# Rituximab products

Humana

## Pharmacy Coverage Policy

**Effective Date:** January 01, 2021
**Revision Date:** July 27, 2022
**Review Date:** July 20, 2022
**Line of Business:** Medicaid - Humana, Medicaid - Ohio
**Policy Type:** Prior Authorization







### Disclaimer

State and federal law, as well as contract language, including definitions and specific inclusions/exclusions, take precedence over clinical policy and must be considered first in determining eligibility for coverage. Coverage may also differ for our Medicare and/or Medicaid members based on any applicable Centers for Medicare & Medicaid Services (CMS) coverage statements including National Coverage Determinations (NCD), Local Medical Review Policies (LMRP) and/or Local Coverage Determinations. See the CMS website at http://www.cms.hhs.gov/. The member's health plan benefits in effect on the date services are rendered must be used. Clinical policy is not intended to pre-empt the judgment of the reviewing medical director or dictate to health care providers how to practice medicine. Health care providers are expected to exercise their medical judgment in rendering appropriate care. Clinical technology is constantly evolving, and we reserve the right to review and update this policy periodically. 

### Description

Rituxan (rituximab), a murine/human monoclonal antibody, binds to the antigen CD20 (human B-lymphocyte–restricted differentiation antigen, Bp35). This antigen is a hydrophobic transmembrane protein that is located on pre-B and mature B lymphocytes. It is also expressed on more than 90% of B-cell non-Hodgkin's lymphomas but not expressed on hematopoietic stem cells, pro-B cells, normal plasma cells, or other normal tissues. CD20 regulates an early step or steps in the activation process for cell cycle initiation and differentiation and may also function as a calcium ion channel. It is not shed from the cell surface and does not internalize upon antibody binding. No free CD20 antigen is found in the circulation.

The mechanism of antineoplastic action may involve mediation of B cell lysis by means of binding of the Fab domain of rituximab to the CD20 antigen on B lymphocytes and by recruitment of immune effector functions by the Fc domain. Cell lysis may be the result of complement-dependent cytotoxicity (CDC) and antibody-dependent cellular cytotoxicity (ADCC). In addition, the antibody has been shown to induce apoptosis in the DHL-4 human B-cell lymphoma line.

Rituxan (rituximab) binds to lymphoid cells in the thymus, the white pulp of the spleen,

and a majority of B lymphocytes in peripheral blood and lymph nodes. However, there appears to be little or no binding to non-lymphoid tissues.

Rituximab is indicated for the treatment of:

- Non-Hodgkin's lymphoma, Diffuse, large B-cell, CD20-positive, in combination for first-line treatment
- Non-Hodgkin's lymphoma, Follicular, CD20-positive, B-cell, in combination with CVP (cyclophosphamide, vincristine, and prednisone) chemotherapy for first-line treatment
- Non-Hodgkin's lymphoma, Low-grade, CD20-positive, B-cell, stable or responsive to prior CVP (cyclophosphamide, vincristine, and prednisone) chemotherapy
- Non-Hodgkin's lymphoma, Relapsed or refractory, low-grade or follicular, CD20-positive, B-cell
- Chronic Lymphocytic Leukemia (CLL) in combination with fludarabine and cyclophosphamide (FC)
- Rheumatoid arthritis (Moderate to Severe), in combination with methotrexate, in patients who had an inadequate response to one or more tumor-necrosis-factor antagonist therapies.
- Adult and pediatric patients 2 years of age and older with granulomatosis with polyangitis (GPA)(Wegener’s Granulomatosis) and microscopic polyangiitis (MPA) in combination with glucocorticoids
- Adult patients with moderate to severe pemphigus vulgaris.

Rituximab is available as Rituxan (10 MG/ML) in 100mg/10 mL and 500 mg/50 mL single-use vials.

Rituximab-abbs is available as Truxima 10 mg/mL injection (100 mg and 500 mg vials) in single-dose vials.

Rituximab-pvvr is available as Ruxience in 10 mg/mL injection (100 mg and 500 mg vials) in single-dose vials.

Rituximab-arrx is available as Riabni in 10mg/mL injection (100 mg and 500 mg vials) in single-dose vials.

## Coverage Determination

Please note the following regarding medically accepted indications:

All reasonable efforts have been made to ensure consideration of medically accepted indications in this policy. Medically accepted indications are defined by CMS as those uses of a covered Part D drug that are approved under the federal Food, Drug and Cosmetic Act, or the use of which is supported by one or more citations included or approved for inclusion in any of the compendia described in section 1927(g)(1)(B)(i) of the Act. These compendia guide review of off-label and off-evidence prescribing and are subject to minimum evidence standards for each compendium. Currently, this review includes the following references when applicable and may be subject to change per CMS:

- American Hospital Formulary Service-Drug Information (AHFS-DI)
- National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium
- Truven Health Analytics Micromedex DrugDEX
- Elsevier/Gold Standard Clinical Pharmacology
- Wolters Kluwer Lexi-Drugs

Rituxan (rituximab) or Truxima (rituximab-abbs) or Ruxience (rituximab-pvvr) or Riabni (rituximab-arrx) will require prior authorization. These agents may be considered medically necessary for the following indications:

*Truxima (rituximab-abbs) requests are for these indications: non-Hodgkin's lymphoma (NHL), chronic lymphocytic leukemia (CLL), rheumatoid arthritis (RA), and granulomatosis with polyangiitis (GPA) (Wegener's Granulomatosis) and microscopic polyangiitis (MPA).

*Ruxience (rituximab-pvvr) requests are for these indications: non-Hodgkin's lymphoma (NHL), chronic lymphocytic leukemia (CLL), rheumatoid arthritis (RA), and granulomatosis with polyangiitis (GPA) (Wegener's Granulomatosis) and microscopic polyangiitis (MPA).

*Riabni (rituximab-arrx) requests are for these indications: non-Hodgkin's lymphoma (NHL), chronic lymphocytic leukemia (CLL), rheumatoid arthritis (RA) and granulomatosis with polyangiitis (GPA) (Wegener's Granulomatosis) and microscopic polyangiitis (MPA).

**Chronic Lymphocytic Leukemia**

- The member must have a diagnosis of chronic lymphocytic leukemia.

**Immune or Idiopathic Thrombocytopenic Purpura**

- The member must have a diagnosis of refractory primary immune or idiopathic thrombocytopenic purpura.

- Member has not had a splenectomy, but has had an insufficient response or is intolerant to corticosteroids, **AND** immunoglobulins (IVIG), **OR**

- Member has had a splenectomy with an inadequate response or is intolerant to

procedure **AND** had an insufficient response or is intolerant to post-splenectomy corticosteroids.
- The member must have had an inadequate response to post-splenectomy corticosteroid therapy for four consecutive weeks within the last three months.

**Note:** Refractory response is characterized as EITHER:

- Platelet count <25,000/µL **OR**
- Active bleeding due to inadequate platelet function.

**Non-Hodgkin's Lymphoma (CD-20 positive/B-cell)**

- The member has a diagnosis of CD-20 positive/B-cell Non-Hodgkin's lymphoma .

**Hodgkin's Disease (Hodgkin's Lymphoma)**

- The member has a diagnosis of Hodgkin's Disease
- The member will be using rituximab for primary treatment or for relapsed or progressive disease

- Disease has confirmed CD20 positivity.

**Rheumatoid Arthritis**

- The member must have a diagnosis of moderately- to severely-active rheumatoid arthritis **AND**
- The member has had prior therapy, contraindication or intolerance to tumor necrosis factor (TNF) antagonist therapy (e.g. Inflectra) **AND**
- The member must be on concomitant treatment with methotrexate during rituximab therapy, unless contraindicated or intolerant to methotrexate.

**Waldenstrom's Macroglobulinemia**

- The member must have a diagnosis of Waldenstrom’s macroglobulinemia.

**Post-transplant Lymphoproliferative Disorder**

- The member has a diagnosis of Post-transplant Lymphoproliferative disease.

**Wegener's Granulomatosis (WG) and Microscopic Polyangiitis (MPA)**

- The member has a diagnosis of Wegener’s Granulomatosis (WG) OR Microscopic Polyangiitis (MPA)

- The member is 2 years of age or older.
- The member is taking rituximab in combination with glucocorticoids.

**Pemphigus Vulgaris (PV)**

- The member must have a diagnosis of moderate to severe Pemphigus Vulgaris

Rituxan (rituximab) or Truxima (rituximab-abbs) or Ruxience (rituximab-pvvr) or Riabni (rituximab-arrx) will be approved in plan year duration or as deemed appropriate by clinical review.

*Coverage Limitations*

Rituxan (rituximab) or Truxima (rituximab-abbs) or Ruxience (rituximab-pvvr) or Riabni (rituximab-arrx) therapy is not considered medically necessary for members with the following concomitant conditions:

- 'High dose' CLL therapies (doses >500mg/m$^2$)
- The member will be using rituximab as maintenance therapy for diffuse large B cell lymphoma (DLBCL)
- The length of maintenance therapy exceeds 2 years for low-grade non-Hodgkin's lymphoma (e.g. follicular lymphoma, marginal zone lymphoma)
- The length of maintenance therapy exceeds 2 years for chronic lymphocytic leukemia

- Experimental/Investigational Use – Indications not supported by CMS recognized

compendia or acceptable peer reviewed literature.

## Background

This is a prior authorization policy about Rituxan (rituximab) or Truxima (rituximab-abbs) or Ruxience (rituximab-pvvr) or Riabni (rituximab-arrx).

The Hematology/Oncology Pharmacy Associated (HOPA) recommends that monoclonal antibodies and other biologic agents currently available be dose rounded to the nearest vial size within 10% of the prescribed dose.

**Black Box Warnings**

- Infusion Reactions: Rituximab administration can result in serious, including fatal, infusion reactions. Deaths within 24 hours of rituximab infusion have occurred. Approximately 80% of fatal infusion reactions occurred in association with the first infusion. Carefully monitor patients during infusions. Discontinue rituximab infusion and provide medical treatment for Grade 3 or 4 infusion reactions.

- Hepatitis B virus (HBV) reactivation: In some cases resulting in fulminant hepatitis, hepatic failure, and death.

- Severe Mucocutaneous Reactions: Severe, including fatal, mucocutaneous reactions can occur in patients receiving rituximab.

- Progressive Multifocal Leukoencephalopathy (PML): JC virus infection resulting in PML and death can occur in patients receiving rituximab (Prod Info RITUXAN(R) IV injection, 2008).

Rituximab use is not indicated in patients with:

- A known hypersensitivity to murine products or other components of the formulation

- Safety and effectiveness have not been established in pediatric patients <18 years old
- Prior severe infusion reaction (IgE mediated) to rituximab treatment
- Women who are pregnant or lactating that have not been apprised of the risk associated with rituximab therapy
- Prior history of progressive multifocal leukoencephalopathy likely due to rituximab therapy
- Multiple sclerosis or other demyelinating events
- Undifferentiated cytopenias
- Combination therapy with cisplatin
- T-cell lymphomas or plasma cell disorders/multiple myeloma (other than Waldenström's Macroglobulinemia)
- HLA desensitization during transplant with or without IVIG
- Combination therapy with other biologicals such as Arzerra, Enbrel, Humira, Cimzia Simponi, Remicade, Orencia, Stelara, or Kineret
- See also 'Coverage Limitations' section.

Contraindications to splenectomy could potentially include: diabetes mellitus, congestive heart failure, ischemic heart disease, cerebrovascular disease, asthma and chronic obstructive pulmonary disease and older age (over 70 or 80 years). Generally speaking, splenectomy should be avoided in pregnant patients and in patients with severe cardiac or pulmonary disease who are at risk for any major surgery.

For use in HLA desensitization protocols during transplant with or without IVIG,

rituximab has not yet been recommended as a validated treatment option—see NEJM reference.

**Dosage Adjustments**
Non-IgE-mediated hypersensitivity reaction: slow or stop infusion; may resume at 50% reduction in infusion rate when symptoms have completely resolved.

Rituxan should be stopped if patient experiences a severe (anaphylactic) reaction.

## Provider Claims Codes

For medically billed requests, please visit www.humana.com/PAL. Select applicable Preauthorization and Notification List(s) for medical and procedural coding information.

## Medical Terms

Rituxan; rituximab; Truxima; rituximab-abbs; Ruxience; rituximab-pvvr; Riabni; rituximab-arrx; Non-Hodgkin's Lymphoma, Hodgkin's Disease, Waldenström's Macroglobulinemia, Post-transplant lymphoproliferative disorder**,** Rheumatoid Arthritis; pemphigus vulgaris; intravenous infusion; pharmacy

## References

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NCCN Drug and Biologics Compendium. Fort Washington, PA: National Comprehensive Cancer Network (NCCN); Updated periodically.

Hematology/Oncology Pharmacy Associated (HOPA) Dose Rounding Position Paper: http://hoparx.org/images/hopa/resource-library/professional-tools/Dose-Rounding-Position-Paper-2017-10-23.pdf

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Ruxience (rituximab-pvvr) Prescribing Information. Pfizer. New York, NY. November 2021.

Truxima (rituximab-abbs) Prescribing Information. Teva. North Wales, PA. February 2022.