Utilization Review Policy 209A

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

EFFECTIVE DATE: 7/1/2021
LAST REVISION DATE: 05/07/2025

COVERAGE CRITERIA FOR: UCare Medical Assistance and Exchange Plans Only (PMAP, Connect, MSC+, MnCare, all Individual and Family Plans)

OVERVIEW

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

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.
2. **Chronic lymphocytic leukemia**, in combination with FC (fludarabine + cyclophosphamide) for previously treated and previously untreated disease.
3. **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]
- **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.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Rituxan Hycela is recommended for requests meeting both the preferred product step therapy requirements and indication requirements.

Preferred Product(s): Truxima, Ruxience, Riabni
Non-Preferred Products(s): Rituxan Hycela

Step Therapy Requirements:

Authorization for a non-preferred biologic product or biosimilar will be granted if the patient has had *any <u>one</u> of the listed issues below (A, B, C, or D) with all preferred product(s)*. *Chart notes documenting* the issue must be provided at time of request:

A. Allergic reaction to a specific inactive ingredient in all preferred biologic products or biosimilars OR

B. Adverse reaction to a specific inactive ingredient in all preferred biologic products or biosimilars OR

C. Therapeutic success while taking a non-preferred biologic product or biosimilar and therapeutic failure during an adequate trial of all preferred biologic products or biosimilars which allowed sufficient time for a positive treatment outcome documented by medical chart notes OR

D. The patient has a diagnosis not included in the FDA-approved indications of all preferred products, but is included in the FDA-approved indications of the non-preferred product

Please note:

- Factors such as patient or prescriber preference or healthcare facility's or pharmacy's inability or unwillingness to order or stock the preferred product(s) will not be considered
- Common side effects to all products and infusion-related reactions are not considered documented allergic reactions to a preferred product as they would be expected with the innovator and biosimilar products
- Continuation of therapy overrides are not available to bypass required trial(s) of preferred biosimilar or biologic reference product
- Generally, an adequate trial of a drug is considered to be three months or longer in order to allow time for efficacy to be established

FDA-Approved Indications

1. B-Cell Lymphoma. Approve for 1 year if the patient meets ALL of the following (A, B, C, <u>and</u> D):
<u>Note</u>: 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.

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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 5.2022 – July 12, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on December 13, 2022.
3. The NCCN Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Clinical Practice Guidelines in Oncology (version 1.2023 – August 30, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on August 30, 2022.
4. The NCCN Hairy Cell Leukemia Clinical Practice Guidelines in Oncology (version 1.2023 – August 30, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on December 13, 2022.

5. The NCCN Waldenstrom's Macroglobulinemia/Lymphoplasmacytic Lymphoma Clinical Practice Guidelines in Oncology (version 1.2023 – July 6, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on December 13, 2022.
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 2.2022 – June 8, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on December 13, 2022.
8. The NCCN Hodgkin Lymphoma Clinical Practice Guidelines in Oncology (version 2.2023 – November 8, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on December 13, 2022.

HISTORY

Type of Revision	Summary of Changes*	Date
New Policy	--	09/19/2018
Policy revision	Reviewed and revised original policy created 07/11/2018 in accordance with Local Coverage Article A52452 and Oncology – Rituxan Hycela Care Continuum Utilization Review Policy.	10/16/2019
Policy revision	Completion of 2019 monthly monitoring process in accordance with Local Coverage Determination L33394, Local Coverage Article A52452, and Oncology – Rituxan Hycela Care Continuum Utilization Review Policy.	11/27/2019
Policy revision	Non-clinical update to policy to add the statement "This policy incorporates Medicare coverage guidance as set forth in National Coverage Determinations (NCDs) and Local Coverage Determinations (LCDs), as well as in companion policy articles and other guidance applicable to the relevant service areas. These documents are cited in the References section of this policy. In some cases, this guidance includes specific lists of HCPCS and ICD-10 codes to help inform the coverage determination process. The Articles that include specific lists for billing and coding purposes will be included in the Reference section of this policy. However, to the extent that this policy cites such lists of HCPCS and ICD-10 codes, they should be used for reference purposes only. The presence of a specific HCPCS or ICD-10 code in a chart or companion article to an LCD is not by itself sufficient to approve coverage. Similarly, the absence of such a code does not necessarily mean that the applicable condition or diagnosis is excluded from coverage."	1/30/2020
Policy revision	*Non-clinical update to policy to add the statement "Note: Conditions for coverage outlined in this Medicare Advantage Medical Policy may be less restrictive than those found in applicable National Coverage Determinations, Local Coverage Determinations and/or Local Coverage Articles. Examples of situations where this clinical policy may be less restrictive include, but are not limited to, coverage of additional indications supported by CMS-approved compendia and the exclusion from this policy of additional coverage criteria requirements outlined in applicable National Coverage Determinations, Local Coverage Determinations and/or Local Coverage Articles." *Updated references *Non-clinical formatting changes	06/15/2020
Policy revision	**Chronic Lymphocytic Leukemia or Small Lymphocytic Lymphoma:** Dosing was clarified to state that the dose is given subcutaneously. **B-Cell Lymphoma:** Dosing was clarified to state that the dose is given subcutaneously. **Hairy Cell Leukemia:** Dosing was clarified to state that the dose is given subcutaneously. **Waldenstrom's Macroglobulinemia/Lymphoplasmacytic Lymphoma:** This indication was added to the policy as an Other Use with Supportive Evidence. Criteria approve for 1 year if patient has already received at least one dose of rituximab intravenous.	11/04/2020
Policy revision	Addition of biosimilar step therapy requirements	4/12/2021

Annual Revision	No criteria changes.	12/01/2021
Annual UCare Revision	Verified Local Coverage Article A52452 and Oncology – Rituxan Hycela and identified no significant updates that require updates to current policy	1/11/2022
Annual Revision	B-Cell Lymphoma: A requirement that the patient is ≥ 18 years of age was added. Chronic Lymphocytic Leukemia or Small Lymphocytic Lymphoma: A requirement that the patient is ≥ 18 years of age was added. Hairy Cell Leukemia: A requirement that the patient is ≥ 18 years of age was added. Hodgkin Lymphoma: This condition was added to the policy under Other Uses with Supportive Evidence. Waldenstrom's Macroglobulinemia/Lymphoplasmacytic Lymphoma: A requirement that the patient is ≥ 18 years of age was added.	12/21/2022
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
UCare P&T Review	Policy reviewed and approved by UCare P&T committee. Annual review process	09/16/2024
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
UCare Update	Updated step therapy criteria to require clinical need for non-preferred product over the preferred products including chart note documentation to support the need for a non-preferred product.	05/07/2025