Evolent Clinical Guideline 3046 for Rituximab Products

Guideline Number:	Applicable Codes	
Evolent_CG_3046		
"Evolent" refers to Evolent Health LLC and Evolent Specialty Services, Inc.		
© 2011 - 2026 Evolent. All rights Reserved.		
Original Date:	**Last Revised Date:**	**Implementation Date:**
July 2011	March 2026	March 2026

TABLE OF CONTENTS

STATEMENT **2**
PURPOSE 2
INDICATIONS **2**
CD-20 POSITIVE B-CELL NON-HODGKIN'S LYMPHOMAS (NHL) AND ACUTE LYMPHOBLASTIC LEUKEMIA (B-ALL) 2
CHRONIC LYMPHOCYTIC LEUKEMIA (CLL)/SMALL LYMPHOCYTIC LYMPHOMA (SLL) 3
HODGKIN'S LYMPHOMA - NODULAR LYMPHOCYTE PREDOMINANT CD-20 POSITIVE HODGKIN'S LYMPHOMA 3
IDIOPATHIC THROMBOCYTOPENIC PURPURA (ITP) 3
WALDENSTROM MACROGLOBULINEMIA/LYMPHOPLASMACYTIC LYMPHOMA 4
CONTRAINDICATIONS/WARNINGS **4**
EXCLUSION CRITERIA **4**
CODING AND STANDARDS **5**
CODES 5
APPLICABLE LINES OF BUSINESS 6
POLICY HISTORY **6**
LEGAL AND COMPLIANCE **6**
GUIDELINE APPROVAL 6
Committee *6*
DISCLAIMER 6
REFERENCES **7**

STATEMENT

Purpose

To define and describe the accepted indications for Rituximab Products [Rituxan (rituximab), Truxima (rituximab-abbs), Ruxience (rituximab-pvvr), Riabni (rituximab-arrx), Rituxan Hycela (rituximab and hyaluronidase)] usage in the treatment of cancer, including FDA approved indications, and off-label indications.

Evolent is responsible for processing all medication requests from network ordering providers. Medications not authorized by Evolent may be deemed as not approvable and therefore not reimbursable.

The use of this drug must be supported by one of the following: FDA approved product labeling, CMS-approved compendia, National Comprehensive Cancer Network (NCCN), American Society of Clinical Oncology (ASCO) clinical guidelines, or peer-reviewed literature that meets the requirements of the CMS Medicare Benefit Policy Manual Chapter 15.

INDICATIONS

Continuation requests for a not-approvable medication shall be exempt from this Evolent policy provided

- The member has not experienced disease progression on the requested medication AND
- The requested medication was used within the last year without a lapse of more than 30 days of having an active authorization AND
- Additional medication(s) are not being added to the continuation request.

CD-20 positive B-Cell Non-Hodgkin's Lymphomas (NHL) and Acute Lymphoblastic Leukemia (B-ALL)

- The member is an adult or pediatric member greater than or equal to 6 months of age who has CD20 positive B-cell NHL (e.g., follicular, diffuse large B-cell, Mantle Cell Lymphoma, pediatric aggressive mature B-Cell Lymphomas) or B-ALL, and rituximab/rituximab biosimilar may be used as a single agent or in combination with chemotherapy for ANY of the following:
    - Initial therapy (for use in combination with chemotherapy only) OR
    - Treatment of relapsed or refractory disease OR
    - Maintenance therapy:
        - For up to two years for Indolent B-Cell Lymphomas (Follicular B Cell Lymphoma and all subtypes of Marginal Zone Lymphoma).
        - For up to disease progression or intolerable toxicity for Mantle Cell Lymphoma.
    - In members with DLBLC or High-Grade B-Cell Lymphoma (HGBL): Use of R-polatuzumab-CHP (rituximab + polatuzumab + cyclophosphamide + doxorubicin + prednisone) as first line/initial treatment for an International Prognostic Index

(IPI) score of 2 or greater.

- Rituximab/rituximab biosimilar may be used in combination with Revlimid (lenalidomide) and Adcetris (brentuximab vedotin) in adult members with relapsed or refractory large B-cell lymphoma (LBCL), including diffuse large B-cell lymphoma (DLBCL) not otherwise specified (NOS), DLBCL arising from indolent lymphoma, or high-grade B-cell lymphoma (HGBL), after two or more lines of systemic therapy who are ineligible for autologous hematopoietic stem cell transplantation (auto-HSCT) or CAR T-cell therapy.
- NOTE: The following regimens are not supported by Evolent Policy due to a lack of Level 1 Evidence (randomized clinical trials and/or meta-analyses) to show superior outcomes/lower toxicity compared to alternative agents/regimens, including but not limited to regimens at **Evolent Pathways**.
  - In relapsed/refractory DLBCL: Gemcitabine + vinorelbine +/- rituximab (any rituximab product)
  - Maintenance for DLBCL: single agent rituximab (any rituximab product)
  - As initial therapy for Marginal Zone Lymphoma: lenalidomide + rituximab (any rituximab product)
  - As second line or subsequent therapy for Mantle Cell Lymphoma: Ibrutinib + lenalidomide + rituximab (any rituximab product); venetoclax + rituximab (any rituximab product).

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

- Rituximab/rituximab biosimilar may be used for first or subsequent line of therapy:
  - In combination with chemotherapy OR
  - As maintenance therapy for up to 2 years
- NOTE: The following regimens are not supported by Evolent Policy due to the lack of Level 1 Evidence (randomized clinical trial and/or meta-analyses) to show superior outcomes compared to alternative agents/regimens, including but not limited to regimens at **Evolent Pathways**.
  - Initial therapy: ibrutinib + rituximab (any rituximab product)
  - Subsequent therapy: lenalidomide +/- rituximab (any rituximab product).

Hodgkin’s Lymphoma - Nodular Lymphocyte Predominant CD-20 positive Hodgkin’s Lymphoma

- The member has nodular lymphocyte predominant Hodgkin’s Lymphoma and rituximab/rituximab biosimilar may be used as a single agent or in combination with chemotherapy for initial or subsequent therapy OR
- Rituximab/rituximab biosimilar may be used for maintenance therapy for up to 2 years.

Idiopathic Thrombocytopenic Purpura (ITP)

- The member has acute ITP and rituximab/rituximab biosimilar may be used as a single agent AND the following:

- The member has ITP that is refractory to corticosteroids AND
- The platelet count is less than 30 x 10^9/L OR
- There are other clinical indications for therapy.

Waldenstrom Macroglobulinemia/Lymphoplasmacytic Lymphoma

- The member has Waldenstrom Macroglobulinemia/Lymphoplasmacytic Lymphoma and rituximab/rituximab biosimilar may be used in combination with chemotherapy and/or a BTK inhibitor (e.g., ibrutinib + rituximab) as primary therapy or as therapy for relapsed/refractory disease.

CONTRAINDICATIONS/WARNINGS

- Contraindications
  - None
- US Boxed Warning
  - Rituximab administration can result in serious, including fatal, infusion-related reactions. Deaths within 24 hours of rituximab infusion have occurred. Approximately 80% of fatal infusion-related reactions occurred in association with the first infusion. Monitor patients closely. Discontinue rituximab infusion for severe reactions and provide medical treatment for grade 3 or 4 infusion-related reactions.
  - Severe, including fatal, mucocutaneous reactions can occur in patients receiving rituximab products.
  - Hepatitis B virus (HBV) reactivation can occur in patients treated with rituximab products, in some cases resulting in fulminant hepatitis, hepatic failure, and death. Screen all patients for HBV infection before treatment initiation, and monitor patients during and after treatment with rituximab. Discontinue rituximab and concomitant medications in the event of HBV reactivation.
  - Progressive multifocal leukoencephalopathy (PML), including fatal PML, can occur in patients receiving rituximab products.

EXCLUSION CRITERIA

- Use of any Rituximab product (Rituxan, Rituxan Hycela, Truxima, Ruxience, Riabni) as maintenance therapy after primary treatment of Diffuse Large B-Cell Lymphoma (DLBCL).
- Treatment exceeds the maximum months duration limit of 2 years when used in combination with Venclexta (venetoclax) for the treatment of CLL.
- Dosing exceeds single dose limit of rituximab products 500 mg/m² (CLL) and 375 mg/m^2 (NHL); Rituxan Hycela 1600 mg (CLL) and 1400 mg (NHL).
- Investigational use of Rituximab Products (Rituxan, Rituxan Hycela, Truxima, Ruxience, Riabni) with an off-label indication that is not sufficient in evidence or is not

generally accepted by the medical community. Sufficient evidence that is not recommended by CMS recognized compendia or acceptable peer reviewed literature is defined as any of the following:

- Whether the clinical characteristics of the patient and the cancer are adequately represented in the published evidence.
- Whether the administered chemotherapy/biologic therapy/immune therapy/targeted therapy/other oncologic therapy regimen is adequately represented in the published evidence.
- Whether the reported study outcomes represent clinically meaningful outcomes experienced by patients. Generally, the definitions of Clinically Meaningful outcomes are those recommended by ASCO, e.g., Hazard Ratio of less than 0.80 and the recommended survival benefit for OS and PFS should be at least 3 months.
- Whether the experimental design, considering the drugs and conditions under investigation, is appropriate to address the investigative question. (For example, in some clinical studies, it may be unnecessary or not feasible to use randomization, double blind trials, placebos, or crossover).
- That non-randomized clinical trials with a significant number of subjects may be a basis for supportive clinical evidence for determining accepted uses of drugs.
- That case reports are generally considered uncontrolled and anecdotal information and do not provide adequate supportive clinical evidence for determining accepted uses of drugs.
- That abstracts (including meeting abstracts) without the full article from the approved peer-reviewed journals lack supporting clinical evidence for determining accepted uses of drugs.

CODING AND STANDARDS

Codes

- J9311 - Injection, rituximab 10 mg and hyaluronidase
- J9312 - Injection, rituximab, 10 mg
- Q5115 - Injection, rituximab-abbs, biosimilar, (truxima), 10 mg
- Q5119 - Injection, rituximab-pvvr, biosimilar, (ruxience), 10 mg
- Q5123 - Injection, rituximab-arrx, biosimilar, (riabni), 10 mg

Applicable Lines of Business

☐	CHIP (Children's Health Insurance Program)
☒	Commercial
☒	Exchange/Marketplace
☒	Medicaid
☐	Medicare Advantage

POLICY HISTORY

Date	Summary
March 2026	• Updated contraindications/warnings section • Updated references
March 2025	• Converted to new Evolent guideline template • This guideline replaces UM ONC_1132 Rituximab Products • Added new indication • Updated references
June 2024	• Updated NCH verbiage to Evolent

LEGAL AND COMPLIANCE

Guideline Approval

Committee

Reviewed / Approved by Evolent Specialty Services Clinical Guideline Review Committee

Disclaimer

Evolent Clinical Guidelines do not constitute medical advice. Treating health care professionals are solely responsible for diagnosis, treatment, and medical advice. Evolent uses Clinical Guidelines in accordance with its contractual obligations to provide utilization management. Coverage for services varies for individual members according to the terms of their health care coverage or government program. Individual members' health care coverage may not utilize some Evolent Clinical Guidelines. Evolent clinical guidelines contain guidance that requires prior authorization and service limitations. A list of procedure codes, services or drugs may not be all inclusive and does not imply that a service or drug is

a covered or non-covered service or drug. Evolent reserves the right to review and update this Clinical Guideline in its sole discretion. Notice of any changes shall be provided as required by applicable provider agreements and laws or regulations. Members should contact their Plan customer service representative for specific coverage information.

REFERENCES

1. Kim JA, et al. Brentuximab vedotin in combination with lenalidomide and rituximab in patients with relapsed/refractory diffuse large B-cell lymphoma: Results from the phase 3 ECHELON-3 study. *Journal of Clinical Oncology*. 2024 June 5; 42(17). https://doi.org/10.1200/JCO.2024.42.17_suppl.LBA7005.
2. Tilly H, et al. Polatuzumab Vedotin in Previously Untreated Diffuse Large B-Cell Lymphoma. *N Engl J Med*. 2022 Jan 27;386(4):351-363. doi: 10.1056/NEJMoa2115304.
3. Rozental A, et al. The role of maintenance therapy in patients with diffuse large B cell lymphoma: A systematic review and meta-analysis. *Hematol Oncol*. 2019 Feb;37(1):27-34. doi: 10.1002/hon.2561.
4. Leonard JP, et al; AUGMENT Trial Investigators. AUGMENT: A Phase III Study of Lenalidomide Plus Rituximab Versus Placebo Plus Rituximab in Relapsed or Refractory Indolent Lymphoma. *J Clin Oncol*. 2019 May 10;37(14):1188-1199. doi: 10.1200/JCO.19.00010.
5. Riabni prescribing information. Amgen, Inc. Thousand Oaks, CA 2025.
6. Rituxan Hycela prescribing information. Genentech, Inc. South San Francisco, CA 2021.
7. Truxima prescribing information. CELLTRION, Inc. Republic of Korea 2025.
8. Rituxan prescribing information. Genentech, Inc. South San Francisco, CA 2021.
9. Ruxience prescribing information. Pfizer Inc. New York, NY 2025.
10. Clinical Pharmacology Elsevier Gold Standard 2026.
11. Micromedex® Healthcare Series: Micromedex Drugdex Ann Arbor, Michigan 2026.
12. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium 2026.
13. AHFS Drug Information. American Society of Health-Systems Pharmacists or Wolters Kluwer Lexi-Drugs. Bethesda, MD 2026.
14. Ellis LM, et al. American Society of Clinical Oncology perspective: Raising the bar for clinical trials by defining clinically meaningful outcomes. *J Clin Oncol*. 2014 Apr 20;32(12):1277-80.
15. Medicare Benefit Policy Manual Chapter 15 Covered Medical and Other Health Services: https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/bp102c15.pdf.
16. Current and Resolved Drug Shortages and Discontinuations Reported to the FDA: http://www.accessdata.fda.gov/scripts/drugshortages/default.cfm.