LifeWise
Health Plan of Washington

MEDICAL POLICY – 2.03.502

Monoclonal Antibodies for the Treatment of Lymphoma

BCBSA Ref. Policy: 5.01.24

Effective Date:	**Jan. 1, 2027***
Last Revised:	Sep. 8, 2026
Replaces:	N/A

*This policy has been revised. Click here to view the current version.

RELATED MEDICAL POLICIES:

5.01.549	Off-Label Use of Drugs and Biologic Agents
5.01.550	Pharmacotherapy of Arthropathies
5.01.556	Rituximab: Non-oncologic and Miscellaneous Uses

Select a hyperlink below to be directed to that section.

POLICY CRITERIA | DOCUMENTATION REQUIREMENTS | CODING
RELATED INFORMATION | EVIDENCE REVIEW | REFERENCES | HISTORY

∞ Clicking this icon returns you to the hyperlinks menu above.

Introduction

An antibody is a blood protein. When the immune system detects an unhealthy cell, antibodies attach themselves to a molecule known as an antigen on that unhealthy cell. The antibody then acts as flag for other immune system cells, causing those other immune system cells to swarm to the area and fight the unhealthy cell. Cancer cells can evade the immune system by reproducing very quickly, avoiding detection, or completely blocking the immune system. Monoclonal antibodies are drugs that work with the body's natural immune response. Monoclonal antibodies are produced in a laboratory and made to specifically attach to the antigens which are typically found in high numbers on cancer cells. This policy describes when treatment with monoclonal antibodies may be approved to treat lymphoma.

Note: The Introduction section is for your general knowledge and is not to be taken as policy coverage criteria. The rest of the policy uses specific words and concepts familiar to medical professionals. It is intended for providers. A provider can be a person, such as a doctor, nurse, psychologist, or dentist. A provider also can be a place where medical care is given, like a hospital, clinic, or lab. This policy informs them about when a service may be covered.

Policy Coverage Criteria

Note: Riabni (rituximab-arrx), Rituxan (rituximab), Ruxience (rituximab-pvvr), and Truxima (rituximab-abbs) are not subject to Site of Service review when used for the treatment of lymphoma.

Drug	Medical Necessity
First-line • **Riabni (rituximab-arrx)** • **Ruxience (rituximab-pvvr)**	**Riabni (rituximab-arrx) and Ruxience (rituximab-pvvr) are a CD20-directed cytolytic antibody and may be considered medically necessary for the treatment of individuals with the following labeled indications:** • Non-Hodgkin's Lymphoma (NHL) • Chronic Lymphocytic Leukemia (CLL) **Riabni (rituximab-arrx) and Ruxience (rituximab-pvvr) may be considered medically necessary for the treatment of individuals with the following off-label indications:** • Treatment of any B-cell or other Lymphoid malignancies with documented CD20 antigen expression ○ ALL, Chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) ○ Primary CNS lymphomas ○ AIDS-related B-cell lymphoma ○ Follicular lymphoma ○ Hairy cell leukemia ○ Lymphoblastic lymphoma ○ MALT lymphoma ○ Hodgkin's lymphoma ○ Burkitt's lymphoma ○ Mantle cell lymphoma ○ Splenic marginal zone lymphoma ○ Multiple myeloma ○ Waldenstrom's macroglobulinemia ○ CD-20 positive leptomeningeal metastases • Treatment of posttransplant lymphoproliferative disorder • First-line therapy of monomorphic or polymorphic post-transplant lymphoproliferative disorder (PTLD)

Drug	Medical Necessity
	• Second-line therapy for persistent or progressive PTLD • Maintenance therapy for polymorphic PTLD
Second-line • **Rituxan (rituximab)** • **Truxima (rituximab-abbs)**	**Rituxan (rituximab) and Truxima (rituximab-abbs) are a CD20-directed cytolytic antibody and may be considered medically necessary for the treatment of individuals with the following labeled indications:** • Non-Hodgkin's Lymphoma (NHL) • Chronic Lymphocytic Leukemia (CLL) **AND** • The individual has had an inadequate response or intolerance to Riabni (rituximab-arrx) **AND** Ruxience (rituximab-pvvr) **Rituxan (rituximab) and Truxima (rituximab-abbs) may be considered medically necessary for the treatment of individuals with the following off-label indications:** • Treatment of any B-cell or other Lymphoid malignancies with documented CD20 antigen expression ○ ALL, Chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) ○ Primary CNS lymphomas ○ AIDS-related B-cell lymphoma ○ Follicular lymphoma ○ Hairy cell leukemia ○ Lymphoblastic lymphoma ○ MALT lymphoma ○ Hodgkin's lymphoma ○ Burkitt's lymphoma ○ Mantle cell lymphoma ○ Splenic marginal zone lymphoma ○ Multiple myeloma ○ Waldenstrom's macroglobulinemia ○ CD-20 positive leptomeningeal metastases • Treatment of posttransplant lymphoproliferative disorder • First-line therapy of monomorphic or polymorphic post-transplant lymphoproliferative disorder (PTLD) • Second-line therapy for persistent or progressive PTLD

Drug	Medical Necessity
	• Maintenance therapy for polymorphic PTLD **AND** • The individual has had an inadequate response or intolerance to Riabni (rituximab-arrx) **AND** Ruxience (rituximab-pvvr)
Second-line • **Rituxan Hycela (rituximab and hyaluronidase human)**	**Rituxan Hycela (rituximab and hyaluronidase human) may be considered medically necessary for the treatment of adult individuals with documented CD20 antigen expression for the following conditions:** • Follicular Lymphoma (FL) ○ Used as a single agent for relapsed or refractory FL ○ Used in combination with first-line chemotherapy for previously untreated FL ○ Used as single agent maintenance therapy in individuals achieving a complete or partial response to rituximab in combination with chemotherapy ○ Used as a single agent after first-line cyclophosphamide, vincristine, and prednisone (CVP) chemotherapy for non-progressing (including stable disease) • Diffuse Large B-cell Lymphoma (DLBCL) ○ In combination with cyclophosphamide, doxorubicin, vincristine, prednisone (CHOP) or other anthracycline-based chemotherapy regimens for previously untreated diffuse large B-cell lymphoma • Chronic Lymphocytic Leukemia (CLL) ○ In combination with fludarabine and cyclophosphamide (FC) for previously untreated and previously treated CLL **AND** • Individual has had an inadequate response or intolerance to Riabni (rituximab-arrx) **AND** Ruxience (rituximab-pvvr) ○ **Exception:** This may be granted when documentation is provided of difficult venous access. **Rituxan Hycela (rituximab and hyaluronidase human) may be considered medically necessary for the treatment of individuals with the following labeled or off-label indications:** • Non-Hodgkin's Lymphoma (NHL) • Chronic Lymphocytic Leukemia (CLL)

Drug	Medical Necessity
	• Treatment of any B-cell or other Lymphoid malignancies with documented CD20 antigen expression ○ ALL, Chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) ○ Primary CNS lymphomas ○ AIDS-related B-cell lymphoma ○ Follicular lymphoma ○ Hairy cell leukemia ○ Lymphoblastic lymphoma ○ MALT lymphoma ○ Hodgkin's lymphoma ○ Burkitt's lymphoma ○ Mantle cell lymphoma ○ Splenic marginal zone lymphoma ○ Multiple myeloma ○ Waldenstrom's macroglobulinemia ○ CD-20 positive leptomeningeal metastases • Treatment of posttransplant lymphoproliferative disorder • First-line therapy of monomorphic or polymorphic post-transplant lymphoproliferative disorder (PTLD) • Second-line therapy for persistent or progressive PTLD • Maintenance therapy for polymorphic PTLD **AND** • The individual has had an inadequate response or intolerance to Riabni (rituximab-arrx) **AND** Ruxience (rituximab-pvvr) ○ **Exception:** This may be granted when documentation is provided of difficult venous access. **Note**: Initiate treatment with Rituxan Hycela only after individuals have received at least **ONE FULL DOSE** of a rituximab product by intravenous infusion.
Arzerra (ofatumumab)	**Arzerra (ofatumumab) may be considered medically necessary for the treatment of chronic lymphocytic leukemia (CLL) in the following situations:** • In combination with chlorambucil, for the treatment of previously untreated individuals with CLL for whom fludarabine-based therapy is considered inappropriate

Drug	Medical Necessity
	• In combination with fludarabine and cyclophosphamide for the treatment of individuals with relapsed CLL • For extended treatment of individuals who are in complete or partial response after at least 2 lines of therapy for recurrent or progressive CLL • For the treatment of individuals with CLL refractory to fludarabine and alemtuzumab
Monjuvi (tafasitamab-cxix)	**Monjuvi (tafasitamab-cxix) may be considered medically necessary for the treatment of relapsed or refractory diffuse large B-cell lymphoma (DLBCL) not otherwise specified, including DLBCL arising from low grade lymphoma when all the following criteria are met:** • The individual is aged 18 years and older **AND** • Are not eligible for autologous stem cell transplant (ASCT) **AND** • Has tried at least 2 prior therapies to treat DLBCL **AND** • Monjuvi (tafasitamab-cxix) will be used in combination with lenalidomide **Monjuvi (tafasitamab-cxix) may be considered medically necessary for the treatment of relapsed or refractory follicular lymphoma (FL) when all the following criteria are met:** • The individual is aged 18 years and older **AND** • Has tried at least 1 prior therapy to treat FL **AND** • Monjuvi (tafasitamab-cxix) will be used in combination with lenalidomide and rituximab

Drug	Investigational
• **Riabni (rituximab-arrx)** • **Rituxan (rituximab)**	**Riabni (rituximab-arrx), Rituxan (rituximab), Rituxan Hycela (rituximab and hyaluronidase human), Ruxience (rituximab-pvvr), and Truxima (rituximab-abbs) are considered investigational for the following off-label indication:**

Drug	Investigational
• **Rituxan Hycela (rituximab and hyaluronidase human)** • **Ruxience (rituximab-pvvr)** • **Truxima (rituximab-abbs)**	• Treatment of lymphoid B-cell malignancies that do not express CD20 antigen **All other uses of Riabni (rituximab-arrx), Rituxan (rituximab), Rituxan Hycela (rituximab and hyaluronidase human), Ruxience (rituximab-pvvr), and Truxima (rituximab-abbs) are considered investigational unless listed in a related medical policy.**
• **Arzerra (ofatumumab)** • **Monjuvi (tafasitamab-cxix)**	**All other uses of Arzerra (ofatumumab) and Monjuvi (tafasitamab-cxix) are considered investigational.**
As listed	**The medications listed in this policy are subject to the product's US Food and Drug Administration (FDA) dosage and administration prescribing information.**

Length of Approval	
Approval	**Criteria**
Initial authorization	**All drugs listed in this policy may be approved up to 6 months.**
Re-authorization criteria	**All drugs listed in this policy may be approved up to 12 months as long as the drug-specific coverage criteria are met and chart notes demonstrate that the individual continues to show a positive clinical response to therapy.**

Documentation Requirements
The individual's medical records submitted for review for all conditions should document that medical necessity criteria are met. The record should include the following: • Office visit notes that contain the diagnosis, relevant history, physical evaluation and medication history

Coding

Code	Description
HCPCS	

Code	Description
J9302	Injection, ofatumumab (Arzerra), 10 mg
J9311	Injection, rituximab 10 mg and hyaluronidase (Rituxan Hycela)
J9312	Injection, rituximab (Rituxan), 10 mg
J9349	Injection, tafasitamab-cxix (Monjuvi), 2 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)

Note: CPT codes, descriptions and materials are copyrighted by the American Medical Association (AMA). HCPCS codes, descriptions and materials are copyrighted by Centers for Medicare Services (CMS).

Related Information

Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma

Chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) is classified as an indolent non-Hodgkin's lymphoma (NHL). When CLL/SLL is relapsed or refractory and CD20+ B-cells (not T-cells) are present, treatment is appropriate with rituximab.

Benefit Application

This policy is managed through the medical benefit.

International Prognostic Index

One point is given for each of the characteristics below in the individual for a total score ranging from zero to five.

- 60 years of age or older
- Serum lactate dehydrogenase concentration above normal

- Eastern Cooperative Oncology Group (ECOG) performance status of 2 or greater
- Ann Arbor stage III or IV
- Number of extranodal disease sites greater than 1

Table 1. Eastern Cooperative Oncology Group (ECOG)

Performance Status	Definition
0	Fully active; no performance restrictions.
1	Strenuous physical activity restricted; fully ambulatory and able to carry out light work.
2	Capable of all self-care but unable to carry out any work activities. Up and about greater than 50% of waking hours.
3	Capable of only limited self-care; confined to bed or chair greater than 50% of waking hours.
4	Completely disabled; cannot carry out any self-care; totally confined to bed or chair.

Table 2. Ann Arbor Revised Staging System for Primary Nodal Lymphomas

Stage	Involvement	Extranodal Status
I	One node or a group of adjacent nodes	Single extranodal lesions without nodal involvement
II	Two or more nodal groups on the same side of the diaphragm	Stage I or II by nodal extent with limited contiguous extranodal involvement
II bulky	II as above with "bulky" disease	Not applicable
III	Nodes on both sides of the diaphragm; nodes above the diaphragm with spleen involvement	Not applicable
IV	Additional noncontiguous extralymphatic involvement	Not applicable

Evidence Review

Description

Normal and malignant hematopoietic cells express various antigens on their surfaces, including: CD20 expressed by B-lymphocytes and B-cell malignancies; CD33, present on myeloid progenitors and acute myeloid leukemia (AML); and CD52, expressed by normal and malignant T- and B-lymphocytes. Monoclonal antibodies have been developed to each of the above antigens and have been investigated for the following labeled and off-label uses.

Rituxan (rituximab) is a CD20-directed cytolytic antibody indicated for the treatment of individuals with following labeled indications:

- Non-Hodgkin's Lymphoma (NHL), and
- Chronic Lymphocytic Leukemia (CLL)

Rituximab and hyaluronidase human (Rituxan Hycela) is a CD20-directed cytolytic antibody and hyaluronidase human, indicated for the treatment of adult individuals with the following labeled indications:

- Follicular Lymphoma (FL)
- Diffuse Large B-cell Lymphoma (DLBCL)
- Chronic Lymphocytic Leukemia (CLL)

Arzerra (ofatumumab): human monoclonal antibody to the CD20 antigen. Labeled indications:

- In combination with chlorambucil, for the treatment of previously untreated individuals with CLL for whom fludarabine-based therapy is considered inappropriate
- In combination with fludarabine and cyclophosphamide for the treatment of individuals with relapsed CLL
- For extended treatment of individuals who are in complete or partial response after at least 2 lines of therapy for recurrent or progressive CLL
- For the treatment of individuals with CLL refractory to fludarabine and alemtuzumab

Monjuvi (tafasitamab-cxix) is a CD19-directed cytolytic antibody with the following labeled indications:

- In combination with lenalidomide for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) not otherwise specified, including DLBCL

arising from low grade lymphoma, and who are not eligible for autologous stem cell transplant (ASCT).

- In combination with lenalidomide and rituximab for the treatment of adult patients with relapsed or refractory follicular lymphoma (FL).

National Comprehensive Cancer Network Compendium

The National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium is based directly on the NCCN Clinical Practice Guidelines in Oncology. The compendium lists specific panel recommendations for off-label uses of drugs, and each recommendation is supported by a level of evidence category.

The NCCN Categories of Evidence and Consensus used in the recommendations are:

- Category 1: The recommendation is based on high-level evidence (e.g., randomized controlled trials) and there is uniform NCCN consensus that the intervention is appropriate
- Category 2A: The recommendation is based on lower-level evidence and there is uniform NCCN consensus that the intervention is appropriate
- Category 2B: The recommendation is based on lower-level evidence and there is nonuniform NCCN consensus (but no major disagreement) that the intervention is appropriate
- Category 3: The recommendation is based on any level of evidence but reflects major NCCN disagreement that the intervention is appropriate

In June 2008, the NCCN Compendium became one of four references for the Centers for Medicare & Medicaid Services (CMS) for oncology coverage policy.

In its national coverage decision, CMS states that, in general, a use identified by the NCCN Compendium is medically accepted if the indication is a Category 1 or 2A as defined by NCCN. A use is not medically accepted if the indication is a category 3 in NCCN.

The local CMS contractor, Noridian Administrative Services (NAS), has issued an additional coverage statement regarding Category 2B:

> NAS recognizes NCCN Categories of Evidence Levels Category 1 and Category 2A ONLY as medically accepted indications. If a provider chooses to use NCCN level 2B in support of a chemotherapeutic drug used off-label in an anti-cancer chemotherapeutic regimen, NAS expects that the provider will make available to NAS significant peer-reviewed Phase II or

Phase III studies demonstrating such support. In the absence of such studies, level 2B evidence does not support such use.

The following policy considers only the off-label indications for rituximab and atumumab.

Background

Rituxan (rituximab)

Regarding Rituxan (rituximab) for individuals with intermediate or aggressive NHL, an interim analysis of a randomized controlled trial is available in abstract form. The trial compared rituximab plus combination chemotherapy (cyclophosphamide, doxorubicin, vincristine and prednisone, aka CHOP) to CHOP therapy alone in 400 individuals with previously treated diffuse large B-cell lymphoma. By intent–to-treat analysis, event-free and overall survival (OS) at 12 months was superior in the rituximab plus CHOP arm. In 2002, final results of this trial were published by Coiffier et al., confirming the superior outcomes in the combination arm. In the Coiffier study, event-free survival at 2 years (CI 95%) was 57% in the CHOP + Rituximab arm and 38% in the CHOP alone arm. A 2002 TEC Assessment also found Rituximab met criteria for treatment of individuals with intermediate or aggressive B-cell non-Hodgkin's lymphoma based on the Coiffier study.

In a randomized, Phase III trial of 122 individuals with untreated advanced-stage mantle cell lymphoma, Lenz and colleagues reported individuals receiving cyclophosphamide, doxorubicin, vincristine and prednisone (CHOP) plus rituximab (n=62) had significantly superior outcomes than individuals receiving CHOP alone (n=60). Complete response rates and median time to treatment failure in the CHOP plus rituximab group vs the CHOP alone group were 34% vs. 7% (p=0.00024) and 21 months versus 14 months (p=0.0131), respectively. Toxicities were reported to be acceptable and similar in both treatment groups.

The indications for off-label use of rituximab were determined by:

- Considering the limited but evolving evidence in clinical trials indicating that CD20 expression enhanced susceptibility to this drug, and thus a response was more likely;
- Soliciting the expert opinion of physician specialists on its accepted use; and
- National Comprehensive Cancer Network Clinical Practice Guidelines for Non-Hodgkin's Lymphomas.

Rituxan Hycela (rituximab and hyaluronidase human)

Evidence for efficacy and safety of Rituxan Hycela (rituximab and hyaluronidase human) was evaluated in three studies of each specified indication. All studies demonstrated comparability of the subcutaneous (SC) formulation to the intravenous (IV) formulation of rituximab.

Follicular Lymphoma

The SABRINA study was a randomized, controlled, open-label, multicenter Phase 3 trial that evaluated 410 individuals with previously untreated CD20-positive FL of Grade 1, 2, or 3a who received either IV Rituxan (rituximab) or one cycle of an IV rituximab product followed by SC Rituxan Hyclea (rituximab), plus chemotherapy. The primary endpoint was overall response (complete response, unconfirmed complete response, and partial response) at the end of induction, which amounted to 84.9% (95% CI 79.2 – 89.5) in the IV group and 84.4% (95% CI 78.7 – 89.1) in the SC group, for a difference of -0.5% (95% CI -7.7 – 6.8). The frequency of adverse events was similar in both groups (95% in the IV group and 96% in the SC group).

Diffuse Large B-Cell Lymphoma

The MabEase study was a randomized, controlled, open-label, multicenter Phase 3b trial that evaluated 576 individuals with previously untreated CD20-positive DLBCL who received either IV rituximab or one cycle of an IV rituximab product followed by SC rituximab, plus chemotherapy. The primary endpoint was complete response/unconfirmed complete response (CR/Cru) at the end of induction, which amounted to 50.6% (95% CI 45.3% - 55.9%) in the SC group and 42.4% (95% CI 35.1% - 49.7%) in the IV group (P=0.076). Safety profiles were similar between arms, with no unexpected safety signals.

Chronic Lymphocytic Leukemia

The SAWYER study was a randomized, controlled, open-label, multicenter, non-inferiority Phase 1b trial that evaluated 176 individuals with previously untreated CD20-positive CLL who received either IV rituximab or one cycle of an IV rituximab product followed by SC rituximab, plus chemotherapy. Overall, the study demonstrated non-inferiority of SC rituximab to IV rituximab through the primary endpoint of pharmacokinetic profiles. The geometric mean trough serum

concentration was 97.5 mcg/mL in the SC group and 61.5 mcg/mL in the IV group, with an adjusted geometric mean ratio of 1.53 (90% CI 1.27 – 1.85). The proportion of individuals reporting adverse events was similar between treatment arms.

Arzerra (ofatumumab)

The evidence for efficacy and safety of Arzerra (ofatumumab) is currently limited to uncontrolled clinical studies. This evidence suggests ofatumumab is efficacious for achieving an objective response in approximately 50% individuals with fludrabine- or alemtuzumab-refractory CLL.

The drug also appears to have efficacy in some individuals with rituximab-refractory disease.

Controlled clinical trials are needed to establish the superiority of ofatumumab over other therapeutic alternative (e.g., rituximab). In addition, improved survival remains to be established.

Monjuvi (tafasitamab-cxix)

Phase 2/3 evidence for the efficacy and safety of tafasitamab for relapsed/refractory (R/R) DLBCL consists of two fair quality Phase 2 trials, one in combination with lenalinomide and the other as monotherapy.

L-MIND was an international, single-arm, open-label, Phase 2 trial in 81 adults with R/R DLBCL who were ineligible for high-dose chemotherapy and hematopoietic stem cell therapy (HSCT). Eligible individuals received tafasitamab + lenalidomide for 12 (28-day) cycles, followed by tafasitamab maintenance monotherapy until progressive disease (PD) in individuals with at least stable disease (SD). The primary study endpoint was objective response rate (CR + PR) (ORR). Results showed an ORR of 60%, with 43% complete response (CR) and 18% partial response (PR). Secondary outcomes included an SD of 16%, disease control rate (CR + PR + SD) (DCR) of 74%, duration of response (DOR) of 22 months, median progression-free survival (PFS) of 12 months, time to first subsequent therapy (TFST) of 15 months, and median OS was not reached (at a median 19.6 months follow-up).

In second fair quality, multicenter, single-arm, open-label, Phase 2a study, 92 adults with R/R NHL, including a cohort of 35 with R/R DLBCL, received tafasitamab weekly for 8 weeks, then those with at least SD received additional weekly doses for 4 more weeks, then those with CR or PR could continue Q2W or monthly maintenance therapy until PD. The primary study endpoint was ORR. In the DLBCL cohort, ORR was 26%, with n=2 CR and n=7 PR. Secondary outcomes

included a SD of 14%, a median DOR of 20 months, and median PFS was 2.7 months (after a median follow-up of 21 months).

Indirect comparison of the L-MIND response rate with that for lenalidomide and tafasitamab monotherapy in R/R NHL (including DLBCL) (28-35% and 26%, respectively) suggests tafasitamab + lenalidomide may be more efficacious than either agent alone. However, the response rate for available CAR T-cell therapies ranges from 52%-82% and for polatuzumab + bendamustine + rituximab was 45%, with 40% achieving CR.

Approval of Monjuvi for the treatment of relapsed or refractory follicular lymphoma (FL) was based on data from the pivotal, randomized, double-blind, placebo-controlled Phase III inMIND trial evaluating the efficacy and safety of Monjuvi in combination with rituximab and lenalidomide in adult patients with relapsed or refractory FL. The median number of prior lines of systemic therapy was 1 (range 1-10) with 55% receiving 1 prior line, 25% receiving 2 prior lines, and 20% receiving 3 or more prior lines. In total, 32% had progression of disease within 24 months after initial diagnosis and 43% had refractory disease to prior CD20-directed therapy.

The study met its primary endpoint demonstrating a statistically significant and clinically meaningful improvement in progression-free survival (PFS) by investigator assessment, which demonstrated 27.5% (N=273) of patients with an event in the Monjuvi group vs. 47.6% (N=275) of patients with an event in the control arm. Patients receiving Monjuvi in combination with rituximab and lenalidomide achieved a median PFS by investigator assessment of 22.4 months (95% CI, 19.2-not evaluable [NE]) compared to 13.9 months (95% CI, 11.5-16.4) in the control arm (hazard ratio [HR]: 0.43 [95% CI, 0.32-0.58]; P<0.0001). The PFS assessed by an Independent Review Committee (IRC) was consistent with investigator-based results. Median PFS by IRC was not reached (95% CI, 19.3-NE) in the Monjuvi group versus 16.0 months (95% CI, 13.9-21.1) in the control arm (HR: 0.41 [95% CI, 0.29-0.56]. The PFS benefit was consistent across prespecified patient subgroups, including number of previous lines of therapy.

The safety of Monjuvi in patients with FL was evaluated in 546 patients in the inMIND trial. Serious adverse reactions occurred in 33% of patients who received Monjuvi in combination with rituximab and lenalidomide, including serious infections in 24% of patients (including pneumonia and COVID-19 infection). Other serious adverse reactions in ≥ 2% of patients included renal insufficiency (3.3%), second primary malignancies (2.9%), and febrile neutropenia (2.6%). Fatal adverse reactions occurred in 1.5% of patients, including from COVID-19, sepsis, and adenocarcinoma. The most common adverse reactions (≥ 20%) in recipients of Monjuvi, excluding laboratory abnormalities, were respiratory tract infections (including COVID-19 infection and pneumonia), diarrhea, rash, fatigue, constipation, musculoskeletal pain, and cough. The most common Grade 3 or 4 laboratory abnormalities (≥ 20%) were decreased neutrophils and decreased lymphocytes.

2004 Update

The US Pharmacopoeial Convention (2003) has concluded that Rituxan (rituximab) is accepted for the following off-label indications: a) as first-line treatment of diffuse aggressive NHL; b) treatment of relapsed or refractory diffuse aggressive NHL; c) first-line treatment of intermediate to high-grade NHL; and d) first-line treatment of low-grade NHL.

2006 Update

Studies continue, but have not yet been published, which would indicate the safety and efficacy of Mylotarg as a single-agent treatment for individuals who are CD33-positive with AML in first relapse. Outcomes of these studies are awaited.

2008 Update

NCCN guidelines v.3.2008 recommends rituximab (preferred), or alkylating agents such as cyclophosphamide or chlorambucil as single agents for first-line therapy for follicular lymphoma in elderly or infirm individuals.

2009 Update

Both R-CHOP (rituximab with cyclophosphamide, doxorubicin, vincristine and prednisone) and R-CVP (rituximab with cyclophosphamide, vincristine and prednisone) have been used successfully in the treatment of individuals with symptomatic FL. Ganguly and Patel (2009 conducted a meta-analysis of relevant literature comparing both treatment arms for FL with response being the final endpoint. Two analyses were conducted: The first analysis compared R-CHOP to R-CVP as frontline agents for the treatment of FL and the second analysis included both untreated and relapsed individuals. The authors report that for both studies, R-CVP was superior to R-CHOP when evaluating for complete response (CR). However, for overall response (CR+PR), R-CHOP was superior. The authors concluded that both R-CHOP and R-CVP protocols achieve excellent overall response. In individuals with known cardiac history, omission of anthracyclines is reasonable and R-CVP provides a competitive CR rate. In younger individuals

with FL where cumulative cardio-toxicity may be of importance in the long term and in whom future stem cell transplantation is an option, again R-CVP may be a more appealing option.

The Company recognizes uses of rituximab, ofatumumab, and alemtuzumab listed in the NCCN Drugs and Biologics Compendium with Categories of Evidence and Consensus of 1 and 2A as proven and Categories of Evidence and Consensus of 2B and 3 as unproven. However, Category 2B uses may be considered for coverage if they are substantiated by provider submission of significant peer-reviewed Phase II or Phase III studies demonstrating treatment effectiveness.

2010 Update

Updated to reflect current NCCN Compendium recommendations as of February 2010. Added newly marketed anti-CD20 monoclonal antibody, ofatumumab. Added information concerning the voluntary withdrawal of gemtuzumab from the market.

2011 Update

Policy updated with literature review. Policy statements for Mylotarg and supporting data removed from policy statement and any reference throughout the policy subsequent to FDA withdrawal of approval for this drug.

2012 Update

Policy updated to include NCCN recommendation for treatment of leptomeningeal metastases. (Category 2A) These may occur with various solid tumors, breast and lung being the most common. Therapy is palliative and usually of limited duration, as the average life expectancy of these individuals is only a few weeks.

2013 Update

Policy updated to include NCCN recommendation for addition of rituximab in induction/consolidation treatment of, ALL, CLL/SLL, primary CNS lymphomas, AIDS-related B-cell lymphoma, follicular lymphoma, hairy cell leukemia, and lymphoblastic lymphoma. (Category 2A and above) Also treatment of post-transplant lymphoproliferative disorder. (Category 2A)

Added Arzerra (ofatumumab) NCCN recommended off-label use for Waldenstrom's macroglobulinemia. (Category 2A)

Campath (alemtuzumab) removed from policy as it is no longer commercially available.

2014 Update

Policy updated to include new labeled indication in combination with chlorambucil for the treatment of previously untreated individuals with chronic lymphocytic leukemia (CLL) for whom fludarabine-based therapy is considered inappropriate.

2015 Update

Policy updated with primary literature review and reference to NCCN guidelines. No new evidence was found that would require a change in this policy.

2016 Update

Policy updated with primary literature review and reference to NCCN guidelines. Adcetris criteria, description, and rationale were added to the policy.

2017 Update

Policy updated with primary literature review and reference to NCCN guidelines. Rituxan Hyclea criteria, description, and rationale were added to the policy.

2018 Update

Policy updated with literature review and reference to NCCN guidelines. Moxetumomab pasudotox criteria, description, and rationale were added to the policy.

2019 Update

Reviewed prescribing information for all drugs in policy. Added criteria for the biosimilar Ruxience (rituximab-pvvr). Added criteria for a new medication Polivy (polatuzumab vedotin-piiq) for the treatment of relapsed or refractory DLBCL. No additional evidence was identified that would require changes to other drugs listed in this policy.

2020 Update

Reviewed prescribing information for all drugs in policy. No new evidence found that would change this policy.

2021 Update

Reviewed prescribing information for all drugs in policy. No new evidence found that would change this policy.

2022 Update

Reviewed prescribing information for all drugs in policy. No new evidence found that would change this policy.

2023 Update

Reviewed prescribing information for all drugs in policy. Updated Polivy criteria to indicate coverage in combination with a rituximab product, cyclophosphamide, doxorubicin, and prednisone (R-CHP) for the treatment of adult individuals who have previously untreated diffuse large B-cell lymphoma (DLBCL), not otherwise specified (NOS) or high-grade B-cell lymphoma (HGBL), and who have an International Prognostic Index (IPI) score of 2 or greater. Added coverage criteria for Columvi for the treatment of adult individuals with relapsed or refractory diffuse large B-cell lymphoma, not otherwise specified (DLBCL,NOS) or large B-cell lymphoma (LBCL) arising from follicular lymphoma, after two or more lines of systemic therapies. Updated Ruxience (rituximab-pvvr) to a non-preferred product. Removed Lumoxiti criteria as Astrazenenca has decided to permanently discontinue Lumoxiti from the US market and will not

be available after August 2023. Updated Rituxan Hycela (rituximab and hyaluronidase) to require documentation of CD20 antigen expression. Added coverage criteria for Epkinly (epcoritamab-bysp) for the treatment of certain adults with diffuse large B-cell lymphoma (DLBCL).

2024 Update

Reviewed prescribing information for all drugs in policy. No new evidence found that would change this policy.

2025 Update

Reviewed prescribing information for all drugs in policy. Clarified that non-formulary exception review authorizations for all drugs listed in this policy may be approved up to 12 months. Clarified that the medications listed in this policy are subject to the product's FDA dosage and administration prescribing information. Moved Columvi (glofitamab-gxbm), Epkinly (epcoritamab-bysp), Lunsumio (mosunetuzumab-axgb) from policy 2.03.502 Monoclonal Antibodies for the Treatment of Lymphoma to policy 5.01.650 Bispecific Antibodies. Updated Polivy (polatuzumab vedotin-piiq) coverage criteria to include use for certain individuals as bridging therapy prior to a planned CD-19 CAR-T treatment. Moved Adcetris (brentuximab vedotin) and Polivy (polatuzumab vedotin-piiq) from policy 2.03.502 Monoclonal Antibodies for the Treatment of Lymphoma to policy 5.01.582 Antibody-Drug Conjugate. Updated Riabni (rituximab-arrx) from a non-preferred product to a preferred product. Updated non-preferred rituximab products, Rituxan and Rituxan Hycela, to require trial with all preferred rituximab products.

2026 Update

Reviewed prescribing information for all drugs in policy. Removed reference to non-formulary exception reviews. Removed BCBSA Ref. Policy 2.03.05 as policy has been archived.

References

1. Coiffier B, Lepage E, Briere J et al. CHOP chemotherapy plus rituximab compared with CHOP alone in elderly patients with diffuse large B-cell lymphoma. N Engl J Med 2002; 346(4):235-42.
2. Lundin J, Kimby E, Bjorkholm M et al. Phase II trial of subcutaneous anti-CD52 monoclonal antibody alemtuzumab (Campath-1H) as first-line treatment for patients with B-cell chronic lymphocytic leukemia (B-CLL). Blood 2002; 100(3):768-73.
3. Lang K, Menzin J, Erle CC et al. Outcomes in patients treated with gemtuzumab ozogamicin for relapsed acute myelogenous leukemia. Am J Health Syst Pharm 2002; 59(10):941-8.
4. Hainsworth JD, Litchy S, Burris HA 3rd et al Rituximab as first-line and maintenance therapy for patients with indolent non-Hodgkin's lymphoma. J Clin Oncol 2002; 20(20):4261-7.
5. Hainsworth JD, Litchy S, Barton JH et al. Single-agent rituximab as first-line and maintenance treatment for patients with chronic lymphocytic leukemia or small lymphocytic lymphoma: a phase II trial of the Minnie Pearl Cancer Research Network. J Clin Oncol 2003; 21(9):1746-51.
6. Reyes F (Ed). Multiple applications of Rituximab in optimizing therapy for non-Hodgkin's Lymphoma. Semin Oncol 2004; 31(No. 1, suppl 2):1-37.
7. Kell WJ, Burnett AK, Chopra R et al. A feasibility study of simultaneous administration of Gemtuzumab Ozogamicin with intensive chemotherapy in induction and consolidation in younger patients with acute myeloid leukemia. Blood. 2003 15; 102(13):4277-83.
8. Erba HP. Treatment options for newly diagnosed patients with chronic lymphocytic leukemia. Curr Hematol Rep. 2004; 3(1):47-53.
9. Lenz G, Dreyling M, Hoster E et al. Immunochemotherapy with rituximab and cyclophosphamide, doxorubicin, vincristine and prednisone significantly improves response time to treatment failure, but not long-term outcome in patients with previously untreated mantle cell lymphoma: results of a prospective randomized trial of the German Low Grade Lymphoma Study Group (GLSG). J Clin Oncol. 2005; 23(9):1984-92.
10. Marcus R, Imrie K, Belch A et al. CVP Chemotherapy plus rituximab compared with CVP as first-line treatment for advanced follicular lymphoma. Blood. 2005; 105(4):1417-23.
11. Habermann TM, Weller EA, Morrison VA et al. Rituximab-CHOP versus CHOP alone or with maintenance rituximab in older patients with diffuse large B-cell lymphoma. J Clin Oncol. 2006;24(19):3121-7.
12. Wendtner CM, Rigen M, Schweighofer CD et al. Consolidation with alemtuzumab in patients with chronic lymphocytic leukemia (CLL) in first remission – experience on safety and efficacy within a randomized multicenter phase III trial of the German CLL Study Group (GCLLSG). Leukemia. 2004;18(6):1093-101.
13. Tauro S, Craddock C, Peggs, K et al. Allogeneic stem-cell transplantation using a reduced-intensity conditioning regimen has the capacity to produce durable remission and long-term disease-free survival in patients with high-risk acute myeloid leukemia and myelodysplasia. Clin Oncol. 2005;23(36):9387-93. Epub 2005 Nov 28.
14. van Besien K, Artz A, Smith S et al. Fludarabine, melphalan, and alemtuzumab conditioning in adults with standard-risk advanced acute myeloid leukemia and myelodysplatic syndrome. J Clin Oncol. 2005;23(24):5728-38. Epub 2005 Jul 11.
15. Fiegl M, Falkner A, Hopfinger G et al. Collaborative Study Group on Alemtuzumab in Chronic Lymphocytic Leukemia: Routine clinical use of alemtuzumab in patients with heavily pretreated B-cell chronic lymphocytic leukemia: a nation-wide retrospective study in Austria. Cancer 2006; 107(10):2408-16.
16. Elter T, Borchmann P, Schulz H et al. Fludarabine in combination with alemtuzumab is effective and feasible in patients with relapsed or refractory B-cell chronic lymphocytic leukemia: Results of a phase II trial. J Clin Oncol 2005;23 (28):7024-31. Epub 2005 Sept 6.
17. Tam CS, Wolf M, Prince HM et al. Fludarabine, cyclophosphamide, and rituximab for the treatment of patients with chronic lymphocytic leukemia or indolent non-Hodgkin lymphoma. Cancer 2006;106 (11):2412-20.
18. Swords R, Nolan A, Fay M et al. Treatment of refractory fludarabine induced autoimmune haemolytic with the anti-CD20 monoclonal antibody rituximab. Clin Lab Haematol 2006;28(1):57-9.

19. Byrd JC, Gribben JG, Peterson BL et al. Select high-risk genetic features predict earlier progression following chemoimmunotherapy with fludarabine and rituximab in chronic lymphocytic leukemia: justification for risk-adapted therapy. J Clin Oncol 2006;24(3):437-43. Epub 2005 Dec 12.

20. Taksin AL, Legrand O, Raffoux E et al. High efficacy and safety profile of fractionated doses of Mylotarg as induction therapy in patients with relapsed acute myeloblastic leukemia: a prospective study of the alpha group. Leukemia 2007;21(1):66-71. Epub 2006 Oct 19.

21. Sekeres MA. Non-transplant therapy for older adults with acute myeloid leukemia. J Natl Compr Canc Netw 2006;4(1):51-6. Review.

22. Fenton C, Perry CM. Gemtuzumab ozogamicin: a review of its use in acute myeloid leukemia. Drugs 2005;65(16):2405-27. Review.

23. Ghielmini M, Hsu, Schmitz SF, Cogliatti SB; et al. Prolonged treatment with rituximab in patients with follicular lymphoma significantly increases event-free survival and response duration compared with the standard weekly x 4 schedule. Blood 2004; 103:4416-23.

24. National Comprehensive Cancer Network. The NCCN Drugs and Biologics Compendium.

25. Ganguly S, Patel V. R-CHOP versus R-CVP in the treatment of follicular lymphoma: a meta-analysis and critical appraisal of current literature. J Hematol Oncol 2009;Mar 24;2(1):14.

26. Davies A, Merli F, Mihaljevic B, et al. Efficacy and safety of subcutaneous rituximab versus intravenous rituximab for first-line treatment of follicular lymphoma (SABRINA): a randomised, open-label, phase 3 trial. Lancet Haematol. 2017;4(6): e272-82.

27. Lugtenburg P, Avivi I, Berenschot H, et al. Efficacy and safety of subcutaneous and intravenous rituximab plus cyclophosphamide, doxorubicin, vincristine, and prednisone in first-line diffuse large B-cell lymphoma: the randomized MabEase study. Haematologica. 2017;102(11): 1913-22.

28. Assouline S, Buccheri V, Delmer A, et al. Pharmacokinetics, safety, and efficacy of subcutaneous versus intravenous rituximab plus chemotherapy as treatment for chronic lymphocytic leukaemia (SAWYER): a phase 1b, open-label, randomised controlled non-inferiority trial. Lancet Haematol. 2016;3(3): e128-38.

29. Coiffier B, Lepretre S, Pedersen LM et al. Safety and efficacy of ofatumumab, a fully human monoclonal anti-CD20 antibody, in patients with relapsed or refractory B-cell chronic lymphocytic leukemia: a phase 1-2 study. Blood. 2008; 111:1094-1100.

30. Wierda W, Kipps T, Mayer J et al. Ofatumumab as single-agent CD20 immunotherapy in fludarabine-refractory chronic lymphocytic leukemia 2010 (In press).

31. Wierda WG, Kipps TJ, Durig J et al. Ofatumumab combined with fludarabine and cyclophosphamide (O-FC) shows high activity in patients with previously untreated chronic lymphocytic leukemia (CLL): results from a randomized, multicenter, international, two-dose, parallel group, phase II trial [abstract]. Blood 2009; 114:207.

32. Hagenbeek A, Gadeberg O, Johnson P et al. First clinical use of ofatumumab, a novel fully human anti-CD20 monoclonal antibody in relapsed or refractory follicular lymphoma: results of a phase 1/2 trial. Blood 2008; 111:5486-5495.

33. Foà R. Changes in the treatment landscape for chronic lymphoid leukemia. N Engl J Med. 2014 Jul 17;371(3):273-4.

34. Truxima (rituximab-abbs). Prescribing Information. Teva Pharmaceuticals USA, Inc.; North Wales, PA. Revised June 2025.

35. Ruxience (rituximab-pvvr). Prescribing Information. Pfizer Labs; New York, NY. Revised June 2025.

36. Riabni (rituximab-arrx). Prescribing Information. Amgen, Inc.; Thousand Oaks, CA. Revised February 2023.

37. Rituxan (rituximab). Prescribing Information. Genentech, Inc.; South San Francisco, CA. Revised December 2021.

38. Rituxan Hycela (rituximab and hyaluronidase human). Prescribing Information. Genentech, Inc.; South San Francisco, CA. Revised June 2021.

39. Arzerra (ofatumumab). Prescribing Information. Novartis Pharmaceuticals Corporation; Cambridge, MA. Revised April 2024.

40. Monjuvi (tafasitamab-cxix). Prescribing Information. Incyte Corporation; Wilmington, DE. Revised June 2025.

41. Sehn LH, Herrera AF, Matasar MJ, et al. Polatuzumab vedotin (Pola) plus bendamustine (B) with rituximab (R) or obinutuzumab (G) in patients with relapsed/refractory (R/R) diffuse large B-cell lympohoma (DLBCL): updated results of a Phase (Ph) Ib/II study [abstract]. Blood. 2018;132:1683.

42. Morschhauser F, Flinn IW, Advani R, et al. Polatuzumab vedotin or pinatuzumab vedotin plus rituximab in patients with relapsed or refractory non-Hodgkin lymphoma: final results from a Phase 2 randomized study (ROMULUS). Lancet Haematol. 2019;6:e254-e265.

43. Tilly H, Morschhauser F, Bartlett NL, et al. Polatuzumab vedotin in combination with immunochemotherapy in patients with previously untreated diffuse large B-cell lymphoma: an open-label, nonrandomized, Phase 1b-2 study. Lancet Oncol. 14 May 2019.

44. Salles G, Duell J, Gozalez Barca E, et al. Tafasitamab plus lenalinomide in relapsed or refractory diffuse large B-cell lymphoma (L-MIND): a multicenter, prospective, single-arm, phase 2 study. Lancet Oncol. 2020;21:978-988.

45. Jurczak W, Zinzani PL, Gaidano G, et al. Phase IIa study of the CD19 antibody MOR208 in patients with relapsed or refractory B-cell non-Hodgkin's lymphoma. Ann Oncol. 2018;29:1266-1272.

46. Cheson BD, Fisher RI, Barrington SF, et al. Recommendations for initial evaluation, staging, and response assessment of Hodgkin and non-Hodgkin lymphoma: The Lugano classification. J Clin Oncol 2014; 32(27):3059-67.

47. Oken MM, Creech RH, Tormey DC, et al. Toxicity and response criteria of the Eastern Cooperative Oncology Group. Am J Clin Oncol 1982; 5:649.

48. The International Non-Hodgkin's Lymphoma Prognostic Factors Project. N Engl J Med 1993; 329:987.

History

Date	Comments
08/15/01	Add to Medicine Section - New Policy
08/13/02	Replace Policy - Policy revised; policy statement changed regarding Rituximab for intermediate or aggressive NHL.
07/13/04	Replace Policy - Policy revised with literature updated; added the 2004 US Pharmacopeia and the American Hospital Formulary Service off-label indications to the Benefit Application section; clarification made: mantle cell was removed from investigational status; otherwise, policy statement unchanged.
12/14/04	Replace Policy / New Policy - Policy replaces BC.2.03.05 per direction from OAP 10/29/04 meeting. Indications changed from investigational to medically necessary.
10/11/05	Replace Policy - Scheduled reviewed. Added two off-label indications to Rituximab in policy statement.
02/06/06	Codes updated - No other changes.
06/23/06	Update Scope and Disclaimer - No other changes.
12/12/06	Replace Policy - Policy reviewed by P&T Committee on September 26, 2006; policy statement expanded to include the use of Alemtuzumab (CamPath) in the treatment of malignancies other than CLL that express CD-52 antigen as a medically necessary

Date	Comments
	indication; and the use of Gemtuzumab ozogamicin (Mylotarg) in the treatment of malignancies other than CLL which express CD-33 antigen as a medically necessary indication; malignancies other than CD33-positive remain investigational, but the condition of AML has been removed from this particular statement indication.
02/22/07	Update References - Policy reviewed and recommended by OAP February 22, 2007. No change to policy statement.
04/10/07	Replace Policy - Policy Guidelines amended to indicate that Mylotarg is intended for IV administration.
06/10/08	Replace Policy - Policy updated with literature search. Policy statement under Rituxan updated to include: "Therapy of other B-cell malignancies that express CD-20 antigen including some cases of CD-20 positive Hodgkin's Disease and Monotherapy as first-line follicular lymphoma treatment for elderly individuals, or others who are not good candidates for cytotoxic chemotherapy" as a medically necessary indication. Policy reviewed and recommended by OAP May 22, 2008. P&T reviewed and approved on May 27, 2008.
02/10/09	Code Update - Code 273.3 added; no other changes.
05/12/09	Replace Policy - Policy statements revised to clarify off-label uses. Intent of policy remains unchanged. NCCN categories of evidence added to Description and Rationale. References added.
10/13/09	Cross Reference Update - No other changes.
05/11/10	Cross Reference Update - No other changes.
08/10/10	Replace Policy - Policy updated the Rituximab labeled indications reflecting the latest revision (02/2010) by deleting all the references to the other chemotherapy agents. Reviewed and recommended by P&T in March 2010; by OAP in May 2010. Mylotarg removed. Arzerra added.
10/19/11	Related Policy 5.01.01 added.
09/11/12	Replace policy. Policy updated with literature review. CD20 positive leptomeningeal metastases added to the list of approved off-label indications for rituximab.
11/26/12	Related Policies Update, add 5.01.526.
10/14/13	Replace policy. Within the Policy section, additional examples of off-label indications for Rituxan have been added to the list of those considered medically necessary; Azerra has an added medically necessary indication for salvage treatment of Waldenstrom's Macroglobulinemia / Lymphoplasmacytic lymphoma in rituximab-intolerant individuals; and Campath has been removed from the policy as it is no longer commercially available. Description, Policy Guidelines and Rationale sections updated in support of the changes within the Policy section. HCPCS code J9010 for Campath removed from the coding section.
11/20/13	Update Related Policies. 5.01.01 deleted and replaced with 5.01.549.

Date	Comments
12/18/13	Update Related Policies. Change title to 5.01.526.
03/17/14	Update Related Policies. Add new policy 5.01.550 which replaces 5.01.526 and 5.01.601; they are now deleted.
08/11/14	Annual Review. Policy updated to include new labeled indication in combination with chlorambucil for the treatment of previously untreated individuals with chronic lymphocytic leukemia (CLL) for whom fludarabine-based therapy is considered inappropriate. ICD-9 diagnosis codes removed.
11/05/14	Minor correction. Correct usage to "CD20" throughout the policy to be consistent. No other changes.
01/23/15	Update Related Policies. Add 5.01.556.
10/13/15	Annual Review. Policy updated with literature review; no change in policy statements. Remove CPT codes 96409-96417; these are not primarily utilized in adjudication.
01/01/17	Annual Review, approved December 13, 2016. Adcetris criteria, description, and rationale were added to the policy.
01/13/17	Coding update, added HCPCS code J9042.
12/01/17	Annual Review, approved November 14, 2017. Rituxan Hyclea criteria, description, and rationale were added to the policy.
07/01/18	Interim Review, approved June 5, 2018. Criteria for Rituxan revised for clarity. Removed HCPCS code J9999.
08/01/18	Interim Review, approved July 10, 2018. Updated Adcetris indications.
12/01/18	Annual Review, approved November 13, 2018. Lumoxiti (moxetumomab pasudotox) added. Added HCPCS code J9999.
01/01/19	Coding update, added new HCPCS codes J9311 and J9312 (new codes effective 1/1/19).
02/01/19	Interim Review, approved January 8, 2019. Updated Adcetris indications.
05/01/19	Interim Review, approved April 18, 2019. Added criteria for Truxima (rituximab-abbs) which is a biosimilar of Rituxan (rituximab). Added description Rituxan Hycela to J9311 and Rituxan to J9312 in coding section. Added Truxima and Lumoxiti names in relationship to J9999. Added term date to HCPCS code J9310.
08/01/19	Coding update, added HCPCS code Q5115 (new code effective 7/1/19).
10/01/19	Coding update, added HCPCS code J9313 (new code effective 10/1/19). Removed HCPCS code J9999.
01/01/20	Annual Review, approved December 17, 2019, effective for dates of services on or after April 3, 2020, following provider notification. Added criteria for Polivy (polatuzumab vedotin-piiq). Added criteria for Ruxience (rituximab-pvvr) which is a biosimilar of Rituxan (rituximab). Updated criteria for Truxima (rituximab-abbs). Removed HCPCS

Date	Comments
	code J9310 as it was terminated 1/1/19. Added HCPCS code J9309 (new code effective 1/1/20) and J3590 to report Ruxience. References were added.
07/01/20	Coding update. Added HCPCS code Q5119, removed HCPCS code J3590.
10/01/20	Annual Review, approved September 1, 2020. No change to policy statements.
12/01/20	Interim Review, approved November 10, 2020. Added coverage criteria for Monjuvi (tafasitamab-cxix) for the treatment of DLBCL. Added HCPCS code J3590 for Monjuvi.
01/01/21	Coding update. Added HCPCS code C9070.
02/01/21	Interim Review, approved January 21, 2021. Added the biosimilar Riabni (rituximab-arrx) as a second line product. Added Riabni to J3590.
04/01/21	Coding update, added term date to HCPC C9070 and added new HCPC code J9349.
07/01/21	Coding update, Added HCPCS code Q5123.
09/01/21	Annual Review, approved August 3, 2021. No change to policy statements.
07/01/22	Interim Review, approved June 14, 2022. Moved Truxima (rituximab-abbs) to being a preferred rituximab product. Updated coverage criteria for the non-preferred product Riabni (rituximab-arrx) to require the individual has had an adequate trial and failure with Rituxan, Ruxience, or Truxima. Removed HCPCS codes C9070 and J3590.
12/01/22	Annual Review, approved November 21. 2022. No change to policy statements. Changed the wording from "patient" to "individual" throughout the policy for standardization.
02/01/23	Interim Review, approved January 10, 2023. Added a new indication to Adcetris (brentuximab vedotin) for the treatment of individuals 2 to less than 22 years of age with previously untreated high risk cHL in combination with chemotherapy. Added coverage for Lunsumio (mosunetuzumab-axgb) for the treatment of relapsed or refractory follicular lymphoma. Added HCPC code J3590 for Lunsumio.
06/01/23	Annual Review, approved May 9, 2023. Updated Polivy criteria to indicate coverage in combination with a rituximab product, cyclophosphamide, doxorubicin, and prednisone (R-CHP) for the treatment of adult individuals who have previously untreated diffuse large B-cell lymphoma (DLBCL), not otherwise specified (NOS) or high-grade B-cell lymphoma (HGBL), and who have an International Prognostic Index (IPI) score of 2 or greater.
07/01/23	Coding update. Added new HCPCS code J9350.
08/01/23	Interim Review, approved July 11, 2023. Added coverage criteria for Columvi for the treatment of adult individuals with relapsed or refractory diffuse large B-cell lymphoma, not otherwise specified (DLBCL,NOS) or large B-cell lymphoma (LBCL) arising from follicular lymphoma, after two or more lines of systemic therapies. Updated Related Policies, removed 8.01.533 as it was archived.
09/01/23	Interim Review, approved August 8, 2023. Removed Lumoxiti criteria as Astrazenenca has decided to permanently discontinue Lumoxiti from the US market and will not be

Date	Comments
	available after August 2023. Updated Ruxience (rituximab-pvvr) to a non-preferred product, effective January 1, 2024, following a 90-day provider notification due to changes in the preferred medical benefit drugs.
01/01/24	Interim Review, approved December 12, 2023. Updated Rituxan Hycela (rituximab and hyaluronidase) to require documentation of CD20 antigen expression. Added coverage criteria for Epkinly (epcoritamab-bysp) for the treatment of certain adults with diffuse large B-cell lymphoma (DLBCL), effective April 4, 2024, following a 90-day provider notification. Added HCPCS codes C9155, J9321 and J9286 and termed HCPCS code C9155.
08/01/24	Annual Review, approved July 22, 2024. No change to policy statements.
10/01/24	Interim Review, approved September 10, 2024. Added a new indication to Epkinly (epcoritamab-bysp) for the treatment of adult individuals with relapsed or refractory FL. The following policy changes are effective January 3, 2025, following a 90-day provider notification. Changed Ruxience (rituximab-pvvr) to a preferred rituximab product. Changed Rituxan (rituximab) and Rituxan Hycela (rituximab and hyaluronidase human) to non-preferred rituximab products. Updated coverage criteria for Riabni (rituximab-arrx), Rituxan, and Rituxan Hycela to require the individual has had an adequate trial and failure with Ruxience or Truxima.
03/01/25	Annual Review, approved February 24, 2025. Clarified that non-formulary exception review authorizations for all drugs listed in this policy may be approved up to 12 months. Clarified that the medications listed in this policy are subject to the product's FDA dosage and administration prescribing information. Removed HCPCS codes C9155, J3590 (Columvi), J9313.
04/01/25	Interim Review, approved March 11, 2025. Added a new indication to Adcetris (brentuximab vedotin) for the treatment of relapsed or refractory large B-cell lymphoma (LBCL).
05/01/25	Interim Review, approved April 8, 2025. Moved Columvi (glofitamab-gxbm), Epkinly (epcoritamab-bysp), Lunsumio (mosunetuzumab-axgb) from policy 2.03.502 Monoclonal Antibodies for the Treatment of Lymphoma to policy 5.01.650 Bispecific Antibodies. Updated Polivy (polatuzumab vedotin-piiq) coverage criteria to include use for certain individuals as bridging therapy prior to a planned CD-19 CAR-T treatment. Removed HCPCS J9286, J9321, J9350.
07/01/25	Interim Review, approved June 23, 2025. Moved Adcetris (brentuximab vedotin) and Polivy (polatuzumab vedotin-piiq) from policy 2.03.502 Monoclonal Antibodies for the Treatment of Lymphoma to policy 5.01.582 Antibody-Drug Conjugate. Removed HCPCS codes J9042 and J9309 since Adcetris and Polivy are being moved to policy 5.01.582.
09/01/25	Interim Review, approved August 12, 2025. Added a new indication to Monjuvi (tafasitamab-cxix) for the treatment of relapsed or refractory follicular lymphoma.
10/01/25	Interim Review, approved September 9, 2025. The following policy change is effective January 2, 2026, following 90-day provider notification. Updated Riabni (rituximab-

Date	Comments
	arrx) from a non-preferred product to a preferred product. Updated non-preferred rituximab products, Rituxan and Rituxan Hycela, to require trial with all preferred rituximab products.
06/01/26	Annual Review approved May 25, 2026. Removed reference to non-formulary exception reviews. Removed BCBSA Reference Policy 2.03.05 as policy has been archived.
10/01/26	Interim Review, approved September 8, 2026. The following policy changes are effective January 1, 2027, following 90-day provider notification. Updated Truxima (rituximab-abbs) from a preferred product to a non-preferred product. Updated non-preferred rituximab products removing Truxima from list of preferred rituximab products.

Disclaimer: This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. The Company adopts policies after careful review of published peer-reviewed scientific literature, national guidelines and local standards of practice. Since medical technology is constantly changing, the Company reserves the right to review and update policies as appropriate. Member contracts differ in their benefits. Always consult the member benefit booklet or contact a member service representative to determine coverage for a specific medical service or supply. CPT codes, descriptions and materials are copyrighted by the American Medical Association (AMA). ©2026 Premera All Rights Reserved.

Scope: Medical policies are systematically developed guidelines that serve as a resource for Company staff when determining coverage for specific medical procedures, drugs or devices. Coverage for medical services is subject to the limits and conditions of the member benefit plan. Members and their providers should consult the member benefit booklet or contact a customer service representative to determine whether there are any benefit limitations applicable to this service or supply. This medical policy does not apply to Medicare Advantage.