**Rituxan (rituximab)**

**Line(s) of Business:**
- HMO; PPO; QUEST Integration
- Medicare Advantage

**Original Effective Date:**
- 10/01/2015

**Current Effective Date:**
- 04/01/2018
- 12/01/2018

**POLICY**

**A. INDICATIONS**

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

**FDA-Approved Indications**

- **Non-Hodgkin’s Lymphoma (NHL)**
  - Rituxan is indicated for the treatment of patients with:
    - Relapsed or refractory, low-grade or follicular, CD20-positive, B-cell NHL as a single agent
    - Previously untreated follicular, CD20-positive, B-cell NHL in combination with first line chemotherapy and, in patients achieving a complete or partial response to Rituxan in combination with chemotherapy, as single-agent maintenance therapy
    - Non-progressing (including stable disease), low-grade, CD20-positive, B-cell NHL, as a single agent after first-line CVP (cyclophosphamide, vincristine, and prednisone) chemotherapy
    - Previously untreated diffuse large B-cell, CD20-positive NHL in combination with cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) or other anthracycline-based chemotherapy regimens

- **Chronic Lymphocytic Leukemia (CLL)**
  - Rituxan is indicated, in combination with fludarabine and cyclophosphamide (FC), for the treatment of patients with previously untreated and previously treated CD20-positive CLL.

- **Rheumatoid Arthritis**
  - Rituxan in combination with methotrexate (MTX) is indicated for the treatment of adult patients with moderately to severely active rheumatoid arthritis who have an inadequate response to one or more tumor necrosis factor (TNF) antagonist therapies.

- **Wegener’s Granulomatosis* (WG) and Microscopic Polyangiitis (MPA)**
  - Rituxan, in combination with glucocorticoids, is indicated for the treatment of adult patients with WG and MPA.
    
    *Also known as granulomatosis with polyangiitis (GPA)

**Compendial Uses**

- Acute lymphoblastic leukemia in combination with chemotherapy
- Central nervous system (CNS) cancers
  - Primary CNS lymphoma
  - Leptomeningeal metastases from lymphomas
• Hodgkin’s lymphoma, nodular lymphocyte-predominant
• Non-Hodgkin’s lymphoma
  o Acquired immunodeficiency syndrome (AIDS)-related B-cell lymphoma
  o Burkitt lymphoma, in combination with chemotherapy
  o Castleman’s disease
  o Diffuse large B-cell lymphoma
  o Hairy cell leukemia, relapsed or refractory
  o Lymphoblastic lymphoma
  o Mantle cell lymphoma
  o Marginal zone lymphomas (gastric/non-gastric MALT, nodal, splenic marginal zone lymphoma)
  o Post-transplant lymphoproliferative disorder (PTLD)
  o Primary cutaneous B-cell lymphoma
  o Small lymphocytic lymphoma (SLL)
• Waldenström’s macroglobulinemia/lymphoplasmacytic lymphoma
• Myasthenia gravis, refractory
• Management of immunotherapy-related toxicities
• Autoimmune hemolytic anemia, refractory
• Immune or idiopathic thrombocytopenic purpura, refractory
• Thrombotic thrombocytopenic purpura, refractory

B. REQUIRED DOCUMENTATION
For all approvable oncologic or hematologic indications, acute lymphoblastic leukemia, central nervous system cancers, Hodgkin’s lymphoma, non-Hodgkin’s lymphoma, and Waldenström’s macroglobulinemia/lymphoplasmacytic lymphoma:
• Initial therapy
  o Testing or analysis confirming CD20 protein on the surface of the B-cell (if applicable)
  o Current oncology or hematology notes, clinical notes (including previous treatment history), and any pertinent pathology reports and/or imaging studies
• Continuation therapy
  o Documentation demonstrating lack of disease progression on therapy (e.g., clinical notes, laboratory tests, and any pertinent pathology reports and/or imaging studies)

C. PRESCRIBER RESTRICTION
For all oncologic or hematologic indications, Rituxan must be recommended by an oncologist or a hematologist.

D. CRITERIA FOR INITIAL APPROVAL
1. Oncologic or Hematologic Indications
   For oncologic or hematologic disorders, with the exception of Autoimmune hemolytic anemia, Immune or idiopathic thrombocytopenic purpura, and Thrombotic thrombocytopenic purpura, the tumor must be CD20-positive as confirmed by testing or analysis to identify the CD20 protein on the surface of the B-cell.

   1.1. Acute lymphoblastic leukemia (ALL)
      Initial authorization of 6 months may be granted for members who are prescribed Rituxan as a component of a chemotherapy regimen.
1.2. **Central nervous system (CNS) cancers**

Initial authorization of 6 months may be granted for members who are prescribed Rituxan for any of the following indications:

a. Primary CNS lymphoma
b. Leptomeningeal metastases from lymphoma

1.3. **Hodgkin’s lymphoma**

Initial authorization of 6 months may be granted for members who are prescribed Rituxan for the treatment of nodular lymphocyte-predominant Hodgkin’s lymphoma.
1.4. **Non-Hodgkin’s lymphoma (NHL)**

a. Initial authorization of 6 months may be granted for members who are prescribed Rituxan for any of the following indications:
   i. Diffuse large B-cell lymphoma
   ii. AIDS-related B-cell lymphoma
   iii. Chronic Lymphocytic Leukemia (CLL) / Small lymphocytic lymphoma (SLL)
   iv. Follicular lymphoma
   v. Hairy cell leukemia, relapsed or refractory
   vi. Lymphoblastic lymphoma
   vii. Mantle cell lymphoma
   viii. Marginal zone lymphoma (nodal, splenic or MALT)
   ix. Post-transplant lymphoproliferative disorder (PTLD)
   x. Primary cutaneous B-cell lymphoma
   xi. Castleman’s disease

b. Initial authorization of 6 months may be granted for members who are prescribed Rituxan as a component of a chemotherapy regimen for the treatment of Burkitt lymphoma.

1.5. **Waldenström’s macroglobulinemia/lymphoplasmacytic lymphoma (LPL)**

Initial authorization of 6 months may be granted for members who are prescribed Rituxan for the treatment of Waldenström’s macroglobulinemia/lymphoplasmacytic lymphoma (LPL).

1.6. **Autoimmune hemolytic anemia**

Initial authorization of 6 months may be granted for members who are prescribed Rituxan for the treatment of autoimmune hemolytic anemia that is refractory to steroids.

1.7. **Immune or Idiopathic thrombocytopenic purpura**

Initial authorization of 6 months may be granted for members who are prescribed Rituxan for the treatment of immune or idiopathic thrombocytopenic purpura that is refractory to steroids or intravenous immunoglobulin (IVIG).

1.8. **Thrombotic thrombocytopenic purpura**

Initial authorization of 6 months may be granted for members who are prescribed Rituxan for the treatment of thrombotic thrombocytopenic purpura that is refractory to plasma exchange or steroids.

2. **Moderately to severely active rheumatoid arthritis (RA)**

Initial authorization of 6 months may be granted to members who meet both of the following criteria:

i. Member has either of the following:
   a) Inadequate response to at least a 3-month trial of a TNF inhibitor (e.g., Cimzia, Enbrel, Humira, Remicade, Simponi, Simponi Aria)
   b) Intolerance or contraindication to a TNF inhibitor

ii. Member is prescribed Rituxan in combination with MTX or has a contraindication or intolerance to MTX.
3. Granulomatosis with polyangiitis (GPA; Wegener’s granulomatosis) and microscopic polyangiitis (MPA)  
Initial authorization of 6 months may be granted to members who are prescribed Rituxan for the treatment of GPA or MPA.

4. Myasthenia gravis  
Initial authorization of 6 months may be granted to members who are prescribed Rituxan for the treatment of myasthenia gravis that is refractory to corticosteroids and/or immunomodulating drugs (eg, azathioprine, IVIG).

5. Immunotherapy-related toxicities  
Initial authorization of 6 months may be granted to members who are prescribed Rituxan for the treatment of immunotherapy-related encephalitis who meet the following criteria:
   i. Viral causes have been excluded
   ii. Member tests positive for autoimmune encephalopathy antibody
   iii. Member has had limited improvement or no improvement on methylprednisolone with or without intravenous immune globulin

RE-AUTHORIZATION/CONTINUATION OF THERAPY
Members who have had Rituxan previously authorized by HMSA/CVS are subject to the continuation criteria below for approval. Members without previous authorization are required to meet criteria for initial authorization in section D. above.

E. CONTINUATION OF THERAPY
1. No previous authorization/precertification:
   All members (including new members and members currently receiving treatment without prior authorization) must meet criteria for initial approval in section D.

2. Reauthorization:
   a. ALL, CNS cancers, Hodgkin’s lymphoma, NHL, and Waldenstrom’s macroglobulinemia/lymphoplasmacytic lymphoma: Oncologic or Hematologic indications: Members who were previously approved for Rituxan by HMSA/CVS may request reauthorizations after their initial approval. Approval for an additional 6 months may be granted if the following documentation shows no progression of disease information is supplied:
      • A current oncology note documenting the patient’s response to treatment showing no progression of disease
      • Current imaging studies and other objective measures showing no progression of disease when compared with previous results
   b. All other indications: Rheumatoid arthritis: Authorization of an additional 12 months may be granted for members requesting authorization for continuation of therapy who are benefiting from Rituxan therapy who are prescribed Rituxan for rheumatoid arthritis and who achieve or maintain positive clinical response to therapy as evidenced by low disease activity or improvement in signs and symptoms of the condition as long as Rituxan, and were previously authorized by HMSA/CVS.
   — Granulomatosis with polyangiitis (Wegener’s granulomatosis):
Authorization of 12 months may be granted for members who are prescribed Rituxan for granulomatosis with polyangitis (Wegener’s granulomatosis) who achieve or maintain positive clinical response to therapy as evidenced by low disease activity or improvement in signs and symptoms of the condition as long as Rituxan was previously authorized by HMSA/CVS.

c.—Microscopic polyangitis:
Authorization of 12 months may be granted for members who are prescribed Rituxan for microscopic polyangitis who achieve or maintain positive clinical response to therapy as evidenced by low disease activity or improvement in signs and symptoms of the condition as long as Rituxan was previously authorized by HMSA/CVS.

c.—Myasthenia gravis:
Authorization of 12 months may be granted for members who are prescribed Rituxan for myasthenia gravis who achieve or maintain positive clinical response to therapy as evidenced by low disease activity or improvement in signs and symptoms of the condition as long as Rituxan was previously authorized by HMSA/CVS.

F. DOSAGE AND ADMINISTRATION
Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

G. ADMINISTRATIVE GUIDELINES
Precertification is required. Please refer to the HMSA medical policy web site for the fax form.

H. IMPORTANT REMINDER
The purpose of this Medical Policy is to provide a guide to coverage. This Medical Policy is not intended to dictate to providers how to practice medicine. Nothing in this Medical Policy is intended to discourage or prohibit providing other medical advice or treatment deemed appropriate by the treating physician.

Benefit determinations are subject to applicable member contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

This Medical Policy has been developed through consideration of the medical necessity criteria under Hawaii’s Patients’ Bill of Rights and Responsibilities Act (Hawaii Revised Statutes §432E-1.4), generally accepted standards of medical practice and review of medical literature and government approval status. HMSA has determined that services not covered under this Medical Policy will not be medically necessary under Hawaii law in most cases. If a treating physician disagrees with HMSA/CVS’s determination as to medical necessity in a given case, the physician may request that CVS/caremarkHMSA reconsider the application of the medical necessity criteria to the case at issue in light of any supporting documentation.

I. REFERENCES


Document History

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<thead>
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<th>Date</th>
<th>Event Description</th>
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<tr>
<td>03/2016</td>
<td>Revised prescriber restriction (added hematologist)</td>
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<tr>
<td>11/2016</td>
<td>Editorial revision (added ‘hematology’ to oncology/hematology sections)</td>
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