I. Medication Description

Rituximab binds specifically to the antigen CD20, a hydrophobic transmembrane protein located on pre-B and mature B lymphocytes. The antigen is also expressed on more than 90% of B-cell NHLs, but is not found on hematopoietic stem cells, pro-B-cells, normal plasma cells, or other normal tissues. CD20 regulates an early step(s) in the activation process for cell cycle initiation and differentiation, and possibly functions as a calcium ion channel. CD20 is not shed from the cell surface and does not internalize upon antibody binding. Free CD20 antigen is not found in the circulation.

B-cells are believed to play a role in the pathogenesis of RA and associated chronic synovitis. In this setting, B-cells may be acting at multiple sites in the autoimmune/inflammatory process, including through production of rheumatoid factor (RF) and other auto-antibodies, antigen presentation, T-cell activation, and/or pro-inflammatory cytokine production. The Fab domain of rituximab binds to the CD20 antigen on B lymphocytes, and the Fc domain recruits immune effector functions to mediate B-cell lysis in vitro. Possible mechanisms of cell lysis include complement-dependent cytotoxicity and antibody-dependent cell-mediated cytotoxicity. The antibody has been shown to induce apoptosis in the DHL-4 human B-cell lymphoma line.

II. Position Statement

Coverage is determined through a prior authorization process with supporting clinical documentation for every request.

III. Policy

Coverage of Rituxan and Rituxan Hycela for oncology indications is available when the following criteria have been met:

- The medication is prescribed by a hematologist/oncologist AND
- The requested use is supported by the National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines (NCCN Guidelines®) and/or NCCN Drugs & Biologics Compendium (NCCN Compendium®) with a recommendation of category level 1 or 2A.

Coverage of Rituxan is also available for the following conditions:

- Autoimmune Hemolytic Anemia (AIHA) that has not responded to previous corticosteroid or other immunosuppressive therapy.
- Evan's Syndrome that has not responded to previous corticosteroid therapy
- Steroid Refractory Chronic Graft vs. Host disease
- Microscopic Polyangiitis (MPA) in adult members in combination with glucocorticoids
• Pemphigus vulgaris, refractory
• Post-transplant lymphoproliferative disorder (PTLD)
• Rheumatoid arthritis (moderate to severe disease):
  o Must be used in combination with methotrexate (MTX) AND
  o Prescribed by a rheumatologist AND
  o Member has tried therapy with at least one non-biologic DMARD with either treatment failure after 12 weeks or intolerable side effects (unless DMARDs are contraindicated) AND
  o Member has received an adequate trial and failed therapy with at least one TNF inhibitor.
• Immune thrombocytopenia/ idiopathic thrombocytopenic purpura (ITP) that has not responded to previous corticosteroid therapy
• Untreated idiopathic thrombocytopenic purpura (ITP) in combination with dexamethasone
• Thrombotic thrombocytopenia purpura
• Wegener’s Granulomatosis (WG) in adult members in combination with glucocorticoids

IV. Quantity Limits

Coverage of Rituxan is available as follows:
• Rheumatoid Arthritis:
  o 10 billable units (1,000mg) per administration
  o No more than 2 administrations every 16 weeks
• Chronic Lymphocytic Leukemia:
  o 13 billable units (1,300mg) per administration
  o Administered every 28 days
• Wegener’s Granulomatosis, Microscopic Polyangiitis, and Autoimmune Hemolytic Anemia:
  o 10 billable units (1,000mg) per administration
  o No more than 4 doses
• All other indications:
  o 10 billable units (1,000mg) per administration
  o No more than once every 7 days

Coverage of Rituxan Hycela is available as follows:
• For all indications:
  o Quantity sufficient to allow dosing in accordance with FDA-approved prescribing information and NCCN guidelines

V. Coverage Duration

• Rheumatoid Arthritis- 1 month. Coverage is renewed after at least 4-6 months have passed from the last course of treatment in situations where re-treatment is necessary to control symptoms.
• Wegener’s Granulomatosis, Microscopic Polyangiitis, and Autoimmune Hemolytic Anemia – 1 month.
• Pemphigus – up to 10 months
• 6 months for all other indications. Coverage may be renewed.
VI. Coverage Renewal Criteria

Coverage can be renewed based upon the following criteria:

- Stabilization of disease or in absence of disease progression **AND**
- Absence of unacceptable toxicity from the drug

VII. Billing/Coding Information

- Rituxan (rituximab) - 100mg/10mL and 500mg/10mL solution for injection
  - J9312: 1 billable unit = 10mg
- Rituxan Hycela (Rituximab/Hyaluronidase Human, Recombinant) - 1,400mg-23,400units/11.7mL and 1,600mg-26,800units/13.4mL solution for injection
  - J9311: 1 billable unit = 10mg

VIII. Summary of Policy Changes

- **3/1/11:**
  - Expanded covered indications section
  - Addition of Dosing/Administration section
  - Addition of Quantity limits section
  - Addition of Coverage Renewal Criteria section
  - Addition of Warnings/Precautions
- **6/1/11:**
  - Addition of more Non-Hodgkin’s Lymphoma ICD9s to autopay grid
  - Addition of GVHD to autopay grid
  - Addition of thrombocytopenic purpura to autopay grid
- **4/2011:** Addition of Wegener’s Granulomatosis and Microscopic Polyangiitis to policy per FDA approval
- **6/15/12:** No changes
- **6/15/13:** Additions:
  - ALL—204.00, 204.01
  - Leptomeningeal metastases—198.4
  - Primary CNS Lymphoma—200.50, 200.51
  - Hodgkin Lymphoma: LPHL—201.40-201.48, V10.72
  - Types of NHL
  - Autopay codes for NHL of 202.40-202.48 and 238.77
- **6/15/14:** updated criteria for WM, ALL, leptomeningeal metastases, PCNS lymphoma, Hodgkin’s lymphoma to mirror current NCCN recommendations; added criteria for coverage in AIHA; clarified pemphigus treatment duration; updated diagnosis codes.
- **7/21/14:** updated NCCN-recommended regimens in LPHL, included coverage for SLL
- **7/1/15:** formulary distinctions made
- **10/1/15:** omission of ICD9 references
<table>
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<tr>
<th>Drug Therapy Guidelines</th>
<th>Rituxan® (rituximab)</th>
<th>Last Review Date: 12/2017</th>
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<tbody>
<tr>
<td>12/15/15: coverage criteria for use in LPHL updated</td>
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<td>9/15/16: policy updated to correspond with current NCCN treatment guidelines</td>
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<td>6/13/17: step therapy criteria added</td>
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<td>1/1/18: coverage criteria updated to allow use as supported by current NCCN guidelines; Rituxan Hycela added; requests for all diagnostic codes will require prior authorization; addendum with diagnostic codes exceptions removed</td>
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<td>4/1/18: updated billing/coding information</td>
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<td>1/3/19: updated billing/coding information</td>
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IX. References


The Plan fully expects that only appropriate and medically necessary services will be rendered. The Plan reserves the right to conduct pre-payment and post-payment reviews to assess the medical appropriateness of the above-referenced therapies.

The preceding policy is a guideline to allow for coverage of the pertinent medication/product, and is not meant to serve as a clinical practice guideline.