg

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Revision Details

Type of Revision	Summary of Changes	Date
Selected Revision	**Preferencing Product Table.** **Removed** "Individual has previously started on or is currently receiving Rituxan (rituximab)	7/1/2025
Selected Revision	**Added** documentation instructions **Neuromyelitis Optica Spectrum Disorder** **Updated from** "Documented diagnosis of neuromyelitis optica spectrum disorder" **to** "diagnosis was confirmed by a positive blood serum test for anti-aquaporin-4 antibody **[documentation required]"**	8/15/2025
Annual Revision	**Policy Title**	10/15/2025

	Updated from "Rituximab for Non-Oncology Indication" to "Rituximab Intravenous Products for Non-Oncology Indications" **Antineutrophil Cytoplasmic Antibody (ANCA)-Associated Vasculitis.** <u>Induction Therapy:</u> **Updated** approval duration from 12 months **to** 1 month **Removed** Churg-Strauss syndrome and pauci-immune glomerulonephritis from examples of ANCA-associated vasculitis **Updated** "The medication is being administered in combination with glucocorticoids unless there is a documented failure, contraindication or intolerance to glucocorticoids" **to** "The medication is being administered in combination with glucocorticoids." **Added** pulmonologist to specialty requirement <u>Follow-Up Treatment:</u> **Updated** "Individual achieved disease control with induction treatment" **to** "According to the prescriber, the patient achieved disease control with induction treatment" **Updated** "At least 16 weeks will elapse between courses" **to** "If the patient previously received a course of therapy, at least 16 weeks will elapse between courses" **Removed** "The medication is prescribed by or in consultation with a rheumatologist, nephrologist, or immunologist." <u>Dosing:</u> **Updated** "18 years of age or older: Up to 1,000 mg administered by intravenous infusion every 4 to 6 months based on clinical evaluation, for up to 6 doses" **to** "≥ 18 years of age: Up to 1,000 mg administered by intravenous infusion for 6 doses" **Updated** "Less than 18 Years of age: Two 250 mg/m^2 intravenous infusion separated by two weeks, followed by a 250 mg/m^2 intravenous infusion every 6 months thereafter based on clinical evaluation" **to** "< 18 years of age: Up to 250 mg/m^2 administered by intravenous infusion for two doses **Updated "Pemphigus Vulgaris and Other Refractory Autoimmune Blistering Diseases" to "Pemphigus Vulgaris"** <u>Initial Treatment:</u> **Updated** approval duration **from** 12 months **to** 1 month **Removed** "Note: Examples of other autoimmune blistering diseases include pemphigus foliaceus, bullous pemphigoid, cicatricial pemphigoid,	

	epidermolysis bullosa acquisita, and paraneoplastic pemphigus" **Updated from** Patient who is being treated for a relapse or for maintenance **to** Patient is being treated for a relapse and a patient is being treated for maintenance. <u>Patient is Being Treated for a Relapse of Pemphigus Vulgaris:</u> **Updated** approval duration **from** 1 year **to** 1 month (which is adequate duration to administer one course of therapy). **Added** "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" <u>Patient is Being Treated for Maintenance of Pemphigus Vulgaris:</u> Added criteria that subsequent infusions will be administered no sooner than 16 weeks following the previous infusion of a rituximab product, and the medication is prescribed by or in consultation with a dermatologist. <u>Dosing:</u> **Removed** "at month 12 and every 6 months thereafter or based on clinical evaluation" **Rheumatoid Arthritis** <u>Initial Therapy:</u> **Updated** approval duration from 12 months **to** 1 month <u>Patient has already received one course of a Rituximab Product for Rheumatoid Arthritis:</u> **Updated** approval duration from 12 months **to** 1 month **Added criteria for "Patient has already received two or more courses of a Rituximab Product for Rheumatoid Arthritis"** **Other Uses with Supportive Evidence** **Graft-Versus-Host Disease** <u>Initial Therapy:</u> **Updated** approval duration **from** 12 months **to** 1 month **Added** "Patient has chronic graft-versus-host disease" Updated "Documentation of failure, contraindication, or intolerance to ONE conventional systemic treatment for graft-versus-host disease [for example, systemic corticosteroids (methylprednisolone, prednisone), cyclosporine, tacrolimus, mycophenolate mofetil, Imbruvica (ibrutinib capsules and tablets), imatinib,	

	antithymocyte globulin, Nipent (pentostatin infusion), or an infliximab product]" **to** "Patient has tried at least one systemic medication for graft-versus-host disease. 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" **Added** criteria for "Patient has already Received a Course of a Rituximab Product for Graft-Versus-Host Disease" **Hematopoietic Cell Transplantation** **Added** criteria for this indication **Added** dosing for this indication **Updated from "Immune or Idiopathic Thrombocytopenia (ITP)" to "Immune Thrombocytopenia (ITP)"** <u>Initial Therapy:</u> **Updated** approval duration **from** 12 months **to** 1 month **Updated from** "Documentation of failure, contraindication, or intolerance to ONE other therapy for ITP (for example, intravenous immunoglobulin (IVIG), anti-D (RHO) immunoglobulin, corticosteroids, or splenectomy)" **to** "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." <u>Patient has Already Received a Course of a Rituximab Product for ITP:</u> **Updated** approval duration **from** 12 months **to** 1 month **Updated from** "Documentation that the individual responded to therapy (for example, a platelet count increase from baseline following treatment with a rituximab product)" **to** "Patient responded to therapy as determined by the prescriber. Note: Examples of a response include a platelet count increase from baseline following treatment with a rituximab product" **Removed** "The medication is prescribed by or in consultation with a hematologist"	

	Immunotherapy-Related Toxicities Associated with Checkpoint Inhibitors **Added** "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)." Initial Therapy: **Updated** approval duration **from** 12 months **to** 1 month **Added** "According to the prescriber, patient developed an immunotherapy-related toxicity" **Added** "Patient developed this immunotherapy-related toxicity while receiving a checkpoint inhibitor" **Added** hematologist and nephrologist to specialty requirement Patient has Already Received a Course of a Rituximab Product: **Updated** approval duration **from** 12 months **to** 1 month **Added** hematologist and nephrologist to specialty requirement Dosing: Updated "Up to 500 mg/m2 administered intravenously for 2 doses separated by at least 14 days" **to** "Approve up to 500 mg/m2 or up to 1,000 mg administered intravenously for 2 doses separated by at least 14 days" **Multiple Sclerosis** Initial Therapy: **Updated from** "Documentation of failure, contraindication, or intolerance to at least ONE other disease-modifying agent for multiple sclerosis" to "According to the prescriber, the patient has experienced inadequate efficacy or significant intolerance to at least TWO other disease-modifying agents for multiple sclerosis. Note: See Appendix B for examples of disease-modifying agents used for multiple sclerosis." **Added** criteria for "Patient is Currently Receiving Rituximab" **Neuromyelitis Optica Spectrum Disorder** **Updated** approval duration **from** 12 months **to** 1 month	

	Removed "Diagnosis was confirmed by a positive blood serum test for anti-aquaporin-4 antibody [documentation required]" **Updated from "Systemic Lupus Erythematous (SLE) [Lupus]" to "Systemic Lupus Erythematosus (SLE) [Lupus]"** <u>Initial Therapy:</u> **Updated** approval duration **from** 12 months **to** 1 month **Updated from** "Documentation of failure, contraindication, or intolerance to ONE standard immunomodulating or immunosuppressant agent [for example, hydroxychloroquine, corticosteroids (e.g., prednisone, methylprednisolone), methotrexate, azathioprine, mycophenolate, or cyclophosphamide]" **to** "Patient 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." <u>Individual has Already Received a Course of a Rituximab Product for SLE:</u> **Updated** approval duration **from** 12 months **to** 1 month **Removed** "The individual has had a documented beneficial response to therapy. Examples of a beneficial response include: reduction in flares; reduction in corticosteroid dose; decrease of anti-dsDNA titer; improvement in specific organ dysfunction (for example, musculoskeletal, blood, hematologic, vascular, others)" **Removed** "The medication is prescribed by or in consultation with a rheumatologist, nephrologist, or neurologist." **Added** dosing for this indication	
Selected Revision	**Pemphigus Vulgaris** **Maintenance Therapy: Added** "every 6 months" to dosing regimen **Autoimmune Hemolytic Anemia** **Updated from** "Refractory Autoimmune Hemolytic Anemia" **to** "Autoimmune Hemolytic Anemia" **Updated** authorization duration **from** 12 months **to** 1 month	2/1/2026

	Removed ” Documented failure, contraindication, or intolerance to conventional treatments (for example, corticosteroids, immunosuppressants, or immunoglobulin” **Added** ”The medication is prescribed by or in consultation with a hematologist” **Added** dosing for this use **Immune Thrombocytopenia (ITP)** **Updated** 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" **Interstitial Lung Disease Associated with Systemic Autoimmune Rheumatic Disease** **Added** criteria and dosing for this use **Membranous Nephropathy** **Updated from** ”Membranous Nephropathy/Membranous Glomerular Nephropathy” **to** ”Membranous Nephropathy” **Updated** authorization duration **from** 12 months **to** 1 month **Removed** individual has ONE of the following: Membranous nephropathy and eGFR < 60 ml/min or declining renal function not otherwise explained, Membranous nephropathy with nephrotic syndrome (nephrotic proteinuria, peripheral edema, hypoalbuminemia), Membranous nephropathy with nephrotic proteinuria (> 3.5 gm/day after 6 months conservative therapy with ACEi or ARB), or Recurrent membranous nephropathy with proteinuria > 1 gm/day in a kidney transplant recipient **Added** ”According to the prescriber, the patient is at moderate risk or high risk for the progressive loss of kidney function” **Added** criteria for Patient has already Received a Course of a Rituximab Product for Membranous Nephropathy **Added** dosing for this use **Minimal Change Disease** **Added** criteria and dosing for this use	

	Myasthenia Gravis **Updated** authorization duration **from** 12 months **to** 6 months **Added** "Patient has confirmed anti-muscle-specific tyrosine kinase antibody-positive myasthenia gravis" **Added** "Patient meets ONE of the following (a or b): a.Patient previously received or is currently receiving pyridostigmine b. Patient has had inadequate efficacy, contraindication, or significant intolerance to pyridostigmine" **Updated from** "Documented failure, contraindication, or intolerance to at least TWO immunosuppressive agents (for example, azathioprine, cyclosporine, or methotrexate)" **to** "Patient has tried at least one immunosuppressant therapy. 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." **Added** "Patient has evidence of unresolved symptoms of myasthenia gravis. 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)" **Added** "The medication is prescribed by or in consultation with a neurologist" **Added** criteria for Patient has Already Received a Course of a Rituximab Product for Myasthenia Gravis **Added** dosing for this use **Pediatric Nephrotic Syndrome** **Updated** authorization duration **from** 12 months **to** 1 month **Updated from** "Documentation of failure, contraindication, or intolerance to corticosteroid or immunosuppressive medication (for example, cyclophosphamide, cyclosporine, mycophenolate mofetil)" **to** "Patient has tried at least one	

	glucocorticoid-sparing agent for nephrotic syndrome. Note: Examples of glucocorticoid-sparing agents for nephrotic syndrome include oral calcineurin inhibitors (e.g., tacrolimus, cyclosporine), cyclophosphamide, or mycophenolate mofetil" **Updated from** "Disease is relapsing and steroid-dependent" **to** "Patient has tried at least one systemic corticosteroid. Note: Examples of systemic corticosteroids include prednisone or prednisolone" **Added** "The medication is prescribed by or in consultation with a nephrologist" **Added** criteria for Patient has Already Received a Course of a Rituximab Product for Pediatric Nephrotic Syndrome. **Added** dosing for this use **Solid Organ Transplantation** **Updated from** "Desensitization for highly-allosensitized transplant candidates (to reduce HLA antibodies)" **to** "The medication will be used for desensitization therapy prior to or immediately after transplantation" **Updated from** "Antibody-mediated rejection (AMR)" **to** "The medication will be used for antibody-mediated rejection" **Added** "The medication will be prescribed by or in consultation with a physician affiliated with a transplant center" **Added** dosing for this use **Thrombotic Thrombocytopenic Purpura** **Updated** authorization duration **from** 12 months **to** 1 month **Removed** "Diagnosis of thrombotic thrombocytopenic purpura" **Updated from** "Individual is receiving concurrent therapy with glucocorticoids unless there is a documented failure, contraindication, or intolerance to glucocorticoids" **to** "The medication will be used in combination with systemic corticosteroids. Note: Examples of systemic corticosteroids include prednisone and methylprednisolone" **Updated from** "Rituximab will be used in combination with plasma exchange therapy" **to**	

	"The medication will be used in combination with therapeutic plasma exchange" **Added** dosing for this use **Factor Inhibitors in an Individual with Hemophilia** This use was removed	

The policy effective date is in force until updated or retired

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
Zymfentra® (infliximab-dyyb SC injection)	Inhibition of TNF	CD, 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
Tocilizumab Products (Actemra® IV, biosimilars; Actemra® SC, biosimilars)	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
Omvoh® (mirikizumab IV infusion, SC injection)	Inhibition of IL-23	CD, UC
Ustekinumab Products (Stelara® IV, biosimilars; Stelara® SC, biosimilars)	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, secukinumab IV infusion)	Inhibition of IL-17A	SC formulation: AS, ERA, nr-axSpA, PsO, PsA

		IV formulation: AS, nr-axSpA, PsA
Taltz® (ixekizumab SC injection)	Inhibition of IL-17A	AS, nr-axSpA, PsO, PsA
Bimzelx® (bimekizumab-bkzx SC injection)	Inhibition of IL-17A/17F	AS, nr-axSpA, PsO, PsA
Ilumya® (tildrakizumab-asmn SC injection)	Inhibition of IL-23	PsO
Skyrizi® (risankizumab-rzaa SC injection, risankizumab-rzaa IV infusion)	Inhibition of IL-23	SC formulation: CD, PsA, PsO, UC
		IV formulation: CD, UC
Tremfya® (guselkumab SC injection, guselkumab IV infusion)	Inhibition of IL-23	SC formulation: CD, PsA, PsO, UC
		IV formulation: CD, UC
Entyvio® (vedolizumab IV infusion, vedolizumab SC injection)	Integrin receptor antagonist	CD, UC
Oral Therapies/Targeted Synthetic Oral Small Molecule Drugs		
Otezla® (apremilast tablets)	Inhibition of PDE4	PsO, PsA
Otezla XR™ (apremilast extended-release tablets)	Inhibition of PDE4	PsO, PsA
Cibinqo™ (abrocitinib tablets)	Inhibition of JAK pathways	AD
Olumiant® (baricitinib tablets)	Inhibition of JAK pathways	RA, AA
Litfulo® (ritlecitinib capsules)	Inhibition of JAK pathways	AA
Leqselvi® (deuruxolitinib tablets)	Inhibition of JAK pathways	AA
Rinvoq® (upadacitinib extended-release tablets)	Inhibition of JAK pathways	AD, AS, nr-axSpA, RA, PsA, UC
Rinvoq® LQ (upadacitinib oral solution)	Inhibition of JAK pathways	PsA, PJIA
Sotyktu® (deucravacitinib tablets)	Inhibition of TYK2	PsO
Xeljanz® (tofacitinib tablets)	Inhibition of JAK pathways	RA, PJIA, PsA, UC
Xeljanz® XR (tofacitinib extended-release tablets)	Inhibition of JAK pathways	RA, PsA, UC
Zeposia® (ozanimod tablets)	Sphingosine 1 phosphate receptor modulator	UC
Velsipity® (etrasimod tablets)	Sphingosine 1 phosphate receptor modulator	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; AD – Atopic dermatitis; AA – Alopecia areata; TYK2 – Tyrosine kinase 2.

APPENDIX B

Medication	Mode of Administration
Aubagio® (teriflunomide tablets, generic)	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-xiiy intravenous infusion)	Injection
Copaxone® (glatiramer acetate subcutaneous injection, generic)	Injection (self-administered)
Gilenya® (fingolimod capsules, generic)	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
Ocrevus Zunovo™ (ocrelizumab and hyaluronidase-ocsq subcutaneous injection)	Subcutaneous injection (not self-administered)
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
Tyruko® (natalizumab-sztn intravenous infusion)	Intravenous infusion
Tysabri® (natalizumab intravenous infusion)	Intravenous infusion
Vumerity® (diroximel fumarate delayed-release capsules)	Oral
Zeposia® (ozanimod capsules)	Oral