Rituximab and Hyaluronidase Human (Rituxan Hycela®)

Requires Step Therapy *See* "Step Therapy Requirements for Provider Administered Specialty Medications" Document at: https://www.bcbst.com/docs/providers/Comm_BC_PAD_Step_Therapy_Guide.pdf

IMPORTANT REMINDER

We develop Medical Policies to provide guidance to Members and Providers. This Medical Policy relates only to the services or supplies described in it. The existence of a Medical Policy is not an authorization, certification, explanation of benefits or a contract for the service (or supply) that is referenced in the Medical Policy. For a determination of the benefits that a Member is entitled to receive under his or her health plan, the Member's health plan must be reviewed. If there is a conflict between the medical policy and a health plan or government program (e.g., TennCare), the express terms of the health plan or government program will govern.

POLICY

INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

- Adult patients with follicular lymphoma (FL):
  - Relapsed or refractory, follicular lymphoma as a single agent
  - Previously untreated follicular lymphoma in combination with first line chemotherapy and, in patients achieving a complete or partial response to rituximab in combination with chemotherapy, as single-agent maintenance therapy
  - Non-progressing (including stable disease), follicular lymphoma as a single agent after first-line cyclophosphamide, vincristine, and prednisone (CVP) chemotherapy
- Adult patients with previously untreated diffuse large B-cell lymphoma (DLBCL) in combination with cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) or other anthracycline-based chemotherapy regimens
- Adult patients with previously untreated and previously treated chronic lymphocytic leukemia (CLL), in combination with fludarabine and cyclophosphamide (FC)

Limitations of Use

- Initiate treatment with Rituxan Hycela only after patients have received at least one full dose of a rituximab product by intravenous infusion.
- Rituxan Hycela is not indicated for the treatment of non-malignant conditions.

Compendial Uses

- B-cell lymphomas:
  - Burkitt lymphoma
  - Castleman disease (CD)
  - Diffuse large B-cell lymphoma (DLBCL)
  - Follicular lymphoma
  - High grade B-cell lymphoma (including high-grade B-cell lymphoma with translocations of MYC and BCL2 and/or BCL6 [double/triple hit lymphoma], high-grade B-cell lymphoma, not otherwise specified)
  - Histologic transformation of indolent lymphomas to diffuse large B-cell lymphoma
  - Human immunodeficiency virus (HIV) related B-cell lymphomas

    - Marginal zone lymphomas
        - Nodal marginal zone lymphoma
        - Splenic marginal zone lymphoma
        - Extranodal marginal zone lymphoma (gastric and non-gastric mucosa associated lymphoid tissue [MALT] lymphoma)
    - Mantle cell lymphoma
    - Post-transplant lymphoproliferative disorder (PTLD)
- Hairy cell leukemia
- Primary cutaneous B-cell lymphoma (e.g., cutaneous marginal zone lymphoma or cutaneous follicle center lymphomas)
- Chronic lymphocytic leukemia (CLL)/Small lymphocytic lymphoma (SLL)
- Histologic transformation (Richter transformation) of CLL/SLL to diffuse large B-cell lymphoma
- Waldenström macroglobulinemia/lymphoplasmacytic lymphoma (LPL)/Bing-Neel syndrome
- Hodgkin lymphoma, nodular lymphocyte-predominant
- Kaposi sarcoma-associated herpesvirus (KSHV)-associated inflammatory cytokine syndrome (KICS)

All other indications are considered experimental/investigational and are not medically necessary.

DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: Documentation of laboratory report confirming CD20 protein on the surface of the B-cell

COVERAGE CRITERIA

Prior to initiating therapy, all members must receive at least one full dose of a rituximab product by intravenous infusion without experiencing severe adverse reactions.

B-cell Lymphomas

Authorization of 12 months may be granted for treatment of any of the following CD20-positive oncologic indications:

- Burkitt lymphoma
- Castleman disease (CD)
- Diffuse large B-cell lymphoma (DLBCL)
- Follicular lymphoma
- High grade B-cell lymphoma (including high-grade B-cell lymphoma with translocations of MYC and BCL2 and/or BCL6 [double/triple hit lymphoma], high-grade B-cell lymphoma, not otherwise specified)
- Histologic transformation of indolent lymphomas to diffuse large B-cell lymphoma
- HIV related B-cell lymphomas
- Marginal zone lymphomas
    - Nodal marginal zone lymphoma
    - Splenic marginal zone lymphoma
    - Extranodal marginal zone lymphoma (gastric and non-gastric MALT lymphoma)
- Mantle cell lymphoma
- Post-transplant lymphoproliferative disorder (PTLD)

Hairy Cell Leukemia (HCL)

Authorization of 12 months may be granted for treatment of CD20-positive HCL.

Primary Cutaneous B-cell Lymphoma

Authorization of 12 months may be granted for treatment of CD20-positive primary cutaneous B-cell lymphoma (e.g., cutaneous marginal zone lymphoma or cutaneous follicle center lymphomas).

Chronic Lymphocytic Leukemia (CLL)/Small Lymphocytic Lymphoma (SLL)

Authorization of 12 months may be granted for treatment of CD20-positive CLL or SLL and histologic transformation (Richter transformation) of CLL/SLL to diffuse large B-cell lymphoma.

Waldenström Macroglobulinemia/Lymphoplasmacytic Lymphoma (LPL)/Bing-Neel Syndrome

Authorization of 12 months may be granted for treatment of CD20 positive Waldenström macroglobulinemia/LPL/Bing-Neel syndrome.

Hodgkin Lymphoma, Nodular Lymphocyte-Predominant

Authorization of 12 months may be granted for treatment of CD20-positive Hodgkin lymphoma, nodular lymphocyte-predominant.

Kaposi Sarcoma-Associated Herpesvirus (KSHV)-Associated Inflammatory Cytokine Syndrome (KICS)

Authorization of 12 months may be granted for treatment of CD20-positive KSHV-associated inflammatory cytokine syndrome.

CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in the coverage criteria section when there is no evidence of unacceptable toxicity.

MEDICATION QUANTITY LIMITS

Drug Name	Diagnosis	Maximum Dosing Regimen
Rituxan Hycela (Rituximab-Hyaluronidase Human)	B-Cell Lymphomas: Castleman's Disease	Route of Administration: Subcutaneous 1400/23,400mg-units (frequency and cycle length varies by regimen; should not be more frequent than once a week)
Rituxan Hycela (Rituximab-Hyaluronidase Human)	B-Cell Lymphomas: Diffuse Large B-Cell Lymphoma, High-Grade B-Cell Lymphomas,	Route of Administration: Subcutaneous 1400/23,400mg-units (frequency and cycle length varies by regimen; should not be more frequent than once a week)
Rituxan Hycela (Rituximab-Hyaluronidase Human)	B-Cell Lymphomas: Follicular Lymphoma	Route of Administration: Subcutaneous 1400/23,400mg-units (frequency and cycle length varies by regimen; should not be more frequent than once a week)
Rituxan Hycela (Rituximab-Hyaluronidase Human)	B-Cell Lymphomas: Histological Transformation of Indolent Lymphomas to Diffuse Large B-cell Lymphoma	Route of Administration: Subcutaneous 1400/23,400mg-units (frequency and cycle length varies by regimen; should not be more frequent than every 14 days)

Rituxan Hycela (Rituximab-Hyaluronidase Human)	B-Cell Lymphomas: Mantle Cell Lymphoma	Route of Administration: Subcutaneous 1400/23,400mg-units (frequency and cycle length varies by regimen; should not be more frequent than once a week)
Rituxan Hycela (Rituximab-Hyaluronidase Human)	B-Cell Lymphomas: Marginal Zone Lymphomas [Nodal Marginal Zone Lymphoma, Gastric Mucosa Associated Lymphoid Tissue (GMALT) Lymphoma, Nongastric MALT Lymphoma, Splenic Marginal Zone Lymphoma]	Route of Administration: Subcutaneous 1400/23,400mg-units (frequency and cycle length varies by regimen; should not be more frequent than once a week)
Rituxan Hycela (Rituximab-Hyaluronidase Human)	B-Cell Lymphomas: Post-Transplant Lymphoproliferative Disorders	Route of Administration: Subcutaneous 1400/23,400mg-units (frequency and cycle length varies by regimen; should not be more frequent than once a week)
Rituxan Hycela (Rituximab-Hyaluronidase Human)	Chronic Lymphocytic Leukemia (CLL)/ Small Lymphocytic Lymphoma (SLL)	Route of Administration: Subcutaneous 1600/26,800mg-units (frequency and cycle length varies by regimen; should not be more frequent than once a week)
Rituxan Hycela (Rituximab-Hyaluronidase Human)	Hairy Cell Leukemia	Route of Administration: Subcutaneous 1400/23,400mg-units (frequency and cycle length varies by regimen; should not be more frequent than once a week)
Rituxan Hycela (Rituximab-Hyaluronidase Human)	Hodgkin Lymphoma - Nodular Lymphocyte-Predominant	Route of Administration: Subcutaneous ≥18 Year(s) 1400/23,400mg-units (frequency and cycle length varies by regimen; should not be more frequent than once a week)
Rituxan Hycela (Rituximab-Hyaluronidase Human)	Primary Cutaneous B-Cell Lymphomas	Route of Administration: Subcutaneous 1400/23,400mg-units on Days 8, 15, and 22 of a 28-day cycle for 1 cycle
Rituxan Hycela (Rituximab-Hyaluronidase Human)	Waldenström Macroglobulinemia/ Lymphoplasmacytic Lymphoma	Route of Administration: Subcutaneous 1400/23,400mg-units (frequency and cycle length varies by regimen; should not be more frequent than once a week)

APPLICABLE TENNESSEE STATE MANDATE REQUIREMENTS

BlueCross BlueShield of Tennessee's Medical Policy complies with Tennessee Code Annotated Section 56-7-2352 regarding coverage of off-label indications of Food and Drug Administration (FDA) approved drugs when the off-label use is recognized in one of the statutorily recognized standard reference compendia or in the published peer-reviewed medical literature.

ADDITIONAL INFORMATION

For appropriate chemotherapy regimens, dosage information, contraindications, precautions, warnings, and monitoring information, please refer to one of the standard reference compendia (e.g., the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) published by the National Comprehensive Cancer Network®, Drugdex Evaluations of Micromedex Solutions at Truven Health, or The American Hospital Formulary Service Drug Information).

This document has been classified as public information

REFERENCES

1. Rituxan Hycela [package insert]. South San Francisco, CA: Genentech, Inc.; June 2021.
2. The NCCN Drugs & Biologics Compendium® © 2026 National Comprehensive Cancer Network, Inc. Available at: https://www.nccn.org. Accessed April 6, 2026.

EFFECTIVE DATE 1/30/2027

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