

**POLICY:** Oncology – Rituxan Hycela™ (rituximab and hyaluronidase human injection for subcutaneous use – Biogen and Genentech/Roche)

**APPROVAL DATE:** 10/16/2019

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## 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 rituximab + 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.

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.<sup>2</sup> 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.<sup>3</sup> 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.

## Guidelines

Rituximab features prominently in the National Comprehensive Cancer Network (NCCN) guidelines for treatment of B-cell lymphomas (version 4.2019 – June 18, 2019) and CLL/small lymphocytic lymphoma (version 1.2020 – August 23, 2019) and is included in multiple treatment regimens across the spectrum of disease. In hairy cell leukemia, NCCN guidelines (version 1.2020 – August 23, 2019) recommend rituximab in multiple regimens for relapsed/refractory disease, including in patients with progressive disease after relapsed/refractory therapy. All of these guidelines have been updated to list Rituxan Hycela (noted as rituximab + hyaluronidase) in most clinical scenarios when the intravenous formulation is recommended, if the patient has received the first full dose with rituximab IV.

## Safety

There is a higher risk of hypersensitivity and other acute reactions during the first infusion.<sup>1</sup> Therefore, all patients must receive at least one full dose of rituximab 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 rituximab IV and includes Boxed Warnings regarding severe mucocutaneous reactions, hepatitis B reactivation, and progressive multifocal leukoencephalopathy.

## POLICY STATEMENT

Prior authorization is recommended for medical benefit coverage of Rituxan Hycela. Approval is recommended for those who meet the conditions of coverage for Criteria and Dosing for the listed indications. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below.

Because of the specialized skills required for evaluation and diagnosis of patients treated with Rituxan Hycela 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.

## RECOMMENDED AUTHORIZATION CRITERIA

### FDA-Approved Indications

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- 1. Chronic Lymphocytic Leukemia (CLL) or Small Lymphocytic Lymphoma (SLL).** Approve for 1 year if the patient meets ALL of the following (A, B, and C):
    - A) The patient has already received at least one full dose of rituximab 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.

**Dosing.** 1,600 mg/26,800 units on Day 1 of each cycle.

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- 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, Primary Cutaneous B-Cell Lymphoma). Approve for 1 year if the patient meets ALL of the following (A, B, and C):
    - A) The patient has already received at least one full dose of rituximab 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.

**Dosing.** Dosing must meet both of the following (A and B):

- A) The dose is 1,400 mg/23,400 units; AND
- B) Doses are separated by at least 7 days.

### Other Uses with Supportive Evidence

3. **Hairy Cell Leukemia.** Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):
- A) The patient has relapsed/refractory hairy cell leukemia; AND
  - B) The patient has already received at least one full dose of rituximab IV; AND
  - C) Rituxan Hycela is administered under the care of a healthcare professional; AND
  - D) The agent is prescribed by or in consultation with an oncologist.

**Dosing.** Approve the following (A and B):

- A) The dose is 1,600 mg/26,800 units or 1,400 mg/23,400 units; AND
- B) Doses are separated by at least 7 days.

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#### 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).** Rituximab IV is indicated for treatment of GPA or MPA.<sup>5</sup> Rituxan Hycela has not been evaluated and does not have established dosing for GPA or MPA.
2. **Pemphigus Vulgaris.** Rituximab IV is indicated for treatment of pemphigus vulgaris.<sup>5</sup> Rituxan Hycela has not been evaluated and does not have established dosing for pemphigus vulgaris.
3. **Rheumatoid Arthritis (RA).** Rituximab IV is indicated for treatment of RA.<sup>5</sup> Rituxan Hycela has not been evaluated and does not have established dosing for RA.
4. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

#### 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 Lymphoma Clinical Practice Guidelines in Oncology (Version 4.2019 – June 18, 2019). © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on September 11, 2019.
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 CLL/SLL Clinical Practice Guidelines in Oncology (Version 1.2020 – August 23, 2019). © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on September 11, 2019.
5. Rituxan® intravenous infusion [prescribing information]. South San Francisco, CA: Genentech, Inc.; April 2019.
6. The NCCN Primary Cutaneous Lymphomas Clinical Practice Guidelines in Oncology (Version 2.2019 – December 17, 2018). © 2018 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on September 9, 2019.
7. The NCCN Hairy Cell Leukemia Clinical Practice Guidelines in Oncology (Version 1.2020 – August 23, 2019). © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on September 11, 2019.

**HISTORY**

Type of Revision	Summary of Changes	Approval Date
New Policy	--	08/30/2017
Annual revision	<p><b>B-Cell Lymphoma:</b> To align with NCCN recommendations, combine criteria for B-Cell Lymphomas and list follicular lymphoma and diffuse large B-cell lymphoma among examples of B-Cell Lymphomas (previously FL and DLBCL were listed separately in the policy).</p> <ul style="list-style-type: none"> <li>• Change approval duration to 1 year (previously was 6 months).</li> </ul> <p><b>Chronic Lymphocytic Leukemia (CLL):</b> To align with NCCN guidelines, add SLL as an approvable condition with the same criteria as CLL.</p> <ul style="list-style-type: none"> <li>• Remove criterion that required Rituxan Hycela to be administered in combination with fludarabine and cyclophosphamide.</li> <li>• Change approval duration to 1 year (previously was 6 months).</li> </ul> <p><b>Patient has been Started on Rituxan Hycela:</b> Due to the change in approval duration, remove criteria for patients currently started on therapy (all reviews, including those who are already taking, will go through criteria and dosing in the policy).</p> <p><b>Other Cancer-Related Indications:</b> To align with the Rituxan Hycela PA policy, remove criteria which directs for case-by-case review for other cancer-related indications.</p>	09/19/2018
Annual revision	<p><b>CLL/SLL:</b> To align with other policies that approve for this condition, remove hematologist from the specialists who are required to prescribe or be consulted prior to approval.</p> <p><b>B-Cell Lymphoma:</b> Primary cutaneous B-cell lymphoma was added to the list of examples of a B-cell lymphoma. To align with other policies that approve for this condition, remove hematologist from the specialists who are required to prescribe or be consulted prior to approval. In the dosing section, update to specify the shortest treatment interval that is approvable.</p> <p><b>Hairy Cell Leukemia:</b> This indication was added to the policy as an Other Use with Supportive Evidence. Criteria approve for 1 year if the patient has relapsed or refractory disease and if the agent is prescribed by or in consultation with an oncologist. Similar to other indications, criteria also require that the patient has already received at least one dose of rituximab IV and that Rituxan Hycela will be administered under the care of a healthcare professional.</p> <p><b>Conditions Not Recommended for Approval:</b> Pemphigus vulgaris was added as a condition not recommended for coverage.</p>	10/16/2019