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Subject: Rituximab Products [rituximab (Rituxan[®]), rituximab-abbs(Truxima[®]), rituximab-arrx (Riabni[™]), rituximab-pvvr (Ruxience[™]), and rituximab;hyaluronidase (Rituxan Hycela[™])

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Dosage/ Administration	Position Statement	Billing/Coding	Reimbursement	Program Exceptions	Definitions
Related Guidelines	Other	References	Updates		

DESCRIPTION:

Rituximab (Rituxan[®]) is a chimeric monoclonal antibody that targets CD20, which is primarily located on the surface of immune system B cells. Once rituximab binds to CD20, B-cells are destroyed; consequently, rituximab is used to treat diseases that are characterized by excessive amounts of B cells, by overactive B cells, or by dysfunctional B cells. Examples include lymphomas, leukemias, autoimmune disorders and in transplant rejection.

Rituximab was initially approved by the US Food and Drug Administration (FDA) in November 1997 for the treatment of relapsed or refractory B-cell Non-Hodgkin's Lymphoma (NHL). Additional FDA-labeled indications include Chronic Lymphocytic Leukemia (CLL), rheumatoid arthritis (RA), granulomatosis with polyangiitis (GPA) (Wegener's granulomatosis)/microscopic polyangiitis (MPA), and moderate to severe pemphigus vulgaris (PV). Standard reference compendia (e.g., Clinical Pharmacology, DrugDex) support rituximab use in a plethora of off-label indications include autoimmune blistering diseases, autoimmune hemolytic anemia, neuromyelitis optica, and many more. Three biosimilar forms of rituximab have been FDA approved: rituximab-abbs (Truxima[®]), rituximab-arrx (Riabni[™]), and rituximab-pvvr (Ruxience[™]).

Rituximab;hyaluronidase (Rituxan Hycela[™]) was FDA approved in June 2017 for adult patients with follicular lymphoma, diffuse large B-cell lymphoma, and chronic lymphocytic leukemia.

Rituximab;hyaluronidase is administered subcutaneously and is only recommended following an initial

dose of intravenous rituximab. It is not indicated for the treatment of non-malignant conditions. Hyaluronidase increases the permeability of subcutaneous tissue by temporarily depolymerizing hyaluronan, a polysaccharide in subcutaneous tissue. This results in dispersion and absorption of rituximab when administered subcutaneously in combination with hyaluronidase. Rituximab;hyaluronidase has demonstrated non-inferior trough concentrations and comparable efficacy and safety to intravenous rituximab.

POSITION STATEMENT:

I. **Initiation** of rituximab (Rituxan®), rituximab-abbs (Truxima®), rituximab-arxx (Riabni™), or rituximab-pvvr (Ruxience™) **meets the definition of medical necessity** when the following are met:

1. When used for an indication listed in Table 1 and **ALL** of the indication-specific and maximum-allowable dose criteria are met
2. For Rituxan or Truxima requests only, the member has an inadequate response, contraindication, or intolerance to rituximab-arxx (Riabni) **OR** rituximab-pvvr (Ruxience)^[a]

Table 1

Indications and Specific Criteria		
Indication	Specific Criteria	Maximum Allowable Dose
Non-oncology related		
Autoimmune blistering disease (ANY of the following) <ul style="list-style-type: none"> • Pemphigus vulgaris • Pemphigus foliaceus • Bullous pemphigoid • Cicatricial pemphigoid • Epidermolysis bullosa acquisita • Paraneoplastic pemphigus 	Member meets ONE of the following: <ol style="list-style-type: none"> 1. BOTH of the following are met: <ol style="list-style-type: none"> a. Member had an inadequate response to corticosteroids b. Member had an inadequate response to oral immunosuppressant therapy including ONE or more of the following: <ol style="list-style-type: none"> i. Mycophenolate ii. Azathioprine iii. Cyclosporine iv. Methotrexate 	375 mg/m ² per dose ^[b]

	2. Member is diagnosed with moderate to severe pemphigus vulgaris	
Autoimmune hemolytic anemia, cold type (AIHA) or cold agglutinin disease (CAD)	Diagnosis only	375 mg/m ² per dose
AIHA, warm type	When the member had an inadequate response to a trial of corticosteroids (e.g., prednisone 1 mg/kg/day for 3 weeks)	375 mg/m ² per dose
Evan's syndrome	Documented inadequate response, contraindication, or intolerance to conventional therapy (e.g., corticosteroids, azathioprine, cyclophosphamide, cyclosporine)	375 mg/m ² per dose
Graft versus host disease, chronic (GVHD)	When BOTH of the following are met: <ol style="list-style-type: none"> 1. Member had an inadequate response to corticosteroids 2. Member had an inadequate response to an oral immunosuppressant used for the treatment of GVHD (e.g., cyclosporine, tacrolimus, sirolimus) 	375 mg/m ² per dose
Heart transplant	When the member is receiving therapy for ONE of the following: <ol style="list-style-type: none"> 1. Desensitization for highly-allosensitized transplant candidates 2. Anti-body mediated rejection (AMR) 	375 mg/m ² per dose
Hemophilia, acquired factor inhibitors	When the member has an inadequate response or contraindication to ONE of the following: <ol style="list-style-type: none"> 1. Adequate trial of corticosteroids or cyclophosphamide (e.g., 4-6 weeks) 2. Immune tolerance induction therapy 	375 mg/m ² per dose

<p>Idiopathic or immune thrombocytopenic purpura, chronic (ITP)</p>	<p>When the member is at risk of bleeding and ALL of the following are met:</p> <ol style="list-style-type: none"> 1. The member has demonstrated an inadequate response to ANY of the following: <ol style="list-style-type: none"> a. Adequate trial of corticosteroids (e.g., prednisone 1-2 mg/kg for 2-4 weeks) b. IVIG c. Splenectomy 2. Member's platelet count is less than 30,000 3. Rituximab will not be used concurrently with fostamatinib (Tavalisse®) or a thrombopoietin receptor agonist (e.g., romiplostim [Nplate™], eltrombopag [Promacta], avatrombopag [Doptelet], lusutrombopag [Mulpleta]) 	<p>375 mg/m² per dose</p>
<p>Liver transplant</p>	<p>When used for desensitization prior to ABO-incompatible liver transplant</p>	<p>375 mg/m² per dose</p>
<p>Membranous nephropathy</p>	<p>When BOTH of the following are met:</p> <ol style="list-style-type: none"> 1. Member meets ONE of the following: <ol style="list-style-type: none"> a. eGFR less than or equal to 60 ml/min/1.73 m² b. Proteinuria greater than or equal to 3.5 g/day and no decrease greater than 50% after 6 months of therapy with an angiotensin-converting enzyme inhibitor (ACEi) or angiotensin II receptor blocker (ARB) c. Proteinuria greater than 8g/day for 6 months 2. Member meets ONE of the following: 	<p>1000 mg administered on day 1 and 15 every 24 weeks or 375 mg/m² per dose</p>

	<ul style="list-style-type: none"> a. Inadequate response to a calcineurin inhibitor with or without prednisone b. Inadequate response to cyclophosphamide in combination with glucocorticoids c. Member has ONE of the following risk factors: <ul style="list-style-type: none"> i. Serum albumin less than 25 g/L (measured by bromocresol purple or immunometric assay) ii. Phospholipase A2 receptor antibody (PLA2Rab) greater than 50 RU/ml iii. Urinary alpha1-microglobulin greater than 40 mcg/min iv. Urinary IgG greater than 1 mcg/min v. Urinary B2-microglobulin greater than 250 mg/day vi. Selectivity index greater than 0.20 	
Myasthenia Gravis	<p>When the member has an inadequate response, contraindication, or intolerance to a corticosteroid and at least ONE of the following:</p> <ul style="list-style-type: none"> 1. azathioprine 2. cyclosporine 3. mycophenolate mofetil 4. tacrolimus 5. methotrexate 	375 mg/m ² per dose

Neuromyelitis optica (NMO)	Diagnosis only	1000 mg administered on day 1 and 15 every 24 weeks
Pediatric idiopathic nephrotic syndrome	<p>When BOTH of the following are met:</p> <ol style="list-style-type: none"> 1. Member's disease is dependent on or refractory to corticosteroids 2. Member had an inadequate response to oral immunosuppressant therapy (e.g., tacrolimus, cyclosporine, mycophenolate) 	375 mg/m ² per dose
Relapsing-Remitting Multiple Sclerosis (RRMS)	<p>When ALL of the following are met:</p> <ol style="list-style-type: none"> 1. Member is diagnosed with a relapsing form of multiple sclerosis (i.e., relapsing remitting multiple sclerosis [RRMS], secondary progressive MS [SPMS], progressive-relapsing MS [PRMS]). 2. The member has an inadequate response to TWO of the following: <ol style="list-style-type: none"> a. Alemtuzumab (Lemtrada) b. Cladribine (Mavenclad) c. Dimethyl fumarate (Tecfidera) d. Diroximel fumarate (Vumerity) e. Fingolimod (Gilenya, Tascenso ODT) f. Glatiramer acetate (Copaxone, Glatopa) g. Interferon beta-1a (Avonex, Rebif) h. Interferon beta-1b (Betaseron, Extavia) i. Monomethyl fumarate (Bafiertam) 	1000 mg administered on day 1 and 15 every 24 weeks

	<ul style="list-style-type: none">j. Natalizumab (Tysabri)k. Ocrelizumab (Ocrevus)l. Ofatumumab (Kesimpta)m. Ozanimod (Zeposia)n. Peg-interferon beta-1a (Plegridy)o. Ponesimod (Ponvory)p. Siponimod (Mayzent)q. Teriflunomide (Aubagio) <p>3. Rituximab will not be used in combination with ANY of the following:</p> <ul style="list-style-type: none">a. Alemtuzumab (Lemtrada)b. Cladribine (Mavenclad)c. Dimethyl fumarate (Tecfidera)d. Diroximel fumarate (Vumerity)e. Fingolimod (Gilenya, Tascenso ODT)f. Glatiramer acetate (Copaxone, Glatopa)g. Interferon beta-1a (Avonex, Rebif)h. Interferon beta-1b (Betaseron, Extavia)i. Mitoxantrone (Novantrone)j. Monomethyl fumarate (Bafiertam)k. Natalizumab (Tysabri)l. Ocrelizumab (Ocrevus)m. Ofatumumab (Kesimpta)n. Ozanimod (Zeposia)o. Peg-interferon beta-1a (Plegridy)p. Ponesimod (Ponvory)	
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	<p>q. Siponimod (Mayzent)</p> <p>r. Teriflunomide (Aubagio)</p>	
Renal Transplant	When used to prevent graft rejection in members with anti-donor antibodies (e.g., anti-HLA antibodies)	375 mg/m ² per dose
Rheumatoid Arthritis (RA)	<p>When ALL of the following are met:</p> <ol style="list-style-type: none"> 1. Member's disease is moderately to severely active 2. Rituximab will be used in combination with methotrexate (unless member has a contraindication to methotrexate) 3. Member is 18 years of age or older 4. Member has at least ONE of the following: <ol style="list-style-type: none"> A. Member has an inadequate response to a trial (e.g., 3 months) of a biologic immunomodulator FDA indicated for the treatment of RA B. Member has a history of treated lymphoproliferative malignancy 	1000 mg administered on day 1 and 15 every 16 weeks
Systemic autoimmune diseases	<p>When the member is diagnosed with ONE of the following:</p> <ol style="list-style-type: none"> 1. Cryoglobulinemia 2. Primary Sjögren Syndrome 	375 mg/m ² per dose
Systemic Lupus Erythematosus	<p>When the member has ONE of the following:</p> <ol style="list-style-type: none"> 1. The member has an inadequate response or has a contraindication to at least 2 immunosuppressants (e.g., mycophenolate mofetil, cyclophosphamide, azathioprine) 2. The member has nephritis that has an inadequate response to a trial of 	375 mg/m ² per dose

	immunosuppressant therapy (e.g., 6 months)	
Thrombotic thrombocytopenic purpura (TTP)	When the member has an inadequate response to plasma exchange and corticosteroids	375 mg/m ² per dose
Vasculitides <ul style="list-style-type: none"> • Granulomatosis with Polyangiitis (GPA or Wegener’s granulomatosis) • Churg-Strauss syndrome • Microscopic polyangiitis (MPA) • Pauci-immune glomerulonephritis 	When rituximab will be used in combination with corticosteroids	375 mg/m ² per dose
Oncology-related		
Acute lymphoblastic leukemia (ALL)	When the member’s disease is CD20-positive	375 mg/m ² per dose
Castleman’s Disease	Member meets ONE of the following: <ol style="list-style-type: none"> 1. Diagnosis of Multicentric Castleman’s Disease 2. Unicentric Castleman’s Disease and ONE of the following is met: <ol style="list-style-type: none"> a. Disease is surgically unresectable b. Member is symptomatic following incomplete/partial resection c. Disease is relapsed or refractory 	375 mg/m ² per dose
Central nervous system (CNS) Cancer - Leptomeningeal Metastases	Rituximab will be administered intrathecally or intraventricular	25 mg per dose
Central nervous system (CNS) Cancers – Primary CNS Lymphoma	When ONE of the following is met: <ol style="list-style-type: none"> 1. For induction or consolidation therapy when used as a single 	500 mg/m ² per dose

	<p>agent or in combination with ONE of the following:</p> <ul style="list-style-type: none"> a. High-dose methotrexate, vincristine, procarbazine b. High-dose methotrexate with or without temozolomide c. High-dose methotrexate, cytarabine, and thiotepa d. Temozolomide e. Lenalidomide <p>2. For relapsed or refractory disease when used as a single agent or in combination with ONE of the following:</p> <ul style="list-style-type: none"> a. Temozolomide b. Lenalidomide c. High-dose methotrexate with or without ibrutinib 	
Chronic lymphocytic Leukemia (CLL)/ Small Lymphocytic Lymphoma (SLL)	When the member's disease is CD20-positive	500 mg/m ² per dose
Hairy Cell Leukemia	<p>When used for ONE of the following:</p> <ul style="list-style-type: none"> 1. In combination with cladribine 2. In combination with pentostatin for relapsed or refractory disease 3. As a single agent if unable to receive purine analog therapy for relapsed or refractory disease 4. In combination with vemurafenib (Zelboraf) to treat disease progression when non-responsive to purine analog therapy (e.g., cladribine or pentostatin) 	375 mg/m ² per dose
Hematopoietic Cell Transplantation	When used as conditioning for allogeneic transplant as part of a non-myeloablative regimen in combination with cyclophosphamide and fludarabine	375 mg/m ² before transplant, and 1000 mg/m ² on days 1, 8,

		and 15 after transplant
Hodgkin Lymphoma (Nodular Lymphocyte-predominant Hodgkin Lymphoma)	When the member's disease is CD20-positive	375 mg/m ² per dose
Immune Checkpoint Inhibitor-related toxicity	<p>When used for ONE of the following toxicities that developed after use of a checkpoint inhibitor (e.g., atezolizumab, avelumab, durvalumab, ipilimumab, nivolumab, pembrolizumab):</p> <ol style="list-style-type: none"> 1. Encephalitis when ALL of the following are met: <ol style="list-style-type: none"> a. Member's encephalitis is positive for autoimmune encephalopathy antibody b. Member had an inadequate response to methylprednisolone or IVIG c. Viral causes have been ruled out 2. Moderate or severe Myasthenia gravis (grade 3 or 4) when the member had an inadequate response to plasmapheresis or IVIG 3. Moderate or severe bullous dermatitis (grade 2, 3, or 4) 4. Myalgia or myositis if member has an inadequate response to corticosteroid 	375 mg/m ² per dose ^(b)
Non-Hodgkin's B-cell Lymphomas (e.g., AIDS-related B-cell lymphoma, Burkitt lymphoma, Burkitt-like lymphoma, Diffuse large B-cell lymphoma, Double/Triple Hit Lymphoma, Follicular lymphoma, Gastric MALT lymphoma, Grey Zone lymphoma, High Grade B-cell lymphoma unspecified, Mantle cell lymphoma, Marginal Zone lymphoma, Nodal Marginal zone lymphoma, Non-gastric MALT lymphoma, Pediatric	When the member's disease is CD20-positive	375 mg/m ² per dose

aggressive Mature B-cell lymphomas, Primary Cutaneous Diffuse Large B-cell Lymphoma Leg type, Primary Mediastinal Large B-cell lymphoma, Splenic marginal zone lymphoma)		
Post-transplant lymphoproliferative disease (PTLD)	When used for B-cell type PTLD	375 mg/m ² per dose
Primary Cutaneous B-cell lymphoma (e.g., Cutaneous Marginal Zone lymphoma or Cutaneous Follicle Center lymphomas)	When disease is classified with ONE of the following: <ol style="list-style-type: none"> 1. Generalized skin involvement (T3) 2. Extracutaneous disease 3. Refractory disease 	375 mg/m ² per dose
Rosai-Dorfman Disease	When used as a single agent for IgG4 disease and member has ONE of the following: <ol style="list-style-type: none"> 1. Symptomatic disease 2. Unresectable disease 3. Relapsed or refractory disease 	375 mg/m ² per dose
Waldenström’s macroglobulinemia/Lymphoplasmacytic lymphoma	When used as a single agent or with ONE of the following: <ol style="list-style-type: none"> 1. Bendamustine 2. Bortezomib with or without dexamethasone 3. Carfilzomib and dexamethasone 4. Cladribine 5. Cyclophosphamide and dexamethasone 6. Cyclophosphamide, doxorubicin, vincristine, and prednisone 7. Cyclophosphamide and fludarabine 8. Cyclophosphamide and prednisone 9. Fludarabine 10. Ibrutinib 11. Ixazomib and dexamethasone 	375 mg/m ² per dose

Other FDA-approved or NCCN supported diagnosis (not previously listed above)	<p>When ONE of the following is met:</p> <ol style="list-style-type: none"> 1. Member is diagnosed with a condition that is consistent with an indication listed in the product’s FDA-approved prescribing information (or package insert) AND member meets any additional requirements listed in the “Indications and Usage” section of the FDA-approved prescribing information (or package insert) 2. Indication AND usage is recognized in NCCN Drugs and Biologics Compendium as a Category 1 or 2A recommendation 	Dose does not exceed the maximum FDA-approved dosing
Approval duration: 6 months for all indications except RA (approval duration is 16 weeks).		

II. **Continuation** of rituximab, rituximab-abbs, rituximab-arrx, or rituximab-pvvr **meets the definition of medical necessity** for the indications in Table 1 when **ALL** of the following criteria are met:

- a. Member has a history of beneficial response to therapy
- b. The member has been previously approved by Florida Blue or another healthplan in the past 2 years, **OR** the member has previously met all indication-specific criteria
- c. The dose does not exceed **ANY** of the following based on indication for therapy:
 - i. Neuromyelitis optica and RRMS: 1000 mg administered on day 1 and 15 every 24 weeks
 - ii. Rheumatoid arthritis: 1000 mg administered on day 1 and 15 every 16 weeks
 - iii. Chronic lymphocytic leukemia, Small lymphocytic lymphoma, or Primary CNS Lymphoma: 500 mg/m² per dose
 - iv. CNS cancer, Leptomeningeal Metastases (Intrathecal administration): 25 mg per dose
 - v. Moderate to severe pemphigus vulgaris if initial dose of 1000mg was given on day 1 and 15: 500 mg administered 12 months after initial dose and every 6 months thereafter^[c]
 - vi. Granulomatosis with Polyangiitis (GPA or Wegener’s granulomatosis), Microscopic Polyangiitis (MPA): 500 mg administered on day 1 and 15 followed by 500 mg every 16 weeks
 - vii. Membranous nephropathy: 1000 mg administered on day 1 and 15 every 24 weeks or 375 mg/m² per dose
 - viii. All other indications: 375 mg/m² per dose

Approval duration: 1 year

^[a] Step therapy does not apply if Rituxan is prescribed for pemphigus vulgaris. Also, step therapy does not apply if a prior health plan paid for the medication - documentation of a paid claim within the past 90 days must be submitted

^[b] Alternative dose: 1000 mg given on day 1 and 15 (given in combination with a tapering dose of corticosteroids)

^[c] If disease relapse occurs, a dose of 1000 mg can be administered at least 16 weeks following the previous dose

I. **Initiation** of rituximab hyaluronidase (Rituxan Hycela™) **meets the definition of medical necessity** when **BOTH** of the following are met:

- a. When administered following an initial single dose of IV rituximab for the indications listed in Table 2 and **ALL** of the indication-specific and maximum-allowable dose criteria are met
- b. The member has an inadequate response, contraindication, or intolerance to rituximab-arrx (Riabni) OR rituximab-pvvr (Ruxience)^[d]

Table 2

Indications and Specific Criteria		
Indication	Specific Criteria	Maximum Allowable Dose
Castleman’s Disease (CD)	<p>When used as a substitute for rituximab as a single agent or with other systemic therapies^[e] and member has ONE of the following:</p> <ol style="list-style-type: none"> 1. Multicentric CD 2. Unicentric CD and ONE of the following is met: <ol style="list-style-type: none"> a. Disease is surgically unresectable b. Member is symptomatic following incomplete/partial resection c. Disease is relapsed or refractory 	1400 mg per dose

<p>Chronic Lymphocytic Leukemia (CLL)/ Small Lymphocytic Lymphoma (SLL)</p>	<p>ONE of the following is met:</p> <ol style="list-style-type: none"> 1. When used in combination with fludarabine and cyclophosphamide (FC) 2. When used as a substitute for rituximab as a single agent or with other systemic therapies^[e] and member's disease is CD20-positive 	<p>1600 mg per dose</p>
<p>Diffuse Large B-cell Lymphoma (DLBCL)</p>	<p>ONE of the following is met:</p> <ol style="list-style-type: none"> 1. When BOTH of the following are met: <ol style="list-style-type: none"> a. Member has previously untreated diffuse large B-cell lymphoma b. Use is in combination with cyclophosphamide, doxorubicin, vincristine, prednisone (CHOP) or other anthracycline-based chemotherapy regimens 2. When used as a substitute for rituximab as a single agent or with other systemic therapies^[e] and member's disease is CD20-positive 	<p>1400 mg per dose</p>
<p>Follicular Lymphoma (FL)</p>	<p>ONE of the following is met:</p> <ol style="list-style-type: none"> 1. Use is in combination with first line chemotherapy in previously untreated follicular lymphoma 2. Single agent use for ONE of the following: <ol style="list-style-type: none"> a. Relapsed or refractory, follicular lymphoma b. Maintenance therapy in members achieving a complete or partial response to rituximab in combination with chemotherapy c. Non-progressing (including stable disease), follicular lymphoma after first-line cyclophosphamide, 	<p>1400 mg per dose</p>

	<p>vincristine, and prednisone (CVP) chemotherapy</p> <p>3. When used as a substitute for rituximab as a single agent or with other systemic therapies^[e] and member's disease is CD20-positive</p>	
Gastric MALT Lymphoma	When used as a substitute for rituximab as a single agent or with other systemic therapies ^[e] and member's disease is CD20-positive	1400 mg per dose
Hairy Cell Leukemia	<p>When used as a substitute for rituximab for ONE of the following:</p> <ol style="list-style-type: none"> 1. In combination with cladribine 2. In combination with pentostatin for relapsed or refractory disease 3. As a single agent if unable to receive purine analog therapy for relapsed or refractory disease 4. In combination with vemurafenib (Zelboraf) to treat disease progression when non-responsive to purine analog therapy (e.g., cladribine or pentostatin) 	1400 mg per dose
High-grade B-cell Lymphomas (Double/Triple Hit Lymphoma or unspecified)	When used as a substitute for rituximab as a single agent or with other systemic therapies ^[e] and member's disease is CD20-positive	1400 mg per dose
Mantle Cell Lymphoma	When used as a substitute for rituximab as a single agent or with other systemic therapies ^[e] and member's disease is CD20-positive	1400 mg per dose
Nodal Marginal Zone Lymphoma	When used as a substitute for rituximab as a single agent or with other systemic therapies ^[e] and member's disease is CD20-positive	1400 mg per dose

Nongastric MALT Lymphoma	When used as a substitute for rituximab as a single agent or with other systemic therapies ^[e] and member's disease is CD20-positive	1400 mg per dose
Post-transplant Lymphoproliferative Disorder (PTLD)	When used as a substitute for rituximab as a single agent or with other systemic therapies ^[e] for B-cell type PTLD	1400 mg per dose
Primary Cutaneous B-cell lymphoma (e.g., Cutaneous Marginal Zone lymphoma or Cutaneous Follicle Center lymphomas)	When used as a substitute for rituximab as a single agent or with other systemic therapies ^[e] and disease is classified with ONE of the following: <ol style="list-style-type: none"> 1. Generalized skin involvement (T3) 2. Extracutaneous disease 3. Refractory disease 	1400 mg per dose
Splenic Marginal Zone Lymphoma	When used as a substitute for rituximab as a single agent or with other systemic therapies ^[e] and member's disease is CD20-positive	1400 mg per dose
Waldenström's macroglobulinemia/Lymphoplasmacytic lymphoma	When used as a substitute for rituximab as a single agent or with ONE of the following: <ol style="list-style-type: none"> 1. Bendamustine 2. Bortezomib with or without dexamethasone 3. Carfilzomib and dexamethasone 4. Cladribine 5. Cyclophosphamide and dexamethasone 6. Cyclophosphamide, doxorubicin, vincristine, and prednisone 7. Cyclophosphamide and fludarabine 8. Cyclophosphamide and prednisone 9. Fludarabine 	1400 mg per dose

	10. Ibrutinib 11. Ixazomib and dexamethasone	
Other FDA-approved or NCCN supported diagnosis (not previously listed above)	When ONE of the following is met: 1. Member is diagnosed with a condition that is consistent with an indication listed in the product’s FDA-approved prescribing information (or package insert) AND member meets any additional requirements listed in the “Indications and Usage” section of the FDA-approved prescribing information (or package insert) 2. Indication AND usage is recognized in NCCN Drugs and Biologics Compendium as a Category 1 or 2A recommendation	Dose does not exceed the maximum FDA-approved dosing
Approval duration: 6 months		

II. **Continuation** of rituximab hyaluronidase (Rituxan Hycela™) meets **the definition of medical necessity** for the indications in Table 2 when **ALL** of the following criteria are met:

- a. Member has a history of beneficial response to therapy
- b. The member has been previously approved by Florida Blue or another healthplan in the past 2 years, **OR** the member has previously met all indication-specific criteria
- c. The dose does not exceed indication specific dosing in Table 2.

Approval duration: 1 year

^[d] Step therapy does not apply if a prior health plan paid for the medication - documentation of a paid claim within the past 90 days must be submitted

^[e] Excludes use in combination with ibritumomab tiuxetan (Zevalin)

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER’S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

Rituximab

Rituximab is FDA-approved for treatment of non-Hodgkin’s Lymphoma (NHL), pediatric patients aged 6 months and older with mature B-cell NHL and mature B-cell acute leukemia (B-AL), chronic lymphocytic leukemia (CLL), rheumatoid arthritis (RA), granulomatosis with polyangiitis (GPA) (Wegener’s Granulomatosis), microscopic polyangiitis (MPA) and moderate to severe pemphigus vulgaris (PV). Rituximab should be used in combination with methotrexate in individuals with moderately to severely active RA who have had an inadequate response to one or more TNF antagonist therapies. The recommended dosage regimens for FDA-approved indications are listed in table 3. See prescribing information for dosing information of biosimilar products rituximab-abbs and rituximab-pvvr.

Table 3

FDA-approved indications and dosage regimens	
Indication	Dose
NHL ^[f]	375 mg/m ² (see prescribing information for dosing schedule for adult and pediatric dosing)
CLL	375 mg/m ² prior to initiation of FC, then 500 mg/m ² on day1 of cycles 2-6
RA	Two-1000 mg infusions separated by 2 weeks ^[g] ; subsequent infusions should administered every 24 weeks or based on clinical evaluation. Do not administer sooner than every 16 weeks
GPA/MPA in adults	375 mg/m ² once weekly for 4 weeks ^[h] Follow up treatment for patients who achieve disease control: Two-500 mg infusions ^[g] separated by 2 weeks followed by 500 mg every 6 months thereafter based on clinical evaluation; subsequent infusions should administered every 24 weeks or based on clinical evaluation. Do not administer sooner than every 16 weeks.
GPA/MPA in pediatric patients 2 years and older	375 mg/m ² once weekly for 4 weeks ^[i] Follow up treatment for patients who achieve disease control: Two-250 mg/m ² infusions separated by 2 weeks ^[g] followed by 250 mg/m ² every 6 months thereafter based on clinical evaluation; subsequent infusions should administered every 24 weeks or based on clinical evaluation. Do not administer sooner than every 16 weeks.
PV	Two-1000 mg infusions separated by 2 weeks ^[g] in combination with a tapering course of glucocorticoids; then a 500 mg infusion ^[g] at month 12 and every 6 months thereafter or based on clinical evaluation. Dose upon relapse is a 1000 mg infusion with consideration to resume or increase the glucocorticoid dose based on clinical evaluation. Do not administer sooner than every 16 weeks after the previous infusion.
<p>^[f] Schedule is based on type of NHL, dose is 250 mg/m² if used as a component of Zevalin® for NHL ^[g] Administer methylprednisolone 100 mg IV or its equivalent 30 minutes prior to each infusion ^[h] Administration of methylprednisolone 1000 mg IV daily for 1-3 days followed by oral prednisone ^[i] Administration of methylprednisolone 30 mg/kg IV daily for 3 days (not to exceed 1 g/day) prior to the first infusion and followed by oral steroids</p> <p>NHL, non-Hodgkin’s Lymphoma; CLL, chronic lymphocytic leukemia; FC, fludarabine and cyclophosphamide; RA, rheumatoid arthritis; GPA, granulomatosis with polyangiitis; MPA, microscopic polyangiitis; PV, pemphigus vulgaris.</p>	

Rituximab should be administered as an intravenous (IV) infusion and should not be administered as an IV push or IV bolus. Premedication should be administered prior to each infusion (e.g., acetaminophen, antihistamine). Initially, rituximab should be administered at a rate of 50 mg/hr; in the absence of infusion toxicity, the rate can be increased by 50 mg/hr increments at 30-minute intervals to a maximum of 400 mg/hr.

Rituximab; Hyaluronidase

FDA-approved: rituximab; hyaluronidase is indicated for treatment of Follicular Lymphoma (FL), Diffuse Large B-cell Lymphoma (DLBCL), and Chronic Lymphocytic Leukemia (CLL), Rituximab;hyaluronidase is not indicated for the treatment of non-malignant conditions.

All patients must receive at least one full dose of a rituximab product by intravenous infusion before receiving rituximab;hyaluronidase by subcutaneous injection. Rituximab;hyaluronidase should be administered by a healthcare professional with medical support to manage severe reactions. Premedicate with acetaminophen and antihistamine before each dose and consider premedication with glucocorticoids.

FL/DLBCL: Administer 1,400 mg/23,400 Units (1,400 mg rituximab and 23,400 Units hyaluronidase human) subcutaneously. See prescribing information for recommended schedule and use of concomitant medications.

CLL: Administer 1,600 mg/26,800 Units (1,600 mg rituximab and 26,800 Units hyaluronidase human) subcutaneously. See prescribing information for recommended schedule and use of concomitant medications.

Administer specified volume into subcutaneous tissue of abdomen and observe 15 minutes following administration. Do not administer other subcutaneous medications at the same site of administration.

11.7 mL from 1,400 mg/23,400 Units vial over approximately 5 minutes.

13.4 mL from 1,600 mg/26,800 Units vial over approximately 7 minutes.

Drug Availability:

Rituximab, rituximab-abbs, and rituximab-pvvr are each supplied as a 100 mg/10 ml and 500 mg/50 mL solution in a single-use vial.

Rituximab;hyaluronidase is supplied as 1,400 mg/23,400 units per 11.7 mL and 1,600 mg/26,800 units per 13.4 mL

PRECAUTIONS:

Boxed Warning

- Fatal infusion reactions within 24 hours of rituximab infusion can occur; approximately 80% of fatal reactions occurred with first infusion. Monitor members and discontinue rituximab infusion for severe reactions
- Severe mucocutaneous reactions, some with fatal outcomes can occur.

- Hepatitis B reactivation with fulminant hepatitis, hepatic failure and death; screen patients for HBV prior to initiation and monitor patients during and several months after therapy. Discontinue rituximab if reactivation occurs
- Progressive multifocal leukoencephalopathy (PML) resulting in death can occur in persons receiving rituximab. Monitor neurologic function and discontinue rituximab if PML occurs.

Warnings

- Tumor lysis syndrome (TLS): acute renal failure, hyperkalemia, hypocalcemia, hyperuricemia or hyperphosphatemia, requiring dialysis with instances of fatal outcome can occur in the setting of TLS following treatment of NHL persons with rituximab. Administer aggressive IV hydration, anti-hyperuricemic agents, and monitor renal function
- Infections – serious, fatal infections can occur. Withhold rituximab and institute appropriate anti-infective therapy
- Cardiac arrhythmias and angina can occur and can be life threatening. Monitor individuals with these conditions closely
- Renal toxicity – severe, fatal renal toxicity can occur. Monitor for signs and symptoms of renal failure.
- Bowel obstruction and perforation – some cases have lead to death, evaluate complaints of abdominal pain
- Do not administer live virus vaccines prior to or during rituximab
- Monitor CBC and platelet counts prior to therapy and at regular intervals for severe cytopenias
- Hypersensitivity reactions and local cutaneous reactions may occur during administration or more than 24 hours after subcutaneous administration. Premedicate and Interrupt if severe infusion reaction occurs.
- Embryo-fetal toxicity- may cause harm to a developing fetus and effective contraception should be utilized up to 12 months following administration.

BILLING/CODING INFORMATION:

HCPCS Coding for rituximab:

J9312	Injection, rituximab, 10 mg
Q5115	Injection, rituximab-abbs, biosimilar, (Truxima), 10 mg
Q5119	Injection, rituximab-pvvr, biosimilar, (ruxience), 10 mg
Q5123	Injection, rituximab-arrx, biosimilar, (riabni), 10 mg

HCPCS Coding for rituximab; hyaluronidase:

J9311	Injection, rituximab 10 mg and hyaluronidase
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ICD-10 Diagnosis Codes That Support Medical Necessity for rituximab (J9312, Q5115, Q5119, Q5123):

B10.89	Other human herpes virus infection
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B20	Human immunodeficiency virus [HIV] disease
C79.32	Secondary malignant neoplasm of cerebral meninges
C79.40	Secondary malignant neoplasm of unspecified part of nervous system
C79.49	Secondary malignant neoplasm of other parts of nervous system
C81.00 – C81.09	Nodular lymphocyte predominant Hodgkin lymphoma
C81.40 – C81.49	Lymphocyte-rich Hodgkin lymphoma
C82.00 – C82.69	Follicular lymphoma of various sites
C82.80 – C82.99	Other specified types of follicular lymphoma and unspecified follicular lymphoma
C83.00 – C83.99	Small cell B-cell lymphoma, Mantle cell lymphoma, diffuse large B-cell lymphoma, lymphoblastic (diffuse) lymphoma, Burkitt lymphoma and other non-follicular lymphoma
C84.90 – C84.99	Cutaneous T-cell lymphoma various sites
C84.A0 – C84.A9	Other mature T/NK-cell lymphomas, various sites
C84.Z0 – C84.Z9	Mature T/NK-cell lymphomas, unspecified various sites
C85.10 – C85.99	Other specified and unspecified types of non-Hodgkin lymphoma, various sites
C86.0 – C86.6	Other specified types of T/NK-cell lymphoma
C88.0	Waldenstrom macroglobulinemia
C88.4	Extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue (Malt- lymphoma)
C91.00	Acute lymphoblastic leukemia not having achieved remission
C91.01	Acute lymphoblastic leukemia, in remission
C91.02	Acute lymphoblastic leukemia, in relapse
C91.10	Chronic lymphocytic leukemia of B-cell type not having achieved remission
C91.12	Chronic lymphocytic leukemia of B-cell type in relapse
C91.40 – C91.42	Hairy cell leukemia
C91.90	Lymphoid leukemia, unspecified not having achieved remission
D36.0	Benign neoplasm of lymph nodes
D47.Z1	Post-transplant lymphoproliferative disorder (PTLD)
D47.Z2	Castleman disease
D59.0	Drug-induced autoimmune hemolytic anemia
D59.1 – D59.19	Other autoimmune hemolytic anemias
D66	Hereditary factor VIII deficiency
D67	Hereditary factor IX deficiency
D68.1	Hereditary factor XI deficiency
D68.311	Acquired hemophilia
D69.3 – D69.49	Immune thrombocytopenic purpura, Evans syndrome, congenital and hereditary thrombocytopenia purpura and other primary thrombocytopenia
D69.6	Thrombocytopenia, unspecified
D76.3	Other histiocytosis syndromes
D89.1	Cryoglobulinemia
D89.811 – D89.813	Chronic, graft-versus-host disease
G35	Multiple sclerosis

G36.0	Neuromyelitis optica [Devic]
G70.00 – G70.01	Myasthenia gravis
L10.0 – L10.9	Pemphigus vulgaris and other pemphigus types
L12.0 – L12.9	Pemphigoid of various types
L13.8	Other specified bullous disorders
L13.9	Bullous disorder, unspecified
L14	Bullous disorders in diseases classified elsewhere
L51.2	Toxic epidermal necrolysis [Lyell]
M05.00 – M05.09	Felty's syndrome, various sites
M05.10 – M05.19	Rheumatoid lung disease with rheumatoid arthritis of various sites
M05.20 – M05.29	Rheumatoid vasculitis with rheumatoid arthritis of various sites
M05.30 – M05.39	Rheumatoid heart disease with rheumatoid arthritis of various sites
M05.40 – M05.49	Rheumatoid myopathy with rheumatoid arthritis of various sites
M05.50 – M05.59	Rheumatoid polyneuropathy with rheumatoid arthritis of various sites
M05.60 – M05.69	Rheumatoid arthritis with involvement of other organs and systems, various sites
M05.70 – M05.79, M05.7A	Rheumatoid arthritis with rheumatoid factor without involvement of other organs and systems, various sites
M05.80 – M05.89, M05.8A	Other rheumatoid arthritis with rheumatoid factor of various sites
M05.9	Rheumatoid arthritis with rheumatoid factor, unspecified
M06.00 – M06.09, M06.0A	Rheumatoid arthritis without rheumatoid factor, various sites
M06.1	Adult-onset Still's disease
M06.4	Inflammatory polyarthropathy
M06.80 – M06.89, M06.8A	Other specified rheumatoid arthritis, various sites
M06.9	Rheumatoid arthritis, unspecified
M30.0	Polyarteritis nodosa
M30.1	Polyarteritis with lung involvement [Churg-Strauss]
M31.0	Hypersensitivity angiitis
M31.10	Thrombotic microangiopathy, unspecified
M31.30	Wegener's granulomatosis without renal involvement
M31.31	Wegener's granulomatosis with renal involvement
M31.7	Microscopic polyangiitis
M32.0 – M32.9	Systemic lupus erythematosus, organ or system involvement unspecified
M35.00 – M35.09, M35.0A – M35.0C	Sjogren syndrome, various areas of involvement
N04.0 – N04.9	Nephrotic syndrome
N05.0 – N05.9	Unspecified nephritic syndrome
Q81.0 – Q81.9	Epidermolysis bullosa, unspecified
Q82.9	Congenital malformation of skin, unspecified
Q82.8	Other specified congenital malformations of skin

R59.0 – R59.9	Enlarged lymph nodes, unspecified
T86.00 – T86.02	Complications of bone marrow transplant
T86.09	Other complications of bone marrow transplant
T86.10 – T86.12	Complications of kidney transplant
T86.19	Other complications of kidney transplant
T86.20 – T86.22	Complications of heart transplant
T86.298	Other complications of heart transplant
T86.30 – T86.32	Complications of heart-lung transplant
T86.39	Other complications of heart-lung transplant
T86.40 – T86.42	Complications of liver transplant
T86.49	Other complications of liver transplant
T86.5	Complications of stem cell transplant
T86.810 – T86.811	Complications of lung transplant
T86.818 – T86.819	Other or Unspecified complications of lung transplant
T86.820 – T86.821	Complications of skin graft (allograft) (autograft)
T86.828 – T86.829	Other or unspecified complications of skin graft (allograft) (autograft)
T86.830 – T86.831	Complications of bone graft
T86.838 – T86.839	Other or unspecified complication of bone graft
T86.840 – T86.841	Complications of corneal transplant
T86.848 – T86.849	Other or unspecified complication of corneal transplant
T86.850 – T86.851	Complication of intestine transplant
T86.858 – T86.859	Other or Unspecified complications of intestine transplant
T86.890 – T86.891	Complications of other transplanted tissue
T86.898 – T86.899	Other or Unspecified complication of other transplanted tissue
T86.90 – T86.92	Complication of unspecified transplanted organ and tissue
T86.99	Other complications of unspecified transplanted organ and tissue
Z48.22	Encounter for aftercare following kidney transplant
Z94.0	Kidney transplant status
Z94.81	Bone marrow transplant status
Z94.89 - Z94.9	Transplant organ and tissue status, unspecified

ICD-10 Diagnosis Codes That Support Medical Necessity for rituximab;hyaluronidase (J9311):

C82.00 – 82.99	Follicular lymphoma of various sites
C83.00 – C83.09	Small cell B-cell lymphoma
C83.10 – C83.19	Mantle cell lymphoma
C83.30 – C83.39	Diffuse large B-cell lymphoma
C85.20 – C85.29	Mediastinal (thymic) large B-cell lymphoma
C85.80 – C85.89	Other specified types of non-Hodgkin lymphoma
C88.0	Waldenstrom macroglobulinemia
C88.4	Extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue [MALT-lymphoma]
C91.10	Chronic lymphocytic leukemia of B-cell type not having achieved remission

C91.12	Chronic lymphocytic leukemia of B-cell type in relapse
C91.40	Hairy cell leukemia, not having achieved remission
C91.42	Hairy cell leukemia in relapse
D36.0	Benign neoplasm of lymph nodes
D47.Z1	Post-transplant lymphoproliferative disorder (PTLD)
D47.Z2	Castleman disease
R59.0 – R59.9	Enlarged lymph nodes

REIMBURSEMENT INFORMATION:

Please refer to section entitled [POSITION STATEMENT](#).

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Advantage products: No National Coverage Determination (NCD) or Local Coverage Determination (LCD) was found at the time of the last guideline revised date.

DEFINITIONS:

RA: Rheumatoid Arthritis.

TNF: tumor necrosis factor.

HyperCVAD: hyper-fractionated cyclophosphamide, vincristine, doxorubicin and dexamethasone

RELATED GUIDELINES:

[Abatacept \(Orencia®\), 09-J0000-67](#)

[Adalimumab \(Humira®\), 09-J0000-46](#)

[Anakinra \(Kineret®\), 09-J0000-45](#)

[Certolizumab Pegol \(Cimzia®\), 09-J0000-77](#)

[Etanercept \(Enbrel®\), 09-J0000-38](#)

[Golimumab \(Simponi™\), 09-J1000-11](#)

[Infliximab \(Remicade®\), 09-J0000-39](#)

OTHER:

None applicable.

REFERENCES:

1. AHFS Drug Information. Bethesda (MD): American Society of Health-System Pharmacists, Inc; 2016 [cited 2016-07-25]. In: STAT!Ref Online Electronic Medical Library [Internet]. Available from: <http://online.statref.com/>.

2. Ahmed AR, Spigelman Z, Cavacini LA, et al. Treatment of Pemphigus Vulgaris with Rituximab and Intravenous Immune Globulin *Engl J Med* 2006; 355:1772-1779
3. American College of Rheumatology Position Statement. Biologic Agents for Rheumatic Diseases. Approved by Committee on Rheumatological Care, 06/03/06 and by the Board of Directors, 08/04/06.
4. Assous N, Gossec L, Dieude P, Meyer O, Dougados M, Kahan A, Allanore Y. Rituximab therapy in rheumatoid arthritis in daily practice. *J Rheumatol*. 2008 Jan; 35(1): 31-4. *Epub* 2007 Nov 15.
5. Cree BA, Lamb S, Morgan K, et al. An open label study of the effects of rituximab in neuromyelitis optica. *Neurology*. 2005; 64(7):1270-1272.
6. Clinical Pharmacology [Internet]. Tampa (FL): Gold Standard, Inc.; 2021 [cited 2021 Aug 5]. Available from: <http://www.clinicalpharmacology.com/>.
7. Collins PW, Chalmers E, Hart DP. Diagnosis and treatment of factor VIII and IX in congenital haemophilia: 4th edition. *Br J Haematol*. 2013; 160: 153 - 170
8. Costanzo MR et al. The international society of heart and lung transplantation guidelines for the care of heart transplant recipients. *J Heart Lung Transplant* 2010; 29: 914-956.
9. Cree BA, Lamb S, Morgan K, et al. An open label study of the effects of rituximab in neuromyelitis optica. *Neurology*. 2005; 64(7):1270-1272.
10. Cutler C, Miklos D, Kim HT, et al. Rituximab for steroid-refractory chronic graft-versus-host disease. *Blood*. 2006; 108:756-762.
11. Dignan FL, Amrolia P, Clark A et al. Diagnosis and management of chronic graft-versus-host disease. *Br J Haematol*. 2012; 158: 46-61.
12. DRUGDEX[®] System [Internet]. Greenwood Village (CO): Thomson Micromedex; Updated periodically [cited 2021 Aug 5].
13. Evens AM, David KA, Helenowski I, et al. Multicenter analysis of 80 solid organ transplantation recipients with post-transplantation lymphoproliferative disease: outcomes and prognostic factors in the modern era. *J Clin Oncol*. 2010; 28(6):1038-1046.
14. Franchini M and Mannuccio P. Inhibitors of pro of coagulation (factor VII, IX, and XI): a review of current therapeutic practice. *Br J Clin Pharmacol*. 2011; 72: 553-562.
15. Franchini M, Mengoli C, and Lippi G et al. Immune tolerance with rituximab in congenital haemophilia with inhibitors: a systematic literature review based on individual patients' analysis. *Haemophilia*. 2008; 14: 903-912.
16. Gulati A, Sinha A, Jordan SC et al. Efficacy and safety of treatment with rituximab for difficult steroid-resistant and –dependent nephrotic syndrome: multicentric report. *Clin J Am Soc Nephrol*. 2010; 5: 2207-2212.
17. Hahn BH, McMahon MA, Wilkinson A et al. American College of Rheumatology Guidelines for screening, treatment, and management of lupus nephritis. *Arthritis Care & Research*. 2012; 64: 797-808.
18. HAYES Alert, Novel Biologic Agent Approved for Treatment of Rheumatoid Arthritis, 01/05/06.
19. HAYES, Inc. Expanded Indications for Rituxan. Lansdale, PA: HAYES, Inc., 03/07/06.

20. Heemann U, Abramowicz D, Spasovski G. Endorsement of the kidney disease improving global outcomes (KDIGO) guidelines on kidney transplantation: a European renal best practice (ERBP) position statement. *Nephrol Dial Transplant*. 2011; 26: 2099-2106.
21. Huth-Kuhne A, Baudo F, Collins P et al. International recommendations on the diagnosis and treatment of patients with acquired hemophilia A. *Haematologica* 2009; 94: 566-575.
22. Iijima K, Sako M, Nozu K et al. Rituximab for childhood-onset, complicated, frequently relapsing nephrotic syndrome or steroid-dependent nephrotic syndrome: a multicenter, double-blind, randomized, placebo-controlled trial. *Lancet* 2014; 384: 1273-81.
23. Iijima K, Sako M, Nozu K et al. Rituximab for nephrotic syndrome in children. *Clin Exp Nephrol*. 2016
24. Ingenix HCPCS Level II, Expert 2011.
25. Ingenix ICD-9-CM for Physicians-Volumes 1 & 2, Expert 2011.
26. Jacob A, Weinshenker BG, Violich, J,.. et.al. Treatment of Neuromyelitis Optica With Rituximab: Retrospective Analysis of 25 Patients *Arch Neurol*. 2008;65(11):1443-1448.
27. Jones RB, Tervaert JWC, Hauser T, et al.; for the European Vasculitis Study Group. Rituximab versus cyclophosphamide in ANCA-associated renal vasculitis. *N Engl J Med*. 2010; 363(3):211-220.
28. Jois RN, Masding A, Somerville M, Gaffney K, Scott DG. Rituximab therapy in patients with resistant rheumatoid arthritis: real-life experience. *Rheumatology (Oxford)*. 2007 Jun; 46(6): 980-2. Epub 2007 Mar 23.
29. Joly, P, Mouquet H, Roujeau JC, et al.. A Single Cycle of Rituximab for the Treatment of Severe Pemphigus. *N Engl J Med* 2007; 357:545-552.
30. Kempton CL, Allen G, Hord J. Eradication of factor VIII inhibitors in patients with mild and moderate hemophilia A. *Am J Hematol*. 2012; 87: 933-936.
31. Keystone E, Fleischmann R, Emery P, Furst DE, vanVollenhoven R, Bathon J, Dougados M, Baldassare A, Ferraccioli G, Chubick A, Udell J, Cravets MW, Agarwal S, Cooper S and Magrini F. Safety and Efficacy of Additional Courses of Rituximab in Patients with Active Rheumatoid Arthritis. *Arthritis & Rheumatism*. December 2007, Vol. 56, No. 12, pp 3896-3908.
32. 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.
33. Kidney Disease Improving Global Outcomes (KDIGO) Glomerulonephritis Work Group. KDIGO Clinical Practice Guideline for Glomerulonephritis. *Kidney International Supplements*. 2012; 2 (2): 139 – 274.
34. Kidney Disease Improving Global Outcomes (KDIGO) Glomerulonephritis Work Group. KDIGO Clinical Practice Guideline for Glomerular diseases. *Kidney International Supplements*. 2021; 100 (4S): S1 – S276.
35. Kjwaja A. KDIGO Guidelines for care of the kidney transplant recipient. *Nephron clin Pract* 2010. 116: c27-c28.
36. Lee JJ, Lam MSH, Rosenberg A. Role of chemotherapy and rituximab for treatment of posttransplant lymphoproliferative disorder in solid organ transplantation. *Annals of Pharmacotherapy*. 2007; 41:1648-1659.

37. Lim W, Vesely SK, and George JN. The role of rituximab in the management of patients with acquired thrombotic thrombocytopenic purpura. *Blood*. 2015; 125: 1526-1531.
38. Mavragani CP, Moutsopoulos. Conventional therapy of Sjogren's Syndrome. *Clin Rev Allerg Immunol*. 2007; 32:284-291.
39. Mease PJ. B cell-targeted therapy in autoimmune disease: rationale, mechanisms, and clinical application. *J Rheumatol*. 2008;35(7):1245-1255.
40. Murukesan V, Mukherjee S. Managing post-transplant lymphoproliferative disorders in solid organ transplant recipients: a review of immunosuppressant regimens. *Drugs* 2012;72(12):4631-43.
41. Mylona E, Baraboutis IG, Lekakis LJ, et al. Multicentric Castleman's Disease in HIV infection: a systematic review of the literature. *AIDS Rev*. 2008; 10:25-35.
42. National Institute for Health and Clinical Excellence. Rituximab for the treatment of rheumatoid arthritis. Issue date: August 2007. Review date: July 2010.
43. National Comprehensive Cancer Network. Cancer Guidelines. Cancer Guidelines and Drugs and Biologics Compendium. Accessed 05/12/22.
44. National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology. Version 2.2021. Acute Lymphoblastic Leukemia. Available at http://www.nccn.org/professionals/physician_gls/PDF/all.pdf
45. National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology. Version 4.2021. B-cell Lymphomas. Available from http://www.nccn.org/professionals/physician_gls/PDF/b-cell.pdf
46. National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology. Version 1.2021. Central Nervous System Cancers. Available from http://www.nccn.org/professionals/physician_gls/PDF/cns.pdf
47. National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology. Version 4.2021. Chronic Lymphoblastic Leukemia/ Small Lymphoblastic Leukemia. Available at http://www.nccn.org/professionals/physician_gls/PDF/cll.pdf
48. National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology. Version 2.2021. Hairy Cell Leukemia. Available from http://www.nccn.org/professionals/physician_gls/PDF/hairy_cell.pdf
49. National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology. Version 3.2021. Hematopoietic cell transplantation (HCT). Available from http://www.nccn.org/professionals/physician_gls/PDF/hct.pdf
50. National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology. Version 1.2021. Histiocytic neoplasms. Available from http://www.nccn.org/professionals/physician_gls/PDF/histio.pdf
51. National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology. Version 4.2021. Hodgkin Lymphoma. Available from http://www.nccn.org/professionals/physician_gls/PDF/hodgkins.pdf
52. National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology. Version 3.2021. Management of Immunotherapy-related toxicities. Available from http://www.nccn.org/professionals/physician_gls/PDF/immunotherapy.pdf

53. National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology. Version 2.2021. Pediatric Aggressive Mature B-cell Lymphomas. Available from [http://www.nccn.org/professionals/physician_gls/PDF/ped_b-cell .pdf](http://www.nccn.org/professionals/physician_gls/PDF/ped_b-cell.pdf)
54. National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology. Version 2.2021. Primary Cutaneous B-cell Lymphomas. Available from http://www.nccn.org/professionals/physician_gls/PDF/pcbcl.pdf
55. National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology. Version 1.2022. Waldenstrom's Macroglobulinemia/Lymphoplasmacytic Lymphoma. Available from http://www.nccn.org/professionals/physician_gls/PDF/waldenstroms.pdf
56. Neunert C, Lim W, Crowther M, et. al. The American Society of Hematology 2011 evidence-based practice guideline for immune thrombocytopenia, Blood April 21, 2011 vol. 117 no. 16 4190-4207.
57. Palace J, Leite MI, Jacob A. A practical guide to the treatment of neuromyelitis optica. Pract Neurol 2012;12(4):209-14.
58. Panel on Opportunistic Infections in HIV-infected Adults and Adolescents. Guidelines for the prevention and treatment of opportunistic infections in HIV-infected adults and adolescents: recommendations from the Centers for Disease Control and Prevention, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. Available at: https://aidsinfo.nih.gov/contentfiles/lvguidelines/adult_oi.pdf. Accessed 7/24/2015.
59. Pietrogrande M, De Vita S, Zignego AL, et al. Recommendations for the management of mixed cryoglobulinemia syndrome in hepatitis C virus-infected patients. Autoimmun Rev 2011;10(8): 444-54.
60. Rae-Grant A, Day GS, Marrie RA et al. Practice guideline: Disease-modifying therapies for adults with multiple sclerosis: Report of the guideline development, dissemination, and implementation subcommittee of the American Academy of Neurology. April 2018. Available at: <https://www.aan.com/Guidelines/home/GuidelineDetail/898>
61. Reid E, Nooka A, Blackmon J, et al. Clinical use of rituximab in patients with HIV related lymphoma and Multicentric Castleman's disease. Curr Drug Deliv 2012;9(1):41-51.
62. Riabni (rituximab-arrx) [package insert]. Amgen Inc. Thousand Oaks (CA): December 2020
63. Rituxan® (rituximab) [package insert]. Biogen and Genetech Inc. South San Francisco (CA): December 2022.
64. Rituxan Hycela™ (rituximab hyaluronidase) [package insert]. Biogen and Genetech Inc. South San Francisco (CA): March 2021
65. Rituximab. In McEvoy GK, editor. AHFS drug information 2015 [monograph on the internet]. Bethesda (MD): American Society of Health-System Pharmacists; 2015 [cited July 17, 2015].
66. Ruxience (rituximab-pvvr) [package insert]. Pfizer Inc, NY, NY June 2020.
67. Sanders DB, Wolfe GI, Benatar M et al. International consensus guidance for management of myasthenia gravis. Neurology. 2016; 87:1-7.
68. Singh Ja, Furst DE, Bharat A et al. 2012 update of the 2008 American College of Rheumatology recommendations for the use of disease-modifying antirheumatic drugs and biologic agents in the treatment of rheumatoid arthritis. Arthritis Care & Research. 2012; 64: 625-639.

69. Singh JA, SAAG KG, Bridges L et al. 2015 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. *Arthritis Care & Research*. 2016; 68 (1): 1-25.
70. Teshima T, Nagafuji K, Henzan H, et al. Rituximab for the treatment of corticosteroid-refractory chronic graft-versus-host disease. *Int J Hematol*. 2009; 90:253-260.
71. Tomblyn M, Chiller T, Einsele H et al. Guidelines for preventing infectious complications among hematopoietic cell transplantation recipients: a global perspective. *Biol Blood Marrow Transplant*. 2009; 15: 1143-1238.
72. Truxima (rituximab-abbs) injection, solution.[package insert]. Teva Pharmaceuticals USA, Inc. North Wales, PA: May 2020,
73. 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.
74. von Bonin M, Oelschlägel U, Radke J, et al. Treatment of chronic steroid-refractory graft-versus-host disease with low-dose rituximab. *Transplantation*. 2008; 86(6):875-879.
75. World Federation of Hemophilia. Guidelines for the management of hemophilia. <http://www.wfh.org/en/resources/wfh-treatment-guidelines>. Accessed 8/4/2015.
76. Zaja F, Bacigalupo A, Patriarca F, et al.; for the GITMO (Gruppo Italiano Trapianto Midollo Osseo). Treatment of refractory chronic GVHD with rituximab: a GITMO study. *Bone Marrow Transplant*. 2007; 40:273-277.
77. Zarkhin V, Li L, Kambham N, et al. A randomized, prospective trial of rituximab for acute rejection in pediatric renal transplantation. *Am J Transplant*. 2008; 8(12):2607-2617

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 02/09/22.

GUIDELINE UPDATE INFORMATION:

08/15/06	New Medical Coverage Guideline.
10/15/06	Revised: added highlighted note stating that this MCG only addresses use in rheumatoid arthritis and does not address rituximab use in oncological applications, revised descriptor of HCPCS code and removed Medicare Advantage from program exceptions.
06/15/07	Review and revision; consisting of reformatting guideline, adding Remicade® in parentheses in criteria after failure of TNF antagonists, added ICD-9 codes in order to be compliant with FCSO LCD, updated related guidelines and updated references.
05/15/08	Review and revision; consisting of adding a black box warning under "PRECAUTIONS" and updating references.
11/15/08	Revision; consisting of updating the boxed warning under the Precautions section and removing the experimental and investigational statement from the Position

	Statement and adding "Re-treatment is not supported in the literature sooner than 6 months after initial treatment AND is investigational".
01/01/09	Annual HCPCS coding update: revised descriptor for code J9310; deleted 90765 and 90766; added 96365 and 96366.
05/15/09	Revision; consisting of changing name of guideline, adding oncologic indications, maximum doses and updating references.
09/15/09	Review and revision; consisting of updating references.
10/15/09	Revision; consisting of clarifying dosage and update coding.
08/01/10	Revision; consisting of updating coding.
10/15/10	Revision; consisting of updating coding.
02/01/11	Review and revision; consisting of adding new indication, removing an indication, updating approved dosages, and references and coding.
05/15/11	Revision to guideline; consisting of updating coding and adding alternate dosing regimen.
07/15/11	Revision to guideline; consisting of add 2 new indications.
01/15/11	Review and revision to guideline; consisting of updating references and coding
07/15/12	Review and revision to guideline; consisting of updating position statement, coding, exceptions and references
12/15/12	Revision to guideline; consisting of updating coding.
04/15/13	Revision to guideline; consisting of updating position statement and coding.
09/15/13	Review and revision to guideline; consisting of revising and reformatting position statement, revising description section, dosage/administration section, precautions section, updated program exceptions and references.
09/15/14	Review and revision to guideline; consisting of reformatting the position statement; updating references and coding.
04/15/15	Revision to guidelines; updating coding.
09/15/15	Review and revision to guideline; consisting of revising position statement, dosing/warnings/precautions section, updated coding and references.
10/01/15	Revision consisting of update to Program Exceptions section.
11/01/15	Revision: ICD-9 Codes deleted.
05/15/16	Revision to codes.
06/15/16	Revision to guideline; consisting of updating position statement and references.
10/01/16	Update to ICD-10 codes.
09/15/17	Review and revision to guideline; consisting of updating the position statement; dosing, coding, and references.
10/15/17	Revision to guideline; consisting of updating position statement and references.
03/15/18	Revision to guideline; consisting of updating position statement, coding and references.
04/01/18	Addition of HCPCS code C9467 and deletion of C9399.
07/15/18	Review and revision to guideline; consisting of updating the position statement, coding and references.
08/15/18	Revision to guideline; consisting of updating the position statement and references.

01/01/19	Revision: HCPCS code updates. Added J9311 and J9312, and removed C9467, J9310, and J9999.
10/15/19	Review and revision to guideline; consisting of updating the position statement, description, coding and references.
04/01/20	Review and revision to guideline; consisting of updating the position statement.
04/15/20	Review and revision to guideline; consisting of updating the position statement.
07/01/20	Revision: Added HCPCS code Q5119.
10/01/20	Revision to ICD-10 coding.
10/15/20	Review and revision to guideline; consisting of updating the position statement, dosing, coding, program exceptions, and references.
05/15/21	Revision to guideline; consisting of updating the position statement, description, coding, and references.
07/01/21	Revision: Added HCPCS code Q5123 and deleted code J9999.
10/01/21	Revision to guideline; consisting of updating the position statement, coding, and references.
03/15/22	Revision to guideline; consisting of updating the position statement and references.
06/15/22	Revision to guideline; consisting of updating the position statement and references.