

Rituximab (Rituxan[®], Ruxience[®], Truxima[®])

When requesting a rituximab product (Rituxan[®], Ruxience[®], Truxima[®]) for non-oncology indications, the individual requiring treatment must be diagnosed with an FDA-approved indication or an off-label compendial use and meet the specific coverage guidelines and applicable safety criteria for the covered indication.

FDA-approved Non-oncology Indications

Rituximab is indicated for the treatment of:

- Moderately to severely active rheumatoid arthritis
- Granulomatosis with polyangiitis (GPA) (Wegener's granulomatosis)
- Microscopic polyangiitis (MPA)
- Moderate to severe pemphigus vulgaris

Approved Non-oncology Off-label Compendial Uses

- Immune thrombocytopenia (ITP)
- Multiple sclerosis (MS)
- Neuromyelitis optica (NMO) spectrum disorder
- Systemic lupus erythematosus (SLE)
- Graft-versus-host disease (GVHD)

Coverage Guidelines

The individual must meet the following criteria for select indications:

Rheumatoid arthritis

The individual must meet **all** of the following criteria for initial authorization:

- Had a 3-month trial of at least one biologic agent or at least one conventional synthetic disease-modifying antirheumatic drug (DMARD) (e.g., methotrexate, leflunomide, hydroxychloroquine, sulfasalazine);
- Rituximab will not be used concurrently with another biologic or with a targeted synthetic DMARD; AND
- Rituximab is prescribed by or in consultation with a rheumatologist.

The individual must meet **all** of the following criteria for reauthorization:

- At least 16 weeks have elapsed since last rituximab treatment course; AND
- For an individual who has received at least 2 courses of rituximab therapy, the individual must have responded to rituximab therapy (e.g., less joint pain, less morning stiffness, improved function, decreased soft tissue swelling in joints, etc.).

Approval duration (initial and renewal): 1 month

Pemphigus vulgaris

The individual must meet **all** of the following criteria for initial authorization:

- Rituximab is being initiated in combination with a corticosteroid, unless contraindicated; AND
- Rituximab is prescribed by or in consultation with a dermatologist.

The individual must meet **all** of the following criteria for reauthorization:

- At least 16 weeks have elapsed since last rituximab treatment course; AND
- Rituximab is prescribed by or in consultation with a dermatologist.

Approval duration (initial): 1 month

Approval duration (renewal): 12 months

Granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA):

The individual must meet **all** of the following criteria for initial authorization:

- Rituximab will be used in combination with glucocorticoids; AND
- Rituximab is prescribed by or in consultation with a rheumatologist, nephrologist, or immunologist.

The individual must meet **all** of the following criteria for reauthorization:

- Has achieved disease control with induction treatment (e.g., induction treatment using rituximab infusion or other standard of care immunosuppressants); AND
- For an individual who has received a course of rituximab for induction treatment, at least 16 weeks have elapsed since last rituximab treatment course.

Approval duration (initial): 1 month

Approval duration (renewal): 12 months

Immune thrombocytopenia

The individual must meet **all** of the following criteria for initial authorization:

- Has tried at least one previous therapy (e.g., intravenous immunoglobulin, corticosteroids, splenectomy); AND
- Rituximab is prescribed by or in consultation with a hematologist.

The individual must meet the following criteria for reauthorization:

- Has responded to previous rituximab therapy (e.g., increased platelet counts);
- Has relapsed (e.g., experienced thrombocytopenia after achievement of a remission); AND
- At least 6 months have elapsed since last rituximab treatment course.

Approval duration (initial and renewal): 1 month

Multiple sclerosis (MS)

The individual must meet **all** of the following criteria for authorization:

- Had an inadequate response or intolerance to at least ONE other disease-modifying agent for MS;
- Rituximab will not be used concurrently with another disease-modifying agent;
- Rituximab is prescribed by or in consultation with a physician who specializes in the treatment of MS and/or a neurologist; AND
- At least 6 months will elapse between rituximab treatment courses (for example, 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 rituximab).

For reauthorization, at least 6 months have elapsed since the last rituximab treatment course.

Approval duration: 12 months

Neuromyelitis optica spectrum disorder

Rituximab is prescribed by or in consultation with a neurologist.

Approval duration: 1 month

Graft-versus-host disease (GVHD)

The individual must meet all of the following criteria for authorization:

- Rituximab is prescribed by or in consultation with an oncologist, hematologist, or a physician affiliated with a transplant center; AND
- Has tried at least one immunosuppressant OR is currently receiving at least one of the following medications in combination with rituximab:
 - o Corticosteroids (e.g., methylprednisolone)
 - o Antithymocyte globulin
 - o Cyclosporine
 - o Tacrolimus
 - o Mycophenolate mofetil
 - o Sirolimus
 - o Thalomid
 - o Nipent
 - o Imatinib
 - o Methotrexate.

Approval duration: 12 months

Systemic lupus erythematosus (SLE)

The individual must meet **all** of the following criteria for initial authorization:

- Has tried at least one standard immunomodulating or immunosuppressant agent (e.g., hydroxychloroquine, corticosteroids, methotrexate, azathioprine, mycophenolate mofetil, or cyclophosphamide); AND
- Rituximab is prescribed by or in consultation with a rheumatologist, nephrologist, or neurologist.

For reauthorization, at least 6 months have elapsed since the last rituximab treatment course.

Approval duration (initial and renewal): 1 month

Dosing Recommendations

Rheumatoid arthritis

The recommended dose is two-1000 mg intravenous infusions separated by 2 weeks (one course) every 24 weeks or based on clinical evaluation, but no sooner than every 16 weeks.

Granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA)

The recommended induction dose is 375 mg/m² administered intravenously no more frequently than once weekly. The follow-up dose is two 500 mg intravenous infusions separated by 2 weeks, followed by a 500 mg intravenous infusion no more frequently than once every 6 months.

Pemphigus vulgaris

The recommended dose is two-1000 mg intravenous infusions separated by 2 weeks (one course) for initial treatment or treatment of relapse. For maintenance therapy, approve up to 500 mg per dose administered intravenously.

Neuromyelitis optica (NMO) spectrum disorder

Each single dose must not exceed 375 mg/m² administered as an intravenous infusion not more frequently than once weekly OR up to two-1000 mg doses administered as an intravenous infusion separated by at least 2 weeks.

Multiple sclerosis

Each course is up to 2,000 mg (total) and each course is administered as one or two intravenous infusions over 1 month.

Immune thrombocytopenia (ITP)

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

Graft-versus-host disease (GVHD)

Each single dose must not exceed 375 mg/m² administered as an intravenous infusion with doses separated by at least 7 days.

References

1. Rituxan [prescribing information]. South San Francisco, CA: Genentech, Inc.; March 2020.
2. Ruxience [prescribing information]. New York, NY: Pfizer; July 2019.
3. Truxima [prescribing information]. North Wales, PA: Teva/Celltrion; May 2019.
4. Yates M, Watts RA, Bajema IM, et al. EULAR/ERA-EDTA recommendations for the management of ANCA-associated vasculitis. *Ann Rheum Dis*. 2016;75(9):1583-1594.
5. The NCCN Drugs and Biologics Compendium. © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on September 9, 2019. Search term: rituximab.
6. The NCCN CLL/SLL Clinical Practice Guidelines in Oncology (Version 1.2020 – August 23, 2019). © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on September 11, 2019.
7. The NCCN B-Cell Lymphoma Clinical Practice Guidelines in Oncology (Version 4.2019 – June 18, 2019). © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on September 11, 2019.
8. The NCCN Primary Cutaneous Lymphomas Clinical Practice Guidelines in Oncology (Version 2.2019 – December 17, 2018). © 2018 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on September 9, 2019.
9. The NCCN Acute Lymphoblastic Leukemia Clinical Practice Guidelines in Oncology (Version 2.2019 – May 15, 2019). © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on September 9, 2019.
10. The NCCN Hairy Cell Leukemia Clinical Practice Guidelines in Oncology (Version 1.2020 – August 23, 2019). © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on September 9, 2019.
11. The NCCN Hodgkin Lymphoma Clinical Practice Guidelines in Oncology (Version 2.2019 – July 15, 2019). © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on September 9, 2019.
12. The NCCN Waldenstrom's Macroglobulinemia/Lymphoplasmacytic Lymphoma Clinical Practice Guidelines in Oncology (Version 2.2019 – September 14, 2018). © 2018 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on September 9, 2019.
13. 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.
14. Dignan FL, Amrolia P, Clark A, et al. Diagnosis and management of chronic graft-versus-host disease. *Br J Haematol*. 2012;158(1):46-61.
15. Neunert C, Lim W, Crowther M, et al. The American Society of Hematology 2011 evidence-based practice guideline for immune thrombocytopenia. *Blood*. 2011;117(16):4190-4207.
16. A Consensus Paper by the Multiple Sclerosis Coalition. The use of disease-modifying therapies in multiple sclerosis. Updated June 2019. Available at: http://ms-coalition.org/wp-content/uploads/2019/06/MS_CDMTPaper_062019.pdf. Accessed on September 16, 2019.
17. Rae-Grant A, Day GS, Marrie RA, et al. Practice guideline recommendations summary: disease-modifying therapies for adults with multiple sclerosis. Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. *Neurology*. 2018;90:777-788.
18. Collongues N, de Seze J. An update on the evidence for the efficacy and safety of rituximab in the management of neuromyelitis optica. *Ther Adv Neurol Disord*. 2016;9(3):180-188.
19. Maury S, Chevret S, Thomas X, et al. Rituximab in B-lineage adult acute lymphoblastic leukemia. *N Engl J Med*. 2016;375(11):1044-1053.

20. Chihara D1, Kantarjian H1, O'Brien S, et al. Long-term durable remission by cladribine followed by rituximab in patients with hairy cell leukaemia: update of a phase II trial. *Br J Haematol*. 2016 Sep;174(5):760-766.
21. Gudbrandsdottir S, Birgens HS, Frederiksen H, et al. Rituximab and dexamethasone vs dexamethasone monotherapy in newly diagnosed patients with primary immune thrombocytopenia. *Blood*. 2013;121(11):1976-1981.
22. Castillo-Trivino T, Braithwaite D, Bacchetti P, Waubant E. Rituximab in relapsing and progressive forms of multiple sclerosis: a systematic review. *PLoS One*. 2013;8(7):e66308. Available at: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3699597/pdf/pone.0066308.pdf>. Accessed on August 25, 2017.
23. Hawker K, O'Connor P, Freedman MS, et al. Rituximab in patients with primary progressive multiple sclerosis: results of a randomized double-blind placebo-controlled multicenter trial. *Ann Neurol*. 2009;66(4):460-471.
24. Alping P, Frisell T, Novakova L, et al. Rituximab versus fingolimod after natalizumab in multiple sclerosis patients. *Ann Neurol*. 2016;79(6):950-8.
25. de Flon P, Gunnarsson M, Laurell K, et al. Reduced inflammation in relapsing-remitting multiple sclerosis after therapy switch to rituximab. *Neurology*. 2016;87(2):141-147.
26. Salzer J, Svenningsson R, Alping P, et al. Rituximab in multiple sclerosis: a retrospective observational study on safety and efficacy. *Neurology*. 2016;87(20):2074-2081.
27. Kim SH, Huh SY, Lee SJ, et al. A 5-year follow-up of rituximab treatment in patients with neuromyelitis optica spectrum disorder. *JAMA Neurol*. 2013 Sep 1;70(9):1110-7.
28. Scott TF, Frohman EM, De Seze J, et al. Evidence-based guideline: clinical evaluation and treatment of transverse myelitis: report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. *Neurology*. 2011;77(24):2128-2134.
29. Kim SH, Jeong IH, Hyun JW, et al. Treatment outcomes with rituximab in 100 patients with neuromyelitis optica: influence of FCGR3A polymorphisms on the therapeutic response to rituximab. *JAMA Neurol*. 2015;72(9):989-995.
30. Collongues N, de Seze J. An update on the evidence for the efficacy and safety of rituximab in the management of neuromyelitis optica. *Ther Adv Neurol Disord*. 2016;9(3):180-188.
31. Kapoor P, Ansell SM, Fonseca R, et al. Diagnosis and management of Waldenström Macroglobulinemia: Mayo stratification of macroglobulinemia and risk-adapted therapy (mSMART) guidelines 2016. *JAMA Oncol*. 2017;3(9):1257-1265.
32. Castillo JJ, Meid K, Gustine JN, et al. Prospective clinical trial of ixazomib, dexamethasone, and rituximab as primary therapy in Waldenström macroglobulinemia. *Clin Cancer Res*. 2018;24(14):3247-3252.
33. The NCCN Primary Cutaneous Lymphomas Clinical Practice Guidelines in Oncology (Version 2.2019 – December 17, 2018). © 2018 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on September 9, 2019.
34. The NCCN Hairy Cell Leukemia Clinical Practice Guidelines in Oncology (Version 1.2020 – August 23, 2019). © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on September 9, 2019.
35. Chihara D1, Kantarjian H1, O'Brien S, et al. Long-term durable remission by cladribine followed by rituximab in patients with hairy cell leukaemia: update of a phase II trial. *Br J Haematol*. 2016;174(5):760-766.
36. The NCCN Acute Lymphoblastic Leukemia Clinical Practice Guidelines in Oncology (Version 2.2019 – May 15, 2019). © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on September 9, 2019.
37. The NCCN Hodgkin Lymphoma Clinical Practice Guidelines in Oncology (Version 2.2019 – July 15, 2019). © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on September 9, 2019.
38. The NCCN Waldenström's Macroglobulinemia/Lymphoplasmacytic Lymphoma Clinical Practice Guidelines in Oncology (Version 2.2019 – September 14, 2018). © 2018 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on September 9, 2019.
39. Rituximab (Rituxan®). In: DRUGDEX® System Micromedex. Greenwood Village, CO: Thompson Reuters (Healthcare) Inc. [Updated; March 17, 2020; Accessed April 28, 2020].