Medical Drug Clinical Criteria

Subject:	Rituximab Agents for Oncologic Indications		
Document #:	CC-0167	**Publish Date:**	09/23/2024
Status:	Revised	**Last Review Date:**	08/16/2024

Table of Contents

Overview | Coding | References

Clinical criteria | Document history

Overview

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.

Biosimilar products must be highly similar to the reference product and there must be no clinically meaningful differences between the biological product and the reference product in terms of the safety, purity, and potency of the product. Biosimilars must utilize the same mechanism of action (MOA), route of administration, dosage form and strength as the reference product; and the indications proposed must have been previously approved for the reference product. The potential exists for a biosimilar product to be approved for one or more indications for which the reference product is licensed based on extrapolation of data intended to demonstrate biosimilarity in one indication. Sufficient scientific justification for extrapolating data is necessary for FDA approval. Factors and issues that should be considered for extrapolation include the MOA for each indication, the pharmacokinetics, bio-distribution, and immunogenicity of the product in different patient populations, and differences in expected toxicities in each indication and patient population.

Truxima was originally granted FDA approval in November of 2018 for the treatment of relapsed/refractory low grade or follicular NHL, previously untreated follicular NHL, and non-progressing low-grade NHL. Based on the totality of submitted data, the FDA concluded that Truxima is highly similar to Rituxan, there are no clinically meaningful differences between Truxima and Rituxan, and that there is justification to support licensure for the proposed indications. Clinical review of Truxima included 2 clinical studies that compared Truxima with Rituxan in the oncology setting. Both were randomized, double-blinded, parallel-group studies that enrolled subjects with either advanced follicular lymphoma or low tumor burden follicular lymphoma. Demonstration of biosimilarity was also based on a third study, a randomized, controlled, double-blind, 3-arm study of Truxima, US-Rituxan, and EU-approve MabThera in patients with rheumatoid arthritis (RA). In May of 2019, FDA granted Truxima approval for previously untreated DLBCL and previously untreated CLL. Ruxience and Riabni were granted FDA approval for all the same oncologic indications as the reference product at the time. Approval for Ruxience was, in part, based on a phase 3, randomized double-blind study of Ruxience versus MabThera in patients with low tumor burden follicular lymphoma (NCT02213263). Ruxience has also been studied in rheumatoid arthritis (Cohen 2018). Riabni was studied in two randomized, double-blind studies with Rituxan as a comparator. Riabni demonstrated no difference in overall response rate in follicular lymphoma (Niederwieser 2020) and no difference in disease activity score change for

rheumatoid arthritis (Burmester 2020). After approval of Truxima, Ruxience, and Riabni, Rituxan received an additional oncologic indication 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. NCCN guidelines indicate that FDA-approved biosimilars are an appropriate substitute for rituximab in all recommended uses.

Rituximab products are used in defined treatment periods when used in oncologic indications. The package insert recommends that rituximab be used up to 2 years where it is indicated as maintenance therapy. As treatment periods are definite, NCCN notes that the biosimilar may be substituted for the reference product at the initiation of a course of treatment. Additionally, no biosimilar rituximab agent is approved as interchangeable, so the patient should remain on the same product that was used to initiate treatment during a single course of therapy. At this time, there is insufficient evidence for efficacy and safety of switching between the reference and biosimilar product in the treatment of oncologic indications.

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)
Follicular Lymphoma	X	X	X	X
Gastric/nongastric 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 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

C81.00-C84.99	Various Lymphoma diagnosis
C85.20-C85.29	Mediastinal (thymic) large B-cell lymphoma
C88.0	Waldenström macroglobulinemia
C91.00-C91.52	Lymphoid Leukemias
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

Document History

Revised: 08/16/2024
Document History:

- 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

References

1. Burmester G, Drescher E, Hrycaj P, Chien D, Pan Z, Cohen S. Efficacy and safety results from a randomized double-blind study comparing proposed biosimilar ABP 798 with rituximab reference product in subjects with moderate-to-severe rheumatoid arthritis [published correction appears in Clin Rheumatol. 2020 Sep 23;:]. Clin Rheumatol. 2020;39(11):3341-3352.
2. Cohen SB, Burgos-Vargas R, Emery P, Jin B, Cronenberger C, Vázquez-Abad MD. Extension study of PF-05280586, a potential rituximab biosimilar, versus rituximab in subjects with active rheumatoid arthritis. Arthritis Care Res. 2018;70(11):1598–1606. doi: 10.1002/acr.23586.
3. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm. Accessed: July 5, 2024.
4. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
5. Kim WS, Buske C, Ogura M, et al. Efficacy, pharmacokinetics, and safety of the biosimilar CT-P10 compared with rituximab in patients with previously untreated advanced-stage follicular lymphoma: a randomized, double-blind, parallel-group, non-inferiority phase 3 trial. Lancet Haematol 2017;4:e362-e373.
6. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2024; Updated periodically.
7. NCCN Clinical Practice Guidelines in Oncology™. © 2024 National Comprehensive Cancer Network, Inc. For additional information visit the NCCN website: http://www.nccn.org/index.asp.

8. Niederwieser D, Hamm C, Cobb P, et al. Efficacy and Safety of ABP 798: Results from the JASMINE Trial in Patients with Follicular Lymphoma in Comparison with Rituximab Reference Product [published correction appears in Target Oncol. 2020 Dec;15(6):807]. Target Oncol. 2020;15(5):599-611.
9. Ogura M, Sancho JM, Cho SG, et al. Efficacy, pharmacokinetics, and safety of the biosimilar CT-P10 in comparison with rituximab in patients with previously untreated low-tumor-burden follicular lymphoma: a randomized, double-blind, parallel-group, phase 3 trial. Lancet Haematol 2018;5:e534-e553.

Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.

CC-0167 Rituximab Agents for Oncologic Indications Step Therapy

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