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):**
  - Must be used in combination with methotrexate (MTX) **AND**
  - Prescribed by a rheumatologist **AND**
  - 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**
  - 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:**
  - 10 billable units (1,000mg) per administration
  - No more than 2 administrations every 16 weeks
- **Chronic Lymphocytic Leukemia:**
  - 13 billable units (1,300mg) per administration
  - Administered every 28 days
- **Wegener’s Granulomatosis, Microscopic Polyangiitis, and Autoimmune Hemolytic Anemia:**
  - 10 billable units (1,000mg) per administration
  - No more than 4 doses
- **All other indications:**
  - 10 billable units (1,000mg) per administration
  - No more than once every 7 days

Coverage of Rituxan Hycela is available as follows:

- For all indications:
  - 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
  - J9310 – 1 billable unit is 100mg
- **Rituxan Hycela** (Rituximab/Hyaluronidase Human, Recombinant) - 1,400mg-23,400units/11.7mL and 1,600mg-26,800units/13.4mL solution for injection
  - C9467 – 1 billable unit is 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
Drug Therapy Guidelines

Rituxan® (rituximab)

Last Review Date: 12/2017

- 12/15/15: coverage criteria for use in LPHL updated
- 9/15/16: policy updated to correspond with current NCCN treatment guidelines
- 6/13/17: step therapy criteria added
- 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
- 4/1/18: updated billing/coding information

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.