Policy and Procedure	
PHARMACY PRIOR AUTHORIZATION AND STEP THERAPY POLICY AND CRITERIA ORPTCONC058B.0226	**ANTINEOPLASTIC AGENTS** **RITUXIMAB** See Appendix A for medications covered by policy
Effective Date: 4/1/2026	**Review/Revised Date**: 08/06, 04/07, 12/08, 02/09, 12/09, 04/10, 06/11, 02/13, 06/13, 02/14, 02/15, 06/15, 07/15, 01/16, 12/16, 01/18, 04/18, 08/18, 01/19, 03/19, 09/19, 12/19, 01/20, 12/20, 04/21, 07/21, 01/22. 04/22, 01/23, 05/23, 01/24, 01/25, 10/25 (ML), 12/25, 01/26 (KN)
Original Effective Date: 08/06	**P&T Committee Meeting Date**: 08/06, 04/07, 12/08, 02/09, 12/09, 04/10, 06/11, 02/13 , 06/13, 02/14, 02/15, 06/15, 07/15, 02/16, 02/17, 02/18, 06/18, 10/18, 02/19, 04/19, 10/19, 12/19, 02/20, 06/20, 02/21, 04/21, 08/21, 02/22, 04/22, 02/23, 06/23, 02/24, 02/25, 10/25, 02/26
Approved by: Oregon Region Pharmacy and Therapeutics Committee	

SCOPE:
Providence Health Plan and Providence Health Assurance as applicable (referred to individually as “Company” and collectively as “Companies”).

APPLIES TO:
Medicare Part B

POLICY CRITERIA:

COVERED USES:
All Food and Drug Administration (FDA) approved indications not otherwise excluded from the benefit, some medically- accepted indications (as outlined in the Required Medical Information section).

REQUIRED MEDICAL INFORMATION:
For all requests for non-preferred rituximab products:
Documented trial and failure, intolerance, or contraindication to the use of both preferred biosimilar medications: Riabni (rituximab-arrx) and Truxima (rituximab-abbs)

For initiation of therapy (new starts): Requests for rituximab may be approved for the following indications when the criteria below are met:

1. **Oncologic Diagnoses:**
    a. Use must be for an FDA approved indication or indication supported by National Comprehensive Cancer Network (NCCN) guidelines with recommendation 2A or higher
2. **Antineutrophil Cytoplasmic Antibody (ANCA)- Associated Vasculitis (including Granulomatosis with Polyangiitis [GPA] and Microscopic Polyangiitis [MPA]):**
    a. Concurrent use with glucocorticoids
3. **Autoimmune Hemolytic Anemia (AIHA):**
    a. Warm-reactive disease refractory to or dependent on glucocorticoids

OR

b. Cold agglutinin disease with symptomatic anemia, transfusion-dependence, and/or disabling circulatory symptoms

4. **Idiopathic Membranous Nephropathy**:
   a. Documented diagnosis of idiopathic (primary) membranous nephropathy
   AND
   b. Secondary causes of membranous nephropathy have been ruled out (e.g., infections, autoimmune diseases, malignancies, nutritional supplements [such as lipoic acid], nonsteroidal anti-inflammatory drugs [NSAIDs])
5. **Immune Thrombocytopenic Purpura (ITP):**
   a. Inadequate response, intolerance, or contraindication to systemic corticosteroid therapy
   AND
   b. Active bleeding or increased risk of bleeding as indicated by a platelet count less than 30,000 cells per microliter
6. **Multiple Sclerosis (MS):**
   a. Diagnosis of a relapsing form of MS (i.e., relapsing-remitting MS [RRMS], active secondary progressive disease [SPMS], or clinically isolated syndrome [CIS])
7. **Myasthenia Gravis (MG):**
   a. Muscle-specific tyrosine kinase (MuSK)-antibody positive disease
   AND
   b. Inadequate response to standard first-line therapy (such as glucocorticoids, azathioprine, mycophenolate mofetil, etc.)
8. **Neuromyelitis Optica Spectrum Disorder (NMOSD):**
   a. Confirmed diagnosis
   AND
   b. Alternative diagnoses have been ruled out (such as myelin oligodendrocyte glycoprotein [MOG] antibody disease [MOGAD], MS, sarcoidosis, cancer, chronic infection)
9. **Pemphigus Vulgaris (PV)**:
   a. Diagnosis of moderate to severe disease confirmed by all the following:
      i. One or more of the following clinical features:
         1) Appearance of lesions, erosions, and/or blisters
         2) Nikolsky sign (induction of blistering via mechanical pressure at the edge of a blister or on normal skin)
         3) Characteristic scarring and lesion distribution
      ii. Histopathologic confirmation by skin/mucous membrane biopsy
      iii. Positive direct immunofluorescence (DIF) microscopy result or the presence of autoantibodies as detected by indirect immunofluorescence (IIF) or enzyme-linked immunosorbent assay (ELISA)

AND

b. Other causes of blistering or erosive skin and mucous membrane diseases have been ruled out

10. **Rheumatoid Arthritis (RA):**
    a. Inadequate response, intolerance, or contraindication to at least one tumor necrosis factor (TNF) antagonist

    AND

    b. Concurrent use with methotrexate unless patient has a contraindication or intolerance
11. **Thrombotic Thrombocytopenic Purpura (TTP)**:
    a. Confirmed TTP with baseline ADAMTS 13 deficiency (less than 10% activity)

    AND

    b. One of the following:
        i. Concurrent use with corticosteroids and therapeutic plasma exchange (TPE)

        OR

        ii. Prophylactic monotherapy for patients in remission

For patients established on therapy with the requested product (within the previous year):

1. Response to therapy (e.g., slowing of disease progression or decrease in symptom severity and/or frequency)

EXCLUSION CRITERIA: N/A

AGE RESTRICTIONS:
Age must be appropriate based on FDA-approved indication

PRESCRIBER RESTRICTIONS:
Must be prescribed by, or in consultation with, a specialist for the respective indication such as: an oncologist, hematologist, rheumatologist, neurologist (in the case of RRMS, NMO), dermatologist (in the case of PV), or nephrologist (in the case of renal disease)

COVERAGE DURATION:
For oncologic diagnoses: Authorization will be approved until no longer eligible with the plan, subject to formulary and/or benefit changes

For non-oncologic diagnoses: Initial authorization will be approved for six months and reauthorization will be approved until no longer eligible with the plan, subject to formulary and. or benefit changes

For off-label use criteria please see the Chemotherapy Treatment Utilization Criteria; Coverage for Non-FDA Approved Indications ORPTCOPS105.

Requests for indications that were approved by the FDA within the previous six (6) months may not have been reviewed by the health plan for safety and effectiveness and inclusion on this policy document. These requests will be reviewed using the New Drug and or Indication Awaiting P&T Review; Prior Authorization Request ORPTCOPS047.

Requests for a non-FDA approved (off-label) indication requires the proposed indication be listed in either the American Hospital Formulary System (AHFS), Drugdex, or the National Comprehensive Cancer Network (NCCN) and is considered subject to evaluation of the prescriber's medical rationale, formulary alternatives, the available published evidence-based research and whether the proposed use is determined to be experimental/investigational.

Coverage decisions are made on the basis of individualized determinations of medical necessity and the experimental or investigational character of the treatment in the individual case.

INTRODUCTION:

Rituximab binds to the CD20 antigen on B-lymphocytes and the Fc portion recruits immune functions to mediate B-cell lysis. Recombinant human hyaluronidase is an endoglycosidase used to increase the dispersion and absorption of co-administered drugs when administered subcutaneously.

Rituximab has a boxed warning for severe mucocutaneous reactions, hepatitis B (HBV) reactivation, and progressive multifocal leukoencephalopathy (PML). Intravenous rituximab also has a boxed warning for fatal-infusion related reactions within 24 hours of administration. The majority of these reactions occur with the first infusion.

FDA APPROVED INDICATIONS:

Rituximab and biosimilars, injection for intravenous use

- Non-Hodgkin's Lymphoma (NHL)
    - Relapsed or refractory, low-grade or follicular, CD20-positive, B-cell NHL as a single agent
    - Previously untreated follicular, CD20-positive, B-cell NHL in combination with first line chemotherapy and, in patients achieving a complete or partial response to a rituximab product in combination with chemotherapy, as single-agent maintenance therapy.
    - Non-progressing (including stable disease), low-grade, CD20-positive, B-cell NHL as a single agent after first-line CVP chemotherapy

  - Previously untreated diffuse large B-cell, CD20-positive NHL in combination with CHOP or other anthracycline-based chemotherapy regimens
- Chronic Lymphocytic Leukemia (CLL): in combination with fludarabine and cyclophosphamide (FC) for the treatment of patients with previously untreated and previously treated CD20-positive CLL
- Granulomatosis with Polyangiitis (GPA) (Wegener's Granulomatosis) and Microscopic Polyangiitis (MPA) in adult and pediatric patients two years of age and older in combination with glucocorticoids (Rituxan®, Ruxience®, Truxima® only for adult and pediatric patients; Riabni® for adult patients only)
- Rheumatoid Arthritis (RA): (Moderate to Severe), in combination with methotrexate, in patients who had an inadequate response to one or more tumor-necrosis-factor (TNF) antagonist therapies
- Treatment of adult patients with moderate to severe pemphigus vulgaris

Rituxan® only

- Mature B-cell NHL and mature B-cell acute leukemia (B-AL): previously untreated, advanced stage, CD20-positive, diffuse large B-cell lymphoma (DLBCL), Burkitt-like lymphoma (BLL) or mature B-cell acute leukemia (B-AL) in combination with chemotherapy in pediatric patients age 6 months and older

  Limitations of use: Rituxan® is not recommended for use in patients with severe, active infection.

Rituxan Hycela® (rituximab and hyaluronidase) injection

- Follicular Lymphoma
  - Relapsed or refractory, follicular lymphoma as a single agent
  - Previously untreated follicular lymphoma in combination with first line chemotherapy and, in patients achieving a complete or partial response to rituximab in combination with chemotherapy, as single-agent maintenance therapy
  - Non-progressing (including stable disease), follicular lymphoma as a single agent after first-line cyclophosphamide, vincristine, and prednisone (CVP) chemotherapy
- Diffuse Large B-cell Lymphoma
  - Previously untreated diffuse large B-cell lymphoma in combination with cyclophosphamide, doxorubicin, vincristine, prednisone (CHOP) or other anthracycline-based chemotherapy regimens
- Chronic Lymphocytic Leukemia
  - Previously untreated and previously treated CLL in combination with fludarabine and cyclophosphamide (FC)

Limitations of Use:

- Initiate treatment only after patients have received at least one full dose of a rituximab product by intravenous infusion.
- Not indicated for the treatment of non-malignant conditions.

POSITION STATEMENT:

Biosimilar Products

A biosimilar is a type of biologic drug that is highly similar to an FDA-approved biologic drug, known as the reference product. Biosimilars provide equivalent clinical benefit to the original reference product ("therapeutically equivalent"). These products have been deemed interchangeable with the reference products by the Oregon Region Pharmacy & Therapeutics Committee (ORPTC). Members will be required to utilize a preferred biosimilar, unless clinical documentation is provided outlining medical rationale for using a non-preferred product, as outlined in the criteria above.

Antineutrophil Cytoplasmic Antibody (ANCA)-Associated Vasculitis (AAV)

AAV is a group of conditions marked by necrotizing inflammation of small blood vessels with few or no immunocomplexes in the walls of the blood vessels (pauci-immune). These conditions include granulomatosis with polyangiitis (GPA), microscopic polyangiitis (GPA), and eosinophilic granulomatosis with polyangiitis EGPA). The Kidney Disease Improving Global Outcomes (KDIGO) 2024 Clinical Practice Guidelines recommend first-line treatment with a combination of glucocorticoids and either rituximab or cyclophosphamide. This recommendation is also supported by the 2022 update of the European Alliance of Associations for Rheumatology (EULAR) guidelines for the management of AAV.[10,11]

Autoimmune hemolytic anemia (AIHA)

AIHA is a group of disorders characterized by a malfunction of the immune system that produces autoantibodies, which attack red blood cells as if they were substances foreign to the body. There are no FDA-approved treatments for AIHA. There are two main types of AIHA: Warm AIHA where the autoantibodies attach to and destroy red blood cells (RBC) at normal body temperature and cold AIHA (cold agglutinin disease) where the autoantibodies (IgM) become most active and attack RBC at temperatures below normal body temperature. Warm AIHA is initially treated with glucocorticoids at a dose of 1 mg/kg per day of prednisone or its equivalent for two to three weeks with or without rituximab 1,000 mg on days 1 and 15 (or 375 mg/m^2 weekly for four weeks). Cold AIHA (cold agglutinin disease [CAD]) is treated with rituximab 375 mg/m^2 weekly for four weeks (with or without bendamustine).[13]

Immune Thrombocytopenic Purpura (ITP)

ITP is also known as immune thrombocytopenic purpura or idiopathic thrombocytopenic purpura. This is an autoimmune disease characterized by immunologic destruction of otherwise normal platelets and is typically caused by an unknown trigger. First line treatment is typically with corticosteroids when the platelet count is < $30x10^9$/L and the patient is asymptomatic or has minor bleeding. Second-line options in patients with ITP for at least three months who are either dependent on corticosteroids or experienced a lack of response to corticosteroids include splenectomy, TPO-receptor agonists (e.g., eltrombopag, romiplostim), and rituximab. Splenectomy is the only treatment that provides sustained remission off all treatments at one year and beyond in a high proportion of ITP patients.[3]

Multiple Sclerosis (MS)

Per the American Academy of Neurology, determining initial treatment for relapsing remitting MS (RRMS) should encompass consideration of safety, route of administration, lifestyle, cost, efficacy, common adverse effects (AEs), and tolerability. Rituximab has been used off-label to treat RRMS for many years. A 2021 systematic Cochrane review assessed the beneficial and adverse effects of rituximab as 'first choice' and as 'switching' therapy for adults with MS. In reviewing rituximab as a first choice agent for RRMS, one non-randomized study compared rituximab with interferon beta or glatiramer acetate, dimethyl fumarate, natalizumab, or fingolimod in active relapsing MS at 24 months' follow-up. Rituximab likely results in a large reduction in relapses compared with interferon beta or glatiramer acetate (hazard ratio (HR) 0.14, 95% confidence interval (CI) 0.05 to 0.39; 335 participants; moderate-certainty evidence). Rituximab may reduce relapses compared with dimethyl fumarate (HR 0.29, 95% CI 0.08 to 1.00; 206 participants; low-certainty evidence) and natalizumab (HR 0.24, 95% CI 0.06 to 1.00; 170 participants; low-certainty evidence). It may make little or no difference on relapse compared with fingolimod (HR 0.26, 95% CI 0.04 to 1.69; 137 participants; very low-certainty evidence). In those patients that were switching therapy, one RCT compared rituximab with placebo in relapsing MS at 12 months' follow-up. Rituximab may decrease recurrence of relapses compared with placebo (OR 0.38, 95% CI 0.16 to 0.93; 104 participants; low-certainty evidence). The authors concluded, for preventing relapses in relapsing MS, rituximab as 'first choice' and as 'switching' may compare favorably with a wide range of approved DMTs.[4,5] A comprehensive review on the treatment of multiple sclerosis by Gholamzad et al. 2019 suggested that rituximab for RRMS patients who did not respond to first- and second-line therapies and in cases where RRMS is stabilized after natalizumab treatment and is a candidate for a RRMS therapy with less PML risk.[7]

Myasthenia Gravis (MG)

MG is a neuromuscular transmission disorder which is caused by autoantibody binding in the neuromuscular junction. The initial treatment for most patients involves pyridostigmine. Corticosteroids and immunosuppressive therapy is used a second-line therapy. Nonsteroidal immunosuppressive which can be used include azathioprine, cyclosporine, mycophenolate mofetil, methotrexate, and tacrolimus. Additional options for patients with refractory MG include intravenous immunoglobulin (IVIG) and chronic PLEX, cyclophosphamide, and rituximab. Recommendations include using rituximab early in therapy in patients with MuSK-MG refractory to initial immunotherapy.[6]

Neuromyelitis optica spectrum disorder (NMOSD)
NMOSD is an autoimmune inflammatory disorder of the central nervous system which, if untreated, may lead to significant disability. There is no curative treatment for NMOSD however there are medications which may reduce the number of attacks.[14]

The Neuromyelitis Optica Study Group (NEMOS) provides recommendations for both FDA-approved and off-label treatments. The standard of care for acute attacks includes high-dose glucocorticoids and apheresis therapy. Other experimental therapies include intravenous immunoglobulins (IVIG), early anti-CD20 therapy, and early anti-complement therapy. First-line therapies for prophylaxis include azathioprine, mycophenolate mofetil (MMF), and rituximab, with rituximab showing benefit over azathioprine and MMF. FDA approved therapies for AQP4-IgG-positive NMOSD include eculizumab, inebilizumab, and satralizumab. Rituximab was approved in Japan in 2022 for NMOSD. Studies have shown its effectiveness in both AQP4-IgG-positive and -negative patients.[14]

Pemphigus vulgaris (PV)
PV is an acquired autoimmune disease in which immunoglobulin (IgG) antibodies target desmosomal proteins to produce intraepithelial, mucocutaneous blistering. Rituximab is recommended as first-line treatment for patients with moderate to severe disease as well as those not achieving remission with systemic corticosteroids and/or immunosuppressive agents. Rituximab provides a corticosteroid-sparing effect.[9]

Rheumatoid arthritis (RA)
The American College of Rheumatology (ACR) guidelines, updated in 2021, conditionally recommend rituximab for use in patients with a previous lymphoproliferative disorder (such as B-cell chronic lymphocytic leukemia, non-Hodgkin lymphoma, hairy cell leukemia) with a moderate to high level of disease activity. It is preferred over other disease-modifying antirheumatic drugs (DMARDs) as is not expected to increase the risk of developing or worsening these disorders.[2]

Thrombotic Thrombocytopenic Purpura (TTP)
TTP is a thrombotic microangiopathy caused by autoantibodies against ADAMTS13, the von Willebrand factor-cleaving protease, leading to severe ADAMTS13 deficiency (activity <10 percent). It is considered a medical emergency that is always fatal without prompt identification and appropriate treatment. The combination of therapeutic plasma exchange (TPE) and corticosteroids is the mainstay of TTP treatment, as TPE provides ADAMTS13 from donor plasma and removes the autoantibody against ADAMTS13, while corticosteroids reduce production of the ADAMTS13 inhibitor. Rituximab suppresses autoantibody production, and noncontrolled and respective studies have shown that adding rituximab to TPE and glucocorticoids improves remission and relapse rates. The 2020 International Society on Thrombosis and Haemostasis (ISTH) guidelines conditionally recommend the addition of rituximab to corticosteroids and TPE over corticosteroids and TPE alone, a recommendation that remains unchanged in the 2025 ISTH focused update.[12]

REFERENCE/RESOURCES:

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3. Neunert C, Terrell DR, Arnold DM *et al*. American Society of Hematology 2019 guidelines for immune thrombocytopenia. *Blood Adv*. 2019;3(23):3829-3866.Erratum in: *Blood Adv*. 2020;4(2):252.
4. Filippini G, Kruja J, Del Giovane C. Rituximab for people with multiple sclerosis. Cochrane Database of Systematic Reviews 2021, Issue 11. Art. No.: CD013874. DOI: 10.1002/14651858.CD013874.pub2. Accessed 08 January 2022.
5. Rae-Grant A, Day GS, Marrie, RA, et al. Practice guideline recommendations summary: Disease-modifying therapies for adults with multiple sclerosis. *Neurology*. Apr 2018, 90 (17) 777-88; DOI: 10.1212/WNL.0000000000005347
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7. Ghloamzad M, Ebtekar M, Ardestani MS, et al. A comprehensive review on the treatment approaches of multiple sclerosis: currently and in the future. *Inflammation Research.* 2019; 68:25-38
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12. Zheng XL, Al-Housni Z, Cataland SR, et al. 2025 focused update of the 2020 ISTH guidelines for management of thrombotic thrombocytopenic purpura. *J Thromb Haemost*. 2025;23(11):3711-3732. doi:10.1016/j.jtha.2025.06.002
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APPENDIX A. BILLING GUIDELINES AND CODING:

HCPCS	Coding Description	Brand Name
Preferred Products		
Q5123	Injection, rituximab-arrx, biosimilar, (riabni), 10 mg	Riabni
Q5115	Injection, rituximab-abbs, biosimilar, (truxima), 10 mg	Truxima
Non-preferred Products		
Q5119	Injection, rituximab-pvvr, biosimilar, (ruxience), 10 mg	Ruxience
J9312	Injection, rituximab, 10 mg	Rituxan
J9311	Injection, rituximab 10 mg and hyaluronidase	Rituxan Hycela
ADMINISTRATION CODES◊		
96401	Chemo anti-neopl sq/im	
96413	Chemo iv infusion 1 hr	
96415	Chemo iv infusion addl hr	

*Coding Notes:

• The above code list is provided as a courtesy and may not be all-inclusive. Inclusion or omission of a code from this policy neither implies nor guarantees reimbursement or coverage. Some codes may not require routine review for medical necessity, but they are subject to provider contracts, as well as member benefits, eligibility and potential utilization audit.
• HCPCS/CPT code(s) may be subject to National Correct Coding Initiative (NCCI) procedure-to-procedure (PTP) bundling edits and daily maximum edits known as “medically unlikely edits” (MUEs) published by the Centers for Medicare and Medicaid Services (CMS). This policy does not take precedence over NCCI edits or MUEs. Please refer to the CMS website for coding guidelines and applicable code combinations.