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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-arrx (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 requests only, the member has an inadequate response, contraindication, or intolerance to rituximab-arrx (Riabni), rituximab-pvvr (Ruxience), **AND** rituximab-abbs (Truxima)-documentation must be submitted

Table 1: Indications and Specific Criteria

Indication	Specific Criteria	Maximum Allowable Dose
Non-oncology related		
Autoimmune blistering disease (**ANY** of the following) • Pemphigus vulgaris • Pemphigus foliaceus • Bullous pemphigoid • Cicatricial pemphigoid • Epidermolysis bullosa acquisita • Paraneoplastic pemphigus	Member meets **ONE** of the following: 1. **BOTH** of the following are met: 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: i. Mycophenolate ii. Azathioprine iii. Cyclosporine iv. Methotrexate 2. Member is diagnosed with moderate to severe pemphigus vulgaris	375 mg/m^2 per dose[a]
Autoimmune Encephalitis	Treatment when **ALL** of the following criteria are met:	1000 mg administered on day 1 and 15

	1. Subacute onset (rapid progression of less than 3 months) of working memory deficits (short-term memory loss), altered mental status, or psychiatric symptoms 2. **ONE** of the following: a. New focal CNS findings b. Seizures not explained by a previously known seizure disorder c. CSF pleocytosis (WBC of more than 5 cells per mm^3) d. MRI features suggestive of encephalitis 3. Exclusion of alternative causes (Table 4) 4. The member had an inadequate response or contraindication to corticosteroids and IVIG Approval duration: 6 months	every 24 weeks or 375 mg/m^2 per dose
Acute Disseminated Encephalomyelitis	Treatment when **ALL** of the following criteria are met: 1. A first multifocal, clinical CNS event of presumed inflammatory demyelinating cause 2. Encephalopathy cannot be explained by fever 3. **ONE** of the following abnormal brain MRI findings: a. Diffuse, poorly demarcated, large (>1-2 cm) lesions predominately involving the cerebral white matter b. T1-hypointense lesions in the white matter c. Deep grey matter abnormalities (e.g., thalamus or basal ganglia) present 4. No new clinical or MRI findings after 3 months of symptom onset 5. Exclusion of alternative causes (Table 1) 6. The member had an inadequate response or contraindication to corticosteroids and IVIG Approval duration: 6 months	1000 mg administered on day 1 and 15 every 24 weeks or 375 mg/m^2 per dose

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: 1. Member had an inadequate response to corticosteroids 2. Member had an inadequate response to a conventional therapy 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: 1. Desensitization for highly-allosensitized transplant candidates 2. Anti-body mediated rejection (AMR)	375 mg/m^2 per dose
Hemophagocytic lymphohistiocytosis (HLH) induced by Epstein-Barr virus	Diagnosis	375 mg/m^2 per dose
Hemophilia, acquired factor inhibitors	When the member has an inadequate response or contraindication to **ONE** of the following: 1. Adequate trial of corticosteroids or cyclophosphamide (e.g., 4-6 weeks) 2. Immune tolerance induction therapy	375 mg/m^2 per dose
Idiopathic or immune thrombocytopenic purpura, chronic (ITP)	When the member is at risk of bleeding and **ALL** of the following are met:	375 mg/m^2 per dose

	1. The member has demonstrated an inadequate response to **ANY** of the following: a. Adequate trial of corticosteroids (e.g., prednisone 1-2 mg/kg for 2-4 weeks) b. IVIG c. Splenectomy 2. **ONE** of the following: a. Member's platelet count is less than 30,000 b. The member has symptomatic bleeding or increased risk for bleeding and platelet count is less than 50,000 3. Rituximab will not be used concurrently with fostamatinib (Tavalisse®) or a thrombopoietin receptor agonist (e.g., romiplostim [Nplate™], eltrombopag [Alvaiz, Promacta], avatrombopag [Doptelet], lusutrombopag [Mulpleta])	
Immunoglobulin G4-related disease (IgG4-RD)	Member meets **ALL** of the following: i. Member is diagnosed with IgG4-RD ii. Conditions that mimic IgG4-RD have been ruled out (e.g., malignancy, infection, other autoimmune disorders) iii. At least one of the following organs are affected: pancreas, bile duct/biliary tree, orbits, lungs, kidneys, lacrimal glands, major salivary glands, retroperitoneum, aorta, pachymeninges, or thyroid gland iv. **ONE** of the following: 1. Member has an inadequate response to glucocorticoids	1000 mg administered on day 1 and 15 every 24 weeks or 375 mg/m2 per dose

	2. Member is dependent on glucocorticoids	
Liver transplant	When used for **ONE** of the following: 1. Desensitization prior to ABO-incompatible liver transplant 2. Anti-body mediated rejection (AMR)	375 mg/m^2 per dose
Membranous nephropathy	When **BOTH** of the following are met: 1. Member meets **ONE** of the following: a. eGFR less than or equal to 60 ml/min/1.73 m^2 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: 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: 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	1000 mg administered on day 1 and 15 every 24 weeks or 375 mg/m^2 per dose

	iv. Urinary IgG greater than 1 mcg/min v. Urinary B2-microglobulin greater than 250 mg/day vi. Selectivity index greater than 0.20	
Minimal Change Disease (MCD), frequently relapsing (FR)/steroid-dependent (SD)	When **BOTH** of the following are met: 1. Member has **ONE** of the following types of MCD: a. Frequently relapsing MCD defined as two or more relapses per 6 months or four or more per 12 months b. Steroid resistant MCD defined as persistence of proteinuria greater than or equal to 3.5 g/day or protein-creatinine ratio greater than 3500 mg/g with less than 50% reduction from baseline despite prednisone 1 mg/kg/day or 2 mg/kg every other day for greater than 16 weeks 2. Member had an inadequate response to oral immunosuppressant therapy (e.g., cyclophosphamide, tacrolimus, cyclosporine, mycophenolate)	1000 mg administered on day 1 and 15 every 24 weeks or 375 mg/m^2 per dose
Myasthenia Gravis	When the member has an inadequate response, contraindication, or intolerance to a corticosteroid	1000 mg administered on day 1 and 15 every 24 weeks or 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	When **BOTH** of the following are met:	375 mg/m^2 per dose

	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)	
Relapsing-Remitting Multiple Sclerosis (RRMS)	When **ALL** of the following are met: 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. Rituximab will not be used in combination with **ANY** of the following: 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) q. Siponimod (Mayzent)	1000 mg administered on day 1 and 15 every 24 weeks

	r. Teriflunomide (Aubagio)	
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)	When **ALL** of the following are met: 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: 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	When the member is diagnosed with **ONE** of the following: 1. Cryoglobulinemia 2. Primary Sjögren Syndrome	375 mg/m^2 per dose
Systemic Lupus Erythematosus	When the member has **ONE** of the following: 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 immunosuppressant therapy (e.g., 6 months)	375 mg/m^2 per dose

Thrombotic thrombocytopenic purpura (TTP)	When the member has an inadequate response to plasma exchange and corticosteroids	375 mg/m^2 per dose
Vasculitides • 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[a]
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: 1. Diagnosis of Multicentric Castleman's Disease 2. Unicentric Castleman's Disease and **ONE** of the following is met: 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: 1. For induction or consolidation therapy when used as a single agent or in combination with **ONE** of the following: a. High-dose methotrexate, vincristine, procarbazine b. High-dose methotrexate with or without temozolomide	500 mg/m^2 per dose (IV), 25 mg per dose (intrathecal or intraventricular)

	c. High-dose methotrexate, cytarabine, and thiotepa d. Temozolomide e. Lenalidomide 2. For relapsed or refractory disease when used as a single agent or in combination with **ONE** of the following: a. Temozolomide b. Lenalidomide c. High-dose methotrexate with or without ibrutinib d. High-dose cytarabine and thiotepa followed by use with thiotepa and carmustine e. As a component with methotrexate, carmustine, etoposide and prednisone (R-MBVP) 3. When administered intrathecally or intraventricular	
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	When used for **ONE** of the following: 1. In combination with cladribine 2. In combination with pentostatin for incomplete hematologic recovery, or relapsed or refractory disease 3. As a single agent if unable to receive purine analog therapy for incomplete hematologic recovery, or relapsed or refractory disease 4. In combination with vemurafenib (Zelboraf) for **ONE** of the following: a. When used following purine analog therapy (e.g., cladribine or pentostatin) b. For treatment of individuals who are not candidates for	375 mg/m^2 per dose

	purine analog therapy (e.g., cladribine or pentostatin) c. For incomplete hematologic recovery after initial therapy, or relapsed or refractory disease 5. In combination with venetoclax for relapsed or refractory disease when resistant to BRAF inhibitor therapy (e.g., dabrafenib, vemurafenib)	
Hematopoietic Cell Transplantation	When used for **ONE** of the following: 1. Desensitization of donor-specific anti-HLA antibodies (DSA) prior to transplant 2. 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	When used for **ONE** of the following toxicities that developed after use of a checkpoint inhibitor (e.g., atezolizumab, avelumab, durvalumab, ipilimumab, nivolumab, pembrolizumab): 1. Encephalitis when **ALL** of the following are met: 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)	375 mg/m^2 per dose[a]

	4. Severe myositis or dysphagia if member has an inadequate response to corticosteroids 5. Hemolytic anemia if member has an inadequate response to corticosteroids 6. Thrombocytopenia if member has an inadequate response to corticosteroids 7. Acute kidney injury/elevated serum creatinine if toxicity remains greater than stage 2 after corticosteroid treatment	
Non-Hodgkin's B-cell Lymphomas (e.g., Burkitt lymphoma, Diffuse large B-cell lymphoma (DLBCL), Double/Triple Hit Lymphoma, Follicular lymphoma, Gastric MALT lymphoma, Grey Zone lymphoma, High Grade B-cell lymphoma, Histiologic transformation of indolent lymphomas to DLBCL, HIV-related B-cell lymphoma, Mantle cell lymphoma, Extranodal marginal zone lymphoma, Marginal Zone lymphoma, Nodal Marginal zone lymphoma, Pediatric aggressive Mature B-cell lymphomas, Primary Cutaneous Diffuse Large B-cell Lymphoma Leg type, Primary Mediastinal Large B-cell lymphoma, Splenic marginal zone lymphoma)	When the member's disease is CD20-positive	375 mg/m^2 per dose
Post-transplant lymphoproliferative disease (PTLD)	When used for **ONE** of the following: 1. B-cell type PTLD 2. Prevention of Epstein-Barr virus (EBV)-related 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: 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: 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: 1. Bendamustine 2. Bortezomib with or without dexamethasone 3. Bortezomib, cyclophosphamide and dexamethasone 4. Carfilzomib and dexamethasone 5. Cladribine 6. Cyclophosphamide and dexamethasone 7. Cyclophosphamide, doxorubicin, vincristine, and prednisone 8. Cyclophosphamide and fludarabine 9. Cyclophosphamide and prednisone 10. Cytarabine 11. Fludarabine 12. Ibrutinib 13. Ixazomib and dexamethasone 14. Methotrexate 15. Zanubrutinib	375 mg/m^2 per dose
Other FDA-approved, NCCN, or other compendia 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)	Dose does not exceed the maximum FDA-approved dosing

	2. Indication **AND** usage is recognized in NCCN Drugs and Biologics Compendium as a Category 1 or 2A recommendation 3. Indication **AND** usage is recognized in one or more of the standard reference compendium listed in Table 5	
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 for an indication in Table 1 in the past 2 years, **OR** the member has previously met all indication-specific criteria

c. For Rituxan requests for non-oncology indications, the member has an inadequate response, contraindication, or intolerance to rituximab-arrx (Riabni), rituximab-pvvr (Ruxience), **AND** rituximab-abbs (Truxima)- documentation must be submitted

d. 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/m^2 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[a, b]

   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 [a, b]

   vii. Membranous nephropathy, minimal change disease FR/SD, encephalitis, or encephalomyelitis: 1000 mg administered on day 1 and 15 every 24 weeks or 375 mg/m2 per dose

   viii. All other indications: 375 mg/m^2 per dose or 1000 mg administered on day 1 and 15 every 24 weeks

Approval duration: 1 year (6 month duration for encephalitis and encephalomyelitis indications in Table 1)

[a] Alternative dose: 1000 mg given on day 1 and 15 every 24 weeks

[b] 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), rituximab-pvvr (Ruxience), **AND** rituximab-abbs (Truxima)[c]

Table 2: Indications and Specific Criteria

Indication	**Specific Criteria**	**Maximum Allowable Dose**
Castleman's Disease (CD)	When used as a substitute for rituximab as a single agent or with other systemic therapies and member has ONE of the following: 1. Multicentric CD 2. Unicentric CD and **ONE** of the following is met: a. Disease is surgically unresectable b. Member is symptomatic following incomplete/partial resection c. Disease is relapsed or refractory	1400 mg per dose
Chronic Lymphocytic Leukemia (CLL)/ Small Lymphocytic Lymphoma (SLL)	**ONE** of the following is met: 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 and member's disease is CD20-positive	1600 mg per dose

Diffuse Large B-cell Lymphoma (DLBCL)	**ONE** of the following is met: 1. When **BOTH** of the following are met: 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 and member's disease is CD20-positive	1400 mg per dose
Extranodal Marginal Zone Lymphoma	When used as a substitute for rituximab as a single agent or with other systemic therapies and member's disease is CD20-positive	1400 mg per dose
Follicular Lymphoma (FL)	**ONE** of the following is met: 1. Use is in combination with first line chemotherapy in previously untreated follicular lymphoma 2. Single agent use for **ONE** of the following: 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,	1400 mg per dose

	vincristine, and prednisone (CVP) chemotherapy 3. When used as a substitute for rituximab as a single agent or with other systemic therapies and member's disease is CD20-positive	
Hairy Cell Leukemia	When used as a substitute for rituximab for **ONE** of the following: 1. In combination with cladribine 2. In combination with pentostatin for incomplete hematologic recovery, or relapsed or refractory disease 3. As a single agent if unable to receive purine analog therapy for incomplete hematologic recovery, or relapsed or refractory disease 4. In combination with vemurafenib (Zelboraf) for **ONE** of the following: a. When used following purine analog therapy (e.g., cladribine or pentostatin) b. For treatment of individuals who are not candidates for purine analog therapy (e.g., cladribine or pentostatin) c. For incomplete hematologic recovery after initial therapy, or relapsed or refractory disease 5. In combination with venetoclax for relapsed or refractory disease when resistant to BRAF inhibitor therapy (e.g., dabrafenib, vemurafenib)	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 and member's disease is CD20-positive	1400 mg per dose
Histiologic transformation of indolent lymphomas to DLBCL	When used as a substitute for rituximab as a single agent or with other systemic therapies and member's disease is CD20-positive	1400 mg per dose
Hodgkin Lymphoma (Nodular Lymphocyte-predominant Hodgkin Lymphoma)	When used as a substitute for rituximab as a single agent or with other systemic therapies 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 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 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 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 and disease is classified with **ONE** of the following: 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 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: 1. Bendamustine 2. Bortezomib with or without dexamethasone 3. Bortezomib, cyclophosphamide and dexamethasone 4. Carfilzomib and dexamethasone 5. Cladribine 6. Cyclophosphamide and dexamethasone 7. Cyclophosphamide, doxorubicin, vincristine, and prednisone 8. Cyclophosphamide and fludarabine 9. Cyclophosphamide and prednisone 10. Cytarabine 11. Fludarabine 12. Ibrutinib 13. Ixazomib and dexamethasone 14. Methotrexate 15. Zanubrutinib	1400 mg per dose
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

[c] 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

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	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

years and older	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.
[f] Schedule is based on type of NHL, dose is 250 mg/m^2 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 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.	

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

ICD-10 Diagnosis Codes That Support Medical Necessity for rituximab (J9312, Q5115, Q5119, Q5123):

B10.89	Other human herpes virus infection
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
C86.00 – C86.60	Other specified types of T/NK-cell lymphoma
C88.00	Waldenstrom macroglobulinemia
C88.40	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
D89.84	IgG4-related disease
G04.00 – G04.02	Acute disseminated encephalitis and encephalomyelitis
G04.81	Other encephalitis and encephalomyelitis
G35.A	Relapsing remitting multiple sclerosis
G35.C1	Active secondary progressive 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

M05.A	Abnormal rheumatoid factor and anti-citrullinated protein antibody with rheumatoid arthritis
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, N04.B1, N04.B2	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
T45.AX5A	Adverse effect of immune checkpoint inhibitors and immunostimulant drugs, initial encounter
T45.AX5D	Adverse effect of immune checkpoint inhibitors and immunostimulant drugs, subsequent encounter
T45.AX5S	Adverse effect of immune checkpoint inhibitors and immunostimulant drugs, sequela
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):

C81.00 – C81.09	Nodular lymphocyte predominant Hodgkin lymphoma
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
C88.00	Waldenstrom macroglobulinemia
C88.40	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.

If this Medical Coverage Guideline contains a step therapy requirement, in compliance with Florida law 627.42393, members or providers may request a step therapy protocol exemption to this requirement if based on medical necessity. The process for requesting a protocol exemption can be found at Coverage Protocol Exemption Request.

DEFINITIONS:

RA: Rheumatoid Arthritis.

TNF: tumor necrosis factor.

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

Off-label/unlabeled use: use of a drug for an indication other than those stated in the FDA-approved labeling.

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:

Table 4: Excluded differential diagnosis in autoimmune encephalitis

Disorder
CNS infection
Septic encephalopathy
Metabolic encephalopathy
Drug toxicity (including use of illicit drugs, neurotoxic effect of prescribed medications, posterior reversable encephalopathy, idiosyncratic reaction (neuroleptic malignant syndrome), drug interaction (serotonergic syndrome), or drug withdrawal)
Cerebrovascular disease
Neoplastic disorders
Creutzfeldt-Jakob disease

Epileptic disorders
Rheumatologic disorders (e.g., lupus, sarcoidosis, other)
Kleine-Levin
Reye syndrome (children)
Mitochondrial diseases
Inborn errors of metabolism (children)

Table 5: Designated compendia

Compendium	Covered Uses †
AHFS-DI	**Narrative text is supportive**
NCCN Drugs and Biologics Compendium	Category Levels 1 and 2A
Thomson Micromedex DrugDex	Meets requirements for **BOTH** of the following: • Strength of recommendation: Class I (Recommended) or IIa (Recommended, In Most Cases) • Efficacy: Class I (Effective) or IIa (Evidence Favors Efficacy)
Clinical Pharmacology	Narrative text is supportive
† If covered use criteria are not met, the request should be denied. AHFS-DI, American Hospital Formulary Service Drug Information; NCCN, National Comprehensive Cancer Network. For additional information regarding designated compendia, please refer to the “Definitions” section.	

Table 6: Thomson Micromedex DrugDex Recommendation Ratings: Strength of Recommendation

Class I	Recommended	The given test or treatment has been proven to be useful, and should be performed or administered
Class IIa	Recommended, in most cases	The given test or treatment is generally considered to be useful, and is indicated in most cases.
Class IIb	Recommended in some cases	The given test or treatment may be useful, and is indicated in some, but not most, cases
Class III	Not recommended	The given test or treatment is not useful and should be avoided
Class Indeterminate	Evidence Inconclusive	

Table 7: Thomson Micromedex DrugDex Recommendation Ratings: Efficacy

Class I	Effective	Evidence and/or expert opinion suggests that a given drug treatment for a specific indication is effective
Class IIa	Evidence favors efficacy	Evidence and/or expert opinion is conflicting as to whether a given drug treatment for a specific indication is effective, but the weight of evidence and/or expert opinion favors efficacy.
Class IIb	Evidence is inconclusive	Evidence and/or expert opinion is conflicting as to whether a given drug treatment for a specific indication is effective, but the weight of evidence and/or expert opinion argues against efficacy.

Class III	Ineffective	Evidence and/or expert opinion suggests that a given drug treatment for a specific indication is ineffective

Table 8: NCCN Categories of Evidence Consensus

Category 1	Based upon high-level evidence; there is uniform NCCN consensus that the intervention is appropriate
Category 2A	Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate
Category 2B	Based upon lower-level evidence, there NCCN consensus that the intervention is appropriate
Category 3	Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate

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COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 11/12/25.

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.
08/15/23	Review and revision to guideline; consisting of updating the position statement to include autoimmune encephalitis, Primary CNS Lymphoma, Non-Hodgkin's B-cell lymphomas, Waldenström's macroglobulinemia/Lymphoplasmacytic lymphoma for

	rituximab. Added nodular lymphocyte predominant Hodgkin lymphoma for Rituxan Hycela. Updated coding and references.
10/01/24	ICD-10 coding update.
01/15/25	Review and revision to guideline; consisting of updating to include Epstein Barr virus induced HLH, minimal change disease, and updated ITP for risk of bleeding.
08/15/25	Review and revision to guideline; consisting of updating to include IgG4-related disease, prevention of Epstein Barr virus PTLD, Hairy cell leukemia and Immune checkpoint inhibitor toxicity. Update to continuation criteria for use of preferred biosimilar agents for non-oncology indications.
10/01/25	Update to ICD-10 codes.
12/15/25	Review and revision to guideline; consisting of updating the position statement to include Truxima as a co-preferred biosimilar with Ruxience and Riabni. Update to myasthenia gravis, liver transplant, hematopoietic cell transplant, compendia supported diagnoses, and inclusion of alternate dosing.