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Drug Policy

Policy:	**201732-CC**	**Initial Effective Date: 07/21/2017**
Code(s):	**HCPCS J9311**	**Annual Review Date: 09/20/2018**
SUBJECT:	Rituxan Hycela™ (rituximab and hyaluronidase human injection for subcutaneous use)	**Last Revised Date: 12/26/2018**

Prior approval is required for some or all procedure codes listed in this Corporate Drug Policy.

Overview

Rituxan Hycela is indicated for treatment of adults with the following indications:

1. follicular lymphoma (FL), as a single agent for relapsed or refractory disease; in previously untreated FL in combination with first-line chemotherapy and, as single-agent maintenance therapy in patients achieving a complete or partial response to Rituxan + chemotherapy; and as a single agent after first-line CVP (cyclophosphamide, vincristine, and prednisone) in non-progressing (including stable disease) FL;
2. diffuse large B-cell lymphoma (DLBCL), in combination with CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) or other anthracycline-based chemotherapy regimens in patients with previously untreated disease; and
3. chronic lymphocytic leukemia (CLL), in combination with FC (fludarabine + cyclophosphamide) for previously treated and previously untreated disease.[1]

Rituxan Hycela is a combination of rituximab and hyaluronidase human. It contains the identical molecular antibody of rituximab available in Rituxan IV, but hyaluronidase has been added to facilitate systemic delivery. Rituxan Hycela should be administered under the care of a healthcare professional with appropriate medical support to manage severe and potentially fatal reactions. The dose of Rituxan Hycela is fixed regardless of the patient's body surface area (BSA); dose reductions are not recommended. When given in combination with chemotherapy, reduce the dose of chemotherapeutic drugs to manage adverse events (AEs). Rituxan Hycela is not indicated for treatment of non-malignant conditions.

Disease Overview

Non-Hodgkin lymphoma (NHL) is a heterogeneous group of lymphoproliferative disorders originating in B-lymphocytes.[2] Major subtypes of NHL diagnosed in the US include DLBCL (33% of NHL cases), CLL/small lymphocytic lymphoma (SLL) [19% of NHL cases], and FL (17% of NHL cases). Cell-surface proteins, including CD20, are highly expressed on these B-cell malignancies.[3] Rituxan Hycela is an anti-CD20 monoclonal antibody that, upon binding to CD20 on B-lymphocytes, depletes B cells by several mechanisms, including direct antibody-dependent cellular toxicity, complement-mediated cell death, and signaling apoptosis.

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Guidelines
Rituxan features prominently in the National Comprehensive Cancer Network (NCCN) guidelines for treatment of B-cell lymphomas and CLL/small lymphocytic lymphoma[2,4] and is included in multiple treatment regimens across the spectrum of FL, DLBCL, and/or CLL. The guidelines for CLL have been updated to recommend Rituxan Hycela (noted as rituximab + hyaluronidase) for its approved indication; however, Rituximab IV (noted as rituximab) features prominently throughout the guidelines.

Safety
There is a higher risk of hypersensitivity and other acute reactions during the first infusion.[1] Therefore, all patients must receive at least one full dose of Rituxan IV, which allows for management by slowing or stopping the IV infusion, before receiving Rituxan Hycela. Patients who are unable to complete one full IV infusion should continue to receive subsequent cycles with Rituxan IV and should not switch to Rituxan Hycela until a full IV dose is successfully administered. Safety is otherwise comparable to Rituxan IV and includes Boxed Warnings regarding severe mucocutaneous reactions, hepatitis B reactivation, and progressive multifocal leukoencephalopathy.

Policy Statement
This policy involves the use of Rituxan Hycela. Prior authorization is recommended for medical benefit coverage. Approval is recommended for those who meet the conditions of coverage in the **Criteria**, **Dosing**, **Initial/Extended Approval**, **Duration of Therapy**, and **Labs/Diagnostics** for the diagnosis provided. The requirement that the patient meet the Criteria for coverage of the requested medication applies to the initial authorization only. **Waste Management** applies for all covered conditions. **Conditions Not Recommended for Coverage** are listed following the recommended authorization criteria and Waste Management section. Requests for uses not listed in this policy will be reviewed for evidence of efficacy and for medical necessity on a case-by-case basis.

Because of the specialized skills required for evaluation and diagnosis of patients treated with Rituxan as well as the monitoring required for adverse events (AEs) and long-term efficacy, initial approval requires Rituxan Hycela to be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals for initial therapy are provided for the initial approval duration noted below; if reauthorization is allowed, a response to therapy is required for continuation of therapy.

Recommended Authorization Criteria

FDA-Approved Indications

1. **Chronic Lymphocytic Leukemia (CLL) or Small Lymphocytic Lymphoma (SLL):**

Criteria: *The patient must meet the following criteria (A, B, AND C)*:
A) The patient has already received at least one full dose of Rituxan IV; AND
B) Rituxan Hycela is administered under the care of a healthcare professional; AND
C) Rituxan Hycela is being prescribed by or in consultation with an oncologist or hematologist.

Dosing in CLL/SLL: *Dosing must meet the following:* 1,600 mg/26,800 units on Day 1 of each cycle, beginning with Cycle 2

Initial Approval/Extended Approval:
Initial Approval: 1 year.

Duration of Therapy in CLL/SLL.[1,11] Duration of treatment is usually 6 cycles, which includes one cycle with Rituxan IV and 5 cycles with Rituxan Hycela.

Labs/Diagnostics. None required.

2. **B-Cell Lymphoma** (e.g., Diffuse Large B-cell Lymphoma [DLBCL], Follicular Lymphoma, Acquired Immune Deficiency [AIDS]-Related B-Cell Lymphoma, Burkitt Lymphoma, Castleman's Disease, Marginal Zone Lymphoma [e.g., extranodal or MALT {gastric or nongastric}, nodal, or splenic marginal zone lymphoma], Primary Mediastinal Large B-Cell Lymphoma, Mantle Cell Lymphoma, Post-Transplant Lymphoproliferative Disorders, Gray Zone Lymphoma).

Criteria: *The patient must meet the following criteria (A, B, AND C)*:
A) The patient has already received at least one full dose of Rituxan IV; AND
B) Rituxan Hycela is administered under the care of a healthcare professional; AND
C) Rituxan Hycela is being prescribed by or in consultation with an oncologist or hematologist.

Dosing in DLBCL: *Dosing must meet both of the following (A and B):*
A) The dose is 1,400 mg/23,400 units; AND
B) The Rituxan Hycela dosing interval is one of the following:
  i. Once weekly; OR
  ii. Day 1 of each cycle (e.g., Day 1 of each 21-day cycle).

Initial Approval/Extended Approval:
Initial Approval: 1 year.

Duration of Therapy in DLBCL. Duration of treatment is usually 6 to 8 cycles, which includes one cycle with Rituxan IV and 5 to 7 cycles with Rituxan Hycela.

Labs/Diagnostics. None required.

3. **Other Cancer-Related Indications. Patients with another indication that is not listed but is cited in the National Comprehensive Cancer Network (NCCN) guidelines as a category 1, 2A, or 2B recommendation. Prescriber will provide specific diagnosis for documentation.** Requests under the medical benefit should be sent to the Medical Director for review on a case-by-case basis.

Waste Management for All Indications.
Dosing is a fixed dose (i.e., 1,400 mg/23,400 units per 11.7 mL and 1,600 mg/26,800 units per 13.4 mL vial). Use the vial size that achieves the required dose.

CONDITIONS NOT RECOMMENDED FOR APPROVAL
Rituxan Hycela has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. Rationale for non-coverage for these specific conditions is provided below. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

1. **Granulomatosis with Polyangiitis (GPA) [Wegener's granulomatosis] or Microscopic Polyangiitis (MPA):** Rituxan IV is indicated for treatment of GPA or MPA.[5] Rituxan Hycela has not been evaluated and does not have established dosing for GPA or MPA.

2. **Rheumatoid Arthritis (RA):** Rituxan IV is indicated for treatment of RA.[5] Rituxan Hycela has not been evaluated and does not have established dosing for RA.

3. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

Documentation Requirements:

The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the drug provided or services performed were not medically necessary, investigational or experimental, not within the scope of benefits afforded to the member and/or a pattern of billing or other practice has been found to be either inappropriate or excessive. Additional documentation supporting medical necessity for the services provided must be made available upon request to the Company.

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Documentation requested may include patient records, test results and/or credentials of the provider ordering or performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.

References

1. Rituxan Hycela™ injection for SC use [prescribing information]. South San Francisco, CA: Biogen and Genentech/Roche; April 2018.
2. The NCCN B-Cell Lymphomas Clinical Practice Guidelines in Oncology (Version 4.2018 – Mary 15, 2018). © 2018 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed September 14, 2018.
3. Dotan E, Aggarwal C, Smith MR. Impact of rituximab (Rituxan) on the treatment of B-cell non-Hodgkin's lymphoma. *P T*. 2010; 35(3): 148–157.
4. The NCCN Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Clinical Practice Guidelines in Oncology (Version 1.2019 – August 9, 2018). © 2018 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed September 14, 2018.
5. Rituxan® intravenous infusion [prescribing information]. South San Fransisco, CA: Genentech, Inc.; April 2016.

FOR MEDICAL BENEFIT COVERAGE REQUESTS:

Prior approval is required for HCPCS Codes J9311

HCPCS Code(s):	
J9311	Injection, rituximab 10 mg and hyaluronidase (effective 1/1/2019)