POLICY Document for RITUXAN (rituximab)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, and overall, clinically appropriate use. This document provides specific information to both sections of the overall policy.

Section 1: Preferred Product
- Policy information specific to preferred medications

Section 2: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 3: Oncology Clinical Policy
- Policy information specific to regimen review per NCCN Guidelines.

Section 1: Preferred Product

CAREFIRST: EXCEPTIONS CRITERIA
RITUXIMAB PRODUCTS

PREFERRED PRODUCTS: RUXIENCE , TRUXIMA

Client Requested: The intent of the criteria is to ensure that patients follow selection elements as established by CareFirst.

POLICY
This policy informs prescribers of preferred products and provides an exception process for targeted products through prior authorization.

I. PLAN DESIGN SUMMARY

This program applies to the rituximab products specified in this policy. Coverage for targeted product is provided based on clinical circumstances that would exclude the use of the preferred products. The coverage review process will ascertain situations where a clinical exception can be made. This program applies to all members requesting treatment with a targeted product.

Each referral is reviewed based on all utilization management (UM) programs implemented for the client.

Table. Rituximab Products

	Product(s)
Preferred*	• **Ruxience** (rituximab-pvvr) • **Truxima** (rituximab-abbs)
Targeted	• **Riabni** (rituximab-arrx) • **Rituxan** (rituximab) • **Rituxan Hycela** (rituximab and hyaluronidase human)

*: Medications considered formulary or preferred on your plan may still require a clinical prior authorization review

II. EXCEPTION CRITERIA

Coverage for a targeted product is provided when either of the following criteria is met:

A. Member has a documented inadequate response, contraindication, or intolerable adverse event to both preferred products the adverse event was not an expected adverse event attributed to the active ingredient as described in the prescribing information (i.e., known adverse reaction for both the reference product and biosimilar products)

Section 2: Clinical Criteria

Specialty Guideline Management Rituximab Products Treatment of Hematologic and Oncologic Conditions

Products Referenced by this Document

Drugs that are listed in the following table include both brand and generic and all dosage forms and strengths unless otherwise stated. Over-the-counter (OTC) products are not included unless otherwise stated.

Brand Name	Generic Name
Rituxan	rituximab
Ruxience	rituximab-pvvr
Truxima	rituximab-abbs
Riabni	rituximab-arrx

Indications

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Rituxan is indicated for the treatment of 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.

Rituxan, Ruxience, Truxima, and Riabni are indicated for:

Non-Hodgkin's lymphoma (NHL) in adult patients with:

- Relapsed or refractory, low-grade or follicular, CD20-positive, B-cell NHL as a single agent
- Previously untreated follicular, CD20-positive, B-cell NHL in combination with first line chemotherapy and, in patients achieving a complete or partial response to a rituximab product in combination with chemotherapy, as single-agent maintenance therapy
- Non-progressing (including stable disease), low-grade, CD20-positive, B-cell NHL, as a single agent after first-line CVP (cyclophosphamide, vincristine, and prednisone) chemotherapy
- Previously untreated diffuse large B-cell, CD20-positive NHL in combination with cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) or other anthracycline-based chemotherapy regimens

Chronic lymphocytic leukemia (CLL), in combination with fludarabine and cyclophosphamide (FC), for the treatment of adult patients with previously untreated and previously treated CD20-positive CLL.

Granulomatosis with polyangiitis (Wegener's Granulomatosis) and microscopic polyangiitis (MPA) in combination with glucocorticoids (Not addressed in this policy – Refer to Rituxan-Ruxience-Truxima-Riabni-RA+Other SGM)

Rheumatoid Arthritis (RA) in combination with methotrexate in adult patients with moderately-to severely active RA who have inadequate response to one or more TNF antagonist therapies. (Not addressed in this policy – Refer to Rituxan-Ruxience-Truxima-Riabni-RA+Other SGM)

Rituxan is also indicated for:

Rituxan is indicated for moderate to severe pemphigus vulgaris in adult patients

(Not addressed in this policy – Refer to Rituxan-Ruxience-Truxima-Riabni-RA+Other SGM)

Compendial Uses

- Autoimmune hemolytic anemia
- B-cell acute lymphoblastic leukemia (ALL)
- B-cell lymphomas
  - Human Immunodeficiency Virus (HIV) Related B-Cell lymphomas
  - B-cell lymphoblastic lymphoma
  - Burkitt lymphoma
  - Castleman's disease
  - Diffuse Large B-Cell lymphoma
  - Follicular lymphoma
  - High grade B-cell lymphoma (including high-grade B-cell lymphoma with translocations of MYC and BCL2 and/or BCL6 [double/triple hit lymphoma], high-grade B-cell lymphoma, not otherwise specified)
  - Histological transformation of indolent lymphomas to diffuse large B-cell lymphoma

    - Histological transformation of indolent lymphomas to high-grade B-cell lymphoma with MYC and BCL6 without BCL2 rearrangements
    - Mantle cell lymphoma
    - Marginal zone lymphomas
        - Nodal marginal zone lymphoma
        - Extranodal marginal zone lymphoma (gastric and non-gastric mucosa associated lymphoid tissue {MALT} lymphoma)
        - Splenic marginal zone lymphoma
    - Post-transplant lymphoproliferative disorder (PTLD)
    - Pediatric Aggressive Mature B-Cell Lymphomas
    - Primary Mediastinal Large B-Cell Lymphoma
- Central nervous system (CNS) cancers
    - Leptomeningeal metastases from lymphomas
    - Primary CNS lymphomas
- Chronic graft-versus-host disease (GVHD)
- CLL/Small lymphocytic lymphoma (SLL)
- Hairy cell leukemia
- Rosai-Dorfman disease
- Hodgkin's lymphoma, nodular lymphocyte-predominant
- Immune checkpoint inhibitor-related toxicities
- Prevention of Epstein-Barr virus (EBV)-related PTLD in high risk patients
- Primary cutaneous B-cell lymphoma
- Relapsed/refractory immune or idiopathic thrombocytopenic purpura (ITP)
- Thrombotic thrombocytopenic purpura
- Waldenström's macroglobulinemia/lymphoplasmacytic lymphoma (LPL)/ Bing-Neel syndrome
- Allogeneic transplant conditioning
- For other compendial uses, refer to Rituxan-Ruxience-Truxima-Riabni-RA+Other SGM

All other indications are considered experimental/investigational and not medically necessary.

Documentation

Submission of the following information is necessary to initiate the prior authorization review: Testing or analysis confirming CD20 protein on the surface of the B-cell (if applicable)

Coverage Criteria

Oncologic Indications

Authorization of 12 months may be granted for treatment of any of the following oncologic disorders that are CD20-positive as confirmed by testing or analysis:

- B-cell acute lymphoblastic leukemia (ALL)

- B-cell lymphomas:
  - HIV-Related B-Cell Lymphomas
  - B-cell lymphoblastic lymphoma
  - Burkitt lymphoma
  - Castleman's disease
  - Diffuse large B-cell lymphoma
  - Follicular lymphoma
  - High grade B-cell lymphoma (including high-grade B-cell lymphoma with translocations of MYC and BCL2 and/or BCL6 [double/triple hit lymphoma], high-grade B-cell lymphoma, not otherwise specified)
  - Histological transformation of indolent lymphomas to diffuse large B-cell lymphoma
  - Histological transformation of indolent lymphomas to high-grade B-cell lymphoma with MYC and BCL6 without BCL2 rearrangements
  - Mantle cell lymphoma
  - Marginal zone lymphomas
    - Nodal marginal zone lymphoma
    - Extranodal marginal zone lymphoma (gastric and non-gastric MALT lymphoma)
    - Splenic marginal zone lymphoma
  - Post-transplant lymphoproliferative disorder (PTLD)
  - Pediatric Aggressive Mature B-Cell Lymphomas
  - Primary Mediastinal Large B-Cell Lymphoma
- Central nervous system (CNS) cancers:
  - Leptomeningeal metastases from lymphomas
  - Primary CNS lymphoma
- CLL/Small lymphocytic lymphoma (SLL)
- Hairy cell leukemia
- Rosai-Dorfman disease
- Hodgkin's lymphoma, nodular lymphocyte-predominant
- Primary cutaneous B-cell lymphoma
- Waldenström's macroglobulinemia/lymphoplasmacytic lymphoma (LPL)/Bing-Neel syndrome

Hematologic Indications

Authorization of 12 months may be granted for treatment of any of the following indications:

- Refractory immune or idiopathic thrombocytopenic purpura (ITP)
- Autoimmune hemolytic anemia
- Thrombotic thrombocytopenic purpura
- Chronic graft-versus-host disease (GVHD)
- Prevention of Epstein-Barr virus (EBV)-related PTLD
- As part of a non-myeloablative conditioning regimen for allogeneic transplant

Immune Checkpoint Inhibitor-Related Toxicities

Authorization of 3 months may be granted for treatment of immune checkpoint inhibitor-related toxicities.

Continuation of Therapy

For oncologic indications: Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an oncologic indication listed in coverage criteria section when there is no evidence of unacceptable toxicity.

For immune checkpoint inhibitor-related toxicities: Authorization of 3 months may be granted for continued treatment in members requesting reauthorization for treatment of immune checkpoint inhibitor-related toxicities who are experiencing benefit from therapy.

For all other indications: Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in the coverage criteria section who are experiencing benefit from therapy.

Section 3: Oncology Clinical Policy

PURPOSE

The purpose of this policy is to define the Novologix NCCN® Regimen Prior Authorization Program.

SCOPE

This policy applies to clients who have implemented the Novologix NCCN® Program as a part of their medical and/or pharmacy prior authorization solution.

PROGRAM DESCRIPTION

The National Comprehensive Care Network® (NCCN®) is an alliance of leading cancer centers devoted to patient care, research and education dedicated to improving the quality, effectiveness, and efficiency of cancer care so patients can live better lives.[1] It is comprised of oncology experts who convene regularly to establish the best treatments for patients. NCCN develops various resources for use by stakeholders in the health care delivery system. These resources include, but are not limited to, the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®), the NCCN Drugs & Biologics Compendium (NCCN Compendium®) and the NCCN Chemotherapy Order Templates (NCCN Templates®).

NCCN Templates® are based on NCCN Guidelines® and NCCN Compendium®. The NCCN Compendium lists the appropriate drugs and biologics as treatment options for specific cancers using U.S. Food and Drug Administration (FDA)-approved disease indications and specific NCCN panel recommendations. Each recommendation is supported by a level of evidence category.

NCCN Categories of Evidence and Consensus[2]

- Category 1: Based upon high-level evidence, there is uniform NCCN consensus that the

intervention is appropriate.
• Category 2A: Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
• Category 2B: Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.
• Category 3: Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

POLICY

Policy for Regimen Prior Authorization
A regimen prior authorization allows submission of a single prior authorization request for all oncology drugs or biologics within an NCCN template that require prior authorization.

PROCEDURE

This policy provides coverage of a regimen review when all of the following criteria are met:
1. Regimen prior authorization reviews, based on NCCN templates, are initiated through the provider portal.
- If the prior authorization request is submitted via phone or fax, each drug or biologic will need to be submitted and reviewed as a separate prior authorization request for review with drug-specific criteria.

2. The prior authorization review is requested for an oncology drug or biologic.
3. The member is eligible for regimen review.
4. The indication is for a cancer that is eligible for regimen review. Currently, the cancer types in scope for regimen review include the following:
- Ampullary Adenocarcinoma
- Anal Carcinoma
- B-Cell Lymphomas
- Basal Cell Skin Cancer
- Biliary Tract Cancers
- Bone Cancer
- Breast Cancer
- Bladder Cancer
- Central Nervous System Cancers
- Cervical Cancer
- Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma
- Chronic Myeloid leukemia
- Colon Cancer
- Dermatofibrosarcoma Protuberans
- Esophageal Cancer
- Gastric Cancer
- Gastrointestinal Stromal Tumors
- Gestational Trophoblastic Neoplasms

- Hairy Cell Leukemia
- Head and Neck Cancers
- Histiocytic Neoplasms
- Hodgkin Lymphoma
- Hepatocellular Carcinoma
- Kaposi Sarcoma
- Kidney Cancer
- Melanoma: Cutaneous
- Melanoma: Uveal
- Merkel Cell Carcinoma
- Mesothelioma: Peritoneal
- Mesothelioma: Pleural
- Multiple Myeloma
- Myelodysplastic Syndromes
- Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Gene Fusions
- Myeloproliferative Neoplasms
- Neuroendocrine and Adrenal Tumors
- Non-Small Cell Lung Cancer
- Occult Primary
- Ovarian Cancer
- Pancreatic Cancer
- Penile Cancer
- Primary Cutaneous Lymphomas
- Prostate Cancer
- Rectal Cancer
- Small Bowl Adenocarcinoma
- Small Cell Lung Cancer
- Soft Tissue Sarcoma
- Squamous Cell Skin Cancer
- Systemic Mastocytosis
- Systemic Light Chain Amyloidosis
- T-Cell Lymphomas
- Testicular Cancer
- Thymomas and Thymic Carcinomas
- Thyroid Carcinoma
- Uterine Neoplasms
- Vaginal Cancer
- Vulvar Cancer
- Waldenström Macroglobulinemia / Lymphoplasmacytic Lymphoma
- Wilms Tumor (Nephroblastoma)

In addition, the following criteria must be met for approval:

1. The requested regimen for the drug(s) or biologic(s) and indication is consistent with an NCCN recommendation with a level of evidence category of 1 or 2A.

2. The NCCN template must be accepted by the provider without modification.

Further review may be indicated when the above criteria are not met.

Authorizations may be granted for 12 months or as medically required, based on the member's condition and provider's assessment.

Supportive Care: Myeloid Growth Factor Therapy

Granulocyte colony stimulating factors are recommended for primary prophylaxis based on the febrile neutropenia risk of the chemotherapy regimen. Febrile neutropenia risk levels vary by NCCN Chemotherapy Order template and are listed at the top of the template. Regimens associated with a high or intermediate risk of febrile neutropenia may include a granulocyte colony stimulating factor as part of the prior authorization.

Continuation of Therapy

To submit a request for continuation of therapy, a new regimen prior authorization review must be requested. Upon template selection, the template must be modified to include the appropriate therapies being used for maintenance treatment. The regimen request will be submitted for further review.

Dosage and Administration

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and evidence-based practice guidelines.

REFERENCES:

SECTION 1

1. Riabni [package insert]. Thousand Oaks, CA: Amgen, Inc.;June 2022.
2. Rituxan [package insert]. South San Francisco, CA: Genentech, Inc.; December 2021.
3. Rituxan Hycela [package insert]. South San Francisco, CA: Genentech, Inc.; June 2021.
4. Ruxience [package insert]. New York, NY: Pfizer; October 2023.
5. Truxima [package insert]. North Wales, PA: Teva Pharmaceuticals USA, Inc; February 2022.

SECTION 2

1. Rituxan [package insert]. South San Francisco, CA: Genentech, Inc.; December 2021.
2. Truxima [package insert]. North Wales, PA: Teva Pharmaceuticals USA, Inc.: February 2022.
3. Micromedex Solutions [database online]. Truven Health Analytics, Greenwood Village, Colorado, USA. Available at: http://www.micromedexsolutions.com/. Accessed April 11, 2024.
4. The NCCN Drugs & Biologics Compendium® © 2024 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed April 11, 2024.
5. Arber D, Orazi A, Vardiman J, et al. The 2016 revision to the World Health Organization classification of myeloid neoplasms and acute leukemia. Blood. May 19, 2016;127(20):2391-2405.
6. The NCCN Clinical Practice Guidelines in Oncology® Acute Lymphoblastic Leukemia (Version 4.2023). © 2024 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed April 11, 2024.
7. Lexicomp Online®, AHFS® Drug Information, Hudson, Ohio: Wolters Kluwer Clinical Drug Information, Inc.; http://online.lexi.com [available with subscription]. Accessed April 11, 2024.

8. Tomblyn M, Chiller T, Einsele H, et al. Guidelines for preventing infectious complications among hematopoietic cell transplantation recipients: a global perspective. Biol Blood Marrow Transplant. 2009; 15(10):1143-1238. URL: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3103296/pdf/nihms205400.pdf. Accessed April 30, 2019.
9. Ruxience [package insert]. NY, NY: Pfizer Inc; October 2023.
10. Riabni [package insert]. Thousand Oaks, CA: Amgen Inc.; February 2023.

SECTION 3

1. National Comprehensive Cancer Network. About NCCN website. https://www.nccn.org/home/about, accessed September 9, 2024.
2. National Comprehensive Cancer Network. NCCN Categories of Evidence and Consensus website, https://www.nccn.org/guidelines/guidelines-process/development-and-update-of-guidelines, accessed September 9, 2024.
3. National Comprehensive Cancer Network. NCCN Guidelines website. https://www.nccn.org/guidelines/category_1, accessed September 9, 2024. (Note: An account may be required.)
4. National Comprehensive Cancer Network. NCCN Drugs and Biologics Compendium website https://www.nccn.org/compendia-templates/compendia/drugs-and-biologics-compendia, accessed September 9, 2024. (Note: A subscription may be required.)
5. National Comprehensive Cancer Network. NCCN Chemotherapy Order Templates (NCCN Templates) website. https://www.nccn.org/compendia-templates/nccn-templates-main/browse-by-cancer-type, accessed September 9, 2024. (Note: A subscription may be required.)