

UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Oncology (Injectable – CD20-Directed Antibody) – Rituxan Hycela Utilization Management Medical Policy

- Rituxan Hycela® (rituximab and hyaluronidase human subcutaneous injection – Biogen and Genentech/Roche)

REVIEW DATE: 02/05/2025

OVERVIEW

Rituxan Hycela, a combination of rituximab and hyaluronidase human, is indicated for treatment of adults with the following indications:¹

- **Diffuse large B-cell lymphoma**, in combination with CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) or other anthracycline-based chemotherapy regimens in patients with previously untreated disease.
- **Chronic lymphocytic leukemia**, in combination with FC (fludarabine + cyclophosphamide) for previously treated and previously untreated disease.
- **Follicular lymphoma**, as a single agent for relapsed or refractory disease; in previously untreated disease in combination with first-line chemotherapy; 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) disease.

Rituxan Hycela contains the identical molecular antibody of rituximab available in Rituxan intravenous, 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; dose reductions are not recommended. When given in combination with chemotherapy, reduce the dose of chemotherapeutic drugs to manage adverse events. Rituxan Hycela is not indicated for treatment of non-malignant conditions. Additionally, treatment should only be initiated after receiving at least one full dose of a rituximab product by intravenous infusion.

Guidelines

Rituximab features prominently in the National Comprehensive Cancer Network (NCCN) guidelines for multiple conditions. The following guidelines from NCCN 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 intravenous.

- **B-cell Lymphomas:** In the guidelines (version 1.2025 – December 20, 2024), rituximab is included in multiple treatment regimens across the spectrum of disease.² For primary cutaneous B-cell lymphomas (version 1.2025 – November 11, 2024), rituximab is a treatment option for patients with primary cutaneous B-cell lymphoma.⁷
- **Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma:** Rituximab features prominently in the guidelines (version 1.2025 – October 01, 2024) and is included in multiple treatment regimens across the spectrum of disease.³
- **Hairy Cell Leukemia:** Guidelines (version 1.2025 – September 26, 2024) recommend rituximab in multiple regimens for initial therapy and relapsed/refractory disease, including in patients with progressive disease after relapsed/refractory therapy (all category 2A).⁴

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- **Hodgkin Lymphoma:** Guidelines (version 1.2025 – December 24, 2024) recommend rituximab ± chemotherapy and/or radiation (depending on the clinical presentation) in the first-line setting for nodular lymphocyte-predominant disease.⁸ Rituximab is also used for relapsed/refractory disease and for maintenance.
- **Waldenstrom Macroglobulinemia/Lymphoplasmacytic Lymphoma:** Guidelines (version 2.2025 – December 18, 2024) include rituximab in regimens across the spectrum of disease (primary therapy, previously treated disease, and maintenance).⁵

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 rituximab intravenous, which allows for management by slowing or stopping the infusion, before receiving Rituxan Hycela. Patients who are unable to complete one full intravenous infusion should continue to receive subsequent cycles with Rituxan intravenous and should not switch to Rituxan Hycela until a full intravenous dose is successfully administered. Safety is otherwise comparable to rituximab intravenous.

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of Rituxan Hycela. Approval is recommended for those who meet the **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. In cases where the approval is authorized in months, 1 month is equal to 30 days. 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 and long-term efficacy, approval requires Rituxan Hycela to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Rituxan Hycela is recommended in those who meet one of the following criteria:

FDA-Approved Indications

1. **B-Cell Lymphoma.** Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):
Note: Examples of B-cell lymphomas include diffuse large B-cell lymphoma [DLBCL], follicular lymphoma, human immunodeficiency virus [HIV]-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, high grade B-cell lymphoma, histologic transformation of indolent lymphoma to DLBCL, post-transplant lymphoproliferative disorders, gray zone lymphoma, primary cutaneous B-cell lymphoma.
 - A) Patient is ≥ 18 years of age; AND
 - B) Patient has already received at least one full dose of rituximab intravenous; AND
 - C) Rituxan Hycela is administered under the care of a healthcare professional; AND
 - D) The medication is being prescribed by or in consultation with an oncologist.

Dosing. Approve the following dosing regimen (A and B):

- A) The dose is 1,400 mg of rituximab and 23,400 units of hyaluronidase given subcutaneously; AND

B) Doses are separated by at least 7 days.

2. **Chronic Lymphocytic Leukemia or Small Lymphocytic Lymphoma.** Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):

- A) Patient is ≥ 18 years of age; AND
- B) Patient has already received at least one full dose of rituximab intravenous; AND
- C) Rituxan Hycela is administered under the care of a healthcare professional; AND
- D) The medication is being prescribed by or in consultation with an oncologist.

Dosing. Approve 1,600 mg of rituximab and 26,800 units of hyaluronidase given subcutaneously on Day 1 of each cycle.

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) Patient is ≥ 18 years of age; AND
- B) Patient has already received at least one full dose of rituximab intravenous; AND
- C) Rituxan Hycela is administered under the care of a healthcare professional; AND
- D) The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve the following dosing regimen (A and B):

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

4. **Hodgkin Lymphoma.** Approve for 1 year if the patient meets ALL of the following (A, B, C, D, and E):

- A) Patient is ≥ 18 years of age; AND
- B) Patient has nodular lymphocyte-predominant disease; AND
- C) Patient has already received at least one full dose of rituximab intravenous; AND
- D) Rituxan Hycela is administered under the care of a healthcare professional; AND
- E) The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve the following dosing regimen (A and B):

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

5. **Waldenstrom's Macroglobulinemia/Lymphoplasmacytic Lymphoma.** Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):

- A) Patient is ≥ 18 years of age; AND
- B) Patient has already received at least one full dose of rituximab intravenous; AND
- C) Rituxan Hycela is administered under the care of a healthcare professional; AND
- D) The medication is being prescribed by or in consultation with an oncologist.

Dosing. Approve the following dosing regimen (A and B):

- A) The dose is 1,600 mg of rituximab and 26,800 units of hyaluronidase or 1,400 mg of rituximab and 23,400 units of hyaluronidase given subcutaneously; AND
- B) The patient receives a maximum of four doses per 28-day treatment cycle.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Rituxan Hycela is not recommended in the following situations:

- 1. **Granulomatosis with Polyangiitis (Wegener's granulomatosis) or Microscopic Polyangiitis.** Rituximab intravenous is indicated for treatment of these indications.⁶ Rituxan Hycela has not been evaluated and does not have established dosing in this setting.
- 2. **Pemphigus Vulgaris.** Rituximab intravenous is indicated for treatment of pemphigus vulgaris.⁶ Rituxan Hycela has not been evaluated and does not have established dosing for pemphigus vulgaris.
- 3. **Rheumatoid Arthritis.** Rituximab intravenous is indicated for treatment of rheumatoid arthritis.⁶ Rituxan Hycela has not been evaluated and does not have established dosing for rheumatoid arthritis.
- 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[®] subcutaneous injection [prescribing information]. South San Francisco, CA: Biogen and Genentech/Roche; June 2021.
- 2. The NCCN B-Cell Lymphoma Clinical Practice Guidelines in Oncology (version 1.2025 – December 20, 2024). © 2024 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on January 28, 2025.
- 3. The NCCN Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Clinical Practice Guidelines in Oncology (version 1.2025 – October 01, 2024). © 2024 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on January 28, 2025.
- 4. The NCCN Hairy Cell Leukemia Clinical Practice Guidelines in Oncology (version 1.2025 – September 26, 2024). © 2024 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on January 28, 2025.
- 5. The NCCN Waldenstrom's Macroglobulinemia/Lymphoplasmacytic Lymphoma Clinical Practice Guidelines in Oncology (version 2.2025 – December 18, 2024). © 2024 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on January 28, 2025.
- 6. Rituxan[®] intravenous infusion [prescribing information]. South San Francisco, CA: Biogen and Genentech/Roche; June 2021.
- 7. The NCCN Primary Cutaneous Lymphomas Clinical Practice Guidelines in Oncology (version 1.2025 – November 11, 2024). © 2024 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on January 28, 2025.
- 8. The NCCN Hodgkin Lymphoma Clinical Practice Guidelines in Oncology (version 1.2025 – December 24, 2024). © 2024 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on January 28, 2025.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes. Updated note for B-cell lymphoma to include histologic transformation of indolent lymphomas to diffuse large B-cell lymphoma and high-grade B-cell lymphoma as examples.	01/10/2024
Annual Revision	Hairy Cell Leukemia: Removed criteria requiring the patient to have relapsed/refractory disease since rituximab is included as part of a preferred treatment regimen for initial therapy per NCCN guideline recommendations.	02/05/2025
Update	04/21/2025: The policy name was changed from “Oncology (Injectable) – Rituxan Hycela Medical Policy” to “Oncology (Injectable – CD20-Directed Antibody) – Rituxan Hycela UM Medical Policy”.	N/A

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