

PHARMACY POLICY STATEMENT

Indiana Medicaid

DRUG NAME	Rituxumab (Rituxan*, Truxima, Ruxience, Riabni)
BENEFIT TYPE	Medical
STATUS	Prior Authorization Required

Rituxan is a monoclonal antibody that targets the CD20 antigen expressed on the surface of pre-B and mature B-lymphocytes. Upon binding to CD20, rituximab mediates B-cell lysis. B cells are believed to play a role in the pathogenesis of rheumatoid arthritis (RA) and associated chronic synovitis. In this setting, B cells may be acting at multiple sites in the autoimmune/inflammatory process.

Rituximab will be considered for coverage when the following criteria are met:

Granulomatosis with Polyangiitis (GPA) (Wegener's Granulomatosis) and Microscopic Polyangiitis (MPA)

For **initial** authorization:

1. Member is 2 years old or older; AND
2. Medication must be prescribed by or in consultation with a nephrologist or rheumatologist; AND
3. Member has a diagnosis of one of the following:
 - a) Severe GPA or MPA,
 - b) Non-severe GPA or MPA (non-organ threatening, non-life-threatening) refractory to glucocorticoid in combination with methotrexate or mycophenolate mofetil (MMF); AND
4. Rituxan will be initiated in combination with glucocorticoids.
5. **Dosage allowed/Quantity limit:** Please refer to the Dosing and Administration section of the package insert.

If all the above requirements are met, the medication will be approved for 6 months.

For **reauthorization**:

1. Chart notes demonstrate clinical improvement of disease signs and symptoms.

If all the above requirements are met, the medication will be approved for an additional 12 months.

Pemphigus Vulgaris (PV)

For **initial** authorization:

1. Member is 18 years old or older; AND
2. Must be prescribed by or in consultation with a dermatologist; AND
3. Member has a documented diagnosis of moderate to severe PV; AND
4. Rituxan will be initiated in combination with a corticosteroid taper (unless contraindicated).
5. **Dosage allowed/Quantity limit:** Initial: Two 1000mg doses separated by 2 weeks; Maintenance: 500mg infusion at month 12 and every 6 months thereafter or based on clinical evaluation. Relapse: 1000mg infusion. Subsequent infusions may be administered no sooner than 16 weeks following the previous infusion.

If all the above requirements are met, the medication will be approved for 12 months.

For **reauthorization**:

1. Chart notes demonstrate clinical improvement of signs and symptoms (e.g. healed lesions, fewer new lesions, etc.)

If all the above requirements are met, the medication will be approved for an additional 12 months.

Rheumatoid Arthritis (RA)

For **initial** authorization:

1. Member is 18 years old or older; AND
2. Medication is being prescribed by or in consultation with a rheumatologist; AND
3. Member has a documented diagnosis of moderately- to severely- active RA; AND
4. Rituxan is being used in combination with methotrexate, or another non-biologic DMARD if unable to tolerate methotrexate; AND
5. Member must have inadequate response or intolerance to one or more tumor necrosis factor (TNF) antagonists (e.g. adalimumab, etanercept, infliximab) for at least 3 months each. Note: TNF antagonists require prior authorization.
6. **Dosage allowed/Quantity limit:** Two 1000mg doses separated by 2 weeks; subsequent courses repeated no sooner than every 16 weeks (every 24 weeks is typical).

If all the above requirements are met, the medication will be approved for 6 months.

For **reauthorization**:

1. Chart notes demonstrate improvement of RA signs and symptoms (e.g. fewer number of painful and swollen joints, achievement of remission, etc.)

If all the above requirements are met, the medication will be approved for an additional 12 months.

Acquired Thrombotic Thrombocytopenic Purpura (aTTP)

For **initial** authorization:

1. Member is 18 years old or older; AND
2. Medication must be prescribed by or in consultation with a hematologist; AND
3. Member has a presumptive or confirmed diagnosis of aTTP including ALL of the following:
 - a) Lab results showing thrombocytopenia (platelet count less than 150,000);
 - b) Microangiopathic hemolytic anemia (MAHA) confirmed by presence of schistocytes on blood smear;
 - c) Documentation of a PLASMIC score between 5 and 7 (intermediate to high risk);²⁵
 - d) Testing shows an ADAMTS13 activity level less than 10%, OR test has been ordered and results are pending.
4. Member's platelet count has not responded after at least 4 days of plasma exchange and glucocorticoid; AND
5. Rituxan is being used in addition to plasma exchange and glucocorticoid.
6. **Dosage allowed/Quantity limit:** 375mg/m² once weekly for 4 doses (off label).²⁶

If all the above requirements are met, the medication will be approved for 30 days.

For **reauthorization**:

1. Member is experiencing a relapse of symptoms (thrombocytopenia and MAHA); AND
2. ADAMTS13 activity is less than 20% (lab report required).

If all the above requirements are met, the medication will be approved for an additional 30 days.

Neuromyelitis Optica Spectrum Disorder (NMOSD)

For **initial** authorization:

1. Member is 18 years old or older; AND
2. Medication must be prescribed by or in consultation with a neurologist; AND
3. Member has a diagnosis of NMOSD and is seropositive for aquaporin-4 (AQP4) IgG antibodies (documentation required).
4. **Dosage allowed/Quantity limit:** 1g on day 1 and day 15, then 1g every 6 months³² (off label)

If all the above requirements are met, the medication will be approved for 6 months.

For **reauthorization**:

1. Chart notes must document disease stabilization, symptom improvement, and/or reduced frequency of relapses.

If all the above requirements are met, the medication will be approved for an additional 12 months.

Generalized Myasthenia Gravis (gMG)

For **initial** authorization:

1. Member is at least 18 years of age; AND
2. Medication must be prescribed by or in consultation with a neurologist; AND
3. Member meets one of the following:
 - a) Member has a documented diagnosis of gMG that is seropositive for MuSK antibodies AND has tried and failed corticosteroid treatment with or without a non-steroid immunosuppressant
 - b) Member has a documented diagnosis of refractory gMG that is seropositive for AChR antibodies AND has tried and failed ALL of the following: pyridostigmine, corticosteroid, and at least 2 non-steroid immunosuppressives (e.g., azathioprine, mycophenolate mofetil, tacrolimus)
4. **Dosage allowed/Quantity limit:** Consult updated clinical literature for recommendations. A variety of regimens have shown efficacy. (Off label use)

If all the above requirements are met, the medication will be approved for 6 months.

For **reauthorization**:

1. Chart notes must document clinically meaningful improvement in symptom severity and functioning compared to previous treatment.

If all the above requirements are met, the medication will be approved for an additional 12 months.

Multiple Sclerosis (MS)

For **initial** authorization:

1. Member is at least 18 years of age; AND
2. Medication must be prescribed by or in consultation with a neurologist; AND
3. Member has a diagnosis of MS, including documentation of baseline relapse rate, lesion count, and/or disability status (e.g., EDSS); AND
4. Member has documentation of one of the following:
 - a) For primary progressive MS (PPMS): Trial and failure of Ocrevus
 - b) For relapsing forms of MS (RMS): Trial and failure of at least 2 preferred disease-modifying drugs indicated for MS; AND
5. Rituximab will not be used concurrently with another disease-modifying drug for MS.
6. **Dosage allowed/Quantity limit:** Consult updated clinical literature for recommendations. (Off label use)

If all the above requirements are met, the medication will be approved for 6 months.

For **reauthorization**:

1. Chart notes must indicate a positive clinical response such as lower relapse rate compared to baseline (i.e., for RMS) or overall stability of disease (i.e., for PPMS).

If all the above requirements are met, the medication will be approved for an additional 12 months.

Immune Thrombocytopenia (ITP)

For **initial** authorization:

1. Medication is prescribed by or in consultation with a hematologist; AND
2. Member has a documented diagnosis of ITP of at least 6 months duration; AND
3. Member's platelet count is $<30 \times 10^9$ OR $<50 \times 10^9$ with active symptomatic bleeding or high risk factors for bleeding; AND
4. Member has had an insufficient response to one of the following:
 - a) Corticosteroid
 - b) Immunoglobulin
 - c) Splenectomy; AND
5. Member has had an insufficient response to a thrombopoietin receptor agonist (TPO-RA) such as Promacta, Nplate, or Doptelet; AND
6. Rituximab will not be used in combination with a TPO-RA or Tavalisse.
7. **Dosage allowed/Quantity limit:** Consult updated clinical literature for recommendations. Example (Off-label): 4 weekly doses of 375 mg/m²

If all the above requirements are met, the medication will be approved for 30 days.

For **reauthorization**:

1. Chart notes must document clinically significant improvement in platelet count compared to baseline following a course of rituximab; AND
2. Patient has a relapse of symptoms and meets all initial criteria.

If all the above requirements are met, the medication will be approved for an additional 30 days.

Non-Hodgkin's Lymphoma (NHL)

These requests must be submitted through [NantHealth/Eviti](#) portal.

Chronic Lymphocytic Leukemia (CLL)

These requests must be submitted through [NantHealth/Eviti](#) portal.

CareSource considers Rituximab not medically necessary for the treatment of conditions that are not listed in this document. For any other indication, please refer to the Off-Label policy.

DATE	ACTION/DESCRIPTION
08/20/2013	Change in diagnosis
07/15/2014	Added diagnosis TTP and additional criteria to CD20+ CLL
07/15/2015	Added MCG 19th edition criteria
10/04/2016	Change in diagnoses to FDA approved uses, updated references with supporting guidelines and literature
06/09/2020	Transferred policy to new template, indicated Eviti carve-outs. Revised criteria for vasculitis diagnoses (GPA, MPA); previously listed as ANCA vasculitis – updated age, specified trial for non-severe, simplified the cyclophosphamide trial language. Revised criteria for Rheumatoid Arthritis – changed from trial of 2 TNF to 1 TNF. Added new diagnosis Pemphigus Vulgaris and its criteria
07/28/2020	Added criteria for aTTP.
10/13/2020	Added criteria for NMOSD. For RA, stated they must use another DMARD if they can't use MTX.
02/09/2022	Transferred to new template. RA: Added new reference. GPA/MPA: Added references and made updates per new guidelines. Added MMF to #3. Removed requirement for trial/failure of cyclophosphamide. PV: Added new references. Removed required trial/failure of steroid and adjuvant immunosuppressant. Added new section for myasthenia gravis (off label).
07/27/2022	Added new section for multiple sclerosis (off label).
02/21/2023	Renamed policy as Rituximab and added biosimilars. Added section for off label treatment of ITP.

1. Rituxan [package insert]. South San Francisco, CA: Genentech, Inc.; 2021.
2. Ntatsaki E, Carruthers D, Chakravarty K, et al. BSR and BHPR guideline for the management of adults with ANCA-associated vasculitis. *Rheumatology* April 2014; ket445
3. Stone JH, Merkel PA, Spiera R, et al. Rituximab versus cyclophosphamide for ANCA-associated vasculitis. *N Engl J Med* 2010; 363:221.
4. Jones RB, Tervaert JW, Hauser T, et al. Rituximab versus cyclophosphamide in ANCA-associated renal vasculitis. *N Engl J Med* 2010; 363:211.
5. Jones RB, Tervaert JW, Hauser T, et al. Rituximab versus cyclophosphamide in ANCA-associated renal vasculitis: 2-year results of a randomized trial. *Ann Rheum Dis* 2015; 74(6): 1178-1182.
6. Latimer NR, Carroll C, Wong R, et al. Rituximab in combination with corticosteroids for the treatment of anti-neutrophil cytoplasmic antibody-associated vasculitis: a NICE single technology appraisal. *Pharmacoeconomics* 2014; 32(12): 1171-1183.
7. Pagnoux C. Updates in ANCA-associated vasculitis. *Eur J Rheumatol* 2015
8. Singh JA, Saag KG, Bridges Jr. SL, et al. 2015 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. *Arthritis Care & Research* 2015: 1-25.
9. Leandro MJ. Rituximab: Principles of use and adverse effects in rheumatoid arthritis. *UpToDate*. https://www.uptodate.com/contents/rituximab-principles-of-use-and-adverse-effects-in-rheumatoid-arthritis?search=rheumatoid%20arthritis%20treatment&topicRef=7966&source=see_link. Updated April 3, 2020. Accessed June 9, 2020.

10. Finckh A, Ciurea A, Brulhart L, et al. Which subgroup of patients with rheumatoid arthritis benefits from switching to rituximab versus alternative anti-tumour necrosis factor (TNF) agents after previous failure of an anti-TNF agent? *Annals of the Rheumatic Diseases*. 2009;69(2):387-393. doi:10.1136/ard.2008.105064
11. Solau-Gervais E, Prudhomme C, Philippe P, et al. Efficacy of rituximab in the treatment of rheumatoid arthritis. Influence of serologic status, coprescription of methotrexate and prior TNF-alpha inhibitors exposure. *Joint Bone Spine*. 2012;79(3):281-284. doi:10.1016/j.jbspin.2011.05.002
12. Harrold LR, Reed GW, Magner R, et al. Comparative effectiveness and safety of rituximab versus subsequent anti-tumor necrosis factor therapy in patients with rheumatoid arthritis with prior exposure to anti-tumor necrosis factor therapies in the United States Corrona registry. *Arthritis Research & Therapy*. 2015;17(1). doi:10.1186/s13075-015-0776-1
13. Chatzidionysiou K, Lie E, Nasonov E, et al. Highest clinical effectiveness of rituximab in autoantibody-positive patients with rheumatoid arthritis and in those for whom no more than one previous TNF antagonist has failed: pooled data from 10 European registries. *Annals of the Rheumatic Diseases*. 2011;70(9):1575-1580. doi:10.1136/ard.2010.148759
14. Emery P, Gottenberg JE, Rubbert-Roth A, et al. Rituximab versus an alternative TNF inhibitor in patients with rheumatoid arthritis who failed to respond to a single previous TNF inhibitor: SWITCH-RA, a global, observational, comparative effectiveness study. *Annals of the Rheumatic Diseases*. 2014;74(6):979-984. doi:10.1136/annrheumdis-2013-203993
15. Hertl M, Eming R. Management of refractory pemphigus vulgaris and pemphigus foliaceus. *UpToDate*. https://www.uptodate.com/contents/management-of-refractory-pemphigus-vulgaris-and-pemphigus-foliaceus?search=pemphigus%20vulgaris&source=search_result&selectedTitle=3~40&usage_type=default&display_rank=3. Updated March 5, 2020. Accessed June 11, 2020.
16. Heelan K, Al-Mohammed F, Smith MJ, et al. Durable Remission of Pemphigus With a Fixed-Dose Rituximab Protocol. *JAMA Dermatology*. 2014;150(7):703. doi:10.1001/jamadermatol.2013.6739
17. Murrell DF, Dick S, Ahmed A, et al. Consensus statement on definitions of disease, end points, and therapeutic response for pemphigus. *Journal of the American Academy of Dermatology*. 2008;58(6):1043-1046. doi:10.1016/j.jaad.2008.01.012
18. Agarwal A, Hall RP, Bañez LL, Cardones AR. Comparison of rituximab and conventional adjuvant therapy for pemphigus vulgaris: A retrospective analysis. *Plos One*. 2018;13(9). doi:10.1371/journal.pone.0198074
19. Merkel PA, Kaplan AA, Falk RJ. Granulomatosis with polyangiitis and microscopic polyangiitis: Initial immunosuppressive therapy. *UpToDate*. https://www.uptodate.com/contents/granulomatosis-with-polyangiitis-and-microscopic-polyangiitis-initial-immunosuppressive-therapy?search=Granulomatosis%20with%20polyangiitis%20and%20Microscopic%20Polyangiitis&source=search_result&selectedTitle=2~150&usage_type=default&display_rank=2. Updated January 23, 2019. Accessed June 11, 2020.
20. McGeoch L, Twilt M, Famera L, et al. CanVasc Recommendations for the Management of Antineutrophil Cytoplasm Antibody-associated Vasculitides. *The Journal of Rheumatology*. 2015;43(1):97-120. doi:10.3899/jrheum.150376
21. Yates M, Watts R, Bajema I, et al. OP0053 Eular/ERA-EDTA Recommendations for The Management of Anca-Associated Vasculitis. *Annals of the Rheumatic Diseases*. 2016;75(Suppl 2). doi:10.1136/annrheumdis-2016-eular.1168
22. Terrier B, Pagnoux C, Perrodeau É, et al. Long-term efficacy of remission-maintenance regimens for ANCA-associated vasculitides. *Annals of the Rheumatic Diseases*. 2018;77(8):1150-1156. doi:10.1136/annrheumdis-2017-212768
23. George JN, Cuker A. Acquired TTP: Initial treatment. *UpToDate*. <http://www.uptodate.com>. Updated September 30, 2019. Accessed July 15, 2020.
24. ISTH Guideline for the Diagnosis and Management of Thrombotic Thrombocytopenic Purpura. https://cdn.ymaws.com/www.isth.org/resource/resmgr/guidance_and_guidelines/ttp_guideline/isth_ttp_guideline_september.pdf. Accessed 7/15/2020.
25. Coppo P, Cuker A, George JN. Thrombotic thrombocytopenic purpura: Toward targeted therapy and precision medicine. *Res Pract Thromb Haemost*. 2018;3(1):26-37. Published 2018 Nov 16. doi:10.1002/rth2.12160
26. Scully M, McDonald V, Cavenagh J, et al. A phase 2 study of the safety and efficacy of rituximab with plasma exchange in acute acquired thrombotic thrombocytopenic purpura. *Blood*. 2011;118(7):1746-1753. doi:10.1182/blood-2011-03-341131
27. Sayani FA, Abrams CS. How I treat refractory thrombotic thrombocytopenic purpura [published correction appears in *Blood*. 2017 Oct 5;130(14):1684]. *Blood*. 2015;125(25):3860-3867. doi:10.1182/blood-2014-11-551580

28. Lim W, Vesely SK, George JN. The role of rituximab in the management of patients with acquired thrombotic thrombocytopenic purpura. *Blood*. 2015;125(10):1526-1531. doi:10.1182/blood-2014-10-559211
29. Kessler RA, Mealy MA, Levy M. Treatment of Neuromyelitis Optica Spectrum Disorder: Acute, Preventive, and Symptomatic. *Curr Treat Options Neurol*. 2016;18(1):2. doi:10.1007/s11940-015-0387-9
30. Weinshenker B. Neuromyelitis Optica Spectrum Disorder. NORD (National Organization for Rare Disorders). <https://rarediseases.org/rare-diseases/neuromyelitis-optica/>. Published August 25, 2020. Accessed October 2, 2020.
31. Mealy MA, Wingerchuk DM, Palace J, Greenberg BM, Levy M. Comparison of relapse and treatment failure rates among patients with neuromyelitis optica: multicenter study of treatment efficacy. *JAMA Neurol*. 2014;71(3):324-330. doi:10.1001/jamaneurol.2013.5699
32. Ciron J, Audoin B, Bourre B, et al. Recommendations for the use of Rituximab in neuromyelitis optica spectrum disorders. *Revue Neurologique*. 2018;174(4):255-264. doi:10.1016/j.neurol.2017.11.005
33. Damato V, Evoli A, Iorio R. Efficacy and Safety of Rituximab Therapy in Neuromyelitis Optica Spectrum Disorders: A Systematic Review and Meta-analysis. *JAMA Neurol*. 2016;73(11):1342-1348. doi:10.1001/jamaneurol.2016.1637
34. Tahara M, Oeda T, Okada K, et al. Safety and efficacy of rituximab in neuromyelitis optica spectrum disorders (RIN-1 study): a multicentre, randomised, double-blind, placebo-controlled trial. *The Lancet Neurology*. 2020;19(4):298-306. doi:10.1016/s1474-4422(20)30066-1
35. Fraenkel L, Bathon JM, England BR, et al. 2021 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. *Arthritis Rheumatol*. 2021;73(7):1108-1123. doi:10.1002/art.41752
36. Kidney Disease: Improving Global Outcomes (KDIGO) Glomerular Diseases Work Group. KDIGO 2021 Clinical Practice Guideline for the Management of Glomerular Diseases. *Kidney Int*. 2021;100(4S):S1-S276. doi:10.1016/j.kint.2021.05.021
37. 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 Care Res (Hoboken)*. 2021;73(8):1088-1105. doi:10.1002/acr.24634
38. 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. doi:10.1016/j.jaad.2018.02.021
39. 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. doi:10.1111/jdv.16752
40. Zhao W, Wang J, Zhu H, Pan M. Comparison of Guidelines for Management of Pemphigus: a Review of Systemic Corticosteroids, Rituximab, and Other Immunosuppressive Therapies. *Clin Rev Allergy Immunol*. 2021;61(3):351-362. doi:10.1007/s12016-021-08882-1
41. Narayanaswami P, Sanders DB, Wolfe G, et al. International Consensus Guidance for Management of Myasthenia Gravis: 2020 Update. *Neurology*. 2021;96(3):114-122. doi:10.1212/WNL.0000000000011124
42. Rodolico C, Bonanno C, Toscano A, Vita G. MuSK-Associated Myasthenia Gravis: Clinical Features and Management. *Front Neurol*. 2020;11:660. Published 2020 Jul 23. doi:10.3389/fneur.2020.00660
43. Feng X, Song Z, Wu M, et al. Efficacy and Safety of Immunotherapies in Refractory Myasthenia Gravis: A Systematic Review and Meta-Analysis. *Front Neurol*. 2021;12:725700. Published 2021 Dec 1. doi:10.3389/fneur.2021.725700
44. Young C, McGill SC. Rituximab for the Treatment of Myasthenia Gravis: A 2021 Update [Internet]. Ottawa (ON): Canadian Agency for Drugs and Technologies in Health; 2021 Apr. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK571915/>
45. Sanders DB, Wolfe GI, Benatar M, et al. International consensus guidance for management of myasthenia gravis: Executive summary. *Neurology*. 2016;87(4):419-425. doi:10.1212/WNL.0000000000002790
46. National Multiple Sclerosis Society. The Use of Disease-Modifying Therapies in Multiple Sclerosis: Principles and Current Evidence. A Consensus Paper by the Multiple Sclerosis Coalition; 2019. Available from: https://www.nationalmssociety.org/NationalMSSociety/media/MSNationalFiles/Brochures/DMT_Consensus_MS_Coalition.pdf. Accessed August 18, 2021.
47. Hauser SL, Cree BAC. Treatment of Multiple Sclerosis: A Review. *Am J Med*. 2020;133(12):1380-1390.e2. doi:10.1016/j.amjmed.2020.05.049
48. Filippini G, Kruja J, Del Giovane C. Rituximab for people with multiple sclerosis. *Cochrane Database Syst Rev*. 2021;11(11):CD013874. Published 2021 Nov 8. doi:10.1002/14651858.CD013874.pub2
49. Alldredge B, Jordan A, Imitola J, Racke MK. Safety and Efficacy of Rituximab: Experience of a Single Multiple Sclerosis Center. *Clin Neuropharmacol*. 2018;41(2):56-59. doi:10.1097/WNF.0000000000000268

50. Neunert C, Terrell DR, Arnold DM, et al. American Society of Hematology 2019 guidelines for immune thrombocytopenia [published correction appears in *Blood Adv.* 2020 Jan 28;4(2):252]. *Blood Adv.* 2019;3(23):3829-3866. doi:10.1182/bloodadvances.2019000966
51. Provan D, Arnold DM, Bussel JB, et al. Updated international consensus report on the investigation and management of primary immune thrombocytopenia. *Blood Adv.* 2019;3(22):3780-3817. doi:10.1182/bloodadvances.2019000812

Effective date: 08/01/2023

Revised date: 02/21/2023