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.

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. The use of rituximab in membranous nephropathy is currently under investigation. A recent randomized controlled trial evaluating rituximab plus nonimmunosuppressive antiproteinuric treatment (NIAT) vs NIAT alone did not meet its primary endpoint of complete or partial remission of proteinuria at 6 months (Dahan 2017). KDIGO 2012 guidelines on glomerulonephritis made no recommendation for rituximab due to lack of evidence. However, the 2021 KDIGO Guidelines for the Management of Glomerular Disease recommend the use of rituximab monotherapy for moderate risk disease and monotherapy or combination with a calcineurin inhibitor for high-risk disease. The MENTOR study showed that rituximab is non-inferior to cyclosporine to achieve partial or complete remission of proteinuria at 24 months (Fervenza 2019). Subsequently, the STARMEN study indicated that adding rituximab at six months of tacrolimus therapy resulted in worse complete or partial remission rates at 24 months than altering cycles of corticosteroids and cyclophosphamide (Fernandez-Juarez 2020).

Biosimilar products: Biosimilar products must be highly similar to the reference product and there must be no clinically meaningful differences between the biological product and the reference product in terms of the safety, purity, and potency of the product. Biosimilars must utilize the same mechanism of action (MOA), route of administration, dosage form and strength as the reference product; and the indications proposed must have been previously approved for the reference product. The potential exists for a biosimilar product to be approved for one or more indications for which the reference product is licensed based on extrapolation of data intended to demonstrate biosimilarity in one indication. Sufficient scientific justification for extrapolating data is necessary for FDA approval. Factors and issues that should be considered for extrapolation include the MOA for each indication, the pharmacokinetics, bio-distribution, and immunogenicity of the product in different patient populations, and differences in expected toxicities in each indication and patient population.

Truxima (rituximab-abbs) was originally approved as the first rituximab biosimilar with FDA approval for the same oncologic indications as Rituxan. However, now the reference product Rituxan has an additional oncologic indication for pediatric patients aged 6 months and older with previously untreated, advanced stage, CD20-positive diffuse large B-cell Lymphoma (DLBCL), Burkitt lymphoma (BL), Burkitt-like lymphoma (BLL), or mature B-cell acute leukemia (B-AL) in combination with chemotherapy. Clinical review of Truxima included two clinical studies that compared Truxima with Rituxan in the oncology setting. Demonstration of biosimilarity was also based on a third study (Shim 2019), a randomized, controlled, double-blind, 3-arm study of Truxima, US-Rituxan, and EU-approve MabThera in patients with rheumatoid arthritis (RA). This clinical data in RA was also used to support the clinical scenario where non-treatment naïve patients may undergo a single transition to Truxima based on the similar safety, efficacy, and immunogenicity profile between patients undergoing a single transition from Rituxan or MabThera to Truxima as compared to those who continued treatment with comparator product. Subsequently, Truxima was approved for RA and GPA/MPA. Both Ruxience and Riabni were granted FDA approval for the same oncologic indications as the reference product at the time in addition to GPA/MPA. Both subsequently were approved for RA. Now the reference product Rituxan has an additional oncologic indication for pediatric patients aged 6 months and older with DLBCL, BL, BLL, or B-AL. Approval for Ruxience was, in part, based on a phase 3, randomized double-blind study of Ruxience versus MabThera in patients with low tumor burden follicular lymphoma (NCT02213263). Ruxience has also been studied in rheumatoid arthritis (Cohen 2018). This was an extension study from a previous 3-arm pharmacokinetic study involving Ruxience, Rituxan, and MabThera. Subjects who received reference products Rituxan or MabThera were randomized to continue treatment or switch to Ruxience for one treatment; and then all subjects continued with Ruxience. This study also demonstrated tolerability and acceptable safety with a single transition from reference to biosimilar. Riabni approval data package included a study in follicular lymphoma and a study in rheumatoid arthritis. Subjects with active RA were randomized to Riabni, MapThera, or Rituxan; and subjects receiving Rituxan were transitioned to Riabni after the first two doses. There was no statistical difference on disease activity score change from baseline between patients treated with Riabni or a rituximab product (Burmester 2020). Based on the totality of submitted data, the FDA concluded that these biosimilar agents are highly similar to Rituxan; there are no clinically meaningful differences between them and Rituxan; and that there is justification to support licensure for the proposed indications. Therefore, as biosimilars have demonstrated biosimilarity to Rituxan for FDA indications, it is reasonable for biosimilarity to be extrapolated to off-label indications as well.

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 and 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 and 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 inhibitors in individuals with hemophilia 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. Graft-Versus-Host Disease as third-line of therapy or greater (Cutler 2006, NCCN 2A, DP B IIb);

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 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);

OR

XII. Pediatric nephrotic syndrome when each of the following criteria are met (KDIGO 2021, DP B IIb):
- A. Individual is 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. 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. 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.

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	Y^	Y^	Y^
Acquired inhibitors in hemophilia	Y	Y^	Y^	Y^
Autoimmune hemolytic anemia	Y	Y^	Y^	Y^
Cryoglobulinemia, primary Sjogren Syndrome, or systemic lupus erythematosus	Y	Y^	Y^	Y^
Graft-Versus-Host Disease	Y	Y^	Y^	Y^
Hepatitis C virus infection-related cryoglobulinemic vasculitis	Y	Y^	Y^	Y^
Immunoglobulin G4-related disease	Y	Y^	Y^	Y^
Relapsing multiple sclerosis	Y	Y^	Y^	Y^
Neuromyelitis optica	Y	Y^	Y^	Y^
Pediatric nephrotic syndrome	Y	Y^	Y^	Y^
Renal transplant with reactive human leukocyte antigen (HLA)-specific antibodies	Y	Y^	Y^	Y^
Antibody-mediated solid organ transplant rejection	Y	Y^	Y^	Y^
Thrombocytopenic purpura, immune or idiopathic	Y	Y^	Y^	Y^
Thrombotic thrombocytopenic purpura	Y	Y^	Y^	Y^
Myasthenia gravis	Y	Y^	Y^	Y^

X = FDA approved indication; Y = *Off-label use*; *Y^= 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 and intolerance to one preferred agent; **OR**

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

[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	**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*

mg vial; Ruxience (rituximab-pvvr) 100 mg, 500 mg vial; Truxima (rituximab-abbs) 100 mg, 500 mg vial	**Granulomatosis with Polyangiitis (GPA) (Wegener's Granulomatosis) 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) **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. 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]
G04.81	Other encephalitis and encephalomyelitis
G35	Multiple sclerosis
G36.0	Neuromyelitis optica [Devic]
G70.00-G70.01	Myasthenia gravis
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)
M31.30-M31.31	Wegener's granulomatosis

M31.7	Microscopic polyangiitis
M32.0-M32.9	Systemic lupus erythematosus (SLE)
M35.00-M35.09	Sicca 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]
N01.0-N01.9	Rapidly progressive nephritic syndrome
N04.0-N04.9	Nephrotic 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)
Q81.0-Q81.9	Epidermolysis bullosa
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: 08/19/2022
Document History:

- 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.

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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, NY, 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