rituximab

Medicare Part B Drug Policy

- Medicare coverage is limited to items and services that are reasonable and necessary for the diagnosis or treatment of an illness or injury (and within the scope of a Medicare benefit category).
- Medicare Benefit Policy Manual - Pub. 100-02, Chapter 15, Section 50, describes national policy regarding Medicare guidelines for coverage of drugs and biologicals.
- Blue Shield of California (BSC) follows Medicare statutes, regulations, National Coverage Determinations (NCDs), Local Coverage Determinations (LCDs), and policy articles for determining coverage for Part B drug requests when applicable.
- BSC Medicare Part B Drug Policies will be used when coverage criteria are not fully established or there is an absence of any applicable Medicare statutes, regulations, NCDs or LCDs.

Drug Details

USP Category: ANTINEOPLASTICS
Mechanism of Action: chimeric human-murine anti-human antigen CD20 monoclonal antibody
HCPCS:
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
How Supplied:
100 mg/10 mL, 500 mg/50 mL (single-use)

Condition(s) listed in policy (see coverage criteria for details)

- ANCA-Associated Vasculitis, Microscopic Polyangiitis (MPA), and Granulomatosis with Polyangiitis (GPA) / Wegener's Granulomatosis
- Autoimmune Hemolytic Anemia (AIHA)
- Autoimmune Mucocutaneous Blistering Diseases (AMBDs)
- B-Cell Mediated Cancers
- Graft Versus Host Disease
- Histiocytic Neoplasms for Rosai-Dorfman Disease
- Immunotherapy-Related Toxicities Secondary to Immune-Checkpoint Inhibitor Therapy
- Leptomeningeal Metastases
- Myasthenia Gravis
- Neuromyelitis Optica Spectrum Disorder
- Primary Immune Thrombocytopenia (ITP)
- Rheumatoid Arthritis
- Sjogren's Disease
- Solid Organ Transplants

Any request for a condition not listed in policy must meet the definition of a medically accepted indication. Section 1861(t)(2)(B) of the Act defines "medically-accepted indication," as any use of a prescription drug or biological product which is approved under the Federal Food, Drug, and

Cosmetic Act, or the use of which is supported by one or more citations included (or approved for inclusion) in one or more of the CMS approved compendia.

Special Instructions and Pertinent Information

Provider must submit documentation (such as office chart notes, lab results or other clinical information) to ensure the member has met all medical necessity requirements.

For members enrolled in our Blue Shield Select (PPO) and Blue Shield Medicare (PPO) plans:
Rituxan and Riabni requires step therapy. Step therapy requires you to try other drugs first before a drug can be covered. The BSC preferred step drugs are Ruxience and Truxima. Both of these drugs will need to be tried for members newly initiating Rituxan or Riabni therapy.

Coverage Criteria

The following condition(s) require Prior Authorization/Preservice:

ANCA-Associated Vasculitis, Microscopic Polyangiitis (MPA), and Granulomatosis with Polyangiitis (GPA) / Wegener's Granulomatosis

Meets medical necessity if all the following are met:

1. For PPO request for Riabni or Rituxan: Intolerance or contraindication with the preferred products, Ruxience and Truxima, that is not expected with requested rituximab product

Covered Doses:

Treatment:
Adults:
375 mg/m^2 IV infusion once weekly for 4 doses, or
1000 mg IV infusion on Days 1 and 15

Children:
375 mg/m^2 IV infusion once weekly for 4 doses, or
BSA ≤ 1.5 m^2: 575 mg/m^2 IV infusion on Days 1 and 15, or
BSA > 1.5 m^2: 750 mg/m^2 IV infusion on Days 1 and 15

Maintenance of Remission:
Adults:
1000 mg IV infusion every 4 months

Children:
250 mg/m^2 IV infusion every 6 months

Coverage Period:

Treatment: One course
Maintenance: Yearly

ICD-10:

I77.6, M30.1, M31.30, M31.31, M31.7

Autoimmune Hemolytic Anemia (AIHA)

Meets medical necessity if all the following are met:

1. Diagnosis of autoimmune hemolytic anemia (including AIHA following allogenic bone marrow transplantation)
2. If for cold-type AIHA, current HgB is less than or equal to 10 mg/dL, and not being used with complement inhibitors (i.e., Enjaymo)
3. For PPO request for Riabni or Rituxan: Intolerance or contraindication with the preferred products, Ruxience and Truxima, that is not expected with requested rituximab product

Covered Doses:
Up to 375 mg/m^2 weekly for up to 4 weeks

Coverage Period:
One course

ICD-10:
D59.0

Autoimmune Mucocutaneous Blistering Diseases (AMBDs)
Meets medical necessity if all the following are met:

1. Diagnosis of ONE of the following:
   a. pemphigus foliaceus
   b. pemphigus vulgaris
   c. bullous pemphigoid
   d. cicatricial pemphigoid
   e. epidermolysis bullosa acquisita
2. Diagnosis is confirmed by lesional tissue biopsy or serology
3. For PPO request for Riabni or Rituxan: Intolerance or contraindication with the preferred products, Ruxience and Truxima, that is not expected with requested rituximab product

Covered Doses:
Initial treatment: up to 2,500 mg IV for the first year of treatment, followed by maintenance treatment of up to 2,000 mg total per subsequent year
Maintenance treatment: Up to 2,000 mg total per year
Dose for treatment of relapse: up to 1000 mg IV x1 and no sooner than 4 months (16 weeks) after previous rituximab infusion.

Coverage Period:
Yearly

ICD-10:
L10.0, L10.2, L12.0, L12.1, L13.8

B-Cell Mediated Cancers
Meets medical necessity if all the following are met:

1. Diagnosis of one of the following:
   a. B-cell lymphomas (e.g., AIDS-related B-cell lymphomas, Burkitt, Castleman's disease, Diffuse large B-cell, Follicular, Gastric MALT lymphoma, High-grade B-cell, Histologic transformation of marginal zone lymphoma to diffuse large B-cell lymphoma, Mantle cell,

Nodal marginal zone, Nongastric MALT, Post-transplant lymphoproliferative disorders, Primary cutaneous B-cell, Splenic marginal zone)

b. Acute lymphoblastic leukemia (ALL)
c. Chronic lymphocytic leukemia (CLL) and small lymphocytic lymphoma (SLL)
d. Hairy cell leukemia
e. Hodgkin lymphoma, nodular, CD20+, lymphocyte-predominant
f. Primary central nervous system lymphoma
g. Waldenstrom's macroglobulinemia / lymphoplasmacytic lymphoma, macroglobulinemia, or macroglobulinemia (idiopathic) primary

2. <u>For PPO request for Riabni or Rituxan:</u> Intolerance or contraindication with the preferred products, Ruxience and Truxima, that is not expected with requested rituximab product

Covered Doses:

	Per Treatment Course	Maintenance
• AIDS-related B-cell lymphomas • Burkitt lymphoma • Castleman's disease • Diffuse large B-cell lymphoma • High-grade B-cell lymphoma • Histologic transformation of marginal zone lymphoma to diffuse large B-cell lymphoma • Primary cutaneous B-cell lymphoma	375 mg/m^2 IV for up to 8 doses	
• Post -transplant lymphoproliferative disorders	375 mg/m^2 IV for up to 8 doses	375 mg/m^2 IV for up to 8 doses over 2 years
• Mantle cell lymphoma	375 mg/m^2 IV for up to 18 doses	375 mg/m2 IV every 2 months
• Gastric MALT lymphoma • Nodal marginal zone • Nongastric MALT lymphoma • Splenic marginal zone	375 mg/m^2 IV for up to 20 doses	375 mg/m2 IV for up to 12 doses over 2 years
• Follicular lymphoma	375 mg/m^2 IV for up to 16 doses	375 mg/m2 IV for up to 12 doses over 2 years
• Acute lymphoblastic leukemia (ALL)	375 mg/m^2 IV for up to 12 doses	375 mg/m^2 IV for up to 6 doses
• Chronic lymphocytic leukemia (CLL) and small lymphocytic lymphoma (SLL)	375 mg/m^2 IV for up to 15 doses 375 mg/m^2 IV for the 1st dose followed by 500 mg/m^2 IV for up to 7 doses	375 mg/m2 IV for 8 doses over 2 years 500 mg/m2 IV for 12 doses over 2 years

• Hairy cell leukemia	375 mg/m^2 IV up to 12 doses	
• Hodgkin lymphoma, nodular, CD20+, lymphocyte-predominant	375 mg/m^2 IV for up to 8 doses	375 mg/m^2 IV once weekly for 4 weeks for up to 4 treatments over 2 years
• Primary central nervous system lymphoma	500 mg/m^2 IV for up to 20 doses 25 mg intrathecal/intraventricular for up to 30 doses	25mg intrathecal/intraventricular every 2 weeks
• Waldenstrom's macroglobulinemia / lymphoplasmacytic lymphoma, macroglobulinemia, or macroglobulinemia (idiopathic) primary	375 mg/m^2 IV up to 20 doses	375 mg/m^2 IV weekly for 4 doses for up to 4 treatments for 2 years 375 mg/m2 IV for 8 doses over 2 years

Coverage Period:
See above

ICD-10:
B20, C79.32, C88.0, C88.4, C91.10, C91.12, C91.40, C91.42, D36.0, D47.Z2, R59.0, R59.1, R59.9, Z85.71, Z85.72, Z85.79

Graft Versus Host Disease
Meets medical necessity if all the following are met:

1. Inadequate response to at least one prior drug for GVHD (i.e., systemic corticosteroids, immunosuppressants)
2. For PPO request for Riabni or Rituxan: Intolerance or contraindication with the preferred products, Ruxience and Truxima, that is not expected with requested rituximab product

Covered Doses:
Up to 375 mg/m^2 IV once weekly for up to 8 doses per course

Coverage Period:
yearly

ICD-10:
D89.810, D89.813, T86.09

Histiocytic Neoplasms for Rosai-Dorfman Disease
Meets medical necessity if all the following are met:

1. Being used as a single agent
2. Being used for nodal and immune-cytopenia diseases
3. For PPO request for Riabni or Rituxan: Intolerance or contraindication with the preferred products, Ruxience and Truxima, that is not expected with requested rituximab product

Covered Doses:
Up to 500 mg/m^2 IV once every one or two weeks for up to 6 cycles

Coverage Period:
Length of time for use of 6 doses

ICD-10:
D76.3

Immunotherapy-Related Toxicities Secondary to Immune-Checkpoint Inhibitor Therapy
Meets medical necessity if all the following are met:

1. Treatment of ONE of the following immunotherapy-related toxicities secondary to immune-checkpoint inhibitor therapy
   a. Encephalitis for positive autoimmune encephalopathy antibody or refractory to pulse-dose methylprednisolone
   b. Severe myasthenia gravis refractory to plasmapheresis or intravenous immune globulin (IVIG)
   c. Moderate or severe bullous dermatitis
   d. Steroid-refractory myalgias or myositis
2. **For PPO request for Riabni or Rituxan:** Intolerance or contraindication with the preferred products, Ruxience and Truxima, that is not expected with requested rituximab product

Covered Doses:
Up to 1000 mg per dose for up to two doses

Coverage Period:
Per episode

ICD-10:
G04.81

Leptomeningeal Metastases
Meets medical necessity if all the following are met:

1. **For PPO request for Riabni or Rituxan:** Intolerance or contraindication with the preferred products, Ruxience and Truxima, that is not expected with requested rituximab product

Covered Doses:
Initial Therapy or Retreatment of Active Disease:
Up to 25 mg intrathecal/intraventricular on Days 1 and 4 of a 7-day cycle for 4 cycles

Maintenance:
Up to 25 mg intrathecal/intraventricular on Days 1 and 4 of a 28-day cycle

Coverage Period:
Initial and Retreatment of Active Disease: Up to 8 doses per treatment course
Maintenance: Yearly

ICD-10:
C79.32

Myasthenia Gravis

Meets medical necessity if all the following are met:

1. Prescribed by or in consultation with a neurologist
2. Inadequate response to corticosteroids
3. ONE of the following:
   a. Inadequate response or intolerance to at least one of the following: mycophenolate, azathioprine, cyclosporine, or cyclophosphamide
   b. Patient has MuSK (muscle-specific tyrosine kinase)-Ab+ MG
4. For PPO request for Riabni or Rituxan: Intolerance or contraindication with the preferred products, Ruxience and Truxima, that is not expected with requested rituximab product

Covered Doses:

Up to 375 mg/m^2 IV infusion once weekly for 4 doses every 6 months OR
Up to 1000 mg IV infusion for 2 doses, separated by a 2-week interval, every 6 months

Coverage Period:

Initial: Yearly
Reauthorization: Yearly, based upon continued response to treatment

ICD-10:

G70.00, G70.01

Neuromyelitis Optica Spectrum Disorder

Meets medical necessity if all the following are met:

1. Prescribed by or in consultation with a neurologist
2. Not being used in combination with another drug therapy for NMOSD (e.g., eculizumab, inebilizumab, satralizumab)
3. For PPO request for Riabni or Rituxan: Intolerance or contraindication with the preferred products, Ruxience and Truxima, that is not expected with requested rituximab product

Covered Doses:

Up to 375 mg/m^2 IV infusion once weekly for 4 doses every 6 months OR
Up to 1000 mg IV infusion for 2 doses, separated by a 2-week interval every 6 months

Coverage Period:

Initial: Yearly (2 treatment courses)
Reauthorization: Yearly, with documented reduction in frequency of NMO attacks from baseline.

ICD-10:

G36.0

Primary Immune Thrombocytopenia (ITP)

Meets medical necessity if all the following are met:

1. Patient has chronic, refractory ITP
2. Platelet count <30, 000/mcl (i.e. <30 x10^9/L)
3. Either of the following (a or b):

a. Inadequate response to one of the following treatments: corticosteroids, IVIG, anti-D antibody, or splenectomy or medical rationale why these cannot be used
b. Inadequate response, intolerance, or contraindication to Promacta or NPlate after meeting step therapy requirements for either drug.

4. For PPO request for Riabni or Rituxan: Intolerance or contraindication with the preferred products, Ruxience and Truxima, that is not expected with requested rituximab product

Covered Doses:
Up to 375 mg/m^2 weekly for 4 weeks

Coverage Period:
Cover for one course

ICD-10:
D69.3

Rheumatoid Arthritis
Meets medical necessity if all the following are met:

1. Prescribed by or in consultation with a rheumatologist
2. Inadequate response, intolerable side effect, or contraindication to methotrexate
3. Not used in combination with another targeted immunotherapies (e.g., TNF inhibitors, IL-6 inhibitors, JAK inhibitors)
4. For PPO request for Riabni or Rituxan: Intolerance or contraindication with the preferred products, Ruxience and Truxima, that is not expected with requested rituximab product

Covered Doses:
Up to two 1000 mg IV infusions separated by 2 weeks, given every 6 months

Coverage Period:
Initial: 1 year
Reauthorization: Yearly

ICD-10:
M06.4, M06.9

Sjogren's Disease
Meets medical necessity if all the following are met:

1. Diagnosis of primary Sjogren's disease
2. Prescribed by or in consultation with a rheumatologist or ophthalmologist
3. For PPO request for Riabni or Rituxan: Intolerance or contraindication with the preferred products, Ruxience and Truxima, that is not expected with requested rituximab product

Covered Doses:
Up to 375 mg/m2 IV infusion once weekly for 4 doses every 6 months OR
Up to 1000 mg IV infusion for 2 doses, separated by a 2-week interval every 6 months

Coverage Period:

Initial: 1 year
Reauthorization: Yearly

Solid Organ Transplants
Meets medical necessity if all the following are met:

1. Documented solid organ transplant, including pre/perioperative prevention or for treatment of antibody-mediated rejection of allograft
2. **For PPO request for Riabni or Rituxan:** Intolerance or contraindication with the preferred products, Ruxience and Truxima, that is not expected with requested rituximab product

Covered Doses:
Given intravenously. Dose is highly variable

Coverage Period:
16 weeks per treatment course

ICD-10:
Z94.0, Z94.1, Z94.4

Additional Information

Summary of Evidence
The contents of this policy were created after examining the following resources:

1. The prescribing information for Riabini, Rituxan, Ruxience, and Truxima
2. CMS approved compendium in accordance with the accepted compendia ratings listed:
   a. Micromedex DrugDex - Class I, Class IIa, of Class IIb
   b. American Hospital Formulary Service-Drug Information (AHFS-DI) - supportive narrative text
   c. National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium - Category 1 or 2A
   d. Lexi-Drugs – "Use: Off-Label" and rated as "Evidence Level A" (cancer indications only)
   e. Clinical Pharmacology - supportive narrative text (cancer indications only)
3. Drugs, Biologics and Injection: Noridian Healthcare Solutions Medicare
4. NCCN Guideline: Acute lymphoblastic leukemia
5. NCCN Guideline: B-cell lymphomas
6. NCCN Guideline: Central nervous system cancers
7. NCCN Guideline: Chronic lymphocytic lymphoma/small lymphocytic lymphoma
8. NCCN Guideline: Hairy cell leukemia
9. NCCN Guideline: Hematopoietic cell transplantation
10. NCCN Guideline: Histiocytic neoplasms
11. NCCN Guideline: Hodgkin lymphoma
12. NCCN Guideline: Management of immunotherapy-related toxicities
13. NCCN Guideline: Pediatric aggressive mature B-cell lymphomas
14. NCCN Guideline: Primary cutaneous lymphomas
15. NCCN Guideline: Waldenstrom macroglobulinemia/lymphoplasmacytic lymphoma
16. Recommendations for the use of rituximab (anti-CD20 antibody) in treatment of autoimmune bullous skin diseases

17. International consensus guidance for management of myasthenia gravis: 2020 update
18. Evidence-based guideline: clinical evaluation and treatment of transverse myelitis: report of the therapeutics and technology assessment subcommittee of the American academy neurology
19. The European Federation of Neurological Societies (EFNS) guidelines on diagnosis and management of neuromyelitis optica
20. Update on diagnosis and treatment of neuromyelitis optica. Recommendations of the neuromyelitis optica study group.
21. American society of hematology 2019 guidelines for immune thrombocytopenia
22. Updated S2K guidelines on the management of pemphigus vulgaris and foliaceus initiated by the European academy of dermatology and venereology (EADV)
23. Updated S2K guidelines for the management of bullous pemphigoid initiated by the European Academy of Dermatology and Venereology (EADV)

After reviewing the information in the above resources, the FDA-approved indications listed in the prescribing information for Riabini, Rituxan, Ruxience, and Truxima are covered in addition to the following:

- Autoimmune hemolytic anemia (AIHA)
- Autoimmune mucocutaneous blistering diseases (AMBDs)
  - Pemphigus foliaceus
  - Bullous pemphigoid
  - Cicatricial pemphigoid
  - Epidermolysis bullosa acquisita
- B-cell mediated cancers
  - B-cell acute lymphoblastic leukemia (ALL)
  - B-cell lymphoblastic lymphoma
  - Burkitt lymphoma
  - Castleman's disease
  - CLL/small lymphocytic lymphoma (SLL)
  - Diffuse large B-cell lymphoma (DLBCL)
  - Follicular lymphoma
  - Hairy cell leukemia
  - High-grade B-cell lymphoma (including high-grade B-cell lymphoma with translocations of MYC and BCL2 and/or BCL6 [double/triple hit lymphoma], high-grade B-cell lymphoma, not otherwise specified)
  - Histological transformation of indolent lymphomas to DLBCL
  - Hodgkin's lymphoma, CD20-positive, nodular
  - Hodgkin's lymphoma, lymphocyte-predominant
  - Human immunodeficiency virus (HIV) related B-cell lymphomas
  - Mantle cell lymphoma
  - Marginal zone lymphomas
    - Nodal marginal zone lymphoma
    - Extranodal marginal zone lymphoma
    - Splenic marginal zone lymphoma
  - Pediatric aggressive mature B-cell lymphomas

    - Post-transplant lymphoproliferative disorder (PTLD)
    - Primary mediastinal large B-cell lymphoma
    - Primary CNS lymphomas
    - Primary cutaneous B-cell lymphoma
    - Waldenstrom's macroglobulinemia / lymphoplasmacytic lymphoma, macroglobulinemia, or macroglobulinemia (idiopathic) primary
- Graft versus host disease
- Histiocytic neoplasms for Rosai-Dorfman disease
- Immunotherapy-related toxicities secondary to immune-checkpoint inhibitor therapy
- Leptomeningeal metastases
- Myasthenia gravis
- Neuromyelitis optica spectrum disorder
- Primary immune thrombocytopenia
- Rheumatoid arthritis, in combination with methotrexate, in patients with an inadequate response to methotrexate
- Sjogren's disease
- Solid organ transplants

Explanation of Rationale:

- Support for FDA-approved indications can be found in the manufacturer's prescribing information.
- Support for using biosimilars as step requirement is found in Noridian Health Care Solutions and supported by the FDA. Noridian will accept a biosimilar drug on the same criteria as the drug to which it is a biosimilar unless an article is published to the contrary. Per the FDA, a biosimilar is highly similar to and has no clinically meaningful difference from an existing FDA approved biologic reference drug.
- Support for using biosimilars in oncology can be found in The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) via the footnote on the reference product (an FDA-approved biosimilar is an appropriate substitute) and in the NCCN Drugs & Biologics Compendium® by the notation that a biosimilar agent may be an appropriate substitute for the reference product.
- **Autoimmune hemolytic anemia**: Support for using rituximab for autoimmune hemolytic anemia (AIHA) can be found in DrugDex compendium. DrugDex compendium supports the use of rituximab for AIHA in adult and pediatric patients as a single-agent or in combination with immunosuppressive therapy.
- **Autoimmune mucocutaneous blistering diseases:** Support for using rituximab for autoimmune mucocutaneous blistering diseases (AMBDs) can be found in published treatment guidelines. The European Academy of Dermatology and Venereology (EADV) supports the use of rituximab in patients with bullous pemphigoid who had an inadequate response to corticosteroids and as initial and subsequent therapy in patients with pemphigus foliaceus. Hertl et al (2008) supports the use of rituximab for bullous pemphigoid, epidermolysis bullosa acquisita, and pemphigus foliaceus in the adjuvant setting in addition to standard immunosuppressive treatment.
- Support for the listed indications can be found in the National Comprehensive Cancer Network's (NCCN) Drugs and Biologics Compendium.
    - **B-cell mediated cancers**

        - B-cell acute lymphoblastic leukemia (ALL)
        - B-cell lymphoblastic lymphoma
        - Burkitt lymphoma
        - Castleman's disease
        - CLL/small lymphocytic lymphoma (SLL)
        - Diffuse large B-cell lymphoma (DLBCL)
        - Follicular lymphoma
        - Hairy cell leukemia
        - High-grade B-cell lymphoma (including high-grade B-cell lymphoma with translocations of MYC and BCL2 and/or BCL6 [double/triple hit lymphoma], high-grade B-cell lymphoma, not otherwise specified)
        - Histological transformation of indolent lymphomas to DLBCL
        - Hodgkin's lymphoma, CD20-positive, nodular
        - Hodgkin's lymphoma, lymphocyte-predominant
        - Human immunodeficiency virus (HIV) related B-cell lymphomas
        - Mantle cell lymphoma
        - Marginal zone lymphomas
            - Nodal marginal zone lymphoma
            - Extranodal marginal zone lymphoma
            - Splenic marginal zone lymphoma
        - Pediatric aggressive mature B-cell lymphomas
        - Post-transplant lymphoproliferative disorder (PTLD)
        - Primary mediastinal large B-cell lymphoma
        - Primary CNS lymphomas
        - Primary cutaneous B-cell lymphoma
        - Waldenstrom's macroglobulinemia / lymphoplasmacytic lymphoma, macroglobulinemia, or macroglobulinemia (idiopathic) primary
    - **Histiocytic neoplasms for Rosai-Dorfman disease**
    - **Leptomeningeal metastases**
- **Graft-versus-host disease:** Support for using rituximab for graft versus host disease (GVHD) is found in the National Comprehensive Cancer Network's (NCCN) guideline for hematopoietic cell transplantation. The NCCN guideline for hematopoietic cell transplantation supports the use of rituximab for GVHD as additional therapy in conjunction with systemic corticosteroids following no response (steroid-refractory disease) to first-line therapy options.
- **Immunotherapy-related toxicities secondary to immune-checkpoint inhibitor therapy**: Support for using rituximab for immunotherapy-related toxicities secondary to immune-checkpoint inhibitor therapy is found in the National Comprehensive Cancer Network's (NCCN) guideline for management of immunotherapy-related toxicities. The NCCN guideline for management of immunotherapy-related toxicities supports the use of rituximab for the management of the following immunotherapy-related toxicities:
    - As additional therapy for moderate (G2), severe (G3), or life-threatening (G4) immunotherapy-related bullous dermatitis
    - Moderate, severe, or life-threatening corticosteroid-refractory myositis (proximal muscle weakness, neck flexor weakness, with or without myalgias) for significant dysphagia, life-threatening situations, or cases refractory to corticosteroids

- As additional therapy for severe (G3-4) myasthenia gravis in patients refractory to plasmapheresis or intravenous immune globulin (IVIG)
- For encephalitis in patients positive for autoimmune encephalopathy antibody, or who have had limited or no improvement after 7-14 days on high-dose corticosteroids with or without IVIG.

- **Myasthenia gravis**: Support for using rituximab for myasthenia gravis can be found in a published guideline. Narayanaswami et al (2021) supports the use of rituximab in patients with muscle specific kinase (MuSK)-antibody positive MG after an unsatisfactory response to initial immunotherapy and acetylcholinesterase (AChR)-antibody positive MG in patients who fail or are unable to tolerate other immunosuppressive agents.
- **Neuromyelitis optica spectrum disorder**: Support for using rituximab for neuromyelitis optica spectrum disorder (NMOSD) can be found in published treatment guidelines. The European Federation of Neurological Societies (EFNS) supports the use of rituximab for immunosuppressive treatment of neuromyelitis optica. The American academy of neurology (AAN) supports use of rituximab in patients with transverse myelitis due to neuromyelitis optica to decrease the number of relapses. The neuromyelitis optica study group (NEMOS) supports the use of rituximab as a first-line treatment option for neuromyelitis optica.
- **Primary immune thrombocytopenia**: Support for using rituximab for primary immune thrombocytopenia (ITP) can be found in a published treatment guideline. The American Society of Hematology supports the use of rituximab in patients who have failed first-line therapy with conventional doses of corticosteroids, IV immune globulin (IVIG), or splenectomy and who at risk of bleeding. Rituximab may also be considered as an alternative to splenectomy in patients with chronic ITP and in those who respond poorly to splenectomy.
- **Rheumatoid arthritis, in combination with methotrexate, in patients with an inadequate response to methotrexate:** Support for using rituximab for rheumatoid arthritis in patients with an inadequate response to methotrexate can be found in DrugDex compendium. DrugDex compendium supports the use of rituximab in combination with methotrexate in patients with an inadequate response to methotrexate.
- **Sjogren's disease**: Support for using rituximab for Sjogren's disease can be found in DrugDex compendium. DrugDex compendium supports the use of rituximab in adults for primary Sjogren's syndrome.
- **Solid organ transplants:** Support for using rituximab for solid organ transplants can be found in DrugDex compendium. DrugDex compendium supports the use of rituximab as an adjunct treatment for antibody-mediated liver transplant rejection and antibody-mediated lung transplant rejection.

References

1. CMS Benefit Policy Manual. Chapter 15; § 50 Drugs and Biologicals
2. Medicare Coverage Database. Available at https://www.cms.gov/Medicare-Coverage-Database/search.aspx
3. Social Security Act (Title XVIII) Standard References, Sections: 1862(a)(1)(A) Medically Reasonable & Necessary; 1862(a)(1)(D) Investigational or Experimental; 1833(e) Incomplete Claim; 1861(t) (1) Drugs and Biologicals
4. AHFS. Available by subscription at http://www.lexi.com

5. Chung SA, Langford CA, Maz M, et al: 2021 American College of Rheumatology/Vasculitis Foundation Guideline for the management of antineutrophil cytoplasmic antibody-associated vasculitis. Arthritis Rheumatol 2021; 73(8):1366-1383.
6. DrugDex. Available by subscription at http://www.micromedexsolutions.com/home/dispatch
7. Fanouriakis A, Kostopoulou M, Alunno A, et al. 2019 update of the EULAR recommendations for the management of systemic lupus erythematosus. Ann Rheum Dis. 2019;78(6):736-745. doi:10.1136/annrheumdis-2019-215089
8. Fraenkel L, Bathon JM, England BR, et al. 2021 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. Arthritis Care Res (Hoboken). 2021;73(7):924-939. doi:10.1002/acr.24596
9. Hertl M, Zillikens D, Borradori L et al. Recommendations for the use of rituximab (anti-CD20 antibody) in treatment of autoimmune bullous skin diseases. J Dtsch Dermatol Ges 2008 May; 6(5):366-73.
10. National Comprehensive Cancer Network. Acute Lymphoblastic Leukemia (Version 3.2023). Available at http://www.nccn.org.
11. National Comprehensive Cancer Network. B-cell lymphomas (Version 6.2023). Available at http://www.nccn.org.
12. National Comprehensive Cancer Network. Central Nervous System Cancers (Version 1.2023). Available at http://www.nccn.org.
13. National Comprehensive Cancer Network. Chronic lymphocytic lymphoma/Small lymphocytic lymphoma (Version 1.2024). Available at http://www.nccn.org.
14. National Comprehensive Cancer Network. Hairy cell leukemia (Version 1.2024). Available at http://www.nccn.org.
15. National Comprehensive Cancer Network. Hematopoietic Cell Transplantation (Version 3.2023). Available at: www.nccn.org.
16. National Comprehensive Cancer Network. Histiocytic Neoplasms (Version 1.2023). Available at: www.nccn.org.
17. National Comprehensive Cancer Network. Hodgkin lymphoma (Version 1.2024). Available at http://www.nccn.org.
18. National Comprehensive Cancer Network. Management of immunotherapy-related toxicities (Version 1.2024). Available at http://www.nccn.org.
19. National Comprehensive Cancer Network. Pediatric Aggressive Mature B-Cell Lymphomas (Version 1.2023). Available at: www.nccn.org.
20. National Comprehensive Cancer Network. Primary Cutaneous Lymphomas (Version 1.2024). Available at: www.nccn.org.
21. National Comprehensive Cancer Network. Waldenstrom macroglobulinemia/ Lymphoplasmacytic lymphoma (Version 2.2024). Available at http://www.nccn.org.
22. Narayanaswami P, et al. International Consensus Guidance for Management of Myasthenia Gravis: 2020 Update. Neurology. 2021;96(3):114-122.
23. Neunert C, Terrell DR, Arnold DM, et al. American Society of Hematology 2019 guidelines for immune thrombocytopenia [published correction appears in Blood Adv. 2020 Jan 28;4(2):252]. Blood Adv. 2019;3(23):3829-3866. doi:10.1182/bloodadvances.2019000966
24. Riabni (rituximab-arrx) [Prescribing Information]. Thousand Oaks, CA: Amgen, Inc.; 6/2022.
25. Rituxan (rituximab) [Prescribing Information]. South San Francisco, CA: Biogen-Idec/ Genentech; 2021.
26. Ruxience (rituximab-pvvr) [Prescribing Information]. New York, NY: Pfizer; 2023.

27. Scott TF, Frohman EM, DeSeze J et al Evidence-based guideline: Clinical evaluation and treatment of transverse myelitis: Report of the Therapeutics and Technology Assessment Subcommittee of the American Academy Neurology. Neurology 2011; 77:2128-2134.
28. Sellner J, Bogglid M, Cante M. et al. EFNS guidelines on diagnosis and management of neuromyelitis optica. Eur J Neur 2010, 17:1019-1032.
29. Trebst C, Jarius S, Berthele A, et al. Update on diagnosis and treatment of neuromyelitis optica. Recommendations of the neuromyelitis optica study group (NEMOS). J Neurol 2014 Jan;261(1):1-16.
30. Truxima (rituximab-abbs) [Prescribing Information]. North Wales, PA: Teva Pharmaceuticals USA, Inc.; 2/2022.
31. Wingerchuk DM, Lennon VA, Pittock SJ, et al. Revised diagnostic criteria for neuromyelitis optica. Neurology 2006; 66:1485-1489.
32. Czernik A, Toosi S, Bystryn JC, et al. Intravenous immunoglobulin in the treatment of autoimmune bullous dermatoses: An update. *Autoimmunity* (2012); 45 (1): 111-118
33. Harman KE, Brown D, Exton LS, et al. British Association of Dermatologists' guidelines for the management of pemphigus vulgaris 2017. *British Journal of Dermatology* (2017); 177: 1170-1201
34. Joly P, Beek NV, Feliciani C, et al. Updated S2K guidelines for the management of bullous pemphigoid initiated by the European Academy of Dermatology and Venereology (EADV). *JEADV* (2020); 34: 1900-1913
35. Joly P, Horvath B, Patsatsi A, et al. Updated S2K guidelines on the management of pemphigus vulgaris and foliaceus initiated by the European Academy of Dermatology and Venereology (EADV). *JEADV* 2020; 34: 1900-1913
36. Borradori L, Beek N, Feliciani C, et al. Updated S2K guidelines for the management of bullous pemphigoid initiated by the European Academy of Dermatology and Venereology (EADV). *JEADV* 2022; 36: 1689-1704

Review History

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Changes from previous policy version:

- New Part B policy

Blue Shield of California Medication Policy to Determine Medical Necessity Reviewed by P&T Committee