Rituximab Intravenous Products Clinical Resource

Agents:

Riabni™ (rituximab-arrx intravenous infusion – Amgen)

Rituxan® (rituximab intravenous infusion – Genentech)

Ruxience™ (rituximab-pvvr intravenous infusion – Pfizer)

Truxima® (rituximab-abbs intravenous infusion – Celltrion/Teva)

Rituxan Hycela (rituximab/hyaluronidase- Genentech)

Review Date: 02/26/2025

Overview

Rituximab biosimilar products do not require prior authorization; however, the use of BRAND Rituxan requires an evaluation of medical necessity, prior to approval of use. Requests for Quartz Medicare Advantage members may be subject to National Coverage Determinations and/or Local Coverage Determinations based on the product being requested.

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

- Chronic lymphocytic leukemia (CLL), in combination with fludarabine and cyclophosphamide (FC) for the treatment of patients with previously untreated and previously treated CD20-positive disease.
- Granulomatosis with polyangiitis (Wegener's granulomatosis) and microscopic polyangiitis in adults, in combination with glucocorticoids.
- Non-Hodgkin lymphoma (NHL), for the following uses:
    - Previously untreated follicular, CD20-positive disease, in combination with first-line chemotherapy, and in patients achieving a complete or partial response to rituximab in combination with chemotherapy, as a single-agent maintenance therapy.
    - For relapsed or refractory, low-grade or follicular, CD20-positive, B-cell disease.
    - For non-progressing (including stable disease) low-grade, CD20-positive, B-cell disease as a single agent after first-line cyclophosphamide/vincristine/prednisone (CVP) chemotherapy.

- For previously untreated diffuse large B-cell, CD20-positive disease, in combination with cyclophosphamide/doxorubicin/vincristine/prednisone (CHOP) or other anthracycline-based chemotherapy regimens.

In addition to the above indications, Rituxan intravenous and Truxima are also indicated for treatment of the following condition:

- Rheumatoid arthritis, in adult patients with moderately to severely active disease, in combination with methotrexate for patients who have had an inadequate response to one or more tumor necrosis factor inhibitors (TNFis).

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

- Granulomatosis with polyangiitis (Wegener's granulomatosis) and microscopic polyangiitis in patients ≥ 2 years of age, in combination with glucocorticoids.
- Pemphigus vulgaris, for adults with moderate to severe disease.

Riabni, Ruxience, and Truxima are approved as biosimilar to Rituxan intravenous, indicating no clinically meaningful differences in safety and effectiveness and the same mechanism of action, route of administration, dosage form, and strength as Rituxan intravenous. However, minor differences in clinically inactive components are allowed. At this time, the biosimilars have only demonstrated biosimilarity, not interchangeability. Rituxan is not covered and requires review for medical necessity prior to its use.

Similar to intravenous rituximab products, rituximab/hyaluronidase subcutaneous injection is indicated in follicular lymphoma, previously untreated diffuse large B cell lymphoma and chronic lymphocytic leukemia after patients have received at least one full dose of a rituximab product by intravenous infusion. It has not be evaluated for non-malignant conditions. Rituxan Hycela is NOT interchangeable with other rituximab products.

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.

- Antineutrophil Cytoplasmic Antibody (ANCA)-Associated Vasculitis: Guidelines from the American College of Rheumatology (ACR) [2021] list rituximab among the alternatives for induction or maintenance of remission. Various regimens are recommended with a typical maximum of 1,000 mg/infusion. For maintenance dosing, at least 4 months should separate doses. The optimal dose of rituximab for remission maintenance remains uncertain. Although scheduled maintenance is conditionally recommended over use of CD19+ B-cell

counts and/or ANCA titers to guide retreatment, there are data to support both approaches.

- Immune Thrombocytopenia (ITP): Guidelines from the American Society of Hematology 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
- 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. 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. 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.
- Oncology indications covered in National Comprehensive Cancer Network (NCCN) guidelines:
    - Acute Lymphoblastic Leukemia (ALL): Guidelines (version 1.2021 – April 6, 2021) list rituximab in multiple regimens for Philadelphia chromosome (Ph)-negative disease. 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 4.2021 – May 5, 2021), rituximab is included in multiple treatment regimens across the spectrum of disease.8 Guidelines for pediatric aggressive mature B-cell lymphomas (version 2.2021 – June 7, 2021) 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 B-cell lymphomas (version 2.2021 – March 4, 2021), rituximab is a treatment option for patients with primary cutaneous B-cell lymphoma.
    - CLL/Small Lymphocytic Lymphoma: Rituximab features prominently in the guidelines (version 4.2021 – April 29, 2021) and is included in multiple treatment regimens across the spectrum of disease.
    - Graft-Versus-Host Disease (GVHD): Guidelines (version 2.2021 – April 21, 2021) list rituximab among the agents used for steroid-refractory chronic GVHD.
    - Hairy Cell Leukemia: Guidelines (version 2.2021 – March 11, 2021) 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).

  - Hodgkin Disease: Guidelines (version 4.2021 – April 20, 2021) recommend rituximab ± chemotherapy and/or radiation (depending on the clinical presentation) in the first-line setting for nodular lymphocyte-predominant disease. Rituximab is also used for relapsed/refractory disease and for maintenance.
  - Primary Central Nervous System Lymphoma: Guidelines for central nervous system cancers (version 2.2024 – July 25, 2024) recommend rituximab in multiple regimens for induction therapy and relapsed or refractory primary central nervous system lymphoma.
  - Waldenstrom Macroglobulinemia/Lymphoplasmacytic Lymphoma: Guidelines (version 1.2020 – September 1, 2020) include rituximab in regimens across the spectrum of disease (primary therapy, previously treated disease, and maintenance).

- Immunotherapy-Related Toxicities Associated with Checkpoint Inhibitors: NCCN (version 1.2024 – December 7, 2023) and the American Society of Clinical Oncology (ASCO) guidelines (2021) recommend rituximab as an option for corticosteroid-refractory dermatologic and hematologic immune mediated adverse events, as well as for immune-mediated encephalitis and myositis.
- Pemphigus Vulgaris: British guidelines (2017) list rituximab in combination with corticosteroids as a first-line therapy.
- Rheumatoid Arthritis: Guidelines from the American College of Rheumatology (ACR) [2015] have tumor necrosis factor (TNF) inhibitors and non-TNF biologics (including rituximab), equally positioned following a trial of a conventional synthetic disease-modifying antirheumatic drug (DMARD).
- Systemic Lupus Erythematous (SLE): European League Against Rheumatism (EULAR) recommendations for the management of SLE (2019) mention rituximab as a therapeutic option for patients who are refractory to standard immunosuppressive therapies.

Clinical Guidance for Use

Use of rituximab intravenous products is recommended in those who meet the following criteria:

Antineutrophil Cytoplasmic Antibody (ANCA)-Associated Vasculitis.

- Induction Treatment: Patient has an ANCA-associated vasculotide; AND the medication is being administered in combination with glucocorticoids; AND the medication is prescribed by or in consultation with a rheumatologist, nephrologist, or immunologist.

Note: Examples of ANCA-associated vasculitis include granulomatosis with polyangiitis (Wegener's granulomatosis) or microscopic polyangiitis.

- Follow-Up Treatment of Patients Who Have Received Induction Treatment for ANCA-Associated Vasculitis. Note: This includes a patient who received induction treatment using a rituximab product or other standard of care immunosuppressants. AND According to the prescriber, the patient achieved disease control with induction treatment; AND if the patient previously received a course of therapy, at least 16 weeks will elapse between courses.

Dosing. Initial Therapy:

- 375 mg/m2 per dose administered intravenously for 4 doses separated by at least 7 days; OR
- Up to two 1,000 mg intravenous doses separated by at least 2 weeks.

Dosing Follow-Up Treatment of a Patient Who Has Received Induction Treatment for ANCA-Associated Vasculitis:

- ≥ 18 years of age: Up to 1,000 mg administered by intravenous infusion for 6 doses; OR
- < 18 Years of age: Up to 250 mg/m2 administered by intravenous infusion for 2 doses.

B-Cell Lymphoma. Note: Examples of B-Cell Lymphomas include Follicular Lymphoma, Diffuse Large B-Cell Lymphoma, Acquired Immune Deficiency (AIDS)-Related B-Cell Lymphoma, Burkitt Lymphoma, Castleman's Disease, Marginal Zone Lymphoma (e.g., extranodal or MALT [gastric or nongastric], nodal, or splenic marginal zone lymphoma), Primary Mediastinal Large B-Cell Lymphoma, Mantle Cell Lymphoma, Post-Transplant Lymphoproliferative Disorders, Gray Zone Lymphoma, Primary Cutaneous B-Cell Lymphoma, Pediatric Aggressive Mature B-cell Lymphomas.

Dosing. Use up to 375 mg/m2 per dose administered intravenously with doses separated by at least 7 days OR up to 375mg/m2 per dose on two days of each cycle.

Chronic Lymphocytic Leukemia or Small Lymphocytic Lymphoma.

Dosing. Use up to 500 mg/m2 administered as an intravenous infusion on 1 day of each cycle.

Pemphigus Vulgaris.

- Initial Treatment. Use for 1 month in combination with a corticosteroid unless contraindicated AND the medication is prescribed by or in consultation with a dermatologist.
- Relapse or for Maintenance of Pemphigus Vulgaris. Subsequent infusions will be administered no sooner than 16 weeks following the previous infusion of a rituximab product AND A dermatologist should monitor/ consult on therapy

Dosing.

- Initial Treatment or Treatment of a Relapse. Use 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
- Maintenance Therapy. Use up to 500 mg per dose administered intravenously.

Rheumatoid Arthritis.

- Initial Therapy. Consider use in patient who has tried ONE conventional synthetic disease-modifying antirheumatic drug (DMARD) for at least 3 months AND rituximab will not be used concurrently with another biologic or with a targeted synthetic DMARD AND the medication is being prescribed by or in consultation with a Rheumatologist.
- Maintenance Therapy. 16 weeks or greater will elapse between treatment courses; AND rituximab will not be used concurrently with another biologic or with a targeted synthetic DMARD**.** 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. Use 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

Acute Lymphoblastic Leukemia. Use in CD20-positive disease.

Dosing: Use up to 375 mg/m2 administered intravenously with doses separated by at least 7 days.

Graft-Versus-Host Disease.

Consider use if patient has tried at least one conventional systemic treatment for graft versus host disease. Note: Examples include systemic corticosteroids (methylprednisolone, prednisone), cyclosporine, tacrolimus, mycophenolate mofetil, Imbruvica (ibrutinib capsules and tablets), imatinib. antithymocyte globulin, Nipent (pentostatin infusion), or an infliximab product.

Dosing. Use up to 375 mg/m2 administered intravenously with doses separated by at least 7 days.

Hairy Cell Leukemia.

Dosing. Use up to 375 mg/m2 administered intravenously with doses separated by at least 7 days.

Hodgkin Lymphoma. Consider use if the patient has nodular lymphocyte-predominant disease

Dosing. Use up to 375 mg/m2 administered intravenously with doses separated by at least 7 days.

Immune Thrombocytopenia (ITP).

Consider use if the patient has tried one other therapy such as intravenous immunoglobulin (IVIG), anti-D (RHO) immunoglobulin, corticosteroids, and splenectomy.

If Patient has Already Received a Course of a Rituximab Product for ITP, consider use if after a minimum of 6 months separating the first dose of the previous course and the first dose of the subsequent course of a rituximab product AND patient responded to therapy as determined by the prescriber (e.g. platelet count increase from baseline following treatment with a rituximab product).; AND the prescriber has determined that the patient has relapsed (e.g. patient experiences thrombocytopenia after achievement of a remission

Dosing. Use up to 375 mg/m2 administered intravenously with doses separated by at least 7 days.

Immunotherapy-Related Toxicities Associated with Checkpoint Inhibitors.

Initial Therapy. Patient is symptomatic despite a trial of at least ONE systemic corticosteroid; AND the medication is prescribed by or in consultation with an oncologist, neurologist, rheumatologist, or dermatologist.

Maintenance Therapy. Prescribed by or in consultation with an oncologist, neurologist, rheumatologist, or dermatologist.

Dosing.

- 500 mg/m2 administered intravenously for 2 doses separated by at least 14 days; OR
- 375 mg/m2 administered intravenously for 4 doses separated by at least 7 days.

Multiple Sclerosis.

Consider use if the patient had an inadequate response or was unable to tolerate at least TWO other disease-modifying agents for multiple sclerosis; AND the medication will not be used concurrently with another disease-modifying agent used for multiple sclerosis; AND at least 6 months will elapse between treatment courses (e.g. 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 subsequent course of therapy).

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

Neuromyelitis Optica Spectrum Disorder.

Dosing.

- Up to 375 mg/m2 administered intravenously with doses separated by at least 7 days; OR
- Up to two 1,000-mg doses administered as an intravenous infusion separated by at least 2 weeks.

Primary Central Nervous System Lymphoma.

Dosing: Use up to 375 mg/m2 administered intravenously with doses separated by at least 7 days.

Systemic Lupus Erythematous (SLE) [Lupus] (including nephrotic syndrome in a patient with SLE).

A) Consider use in patient that has tried at least ONE standard immunomodulating or immunosuppressant agent

B) For a patient that has already received a course of a rituximab product for SLE. Use 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 subsequent course of rituximab).

Dosing. Varies

Waldenstrom's Macroglobulinemia/Lymphoplasmacytic Lymphoma.

Dosing. Use up to 375 mg/m2 administered intravenously with doses separated by at least 7 days.

Conditions Not Recommended for Approval

Use is not recommended for circumstances where data do not support its use.

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