Medical Drug Clinical Criteria

Subject:	Rituximab Agents for Oncologic Indications		
Document #:	CC-0167	**Publish Date:**	~~09/23/2024~~10/01/2025
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Overview

This document addresses step therapy for oncologic indications of rituximab products. Please refer to the following r This document addresses step therapy for oncologic indications of rituximab products. Please refer to the following related clinical criteria for additional information

- CC-0075 Rituximab Agents for Non-Oncologic Indications
- Rituxan Hycela (rituximab and hyaluronidase)

Rituxan and Biosimilar Products for Oncologic Indications

The reference product Rituxan (rituximab) is FDA approved for the treatment of CD20-positive Non-hodgkin's lymphomas (NHL) including relapsed/refractory low-grade or follicular NHL, previously untreated follicular lymphoma, non-progressing low-grade NHL, and previously untreated diffuse large B-cell lymphoma. NCCN defines low-grade lymphomas as follicular lymphoma and marginal zone lymphoma which includes Malt lymphomas and nodal/splenic type. Rituxan is also FDA approved to treat chronic lymphocytic leukemia (CLL) in combination with fludarabine and cyclophosphamide and for pediatric patients aged 6 months and older with previously untreated, advanced stage, CD20-positive diffuse large B-cell Lymphoma (DLBCL), Burkitt lymphoma (BL), Burkitt-like lymphoma (BLL), or mature B-cell acute leukemia (B-AL) in combination with chemotherapy. Three biosimilars to Rituxan, Truxima (rituximab-abbs), Ruxience (rituximab-pvvr), and Riabni (rituximab-arrx) have been approved by the FDA.

Rituxan, Truxima, Ruxience, and Riabni have black box warnings for fatal infusion reactions, severe mucocutaneous reactions, hepatitis B virus (HBV) reactivation, and progressive multifocal leukoencephalopathy (PML). Rituximab administration can result in serious, including fatal, infusion reactions and deaths within 24 hours of infusion have occurred, most in association with the first infusion. Monitor individuals closely and discontinue rituximab infusion for severe reactions and provide medical treatment for grade 3 or 4 reactions. Severe, including fatal, mucocutaneous reactions can occur. HBV reactivation can occur and in some cases resulting in fulminant hepatitis, hepatic failure, and death. Screen all individuals for HBV infection before treatment initiation and monitor during and after treatment with rituximab. Discontinue rituximab and concomitant medications in the event of HBV reactivation. PML, including fatal PML, can occur.

Clinical Criteria

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Rituxan (rituximab); Truxima (rituximab-abbs); Ruxience (rituximab-pvvr); Riabni (rituximab-arrx)

Requests for Rituxan (rituximab), Truxima (rituximab-abbs), Riabni (rituximab-arrx) or Ruxience (rituximab-pvvr) may be approved for oncologic indications.

Step Therapy

Summary of FDA-approved and Off-label Oncologic Indications for Rituximab Products

	Rituxan (rituximab)	Truxima (rituximab-abbs)	Ruxience (rituximab-pvvr)	Riabni (rituximab-arrx)
B-Cell Follicular Lymphoma	X	X	X	X
Extranodal Marginal Zone Lymphoma [Gastric/nongastric ~~malt~~MALT Lymphoma]	X/NCCN*	X/NCCN*	X/NCCN*	X/NCCN*
Nodal/Splenic Marginal Zone Lymphoma	X/NCCN*	X/NCCN*	X/NCCN*	X/NCCN*
Histologic transformation of Indolent lymphoma to DLBCL	Y	Y	Y	Y
Post-transplant lymphoproliferative disorders	Y	Y	Y	Y
Castleman's disease	Y	Y	Y	Y
Mantle Cell lymphoma	Y	Y	Y	Y
DLBCL	X	X	X	X
High-Grade B-Cell lymphomas	Y	Y	Y	Y
Burkitt Lymphoma	X	Y	Y	Y
HIV-related B-cell Lymphomas	Y	Y	Y	Y
Chronic Lymphocytic Leukemia/ Small Lymphocytic Lymphoma	X	X	X	X
Primary Cutaneous B-Cell Lymphomas	Y	Y	Y	Y
Pediatric Aggressive Mature B-Cell Lymphomas	X	Y	Y	Y
Acute lymphoblastic Leukemia	Y	Y	Y	Y
Primary CNS Lymphoma	Y	Y	Y	Y
Leptomeningeal Metastases	Y	Y	Y	Y
Hairy Cell Leukemia	Y	Y	Y	Y
Hematopoietic Cell Transplantation	Y	Y	Y	Y
Histiocytic Neoplasms	Y	Y	Y	Y
Hodgkin Lymphoma	Y	Y	Y	Y
Waldenstrom Macroglobulinemia/ Lymphoplasmacytic Lymphoma	Y	Y	Y	Y

X= FDA approved use; Y= Off-label use.
**NCCN defines low grade non-hodgkins lymphomas as MALT lymphoma and marginal zone lymphoma*

Note: When a rituximab agent is deemed approvable based on the clinical criteria above, the benefit plan may have additional criteria requiring the use of a preferred[1] agent or agents.

Rituximab Reference and Biosimilar Agents for Oncologic Indications Step Therapy

A list of the preferred rituximab agents is available here.

Requests for a non-preferred rituximab agent for an oncologic indication may be approved when the following criteria are met:

I. Individual has had a trial of and has an allergy or severe intolerance to an inactive ingredient in one preferred agent which interferes with the individual's ability to use the product, and the same allergy/severe intolerance is not expected with the non-preferred product.

~~I. Individual has had a trial and intolerance to one preferred[1] agent; **OR**~~

~~II. Individual is currently stabilized on the requested non-preferred rituximab agent.~~

[1]Preferred, as used herein, refers to agents that were deemed to be clinically comparable to other agents in the same class or disease category but are preferred based upon clinical evidence and cost effectiveness.

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

HCPCS

J9312	Injection, rituximab, 10 mg [Rituxan]
Q5115	Injection, rituximab-abbs, biosimilar, (Truxima), 10 mg
Q5119	Injection, rituximab-pvvr, biosimilar, (RUXIENCE), 10 mg
Q5123	Injection, rituximab-arrx, biosimilar, (3iabni), 10 mg [RIABNI™]

ICD-10 Diagnosis

B20	Human immunodeficiency virus [HIV] disease
C79.32	Secondary malignant neoplasm of cerebral meninges
C81.00-C84.99	Various Lymphoma diagnosis
C85.10-C85.19~~C85.20-C85.29~~	Unspecified B-cell lymphoma~~Mediastinal (thymic) large B-cell lymphoma~~
~~C88.0~~	~~Waldenström macroglobulinemia~~
~~C91.00-C91.52~~	~~Lymphoid Leukemias~~
C85.20-C85.29	Mediastinal (thymic) large B-cell lymphoma
C85.80-C85.89	Other specified types of non-Hodgkin lymphoma
C88.00	Waldenström macroglobulinemia not having achieved remission
C88.40	Extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue [MALT-lymphoma] not having achieved remission
C91.0-C91.02	Acute lymphoblastic leukemia [ALL]
C91.10-C91.12	Chronic lymphocytic leukemia of B-cell type
C91.40-C91.42	Hairy cell leukemia
D47.Z1	Post-transplant lymphoproliferative disorder (PTLD)
D47.Z2	Castleman's Disease
D76.3	Other histiocytosis syndromes
D89.811	Chronic graft-versus-host disease
D89.812	Acute on chronic graft-versus-host disease
D89.813	Graft-versus-host disease, unspecified
T86.09	Other complications of bone marrow transplant
Z94.81	Bone marrow transplant status
Z94.84	Stem cells transplant status

Document History

Revised: 08/15/2025
Document History:

- 08/15/2025 – Annual Review: Remove step therapy override for individuals stable on non-preferred agent; update step therapy language for consistency with other documents. Update to step therapy tables to remove obsolete line of business. Coding Reviewed: Removed ICD-10-CM C88.0. Removed C91.30-C91.32 and C91.50-C91.52 from range C91.00-C91.52 and updated descriptions. Added ICD-10-CM B20, C79.32, C85.10-C85.19, C85.80-C85.89, C88.00, C88.40, Z94.84.

- 08/15/2025 – Annual Review: Remove step therapy override for individuals stable on non-preferred agent; update step therapy language for consistency with other documents. Coding Reviewed: Removed ICD-10-CM C88.0. Removed C91.30-C91.32 and C91.50-C91.52 from range C91.00-C91.52 and updated descriptions. Added ICD-10-CM B20, C79.32, C85.10-C85.19, C85.80-C85.89, C88.00, C88.40, Z94.84.
- 08/16/2024 – Annual Review: Update indication table. No criteria changes. Coding Reviewed: Added ICD-10-CM C85.20-C85.29, D47.Z1, D76.3, D89.811, D89.812, D89.813, T86.09, Z94.81.
- 08/18/2023 – Annual Review: Update indication table. No criteria changes. Coding Reviewed: No changes.
- 05/15/2023 – Step therapy table updates.
- 03/27/2023 – Step therapy table updates.
- 01/25/2023 – Step therapy table updates.
- 08/19/2022 – Annual Review: Update indication table. Step therapy table updates. Coding reviewed: No changes.
- 07/25/2022 – Step therapy table updates.
- 04/25/2022 – Step therapy table updates.
- 03/28/2022 – Step therapy table updates.
- 11/19/2021 – Select Review: Administrative update to clarify that oncologic uses may be approved; update document title. Coding Reviewed: Extended code ranges C81.00-C84.99, C91.00-C91.52.
- 11/19/2021 – Select Review: Administrative update to clarify that oncologic uses may be approved; update document title. Step therapy table updates.
- 11/01/2021 – Step therapy table updates.
- 08/20/2021 – Annual Review: Update indication table; clarify that oncologic uses may be approved. Coding reviewed: Removed HCPCS J9310, Added HCPCS J9312.
- 02/19/2021 – Select Review: Add new biosimilar agent Riabni to step therapy; update indication table. Coding Reviewed: Added HPCS J3590, J9999, C9399. All diagnosis pend for Riabni. Step Therapy table updates. Effective 7/1/2021 Added Q5123. Removed J9999, J3590, C9399. Removed all diagnosis pend for Riabni.
- 12/21/2020 – Add step therapy for Medicaid line of business.
- 08/21/2020 – Annual Review: No changes. Coding Review: Removed J3490, J9311. Added HCPCS Q5119
- 08/16/2019 – Select Review: Add step therapy for non-preferred reference and biosimilar rituximab products in oncologic indications. Coding Reviewed: Added HCPCS codes J9310, J9311, Q5115, J3490. ICD-10 codes: C81.0-84.10, C91.0-C91.5, D47.Z2, C88.0

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Commercial Medical Benefit

Effective Date	Preferred Agents	Non-Preferred Agents
02/01/2022	Rituxan Riabni	Ruxience Truxima
~~04/01/2022 CalPERS~~ ~~For members 18 years and older, step therapy criteria applies to new starts only (defined as no use of Rituxan in the last 12 months)~~	~~Riabni~~ ~~Ruxience~~ ~~Truxima~~	~~Rituxan~~

Medicaid Medical Benefit

Effective Date	Preferred Agents	Non-Preferred Agents
04/15/2022: MD, NJ, NV, SC, VA, WI, WNY 05/01/2022: IA 05/15/2022: IN, GA, TN 06/15/2022: AR, CA 08/01/2022: LA 09/15/2022: KY 02/01/2023: OH 04/01/2023: DC	Riabni	Rituxan Ruxience Truxima

Medicare Medical Benefit

Effective Date	Preferred Agents	Non-Preferred Agents
02/01/2022	Rituxan Riabni	Ruxience Truxima