Market Applicability							
Market	**DC**	**GA**	**KY**	**MD**	**NJ**	**NY**	**WA**
Applicable	X	X	X	X	X	X	X

Rituximab
[Rituxan (rituximab) Truxima (rituximab-abbs), or Ruxience (rituximab-pvvr)]

Override(s)	Approval Duration
Prior Authorization	1 year; unless state regulations require otherwise

Medications
Rituxan (rituximab)
Ruxience (rituximab-pvvr)
Truxima (rituximab-abbs)

Rituximab Dosing Limit

Drug	Limit Per Indication
Rituxan (rituximab) 100 mg, 500 mg vial; Truxima (rituximab-abbs) 100 mg, 500 mg vial; Ruxience (rituximab-pvvr) 100 mg, 500 mg vial	**Rheumatoid arthritis (RA):** 1000 mg on days 1 and 15; repeated as frequent as every 16 weeks **Pemphigus Vulgaris & other autoimmune blistering skin diseases; maintenance**: 500 mg as frequently as every 16 weeks* **Granulomatosis with Polyangiitis (GPA) and Microscopic Polyangiitis (MPA) maintenance:** 500 mg every 6 months† **Myasthenia Gravis**: 375 mg/m^2 monthly (DP)^ **Autoimmune Hemolytic Anemia:** 375 mg/m^2 weekly for 4 weeks (DP) **Idiopathic Thrombocytopenic Purpura:** 375 mg/m^2 weekly for up to 6 weeks (DP) **Primary Sjogren's Syndrome:** 1000 mg on days 1 and 15 (2000 mg total) (DP)
Override Criteria	
*For initiation of therapy, may approve two 1000mg doses separated by 2 weeks. May also approve one 1000 mg infusion upon relapse †For induction treatment, may approve 375 mg/m^2 weekly for 4 weeks. After induction (at least 16 weeks later), may approve two 500mg infusions separated by 2 weeks followed by maintenance therapy ^For initiation of therapy, may approve 375 mg/m^2 weekly for 4 weeks	

Market Applicability							
Market	**DC**	**GA**	**KY**	**MD**	**NJ**	**NY**	**WA**
Applicable	X	X	X	X	X	X	X

APPROVAL CRITERIA

Requests for Rituxan (rituximab) Truxima (rituximab-abbs), or Ruxience (rituximab-pvvr) may be approved for the following:

I. Rheumatoid arthritis (RA) when each of the following criteria are met:
   A. Individual is 18 years of age or older with moderate to severe (RA); **AND**
   B. Individual has had an inadequate response to, is intolerant of, or has a contraindication to conventional therapy [nonbiologic disease modifying anti-rheumatic drugs (DMARDs) (such as methotrexate, sulfasalazine, leflunomide, or hydroxychloroquine)] (ACR 2015); **AND**
   C. Individual had an inadequate response, is intolerant of, or has a contraindication to one or more tumor necrosis factor (TNF) antagonist therapies;

OR

II. Granulomatosis with Polyangiitis and Microscopic Polyangiitis (MPA) when each of the following criteria are met:
   A. Individual is 2 years of age or older with Granulomatosis with Polyangiitis and MPA; **AND**
   B. Individual is using concomitantly with glucocorticoids;

OR

III. Autoimmune blistering skin diseases (such as but not limited to pemphigus vulgaris, pemphigus foliaceus, bullous pemphigoid, cicatricial pemphigoid, epidermolysis bullosa acquisita and paraneoplastic pemphigus) (Ahmed 2016, Maley 2016) when either of the following criteria are met:
   A. As first-line treatment in adults with moderate to severe pemphigus vulgaris; **OR**
   B. Disease is treatment-refractory;

OR

IV. Acquired inhibitors in individuals with hemophilia who fail cyclophosphamide and prednisone therapy (Collins 2009, Rossi 2016); **OR**

V. Autoimmune hemolytic anemia, refractory (Birgens 2013, Michel 2017, DP B IIb); **OR**

VI. Cryoglobulinemia, primary Sjogren Syndrome, or systemic lupus erythematosus refractory to standard therapy (Ramos 2009, DP B IIb) including:
   A. Corticosteroids; **AND**
   B. Two (2) or more immunosuppressive agents (such as but not limited to azathioprine, cyclosporine, methotrexate, or hydroxychloroquine);

OR

VII. Graft-Versus-Host Disease as third-line of therapy or greater(Cutler 2006, DP B IIb);

Market Applicability							
Market	**DC**	**GA**	**KY**	**MD**	**NJ**	**NY**	**WA**
Applicable	X	X	X	X	X	X	X

OR

VIII. Hepatitis C virus infection-related cryoglobulinemic vasculitis in conjunction with intravenous methylprednisolone, and concomitant antiviral therapy [or as monotherapy for non-response or intolerance to antiviral therapy] for individuals with any of the following (KDIGO 2018):
   A. Nephrotic proteinuria; **OR**
   B. Evidence of rapidly progressive kidney disease; **OR**
   C. Uncontrolled nephrotic syndrome; **OR**
   D. Acute flare of cryoglobulinemia;

OR

IX. Immunoglobulin G4-related disease when any of the following are met (Khosroshahi 2015):
   A. Failure to respond to prednisone or other corticosteroid agents; **OR**
   B. Unable to tolerate tapering of prednisone or other corticosteroid agents; **OR**
   C. Has a medical contraindication to prednisone or other corticosteroid agents;

OR

X. Relapsing multiple sclerosis (AAN 2018, DP B IIb);

OR

XI. Neuromyelitis optica (Scott 2011);

OR

XII. Pediatric nephrotic syndrome when each of the following criteria are met (KDIGO 2012, DP B IIb):
   A. Individual 18 years of age or younger; **AND**
   B. Individual has steroid-dependent, relapsing disease; **AND**
   C. Individual has had an inadequate response to, is intolerant of, or has a contraindication to corticosteroids or immunosuppressive agents (such as but not limited to cyclosporine, cyclophosphamide, or mycophenolate);

OR

XIII. Renal transplant setting for either of the following indications (Vo 2010, KDIGO 2017):
   A. Pre-transplant to suppress panel reactive anti-human leukocyte antigens (HLA) antibodies in individuals with high panel reactive antibody (PRA) levels to HLAs; **OR**
   B. Post-transplant in individuals with acute rejection who had received rituximab treatment pre-transplant;

OR

XIV. Antibody-mediated solid organ transplant rejection (KDIGO 2009, ISHLT 2010);

OR

XV. Thrombocytopenic purpura, immune or idiopathic (ASH 2011);

OR

XVI. Immune mediated thrombotic thrombocytopenic purpura (TTP) when each of the following criteria are met (Scully 2012, DP B IIb):
   A. TTP is confirmed by severely reduced baseline activity of ADAMTS 13 (less than 5%), with the presence of an ADAMTS 13 inhibitor; **AND**

Market Applicability							
Market	**DC**	**GA**	**KY**	**MD**	**NJ**	**NY**	**WA**
Applicable	X	X	X	X	X	X	X

B. Individual has refractory or relapsing disease as defined by lack of response to plasma exchange therapy and glucocorticoids;

OR

XVII. Myasthenia gravis when the following criteria are met (MGFA 2016, DP B I):
A. Individual is 18 years of age or older with myasthenia gravis; **AND**
B. Individual has had an inadequate response to, is intolerant of, or has a contraindication to two or more immunosuppressive drug agents (such as azathioprine, cyclosporine, or methotrexate).

Requests for Rituxan (rituximab), Truxima (rituximab-abbs), or Ruxience (rituximab-pvvr) may not be approved when the above criteria are not met and for all other non-oncologic indications.

Key References:

1. Fervenza FC, Appel GB, Barbour SJ. et al. Rituximab or cyclosporine in the treatment of membranous nephropathy. N Engl J Med 2019; 381: 36–46.
2. Dahan, K., Debiec, H., Plaisier, E. et al. Rituximab for severe membranous nephropathy: a 6-month trial with extended follow-up. *J Am Soc Nephrol*. 2017; 28: 348–358
3. Management and treatment of glomerular diseases (part 1): conclusions from a KDIGO (Kidney Disease Improving Global Outcomes) Controversies Conference. February 2019. Available at https://www.kidney-international.org/article/S0085-2538(18)30809-3/fulltext#sec3.5. Accessed on October 21, 2019.
4. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.: 2018. URL: http://www.clinicalpharmacology.com. Updated periodically.
5. Cohen SB, Burgos-Vargas R, Emery P, Jin B, Cronenberger C, Vázquez-Abad MD. Extension study of PF-05280586, a potential rituximab biosimilar, versus rituximab in subjects with active rheumatoid arthritis. Arthritis Care Res. 2018;70(11):1598–1606. doi: 10.1002/acr.23586.
6. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm. Accessed: October 17, 2018.
7. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
8. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2018; Updated periodically.
9. Singh JA, Saag KG, Bridges SL et al. 2015 American College of Rheumatology Guideline for the treatment of rheumatoid arthritis. *Arthritis Rheum*. 2016;68:1-26.
10. Ahmed AR, Shetty S, Kaveri S, Spigelman ZS. Treatment of recalcitrant bullous pemphigoid (BP) with a novel protocol: a retrospective study with a 6-year follow-up. J Am Acad Dermatol. 2016; 74(4):700-708.
11. Maley A, Warren M, Haberman I, et al. Rituximab combined with conventional therapy versus conventional therapy alone for the treatment of mucous membrane pemphigoid (MMP). J Am Acad Dermatol. 2016; 74(5):835-840.
12. Collins PW, Mathias M, Hanley J, et al. Rituximab and immune tolerance in severe hemophilia A: a consecutive national cohort. J Thromb Haemot. 2009; 7(5):787-794.
13. Kruse-Jarres R, Kempton CL, Baudo F, et. Al. Acquired hemophilia A: Updated review of evidence and treatment guidance. American Journal of Hematology. 2017; 92:695-705.
14. Rossi B, Blanche P, Roussel-Robert V, et al. Rituximab as first-line therapy for acquired haemophilia A: a single-centre 10-year experience. Haemophilia. 2016; 22(4):e338-41.
15. Birgens H, Frederiksen H, Hasselbalch HC, et al. A phase III randomized trial comparing glucocorticoid monotherapy versus glucocorticoid and rituximab in patients with autoimmune haemolytic anaemia. Br J Haematol. 2013; 163(3):393-399.

This policy does not apply to health plans or member categories that do not have pharmacy benefits, nor does it apply to Medicare. Note that market specific restrictions or transition-of-care benefit limitations may apply.

Market Applicability							
Market	**DC**	**GA**	**KY**	**MD**	**NJ**	**NY**	**WA**
Applicable	X	X	X	X	X	X	X

16. Michel M, Terriou L, Roudot-Thoraval F, et al. A randomized and double-blind controlled trial evaluating the safety and efficacy of rituximab for warm auto-immune hemolytic anemia in adults (the RAIHA study). Am J Hematol. 2017; 92(1):23-27.
17. Ramos-Casals M, Soto MJ, Cuadrado MJ, Khamashta MA. Rituximab in systemic lupus erythematosus: a systematic review of off-label use in 188 cases. Lupus. 2009; 18(9):767-776.
18. Cutler C, Miklos D, Kim HT, et al. Rituximab for steroid-refractory chronic graft-versus-host disease. Blood. 2006; 108:756-762.
19. Kharfan-Dabaja MA, Mhaskar AR, Djulbegovic B, et al. Efficacy of rituximab in the setting of steroid-refractory chronic graft-versus-host disease: a systematic review and meta-analysis. Biol Blood Marrow Transplant. 2009; 15:1005-1013.
20. Kharfan-Dabaja MA, Cutler CS. Rituximab for prevention and treatment of graft-versus-host disease. Int J Hematol. 2011; 93(5):578-585.
21. KDIGO (Kidney Disease Improving Global Outcomes) clinical practice guideline for glomerulonephritis (GN). June 2012. Available at: http://kdigo.org/home/glomerulonephritis-gn/. Accessed on: October 17, 2019.
22. Khosroshahi A, Wallace ZS, Crowe JL, et al; Second International Symposium on IgG4-Related Disease. International Consensus Guidance Statement on the Management and Treatment of IgG4-Related Disease. Arthritis Rheumatol. 2015; 67(7):1688-1699.
23. 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(17):777-788.
24. Alping P, Frisell T, Novakova L, et al. Rituximab versus fingolimod after natalizumab in multiple sclerosis patients. Ann Neurol. 2016; 79(6):950-958.
25. 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.
26. Vo AA, Peng A, Toyoda M, et al. Use of intravenous immune globulin and rituximab for desensitization of highly HLA-sensitized patients awaiting kidney transplantation. Transplantation. 2010; 89(9):1095-1102.
27. KDIGO (Kidney Disease Improving Global Outcomes) clinical practice guideline on the evaluation and care of living kidney donors. August 2017. Available at: https://kdigo.org/wp-content/uploads/2017/07/2017-KDIGO-LD-GL.pdf. Accessed on October 17, 2018.
28. KDIGO (Kidney Disease Improving Global Outcomes) Transplant Work Group: KDIGO clinical practice guideline for the care of kidney transplant recipients. Am J Transplant. 2009; 9(3): S1-S157.
29. KDIGO 2018 Clinical Practice Guideline for the Prevention, Diagnosis, Evaluation, and Treatment of Hepatitis C in Chronic Kidney Disease. Kidney International Supplements (2018) 8(3): 91-165.
30. Costanzo MR, Dipchand A, Starling R, et al. The International Society of Heart and Lung Transplantation (ISHLT) Guidelines for the care of heart transplant recipients. J Heart Lung Transplant. 2010; 29(8):914-956.
31. Neunert C, Lim W, et al. The American Society of Hematology 2011 evidence-based practice guideline for immune thrombocytopenia. Blood. 2011;117(16):4190-4207.
32. Scully M, Hunt BJ, Benjamin S, et al; British Committee for Standards in Haematology. Guidelines on the diagnosis and management of thrombotic thrombocytopenic purpura and other thrombotic microangiopathies. Br J Haematol. 2012; 158(3):323-335.
33. Shim SC, Bozic-Majstorovic L, Kasay AB, et al. Efficacy and Safety of switching from rituximab to biosimilar CT-P10 in rheumatoid arthritis: 72-week data from a randomized Phase 3 trial. Rheumatology 2019, kez152, https://doi.org/10.1093/rheumatology/kez152.
34. Sanders DB, Wolfe GI, Benatar M, et al for the Task Force of the Myasthenia Gravis Foundation of America (MGFA). International consensus guidance for management of myasthenia gravis. Neurology 2016; 87:419.