Medical Drug Clinical Criteria

Subject:	Rituximab agents for Non-Oncologic Indications		
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Overview

This document addresses the approved and off-label non-oncologic indications for use of rituximab agents, Rituxan (rituximab) and the biosimilars Truxima (rituximab-abbs), Riabni (rituximab-arrx), and Ruxience (rituximab-pvvr). Rituximab is a genetically engineered monoclonal antibody that targets a specific protein, known as CD20 found on the surface of normal and malignant B-lymphocytes. It is FDA approved for the non-oncologic uses of rheumatoid arthritis, pemphigus vulgaris, and granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA).

Note: This document does not address any FDA approved oncologic indications or off-label oncologic uses of rituximab (including conditions such as multicentric Castleman disease [MCD], post-transplant lymphoproliferative disease [PTLD], or when used as a conditioning regimen for allogenic transplant).

Rheumatoid Arthritis: The American College of Rheumatology (ACR) guidelines recommend disease-modifying antirheumatic drug (DMARD) monotherapy as first-line treatment in individuals with RA with moderate to high disease activity. Methotrexate (MTX) monotherapy, titrated to a dose of at least 15 mg, is recommended over hydroxychloroquine, sulfasalazine, and leflunomide. Methotrexate monotherapy is also recommended over monotherapy with biologics (TNFi, IL-6 inhibitors, abatacept) or JAK inhibitors. For individuals taking maximally tolerated doses MTX who are not at target, the addition of a biologic or JAK inhibitor is recommended. Non-TNFi biologics or JAK inhibitors are conditionally recommended over TNFi in individuals with heart failure.

ANCA-associated vasculitis: Antineutrophil cytoplasmic antibody (ANCA)- associated vasculitis AAV is a collection of relatively rare autoimmune diseases of unknown causes, characterized by inflammatory cell infiltration causing necrosis of blood vessels. The clinical presentation of disease can vary, ranging from a skin rash to fulminant multisystem disease. Three subtypes of the disease include granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA), and Eosinophilic granulomatosis with polyangiitis (EGPA-previously known as Churg-Strauss). Rituximab, in combination with glucocorticoids, is indicated for the treatment of patients age 2 and above with GPA or MPA. The American College of Rheumatology (ACR)/ Vasculitis Foundation guidelines recommend rituximab for remission induction for active, severe disease and for remission maintenance in those that have entered remission after treatment with cyclophosphamide or rituximab.

Pemphigus vulgaris and other autoimmune blistering skin diseases: Pemphigus is a life-threatening autoimmune blistering disease affecting the skin and mucosa and is comprised of three major forms characterized by autoantibodies directed against epidermal cell junctions: pemphigus vulgaris, pemphigus foliaceus, and paraneoplastic pemphigus (PNP). Rituximab (Rituxan) is FDA approved for moderate to severe pemphigus vulgaris and there is literature to support its use as first-line therapy and in treatment refractory disease. In addition, there are case series and retrospective comparative studies that support the use of rituximab in refractory pemphigoid disease [bullous pemphigoid and mucous membrane pemphigoid (such as cicatricial pemphigoid and epidermolysis bullosa acquisita)].

Myasthenia Gravis (MG): MG is a common disorder of neuromuscular transmission characterized by a variable combination of weakness in ocular, bulbar, limb, and respiratory muscles. Treatment strategies include symptomatic therapy (with anticholinesterase agents such as pyridostigmine), chronic immunotherapy with steroids or other immunosuppressive drugs (such as azathioprine, cyclosporine, or methotrexate), rapid immunotherapy (with plasmapheresis or IVIG), and/or surgical treatment. The Myasthenia Gravis Foundation of America (MGFA)

international consensus guidelines recommend immunosuppressive drugs (such as azathioprine or cyclosporine) and/or corticosteroids for individuals who have not met treatment goals after an adequate trial of pyridostigmine. Rapid immunotherapy (with IVIG or plasmapheresis), cyclophosphamide, or rituximab may be considered for refractory MG. Rituximab can be considered in those who have an unsatisfactory response to initial immunotherapy, or in those who do not tolerate other immunosuppressive agents.

Antibody-Mediated Solid Organ Transplant Rejection: Antibody-mediated rejection is caused by anti-donor-specific antibodies, mostly anti-HLA antibodies. Treatment for acute antibody-mediated rejection generally consists of IVIG and rituximab, with or without plasma exchange. Chronic AMR has remained a significant problem with a lack of standardized treatment and limited therapeutic options. Literature and guideline recommendations (KDIGO 2009, ISHLT 2010) support rituximab as a potential treatment option for antibody-mediated rejection. Based on guideline recommendations, available literature, limited alternative treatment options, and views of relevant medical specialists, the use of rituximab may be considered for antibody-mediated rejection.

Systemic Sclerosis-Associated Interstitial Lung Disease (SSc-ILD): Interstitial lung disease (ILD) is a common pulmonary manifestation of systemic sclerosis (SSc) and is a leading cause of systemic sclerosis-related death. SSc-ILD presents with fatigue, shortness of breath and dry cough. Diagnosis is based on the presence of characteristic findings of ILD on chest high resolution computed tomography (HRCT) in an individual with SSc and exclusion of other causes of ILD. The American Thoracic Society (ATS) clinical practice guideline on the treatment of systemic sclerosis-associated interstitial lung disease provides recommendations for the use of mycophenolate (strong recommendation), cyclophosphamide (conditional recommendation), tocilizumab (conditional recommendation), and rituximab (conditional recommendation). Recommendations are based on low or very low-quality evidence. The American College of Rheumatology/American College of Chest Physicians guideline for the treatment of interstitial lung disease in people with systemic autoimmune rheumatic diseases (SARD) provides conditional recommendations for rituximab, mycophenolate and cyclophosphamide as first-line therapy options for ILD associated with SARDs in general (including systemic sclerosis [SSc], rheumatoid arthritis [RA], idiopathic inflammatory myopathies [IIM including polymyositis, dermatomyositis, antisynthetase syndrome, immune-mediated necrotizing myopathy], mixed connective tissue disease [MCTD], or Sjogren disease [SjD]). There is also limited evidence that rituximab is useful in skin manifestation of systemic sclerosis. The EULAR recommendations for the treatment of systemic sclerosis: 2023 update state that mycophenolate, methotrexate, and/or rituximab should be considered for systemic sclerosis skin fibrosis.

Other Uses: Based on the results from published data in the peer-reviewed medical literature, rituximab is also used to treat additional non-oncologic indications that are not currently approved by the FDA. Supporting literature includes guideline recommendations, randomized controlled trials, retrospective studies, case series, case reports, and specialty consensus opinion. International Acquired Hemophilia A guidelines suggest adding rituximab to first-line therapy in individuals with inhibitor titer >20 BU, and as a second-line agent in refractory individuals (Tiede 2020). Rituximab is also used as treatment for autoimmune hemolytic anemia, including warm autoimmune hemolytic anemia and cold agglutinin disease (Jager 2020). It has also been studied in autoimmune diseases such as cryoglobulinemia, sjogren syndrome, and systemic lupus erythematosus that are refractory to standard treatment (Fanouriakis 2019, Ramos-Casals 2020) and as treatment for refractory Graft Versus Host Disease (NCCN 2A). KDIGO guidelines review the use of rituximab in Hepatitis C virus infection-related glomerulonephritis, pediatric nephrotic syndrome, membranous nephropathy, and renal transplant (pre- and post- transplant). The American Academy of Neurology (AAN) guidelines recommend disease modifying therapies (DMTs), such as rituximab, in individuals with relapsing forms of MS with recent clinical relapses or MRI activity. The American Society of Hematology 2019 guidelines suggest rituximab for initial or second-line treatment of Immune thrombocytopenia (ITP), also called idiopathic thrombocytopenic purpura or immune thrombocytopenic purpura. The International Society on Thrombosis and Haemostasis (ISTH) Guidelines for treatment of thrombotic thrombocytopenic purpura recommend rituximab for treatment of acute events and relapses, and as prophylaxis for individuals who are in remission. Consensus recommendations for the management of autoimmune encephalitis suggest rituximab for disease refractory to initial therapy with immunoglobulin or plasma exchange therapy (Zuliani 2019, Abboud 2021).

Rituxan, Truxima, Riabni, and Ruxience have black box warnings for fatal infusion reactions, severe mucocutaneous reactions, hepatitis B virus (HBV) reactivation, and progressive multifocal leukoencephalopathy (PML). Rituximab administration can result in serious, including fatal, infusion reactions and deaths within 24 hours of infusion have occurred, most in association with the first infusion. Monitor individuals closely; discontinue rituximab infusion for severe reactions and provide medical treatment for grade 3 or 4 reactions. Severe, including fatal, mucocutaneous reactions can occur. HBV reactivation can occur, in some cases resulting in fulminant hepatitis, hepatic failure, and death. Screen all individuals for HBV infection before treatment initiation and monitor during and after treatment with rituximab. Discontinue rituximab and concomitant medications in the event of HBV reactivation. PML, including fatal PML, can occur.

Clinical Criteria

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Rituxan (rituximab); Riabni (rituximab-arrx); Ruxience (rituximab-pvvr); Truxima (rituximab-abbs)

All requests require documentation provided for diagnosis.

Requests for Rituxan (rituximab), Riabni (rituximab-arrx), Ruxience (rituximab-pvvr) or Truxima (rituximab-abbs) 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 methotrexate titrated to maximally tolerated dose (ACR 2021); **OR**
   C. If methotrexate is not tolerated or contraindicated, individual has had an inadequate response to, is intolerant of, or has a contraindication to other conventional therapy [sulfasalazine, leflunomide, or hydroxychloroquine]; **AND**
   D. 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 (GPA) 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 (GPA) and MPA; **AND**
   B. Individual is using concomitantly with glucocorticoids with or without avacopan for induction treatment; **OR**
   C. Individual is using as follow up treatment after achieving disease control with induction treatment;

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 hemophilia or acquired inhibitors in individuals with hemophilia when used in combination with corticosteroids or in individuals who have had an inadequate response, are intolerant of, or have a contraindication to corticosteroid and cytotoxic therapy (Collins 2009, Tiede 2020);

OR

V. Autoimmune hemolytic anemia (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. Steroid-refractory Graft-Versus-Host Disease (Cutler 2006, NCCN 2A, DP B IIb);

OR

VIII. Hepatitis C virus infection-related glomerulonephritis in individuals with cryoglobulinemic flare, rapidly progressing glomerulonephritis, or nephrotic syndrome (KDIGO 2022);

OR

IX. Immunoglobulin G4-related disease when any of the following criteria 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 contraindication to prednisone or other corticosteroid agents;

OR

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

OR

XI. Neuromyelitis optica (Nikoo 2017, Tahara 2020, DP B IIa));

OR

XII. Pediatric nephrotic syndrome when each of the following criteria are met (KDIGO ~~2021~~2025, DP B IIb):
A. Individual is 18 years of age or younger; **AND**
B. Individual has frequently relapsing or 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. Membranous Nephropathy (MN) when each of the following criteria are met (KDIGO 2021):
A. Individual has moderate to high risk MN as shown by one of the following:
1. Individual has proteinuria > 3.5 g/d and proteinuria has not decreased > 50% after 6 months of conservative therapy with angiotensin converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs); **OR**
2. Individual has an estimated glomerular filtration rate (eGFR) < 60 mL/min/1.73 m^2;

OR

XIV. Renal transplant setting for either of the following indications (Vo 2010, KDIGO 2020):
A. Pre-transplant to suppress panel reactive anti-human leukocyte antigens (HLA) antibodies in individuals with high panel reactive antibody (PRA or cPRA [corrected PRA]) levels to HLAs **or** in individuals with a history of high levels of donor-specific antibodies (DSAs); **OR**
B. Post-transplant in individuals with acute rejection who had received rituximab treatment pre-transplant;

OR

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

OR

XVI. Thrombocytopenic purpura, immune or idiopathic (ITP) (ASH 2019);

OR

XVII. Immune mediated thrombotic thrombocytopenic purpura (TTP) when each of the following criteria are met (ISTH 2020):
A. TTP is confirmed by severely reduced baseline activity of ADAMTS 13 (less than 10%), with the presence of an ADAMTS 13 inhibitor or anti-ADAMTS13 IgG; **AND**
B. Individual is using in combination with plasma exchange therapy and glucocorticoids for treatment of acute event or relapse;
OR
C. Individual is in remission and using for prevention of relapse;

OR

XVIII. Myasthenia gravis when the following criteria are met (MGFA 2020, DP B I):
A. Individual is 18 years of age or older with myasthenia gravis; **AND**
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).

OR

XIX. Systemic Sclerosis-associated skin fibrosis when the following criteria are met (DP BIIa, Del Galdo 2023):
A. Individual has a diagnosis of systemic sclerosis-associated skin fibrosis; **AND**
B. Individual has had a trial and inadequate response to, is intolerant of, or has a contraindication to mycophenolate or methotrexate;

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OR

XX. Systemic Autoimmune Rheumatic Disease- associated Interstitial Lung Disease (SARD-ILD) when the following criteria are met (DP BIIa, ATS 2023, ACR 2023):

A. Individual has a diagnosis of Systemic Autoimmune Rheumatic Disease (including systemic sclerosis [SSc], rheumatoid arthritis [RA], idiopathic inflammatory myopathies [IIM including polymyositis, dermatomyositis, antisynthetase syndrome, immune-mediated necrotizing myopathy], mixed connective tissue disease [MCTD], or Sjogren disease [SjD]) - associated Interstitial Lung Disease (SARD-ILD); **AND**

B. Diagnosis has been verified through chest high resolution computed tomography (HRCT) showing characteristic features of ILD in an individual with a known systemic autoimmune rheumatic disease (including SSc, RA, IIM, MCTD, or SjD); **AND**

C. Individual has had a trial and inadequate response to, is intolerant of, or has a contraindication to mycophenolate or cyclophosphamide;

OR

~~XIX.~~XXI. Immune-mediated encephalitis, including paraneoplastic and autoimmune encephalitis when the following criteria are met (Zuliani 2019, Lancaster 2016):

A. Diagnosis is confirmed by detection of a specific autoantibody associated with encephalitis [including but not limited to: NMDAR, LGI1, Caspr2, AMPAR, GABA-A or GABA-B receptor, IgLON5, DPPX, GlyR, mGluR1, mGluR2, mGluR5, Neurexin 3-alpha, or dopamine-2 receptor (D2R)]; **AND**

B. Individual has had an inadequate response to, is intolerant of, or has a contraindication to first line agent(s) including immunoglobulin therapy *or* plasma exchange;

OR

~~XX.~~XXII. Immune Checkpoint Inhibitor ~~Immunotherapy~~-related toxicities including (NCCN 2A):

A. Moderate, severe, or life-threatening bullous pemphigoid or bullous dermatitis; **OR**

B. Hemolytic anemia or thrombocytopenia refractory to corticosteroids; **OR**

C. Acute kidney injury/elevated serum creatinine if toxicity remains greater than stage 2 after 4-6 weeks of corticosteroids or if creatinine increases during steroid taper (or once off steroids); **OR**

~~B.~~D. Moderate, severe, or life-threatening myositis for significant dysphagia, life-threatening situations, or cases refractory to corticosteroids; **OR**

~~C.~~E. Severe myasthenia gravis refractory to prior therapy; **OR**

~~D.~~F. Encephalitis refractory to prior therapy in individuals positive for autoimmune encephalopathy antibody.

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

Step Therapy

Summary of FDA-approved and off-label non-oncologic indications for rituximab agents

	Rituxan (rituximab)	Truxima (rituximab-abbs)	Ruxience (rituximab-pvvr)	Riabni (rituximab-arrx)
Rheumatoid Arthritis	X	X	X	X
Granulomatosis with Polyangiitis and Microscopic Polyangiitis	X	X	X	X
Pemphigus vulgaris	X	X~~Y~~$^{\Delta}$	X~~Y~~$^{\Delta}$	X~~Y~~$^{\Delta}$
Acquired hemophilia or inhibitors in hemophilia	Y	Y$^{\Delta}$	Y$^{\Delta}$	Y$^{\Delta}$
Autoimmune hemolytic anemia	Y	Y$^{\Delta}$	Y$^{\Delta}$	Y$^{\Delta}$
Cryoglobulinemia, primary Sjogren Syndrome, or systemic lupus erythematosus	Y	Y$^{\Delta}$	Y$^{\Delta}$	Y$^{\Delta}$
Graft-Versus-Host Disease	Y	Y$^{\Delta}$	Y$^{\Delta}$	Y$^{\Delta}$
Hepatitis C virus infection-related glomerulonephritis	Y	Y$^{\Delta}$	Y$^{\Delta}$	Y$^{\Delta}$
Immunoglobulin G4-related disease	Y	Y$^{\Delta}$	Y$^{\Delta}$	Y$^{\Delta}$
Relapsing multiple sclerosis	Y	Y$^{\Delta}$	Y$^{\Delta}$	Y$^{\Delta}$

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Neuromyelitis optica	Y	Y^Δ	Y^Δ	Y^Δ
Pediatric nephrotic syndrome	Y	Y^Δ	Y^Δ	Y^Δ
Membranous nephropathy	Y	Y^Δ	Y^Δ	Y^Δ
Renal transplant with reactive human leukocyte antigen (HLA)-specific antibodies	Y	Y^Δ	Y^Δ	Y^Δ
Antibody-mediated solid organ transplant rejection	Y	Y^Δ	Y^Δ	Y^Δ
Thrombocytopenic purpura, immune or idiopathic	Y	Y^Δ	Y^Δ	Y^Δ
Thrombotic thrombocytopenic purpura	Y	Y^Δ	Y^Δ	Y^Δ
Myasthenia gravis	Y	Y^Δ	Y^Δ	Y^Δ
Immunotherapy-related toxicities	Y	Y^Δ	Y^Δ	Y^Δ

X = FDA approved indication; Y = *Off-label use*; ~~*Y^Δ = Off-label indication based on clinical judgement of biosimilarity by 1Q 2021 P&T committee*~~

Note: When a rituximab agent is deemed approvable based on the clinical criteria above, the benefit plan may have additional criteria requiring the use of a preferred[1] agent or agents.

Rituximab Reference and Biosimilar Agents for Non-Oncologic Indications Step Therapy

A list of the preferred rituximab agents is available here.

Requests for a non-preferred rituximab agent for a non-oncologic indication may be approved when the following criteria are met:

~~I.~~ Individual has had a trial of and has an allergy or severe intolerance to an inactive ingredient in one preferred agent which interferes with the individual's ability to use the product, and the same allergy/severe intolerance is not expected with the non-preferred product;~~Individual has had a trial and intolerance to one preferred agent; **OR**~~

~~II.~~I. ~~Individual is currently stabilized on the requested non-preferred rituximab agent~~.

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[1]Preferred, as used herein, refers to agents that were deemed to be clinically comparable to other agents in the same class or disease category but are preferred based upon clinical evidence and cost effectiveness.

Quantity Limits

Rituximab for Non-Oncologic Indications Quantity Limit

Drug	Limit Per Indication
Rituxan (rituximab) 100 mg, 500 mg vial; Riabni (rituximab-arrx) 100 mg, 500 mg vial; Ruxience (rituximab-pvvr) 100 mg, 500 mg vial; Truxima (rituximab-abbs) 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) (Wegener's Granulomatosis) and Microscopic Polyangiitis (MPA) maintenance:** 1000mg every 4 months† **Myasthenia Gravis**: 375 mg/m^2 monthly (DP)^ **Autoimmune Hemolytic Anemia:** 375 mg/m^2 weekly for 4 weeks (DP) **Immune Thrombocytopenia (ITP):** 375 mg/m^2 weekly for up to 4 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 (Label) or 1000 mg on days 1 and 15 (DP). After induction (at least 16 weeks after rituximab induction or within 4 weeks after achieving disease control from	

induction with other standard of care immunosuppressants), may approve two 500mg infusions separated by 2 weeks followed by maintenance therapy.

^May approve 375 mg/m^2 weekly for 4 weeks when initiating therapy or as clinically indicated upon relapse.

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

HCPCS	
J9312	Injection, rituximab, 10 mg [Rituxan]
Q5115	Injection, rituximab-abbs, biosimilar, (Truxima), 10 mg
Q5119	Injection, rituximab-pvvr, biosimilar, (Ruxience), 10 mg
Q5123	Injection, rituximab-arrx, biosimilar, [Riabni], 10 mg

ICD-10 Diagnosis	
B17.10-B17.11	Acute hepatitis C
B18.2	Chronic viral hepatitis C
B19.20-B19.21	Unspecified viral hepatitis C
D59.0-D59.19	Drug-induced, other autoimmune hemolytic anemias
D68.311	Acquired hemophilia
D69.3	Immune thrombocytopenic purpura (idiopathic thrombocytopenic purpura)
D89.1	Cryoglobulinemia
~~D89.810-D89.89~~	~~Other specified disorders involving the immune mechanism, not elsewhere classified [Graft-versus-host disease, ALPS]~~
D89.810-D89.813	Graft-versus-host disease
D89.84	IgG4-related disease
G04.81	Other encephalitis and encephalomyelitis
G35	Multiple sclerosis
G36.0	Neuromyelitis optica [Devic]
G70.00-G70.01	Myasthenia gravis
G72.49	Other inflammatory and immune myopathies, not elsewhere classified
J84.170-J84.178	Other interstitial pulmonary diseases with fibrosis in diseases classified elsewhere [systemic autoimmune rheumatic disease-associated interstitial lung disease (SARD-ILD)]
L10.0-L10.9	Pemphigus
L12.0-L12.9	Pemphigoid ~~(epidermolysis bullosa)~~
M05.00-M05.9	Rheumatoid arthritis with rheumatoid factor
M06.00-M06.09	Rheumatoid arthritis without rheumatoid factor
M06.80-M06.9	Other specified rheumatoid arthritis and rheumatoid arthritis, unspecified
M31.10	Thrombotic microangiopathy (thrombotic thrombocytopenic purpura)
M31.19	Other thrombotic microangiopathy (thrombotic thrombocytopenic purpura)
M31.30-M31.31	Wegener's granulomatosis
M31.7	Microscopic polyangiitis
M32.0-M32.9	Systemic lupus erythematosus (SLE)

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M33.00-M33.99	Dermatopolymyositis [systemic autoimmune rheumatic disease]
M34.0-M34.9	Systemic sclerosis [scleroderma]
M35.00-M35.09	SjögrenSicca syndrome (Sjögren)
M35.5	Multifocal fibrosclerosis [when specified as immunoglobulin G4-related disease]
M35.9	Systemic involvement of connective tissue, unspecified [when specified as immunoglobulin G4-related disease]
M60.80-M60.9	Other myositis, myositis unspecified [immune checkpoint inhibitor-related toxicity]
N01.0-N01.9	Rapidly progressive nephritic syndrome
N03.0-N03.A	Chronic nephritic syndrome
N04.0-N04.9A	Nephrotic syndrome
N05.0-N05.A	Unspecified nephritic syndrome
N06.0-N06.9	Isolated proteinuria with specified morphological lesion
N08	Glomerular disorders in diseases classified elsewhere
N18.1-N18.9	Chronic kidney disease (CKD)
N17.9	Acute kidney failure, unspecified [immune checkpoint inhibitor-related toxicity]
Q81.0-Q81.9	Epidermolysis bullosa
T45.AX5A-T45.AX5S	Adverse effect of immune checkpoint inhibitors and immunostimulant drugs
T86.00-T86.99	Complications of transplanted organs and tissue
Z48.22	Encounter for aftercare following kidney transplant
Z94.0	Kidney transplant status

Document History

Revised: 08/15/2025
Document History:

- 08/15/2025 – Annual Review: Add off label use in systemic sclerosis-related skin fibrosis and rheumatic disease-associated interstitial lung disease; update immunotherapy related toxicities per NCCN; update step therapy with standard biosimilar step language; update references; wording and formatting updates. Coding Reviewed: Updated description for ICD-10-CM L12.0-L12.9, M35.00-M35.09, M35.9. Added ICD-10-CM G72.49, J84.170-J84.178, M31.19, M33.00-M33.99, M34.0-M34.9, M60.80-M60.9, N04.A to range N04.0-N04.9, N03.0-N03.A, N05.0-N05.A, N17.9, T45.AX5A-T45.AX5S. Removed ICD-10-CM M35.5, N18.1-N18.9, D89.831-D89.839, D89.89.
- 08/16/2024 – Annual Review: No changes. Coding Reviewed: No changes.
- 12/11/2023 – Select Review: Update GPA/MPA quantity limit per compendia/guidelines. Coding Reviewed: No changes.
- 08/18/2023 – Annual Review: Update acquired hemophilia criteria to include combination use with corticosteroids; update graft-versus-host disease to “steroid-refractory”; add use in certain immunotherapy-related toxicities per NCCN; update Hepatitis C virus infection-related glomerulonephritis criteria per KDIGO guidelines; include additional induction regimen for GPA/MPA in quantity limit; update table. Coding Reviewed: No changes.
- 05/15/2023 – Step therapy table updates.
- 03/27/2023 – Step therapy table updates.
- 01/25/2023 – Step therapy table updates.
- 08/19/2022 – Annual Review: Update criteria to include new off-label use in membranous nephropathy based on KDIGO guidelines; update references; update ITP quantity limit per compendia. Step therapy table update. Coding Reviewed: Added ICD-10-CM M31.10, N04.0-N04.9.
- 07/25/2022 – Administrative update to add documentation. Step therapy table update.
- 04/25/2022 – Step therapy table update.
- 03/28/2022 – Step therapy table update.
- 11/19/2021 – Select Review: Update RA criteria to align with new guidelines; update GPA/MPA criteria to allow combination with avacopan; update GPA/MPA QL to align with label. Coding Reviewed. No changes. Step therapy table updates.

- 11/01/2021 – Add step therapy and step therapy table.
- 08/20/2021 – Annual Review: Update GPA/MPA criteria and quantity limit to clarify use as follow up treatment; update encephalitis criteria to clarify use in any immune-mediated encephalitis; update acquired inhibitors criteria for clarity, update autoimmune hemolytic anemia to remove “refractory”; update TTP diagnosis and use of rituximab as initial or prophylactic treatment. Coding reviewed: No changes.
- 03/15/2021 – Select Review: Update myasthenia gravis quantity limit. Coding Review: No changes. Effective 7/1/2021 Added HCPCS Q5123. Extended code range to D59.0-D59.19. Removed HCPCS J9999, J3590, C9399. Removed all diagnosis pend for Riabni.
- 02/19/2021 – Select Review: Add new biosimilar agent Riabni to clinical criteria and quantity limit; update indication table. Coding Review: Added J3590, J9999, C9399, All diagnosis pend for Riabni.
- 11/20/2020 – Annual Review: Update transplant criteria to include donor-specific antibodies for clarity; add criteria for refractory autoimmune encephalitis; update references. Coding Reviewed: Added ICD-10-CM G04.81.
- 05/15/2020 – Select Review: Update rheumatoid arthritis quantity limit. Coding Reviewed: Effective 7/1/2020 Added HCPCS Q5119, Delete 6/30/2020 J3490, J3590
- 02/21/2020 – Select Review: Update indication table to note that Truxima is FDA approved for RA and GPA/MPA. Coding Reviewed: Added HCPCS Q J3590 for Ruxience
- 11/15/2019 – Annual Review: Update age for Granulomatosis with Polyangiitis and Microscopic Polyangiitis per label; update cryoglobulinemic vasculitis criteria wording according to new KDIGO guidelines. Wording and formatting changes. Coding reviewed: No Changes.
- 08/16/2019 – Select Review: Apply current prior authorization and quantity limits to rituximab biosimilars Truxima and Ruxience. Remove double prior trial requirement in multiple sclerosis criteria. Add new non-preferred reference or biosimilar step therapy for non-oncologic indications. Coding Reviewed: Added HCPCS codes Q5115, J3490
- 11/16/2018 – Annual Review: Initial P&T review of Rituxan for Non-Oncologic Indications Clinical Guideline. Update approval criteria to add off-label indication for refractory myasthenia gravis in adults which meets off-label policy requirements and is in accordance with MGFA guideline recommendations. Update approval criteria to add off-label indication for antibody-mediated solid organ transplant rejection in accordance with KDIGO and ISHLT guideline recommendations and per AST consultant recommendations. Update RA criteria to delete “active” disease wording. Delete requirement for methotrexate combination therapy for RA indication for consistency with other RA approval criteria and in accordance with ACR guideline recommendations. Update TTP and autoimmune blistering skin disease criteria for clarity per committee recommendations. Add examples of conventional therapy to approval criteria for clarity. Wording and formatting changes to criteria for clarity and consistency. HCPCS and ICD-10 Coding Review: Delete J9310. Add J9312. Add G70.00-G70.01 for Myasthenia gravis indication. Organ transplant ICD-10 already included.

References

1. Autoimmune encephalitis: proposed best practice recommendations for diagnosis and acute management. Abboud H, Probasco JC, Irani S, et al. J Neurol Neurosurg Psychiatry. 2021;92:757–768.
2. 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.
3. Alping P, Frisell T, Novakova L, et al. Rituximab versus fingolimod after natalizumab in multiple sclerosis patients. Ann Neurol. 2016; 79(6):950-958.
4. 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.
5. Burmester G, Drescher E, Hrycaj P, Chien D, Pan Z, Cohen S. Efficacy and safety results from a randomized double-blind study comparing proposed biosimilar ABP 798 with rituximab reference product in subjects with moderate-to-severe rheumatoid arthritis [published correction appears in Clin Rheumatol. 2020 Sep 23;:]. Clin Rheumatol. 2020;39(11):3341-3352. doi:10.1007/s10067-020-05305-y.
6. Chung, SA, Langford CA, Maz M, et al. 2021 American College of Rheumatology/Vasculitis Foundation Guideline for the Management of Antineutrophil Cytoplasmic Antibody-Associated Vaculitis. Arthritis Care & Research. 2021;73(8):1088-1105.
7. 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.

8. 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.
9. 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.
10. Cutler C, Miklos D, Kim HT, et al. Rituximab for steroid-refractory chronic graft-versus-host disease. Blood. 2006; 108:756-762.
11. 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.
12. Del Galdo F, Lescoat A, Conaghan PG, et al: EULAR recommendations for the treatment of systemic sclerosis: 2023 update. Ann Rheum Dis 2025; 84(1):29-40.
13. Fernandez-Juarez G, Rojas-Rivera J, Van de Logt A, et al. The STARMEN trial indicates that alternating treatment with corticosteroids and cyclophosphamide is superior to sequential treatment with tacrolimus and rituximab in primary membranous nephropathy. Kidney Int. 2021;99(4):986-998.
14. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm. Accessed: July 3, 2025.
15. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
16. Fanouriakis A, Kostopoulou M, Alunno A, et al: 2019 update of the EULAR recommendations for the management of systemic lupus erythematosus. Ann Rheum Dis 2019; 78(6):736-745.
17. 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.
18. Fernández-Juárez G, Rojas-Rivera J, Logt AV, et al. The STARMEN trial indicates that alternating treatment with corticosteroids and cyclophosphamide is superior to sequential treatment with tacrolimus and rituximab in primary membranous nephropathy.
19. Fraenkel L, Bathon JM, England BR et al. 2021 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. Arthritis Care & Research. 2021;73(7):924-939.
20. Jager U, Barcellini W, Broome C, et al. Diagnosis and treatment of autoimmune hemolytic anemia in adults: Recommendations from the first International Consensus meeting. Blood Rev. 2020; 41:100648.
21. Johnson S, Bernstein E, Bolster M, et al. 2023 American College of Rheumatology/American College of Chest Physicians (CHEST) Guideline for the Treatment of Interstitial Lung Disease in People with Systemic Autoimmune Rheumatic Diseases. Arthritis Rheum. 2024; 76(8):1182-1200.
22. KDIGO (Kidney Disease Improving Global Outcomes) clinical practice guideline for glomerulonephritis (GN). June 2012.
23. 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.
24. Kidney Disease: Improving Global Outcomes (KDIGO) 2025 Clinical Practice Guideline for the Management of Nephrotic Syndrome in Children. May 2025.
25. KDIGO (Kidney Disease Improving Global Outcomes) clinical practice guideline on the evaluation and care of living kidney donors. August 2017.
26. 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.
27. KDIGO (Kidney Disease: Improving Global Outcomes) Clinical practice guideline on the evaluation and management of candidates for kidney transplantation. *Transplantation*. 2020; 104 (S4).
28. KDIGO 2022 Clinical Practice Guideline for the Prevention, Diagnosis, Evaluation, and Treatment of Hepatitis C in Chronic Kidney Disease. Kidney International Supplements (2022) 102:65.
29. 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.
30. Kharfan-Dabaja MA, Cutler CS. Rituximab for prevention and treatment of graft-versus-host disease. Int J Hematol. 2011; 93(5):578-585.
31. 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.
32. 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.
33. Lancaster, E. The Diagnosis and Treatment of Autoimmune Encephalitis. J Clin Neurol. 2016 Jan;12(1):1-13.
34. Lancaster, E. Autoantibody Encephalitis: Presentation, Diagnosis, and Management. J. Clin Neurol. 2022; 18(4):373-390.
35. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2024; Updated periodically.
36. 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.

37. Management and treatment of glomerular diseases (part 1): conclusions from a KDIGO (Kidney Disease Improving Global Outcomes) Controversies Conference. February 2019.
38. 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.
39. Neunert C, Terrell DR, Arnold DM, et al. The American Society of Hematology 2019 guidelines for immune thrombocytopenia. Blood Adv. 2019; 3 (23):3829-3866.
40. Nikoo Z, Badihian S, Shaygannejad V, et al. Comparison of the efficacy of azathioprine and rituximab in neuromyelitis optica isspectrum disorder: a randomized clinical trial. J Neurol 2017; 264:2003.
41. Raghu G, Montesi SB, Silver RM, et al. Treatment of Systemic Sclerosis-associated Interstitial Lung Disease: Evidence-based Recommendations. An Official American Thoracic Society (ATS) Clinical Practice Guideline. Am J Respir Crit Care Med. 2023.
42. 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.
43. 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.
44. Ramos-Casals M, Brito-Zerón P, Bombardieri S On behalf of the EULAR-Sjögren Syndrome Task Force Group, et al. EULAR recommendations for the management of Sjögren's syndrome with topical and systemic therapies. Annals of the Rheumatic Diseases 2020;79:3-18.
45. 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.
46. 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.
47. Sammaritano LR, Askanase A, Bermas BL, et al. 2024 American College of Rheumatology (ACR) Guideline for the Screening, Treatment, and Management of Lupus Nephritis. Arthritis Rheumatol. 2025 May 7. doi: 10.1002/art.43212.
48. Narayanaswami P, Sanders DB, Wolfe G, et al for the Task Force of the Myasthenia Gravis Foundation of America (MGFA). International consensus guidance for management of myasthenia gravis 2020 update. Neurology 2021; 96:114-122.
49. 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.
50. 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.
51. Fraenkel L, Bathon JM, England BR et al. 2021 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. Arthritis Care & Research. 2021;73(7):924-939.
52. 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. Lancet Neurol 2020; 19:298.
53. Tiede A, Collins P, Knoebl P, et al. International recommendations on the diagnosis and treatment of acquired hemophilia A. Haematologica 2020; 105 (7):1791-1801.
54. 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.
55. Zheng, XL, Vesely, SK, Cataland, SR, et al. ISTH guidelines for treatment of thrombotic thrombocytopenic purpura. J Thromb Haemost. 2020; 18: 2496– 2502. https://doi.org/10.1111/jth.15010.
56. Zheng, XL, Vesely, SK, Cataland, SR, et al. ISTH guidelines for the diagnosis of thrombotic thrombocytopenic purpura. J Thromb Haemost. 2020; 18: 2486– 2495. https://doi.org/10.1111/jth.15006.
57. Zuliani L, Nosadini M, Gastaldi M, et. al. Management of antibody-mediated autoimmune encephalitis in adults and children: literature review and consensus-based practical recommendations. Neurological Sciences 2019. 40:2017-2030.
58. NCCN Clinical Practice Guidelines in Oncology™. © 2025 National Comprehensive Cancer Network, Inc. For additional information visit the NCCN website: http://www.nccn.org/index.asp. Accessed on July 9, 2025.
    a. Management of Immunotherapy-related Toxicities. V1.2025. Revised December 20, 2025.
    b. Hematopoietic Cell Transplantation (HCT). V2.2025. Revised June 3, 2025.

Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.

CC-0075 Rituximab agents for Non-Oncologic Indications

Commercial Medical Benefit

Effective Date	Preferred Agents	Non-Preferred Agents
02/01/2022	Rituxan Riabni	Ruxience Truxima
01/01/2022 CalPERS For members 18 years and older step therapy criteria applies to new starts only (defined as no use of Rituxan in the last 12 months)	Riabni Ruxience Truxima	Rituxan

Medicaid Medical Benefit

Effective Date	Preferred Agents	Non-Preferred Agents
04/15/2022: MD, NJ, NV, SC, VA, WI, WNY 05/01/2022: IA 05/15/2022: IN, GA, TN 06/15/2022: AR, CA 08/01/2022: LA 09/15/2022: KY 02/01/2023: OH 04/01/2023: DC	Riabni	Rituxan Ruxience Truxima

Medicare Medical Benefit

Effective Date	Preferred Agents	Non-Preferred Agents
02/01/2022	Rituxan Riabni	Ruxience Truxima