

# Specialty Guideline Management

## Rituximab Products

### Products Referenced by this Document

Drugs that are listed in the following table include both brand and generic and all dosage forms and strengths unless otherwise stated. Over-the-counter (OTC) products are not included unless otherwise stated.

Note: This criteria is created only for implementation of Pennsylvania Employee Benefit Trust Fund (PA EBTF)

Brand Name	Generic Name
Rituxan	rituximab
Ruxience	rituximab-pvvr
Truxima	rituximab-abbs
Riabni	rituximab-arrx

### Indications

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

#### FDA-Approved Indications<sup>1,2,27,28</sup>

- Non-Hodgkin's lymphoma (NHL) in adult patients with:
  - 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 (cyclophosphamide, vincristine, and prednisone) chemotherapy
- Previously untreated diffuse large B-cell, CD20-positive NHL in combination with cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) or other anthracycline-based chemotherapy regimens
- Chronic lymphocytic leukemia (CLL), in combination with fludarabine and cyclophosphamide (FC), for the treatment of adult 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 2 years of age and older in combination with glucocorticoids (pediatric indication applies to Rituxan only).
- Rheumatoid Arthritis (RA) in combination with methotrexate in adult patients with moderately- to severely-active RA who have an inadequate response to one or more TNF antagonist therapies.
- Pemphigus Vulgaris (PV): Rituxan is indicated for the treatment of adult patients with moderate to severe pemphigus vulgaris.
- Previously untreated, advanced stage, CD20-positive diffuse large B-cell lymphoma (DLBCL), Burkitt lymphoma (BL), Burkitt-like lymphoma (BLL) or mature B-cell acute leukemia (B-AL) in combination with chemotherapy in pediatric patients aged 6 months of age and older.

## Compendial Uses

- Sjögren's syndrome<sup>4-6</sup>
- Multiple sclerosis, relapsing remitting<sup>4,10</sup>
- Neuromyelitis optica (i.e., neuromyelitis optica spectrum disorder, NMOSD, Devic disease)<sup>11,12, 36</sup>
- Autoimmune blistering disease<sup>19,31,32</sup>
- Cryoglobulinemia<sup>13-15</sup>
- Solid organ transplant<sup>17</sup>
- Opsoclonus-myoclonus ataxia<sup>18</sup>
- Systemic lupus erythematosus (SLE)<sup>20,21</sup>
- Non-Hodgkin's lymphoma<sup>22,25</sup>
  - CLL/Small lymphocytic lymphoma (SLL)<sup>22</sup>
  - Mantle cell lymphoma<sup>22,25</sup>
  - Marginal zone lymphomas (nodal, splenic, gastric MALT, nongastric MALT, extranodal)<sup>22</sup>
  - Primary cutaneous B-cell lymphoma<sup>22</sup>
  - High-grade B-cell lymphoma (including high-grade B-cell lymphoma with translocations of MYC and BCL2 and/or BCL6 [double/triple hit lymphoma], high-grade B-cell lymphoma, not otherwise specified)<sup>22</sup>
  - Histological transformation of indolent lymphomas to diffuse large B-cell lymphoma<sup>22</sup>
  - Histological transformation of indolent lymphomas to high-grade B-cell lymphoma with MYC and BCL6 without BCL2 rearrangements<sup>22</sup>

- Castleman's disease<sup>22</sup>
- Human Immunodeficiency Virus (HIV) Related B-cell lymphoma<sup>22</sup>
- Hairy cell leukemia<sup>22</sup>
- Post-transplant lymphoproliferative disorder (PTLD)<sup>22,25</sup>
- Pediatric Aggressive Mature B-cell Lymphoma<sup>22</sup>
- Primary Mediastinal Large B-Cell Lymphoma
- B-cell lymphoblastic lymphoma<sup>22,26</sup>
- Relapsed/refractory immune or idiopathic thrombocytopenic purpura (ITP)<sup>23,25</sup>
- Autoimmune hemolytic anemia<sup>25</sup>
- Waldenström's macroglobulinemia/lymphoplasmacytic lymphoma (LPL)/Bing-Neel syndrome<sup>22,25</sup>
- Thrombotic thrombocytopenic purpura<sup>25</sup>
- Myasthenia gravis, refractory<sup>25</sup>
- Hodgkin's lymphoma, nodular lymphocyte-predominant<sup>22,25</sup>
- Chronic graft-versus-host disease (GVHD)<sup>25</sup>
- Central nervous system (CNS) cancers<sup>22</sup>
  - Leptomeningeal metastases from lymphomas
  - Primary CNS lymphoma
- B-cell acute lymphoblastic leukemia (ALL)<sup>22</sup>
- Prevention of Epstein-Barr virus (EBV)-related PTLD in high risk patients<sup>24,25</sup>
- Immune checkpoint inhibitor-related toxicities<sup>22</sup>
- Rosai-Dorfman disease<sup>22</sup>
- Allogeneic transplant conditioning<sup>22</sup>
- Membranous nephropathy<sup>38</sup>

All other indications are considered experimental/investigational and not medically necessary.

## Documentation

Submission of the following information is necessary to initiate the prior authorization review:

- Rheumatoid Arthritis (RA)
  - Initial requests:
    - Chart notes, medical record documentation, or claims history supporting previous medications tried (if applicable), including response to therapy. If therapy is not advisable, documentation of clinical reason to avoid therapy.
    - Laboratory results, chart notes, or medical record documentation of biomarker testing (i.e., rheumatoid factor [RF], anti-cyclic citrullinated peptide [anti-CCP], and C-reactive protein [CRP] and/or erythrocyte sedimentation rate [ESR]) (if applicable).
  - Continuation requests: Chart notes or medical record documentation supporting positive clinical response.

Reference number(s)
2893-A

- Sjögren's syndrome, cryoglobulinemia, opsoclonus-myoclonus-ataxia, and systemic lupus erythematosus (initial requests only): Chart notes, medical record documentation, or claims history supporting previous medications tried, including response to therapy.

## Prescriber Specialties

This medication must be prescribed by or in consultation with one of the following:

- RA, GPA (Wegener's granulomatosis), MPA, Churg-Strauss, pauci-immune glomerulonephritis, SLE: rheumatologist, immunologist, nephrologist
- Sjögren's syndrome: rheumatologist, ophthalmologist, immunologist
- Multiple sclerosis, NMOSD, myasthenia gravis, opsoclonus-myoclonus-ataxia: neurologist, immunologist, rheumatologist
- Autoimmune blistering disease: dermatologist, immunologist
- Cryoglobulinemia: hematologist, rheumatologist, neurologist, nephrologist
- Solid organ transplant: immunologist, transplant specialist
- Membranous nephropathy: nephrologist

## Exclusions

- Coverage will not be provided for requests for the treatment of rheumatoid arthritis (RA) when planned date of administration is less than 16 weeks since date of last dose received.
- Member will not receive Rituxan, Ruxience, Truxima, or Riabni with any other biologic drug or targeted synthetic drug for RA.
- Member will not receive Rituxan, Ruxience, Truxima, or Riabni with other multiple sclerosis (MS) drugs excluding Ampyra.
- Member will not receive Rituxan, Ruxience, Truxima, or Riabni with other biologics for the treatment of neuromyelitis optica.

## Coverage Criteria

### Oncologic Disorders<sup>1,2,22,25,27</sup>

Indefinite authorization may be granted for all oncologic disorders.

### Rheumatoid Arthritis (RA)<sup>1,2,4,7-9,27,29,30,35</sup>

Authorization of 12 months may be granted for adults who have previously received a biologic or targeted synthetic drug (e.g., Rinvoq, Xeljanz) indicated for the treatment of moderately to severely active

rheumatoid arthritis. The requested medication must be prescribed in combination with methotrexate (MTX) or leflunomide unless the member has a contraindication (see VII. Appendix) or intolerance to MTX or leflunomide.

Authorization of 12 months may be granted for treatment of adults with moderately to severely active RA in combination with MTX or leflunomide unless the member has a contraindication (see VII. Appendix) or intolerance to MTX or leflunomide when all of the following criteria are met:

- The member meets either of the following criteria:
  - The member has been tested for either of the following biomarkers and the test was positive:
    - Rheumatoid factor (RF)
    - Anti-cyclic citrullinated peptide (anti-CCP)
  - The member has been tested for ALL of the following biomarkers:
    - RF
    - Anti-CCP
    - C-reactive protein (CRP) and/or erythrocyte sedimentation rate (ESR)
- The member meets either of the following criteria:
  - The member has experienced an inadequate response to at least a 3-month trial of MTX despite adequate dosing (i.e., titrated to 15 mg/week); or
  - The member had an intolerable adverse effect or contraindication to MTX (see VII. Appendix), and an inadequate response to another conventional drug (e.g., hydroxychloroquine, leflunomide, sulfasalazine).

## Granulomatosis with Polyangiitis (GPA) (Wegener's Granulomatosis), Microscopic Polyangiitis (MPA), Churg-Strauss and Pauci-Immune Glomerulonephritis<sup>1,2,27,28,33,34</sup>

Authorization of 12 months may be granted for treatment of GPA, MPA, Churg-Strauss, or pauci-immune glomerulonephritis.

## Sjögren's Syndrome<sup>4-6</sup>

Authorization of 12 months may be granted for treatment of Sjögren's syndrome when corticosteroids and other immunosuppressive agents were ineffective.

## Multiple Sclerosis<sup>4,10</sup>

Authorization of 12 months may be granted for treatment of relapsing remitting multiple sclerosis (MS).

## Neuromyelitis Optica (I.E., Neuromyelitis Optica Spectrum Disorder, NMOSD, Devic Disease)<sup>11,12,36</sup>

Authorization of 12 months may be granted for treatment of neuromyelitis optica (i.e., neuromyelitis optica spectrum disorder, NMOSD, Devic disease).

## Autoimmune Blistering Disease<sup>19,31,32</sup>

Authorization of 12 months may be granted for treatment of autoimmune blistering disease (e.g., pemphigus vulgaris, pemphigus foliaceus, bullous pemphigoid, cicatricial pemphigoid, epidermolysis bullosa acquisita and paraneoplastic pemphigus).

## Hematologic Indications<sup>23-25</sup>

Authorization of 12 months may be granted for treatment of any of the following indications:

- Refractory immune or idiopathic thrombocytopenic purpura (ITP)
- Autoimmune hemolytic anemia
- Thrombotic thrombocytopenic purpura
- Chronic graft-versus-host disease (GVHD)
- Prevention of Epstein-Barr virus (EBV)-related PTLD

## Myasthenia Gravis<sup>25</sup>

Authorization of 12 months may be granted for treatment of refractory myasthenia gravis.

## Immune Checkpoint Inhibitor-Related Toxicities<sup>22</sup>

Authorization of 3 months may be granted for treatment of immune checkpoint inhibitor-related toxicities.

## Cryoglobulinemia<sup>13-15</sup>

Authorization of 12 months may be granted for treatment of cryoglobulinemia when corticosteroids and other immunosuppressive agents were ineffective.

## Solid Organ Transplant<sup>17</sup>

Authorization of 3 months may be granted for treatment of solid organ transplant and prevention of antibody mediated rejection in solid organ transplant.

## Opsoclonus-Myoclonus-Ataxia<sup>18</sup>

Authorization of 12 months may be granted for treatment of opsoclonus-myoclonus-ataxia associated with neuroblastoma when the member is refractory to steroids and chemotherapy.

## Systemic Lupus Erythematosus<sup>20,21</sup>

Authorization of 12 months may be granted for the treatment of systemic lupus erythematosus that is refractory to immunosuppressive therapy.

## Membranous Nephropathy<sup>37</sup>

Authorization of 12 months may be granted for treatment of membranous nephropathy when the member is at moderate to high risk for disease progression.

# Continuation of Therapy

## Rheumatoid Arthritis<sup>1,2,4,7-9,27,29,30,35</sup>

Authorization of 12 months may be granted for continued treatment in all adult members (including new members) requesting reauthorization who achieve or maintain positive clinical response after at least two doses of therapy with Rituxan, Ruxience, Truxima, or Riabni as evidenced by disease activity improvement of at least 20% from baseline in tender joint count, swollen joint count, pain, or disability.

## Immune Checkpoint Inhibitor-Related Toxicities

Authorization of 3 months may be granted for continued treatment in members requesting reauthorization for treatment of immune checkpoint inhibitor-related toxicities who are experiencing benefit from therapy.

## Hematologic Indications

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in coverage criteria section for hematologic indications who are experiencing benefit from therapy.

## Multiple Sclerosis

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for relapsing remitting multiple sclerosis (MS) who are experiencing disease stability or improvement while receiving Rituxan, Ruxience, Truxima, or Riabni.

## Other Indications

Authorization of 12 months may be granted for continued treatment in all members (including new members) requesting reauthorization who are receiving benefit from therapy.

## Appendix

### Examples of Contraindications to Methotrexate and Leflunomide

- Clinical diagnosis of alcohol use disorder, alcoholic liver disease or other chronic liver disease
- Breastfeeding
- Blood dyscrasias (e.g., thrombocytopenia, leukopenia, significant anemia)
- Elevated liver transaminases
- History of intolerance or adverse event
- Hypersensitivity
- Interstitial pneumonitis or clinically significant pulmonary fibrosis
- Myelodysplasia
- Pregnancy or currently planning pregnancy
- Renal impairment
- Significant drug interaction

## References

1. Rituxan [package insert]. South San Francisco, CA: Genentech, Inc.; December 2021.
2. Truxima [package insert]. North Wales, PA: Teva Pharmaceuticals USA, Inc; February 2022.
3. Methotrexate [package insert]. Cranbury, NJ: Sun Pharmaceutical Industries, Inc.; August 2021.
4. IBM Micromedex [Internet database]. Ann Arbor, MI: Truven Health Analytics. Updated periodically. Accessed April 8, 2024..
5. Dass S, Bowman SJ, Vital EM, et al. Reduction of fatigue in Sjögren syndrome with rituximab: results of a double blind, placebo-controlled study. *Ann Rheum Dis*. 2008;67:1541-1544.
6. Meijer JM, Meiners PM, Vissink A, et al. Effectiveness of rituximab treatment in primary Sjögren's syndrome: a randomized, double-blind, placebo-controlled trial. *Arthritis Rheum*. 2010;62(4):960-8.
7. Smolen JS, Landewé R, Billsma J, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2019 update. *Ann Rheum Dis*. 2020;79:685-699.
8. Singh JA, Saag KG, Bridges SL Jr, et al. 2015 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. *Arthritis Rheumatol*. 2016;68(1):1-26.



9. Saag KG, Teng GG, Patkar NM, et al. American College of Rheumatology 2008 recommendations for the use of nonbiologic and biologic disease-modifying antirheumatic drugs in rheumatoid arthritis. *Arthritis Rheum.* 2008;59(6):762-784.
10. Hauser SL, Waubant E, Arnold DL, et al. B-cell depletion with rituximab in relapsing-remitting multiple sclerosis. *N Engl J Med.* 2008;358:676-688.
11. Scott, T.F., Frohman, E.M., DeSeze, J., (2011). Evidence-based guideline: Clinical evaluation and treatment of transverse myelitis: Report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. *American Academy of Neurology.* 77: 2128-2134.
12. Kumpfel, T., Giglhuber, K., et al. (2023). Update on the diagnosis and treatment of neuromyelitis optica spectrum disorders (NMOSD)- revised recommendations of the Neuromyelitis Optica Study Group (NEMOS). Part II: Attack therapy and long-term management. *J Neurol* 271: 141-176.
13. De Vita S, Quartuccio L, Isola M, et al. A randomized controlled trial of rituximab for the treatment of severe cryoglobulinemic vasculitis. *Arthritis Rheum.* 2012;64(3):843-53.
14. Sneller MC, Hu Z, Langford CA. A randomized controlled trial of rituximab following failure of antiviral therapy for hepatitis C virus-associated cryoglobulinemic vasculitis. *Arthritis Rheum.* 2012 Mar; 64(3):835-42.
15. Terrier B, Krastinova E, Marie I, et al. Management of noninfectious mixed cryoglobulinemia vasculitis: data from 242 cases included in the CryoVas survey. *Blood.* 2012 Jun 21; 119(25):5996-6004.
16. Trappe R, Oertel S, Leblond V, et al. Sequential treatment with rituximab followed by CHOP chemotherapy in adult B-cell post-transplant lymphoproliferative disorder (PTLD): the prospective international multicentre phase 2 PTLD-1 trial. *Lancet Oncol* 2012.
17. The American Society of Transplantation Infectious Diseases Guidelines. *Am J Transplant* 2009; 9 (Suppl 4):S92.
18. Bell J, Moran C, Blatt J. Response to rituximab in a child with neuroblastoma and opsoclonus-myoclonus. *Pediatr Blood Cancer* 2008; 50:370.
19. Hertl M, Geller S. Initial management of pemphigus vulgaris and pemphigus foliaceus. *UpToDate* [online serial]. Waltham, MA: UpToDate; reviewed August 2021.
20. American Society of Health System Pharmacists. AHFS DI. Bethesda, MD. Electronic version, 2020. Available with subscription. URL: <http://online.lexi.com/lco/action/home>. Accessed April 8, 2024.
21. DRUGDEX System (electronic version). Micromedex Truven Health Analytics. Available with subscription. URL: [www.micromedexsolutions.com](http://www.micromedexsolutions.com). Accessed April 8, 2024.
22. The NCCN Drugs & Biologics Compendium® © 2018 National Comprehensive Cancer Network, Inc. <https://www.nccn.org>. Accessed March 27, 2024.
23. Lexicomp Online®, AHFS® Drug Information, Hudson, Ohio: Wolters Kluwer Clinical Drug Information, Inc.; <http://online.lexi.com> [available with subscription]. Accessed April 3, 2023.
24. Tomblyn M, Chiller T, Einsele H, et al. Guidelines for preventing infectious complications among hematopoietic cell transplantation recipients: a global perspective. *Biol Blood Marrow Transplant.* 2009; 15(10):1143-1238. URL: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3103296/pdf/nihms205400.pdf>. Accessed August 2, 2013.

Reference number(s)
2893-A

25. Micromedex Solutions [database online]. Truven Health Analytics, Greenwood Village, Colorado, USA. Available at: <http://www.micromedexsolutions.com/>. Accessed March 27, 2024.
26. Arber D, Orazi A, Vardiman J, et al. The 2016 revision to the World Health Organization classification of myeloid neoplasms and acute leukemia. *Blood*. May 19, 2016;127(20):2391-2405.
27. Ruxience [package insert]. NY, NY: Pfizer Biosimilars; October 2023.
28. Riabni [package insert]. Thousand Oaks, CA: Amgen, Inc.; February 2023.
29. Aletaha D, Neogi T, Silman, et al. 2010 Rheumatoid arthritis classification criteria: an American College of Rheumatology/European League Against Rheumatism collaborative initiative. *Arthritis Rheum*. 2010;62(9):2569-81.
30. Smolen JS, Aletaha D. Assessment of rheumatoid arthritis activity in clinical trials and clinical practice. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. Available with subscription. URL: [www.uptodate.com](http://www.uptodate.com). Accessed November 2, 2021.
31. Murrell DF, Peña S, Joly P, et al. Diagnosis and management of pemphigus: Recommendations of an international panel of experts. *J Am Acad Dermatol*. 2020;82(3):575-585.e1.
32. Joly P, Horvath B, Patsatsi A, et al. Updated S2K guidelines on the management of pemphigus vulgaris and foliaceus initiated by the european academy of dermatology and venereology (EADV). *J Eur Acad Dermatol Venereol*. 2020;34(9):1900-1913.
33. Menditto VG, Rossetti G, Olivari D, et al. Rituximab for eosinophilic granulomatosis with polyangiitis: a systematic review of observational studies. *Rheumatology (Oxford)*. 2021;60(4):1640-1650.
34. Chung SA, Langford CA, Maz M, et al. 2021 American College of Rheumatology/Vasculitis Foundation Guideline for the Management of Antineutrophil Cytoplasmic Antibody-Associated Vasculitis. *Arthritis Rheumatol*. 2021;73(8):1clinic6-1383.
35. Fraenkel L, Bathon JM, England BR, et al. 2021 American College of Rheumatology guideline for the treatment of rheumatoid arthritis. *Arthrit Care Res*. 2021;0:1-16.
36. Poupart J, Giovannelli J, Deschamps R, Audoin B, Ciron J, Maillart E, Papeix C, Collongues N, Bourre B, Cohen M, Wiertlewski S, Outteryck O, Laplaud D, Vukusic S, Marignier R, Zephir H; NOMADMUS study group. Evaluation of efficacy and tolerability of first-line therapies in NMOSD. *Neurology*. 2020 Apr 14;94(15):e1645-e1656.
37. Kidney Disease: Improving Global Outcomes (KDIGO) Glomerular Diseases Work Group. KDIGO 2021 Clinical Practice Guideline for the Management of Glomerular Diseases. *Kidney Int*. 2021 Oct;100(4S):S1-S276.