BlueCross BlueShield
Federal Employee Program
Federal Employee Program®
750 9th St NW
Washington, D.C. 20001
202.942.1000
Fax 202.942.1125

5.21.096

Section:	Prescription Drugs	**Effective Date:**	April 1, 2024
Subsection:	Antineoplastic Agents	**Original Policy Date:**	July 14, 2017
Subject:	Rituxan Hycela	**Page:**	1 of 6

Last Review Date: March 8, 2024

Rituxan Hycela

Description

Rituxan Hycela (rituximab and hyaluronidase human)

Background
Rituxan Hycela (rituximab and hyaluronidase human) is a monoclonal antibody that is manufactured through biotechnology methods rather than by the body's own immune system. The drug works by reducing the number of specific immune cells in the blood, known as B-cells. The drug binds to a particular protein, the CD20 antigen, on the surface of normal and malignant B-cells, making it easier for the patient's immune system to attack the cancer cell as if it were a foreign pathogen. Rituxan Hycela is used in the treatment of chronic lymphocytic leukemia (CLL), a slowly progressing blood and bone marrow cancer that arises from a group of white blood cells known as B-cells, in the treatment of CD20 positive, Non-Hodgkin's Lymphoma (NHL), which is a type of cancer that occurs in B-cells (1).

Regulatory Status
FDA-approved indications: Rituxan Hycela is a combination of rituximab, a CD20-directed cytolytic antibody, and hyaluronidase human, an endoglycosidase, indicated for the treatment of adult patients with: (1)

1. Follicular Lymphoma (FL)
    a. Relapsed or refractory, follicular lymphoma as a single agent
    b. 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

c. Non-progressing (including stable disease), follicular lymphoma as a single agent after first-line cyclophosphamide, vincristine, and prednisone (CVP) chemotherapy

2. Diffuse Large B-cell Lymphoma (DLBCL)
    a. Previously untreated diffuse large B-cell lymphoma in combination with cyclophosphamide, doxorubicin, vincristine, prednisone (CHOP) or other anthracycline-based chemotherapy regimens
3. Chronic Lymphocytic Leukemia (CLL)
    a. Previously untreated and previously treated 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 (1).

Rituxan Hycela has several boxed warnings regarding severe mucocutaneous reactions, Hepatitis B virus (HBV) reactivation can occur, in some cases resulting in fulminant hepatitis, hepatic failure, and progressive multifocal leukoencephalopathy (PML) resulting in death (1).

Acute renal failure, hyperkalemia, hypocalcemia, hyperuricemia, or hyperphosphatemia from tumor lysis, some fatal, can occur. Patients at high risk for tumor lysis syndrome should be administered aggressive intravenous hydration, anti-hyperuricemic agents, and their renal function should be monitored (1).

Serious, including fatal, bacterial, fungal, and new or reactivated viral infections can occur during and following the completion of Rituxan Hycela-based therapy. Discontinue Rituxan Hycela for serious infections and institute appropriate anti-infective therapy (1).

The safety of immunization with live viral vaccines following Rituxan Hycela therapy has not been studied and vaccination with live virus vaccines is not recommended (1).

In patients with lymphoid malignancies, during treatment with Rituxan Hycela monotherapy, obtain complete blood counts (CBC) and platelet counts prior to each Rituxan Hycela course. During treatment with Rituxan Hycela and chemotherapy, obtain CBC and platelet counts at weekly to monthly intervals and more frequently in patients who develop cytopenias (1).

The safety and effectiveness of Rituxan Hycela is patients less than 18 years of age have not been established (1).

Related policies
Arzerra, Gazyva, Rituximab

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Rituxan Hycela may be considered **medically necessary** if the conditions indicated below are met.

Rituxan Hycela may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 18 years of age or older

Diagnoses

Patient must have **ONE** of the following:

1. Follicular lymphoma with **ONE** of the following:
    a. Relapsed or refractory
    b. In combination with first line chemotherapy
    c. Non-progressing after first-line cyclophosphamide, vincristine, and prednisone (CVP) chemotherapy

2. Diffuse large B-cell lymphoma
    a. In combination with cyclophosphamide, doxorubicin, vincristine, prednisone (CHOP) or other anthracycline-based chemotherapy regimens

3. Chronic Lymphocytic Leukemia (CLL)
    a. In combination with fludarabine and cyclophosphamide (FC)

AND ALL of the following:

a. Patient has received at least one full dose of a rituximab product by intravenous infusion
b. **NOT** given concurrently with live vaccines (non-live vaccines should be administered at 4 weeks prior to a course of Rituxan Hycela)
c. If the patient has a history of Hepatitis B (HBV) infection:
    i. Prescriber agrees to monitor for HBV reactivation
d. **NO** severe active infections
e. Prescriber agrees to monitor for signs of progressive multifocal leukoencephalopathy (PML) or severe mucocutaneous reactions

Prior – Approval *Renewal* Requirements

Age 18 years of age or older

Diagnoses

Patient must have **ONE** of the following:

1. Follicular lymphoma
2. Diffuse large B-cell lymphoma
3. Chronic Lymphocytic Leukemia (CLL)

AND ALL of the following:

a. **NO** disease progression or unacceptable toxicity
b. **NOT** given concurrently with live vaccines (non-live vaccines should be administered at 4 weeks prior to a course of Rituxan Hycela)
c. If the patient has a history of Hepatitis B (HBV) infection:
    i. Prescriber agrees to monitor for HBV reactivation
d. **NO** severe active infections
e. Prescriber agrees to monitor for signs of progressive multifocal leukoencephalopathy (PML) or severe mucocutaneous reactions

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Duration 12 months

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary

Rituxan Hycela is a monoclonal antibody that is manufactured through biotechnology methods rather than by the human body's own immune system. The drug works by greatly reducing the number of specific immune cells in the blood, known as B-cells. The drug binds to a particular protein, the CD20 antigen, on the surface of normal and malignant B-cells, making it easier for the patient's immune system to attack the cancer cell as if it were a foreign pathogen. Rituxan Hycela is therefore used to treat diseases which are characterized by excessive numbers of B cells, overactive B cells, or dysfunctional B cells. This includes non-Hodgkin lymphoma (NHL), chronic lymphocytic leukemia (CLL), rheumatoid arthritis (RA), microscopic polyangiitis (MPA), and granulomatosis with polyangiitis (1).

Prior authorization is required to ensure the safe, clinically appropriate, and cost-effective use of Rituxan Hycela (rituximab) while maintaining optimal therapeutic outcomes.

References

1. Rituxan Hycela [package insert]. South San Francisco, CA: Genentech Inc.; June 2021.
2. NCCN Drugs & Biologics Compendium® Rituximab and hyaluronidase human 2024. National Comprehensive Cancer Network, Inc. Accessed on January 22, 2024.

Policy History

Date	Action
July 2017	Addition to PA
September 2017	Annual review
June 2018	Annual editorial review and reference update
March 2019	Annual review and reference update
June 2019	Annual review
March 2020	Annual review and reference update
June 2020	Annual review

December 2020	Annual review and reference update. Added requirement to t/f the preferred products
February 2021	Added Riabni as a preferred product
March 2021	Annual editorial review
June 2021	Annual review and reference update
December 2021	Annual review and reference update
January 2022	Clarified medical exception requirement by adding “if adjudicated through the pharmacy benefit”
March 2022	Annual review and reference update
March 2023	Annual review and reference update. Changed policy number to 5.21.096
December 2023	Annual review and reference update. Per FEP, removed from MedEx program
March 2024	Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 8, 2024 and is effective on April 1, 2024.