POLICY Document for bendamustine products

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

Section 2: Oncology Clinical Policy
- Policy information specific to regimen review per NCCN Guidelines.

Section 1: Clinical Criteria

Specialty Guideline Management bendamustine products

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
Treanda	bendamustine
Bendeka	bendamustine
Belrapzo	bendamustine
Vivimusta	bendamustine

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

- Chronic lymphocytic leukemia (CLL)

- Indolent B-cell non-Hodgkin lymphoma (NHL) that has progressed during or within six months of treatment with rituximab or a rituximab-containing regimen

Compendial Uses

- Classic Hodgkin lymphoma (cHL)
- Nodular lymphocyte predominant Hodgkin lymphoma (NLPHL)
- Multiple myeloma (MM)
- CLL/small lymphocytic lymphoma (SLL)
- B-cell lymphomas:
    - Human immunodeficiency virus (HIV)-related B-cell lymphoma
    - Diffuse large B-cell lymphoma (DLBCL)
    - Follicular lymphoma
    - High grade B-cell lymphoma
    - Histologic transformation of indolent lymphomas to diffuse large B-cell lymphoma
    - Marginal zone lymphoma
        - Nodal marginal zone lymphoma
        - Gastric mucosa associated lymphoid tissue (MALT) lymphoma (extranodal marginal zone lymphoma of the stomach)
        - Nongastric MALT lymphoma (extranodal marginal zone lymphoma of nongastric sites)
        - Splenic marginal zone lymphoma
    - Mantle cell lymphoma (MCL)
    - Post-transplant lymphoproliferative disorders (PTLD)
- T-cell lymphomas:
    - Adult T-cell leukemia/lymphoma (ATLL)
    - Hepatosplenic T-Cell lymphoma
    - Peripheral T-cell lymphoma (PTCL)
    - Breast implant associated anaplastic large cell lymphoma (ALCL)
    - T-cell prolymphocytic leukemia
- Waldenström's macroglobulinemia/lymphoplasmacytic lymphoma/Bing-Neel syndrome
- Systemic light chain amyloidosis
- Hematopoietic cell transplantation
- Cold agglutinin disease
- Mycosis fungoides (MF) and Sezary syndrome (SS)

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

Coverage Criteria

B-Cell Lymphoma

Authorization of 12 months may be granted for treatment of B-cell lymphomas with any of the following subtypes:

- HIV-related B-cell lymphoma (HIV-related diffuse large B-cell lymphoma, primary effusion lymphoma, and human herpesvirus-8 (HHV8)-positive diffuse large B-cell lymphoma, plasmablastic lymphoma) when all of the following criteria are met:
  - The requested drug is used as subsequent therapy
  - The requested drug is used in combination with polatuzumab vedotin-piiq with or without rituximab
  - The member is not a candidate for transplant or the requested drug will be used as a bridging option until CAR T-cell product is available
- Diffuse large B-cell lymphoma (DLBCL) when all of the following criteria are met:
  - The requested drug is used as subsequent therapy
  - The requested drug is used in combination with polatuzumab vedotin-piiq with or without rituximab
  - The member is not a candidate for transplant or the requested drug will be used as a bridging option until CAR T-cell product is available
- Follicular lymphoma
- High-grade B-cell lymphoma when all of the following criteria are met:
  - The requested drug is used as subsequent therapy
  - The requested drug will be used in combination with polatuzumab vedotin-piiq with or without rituximab
  - The member is not a candidate for transplant or the requested drug will be used as a bridging option until CAR T-cell product is available.
- Histologic transformation of indolent lymphomas to diffuse large B-cell lymphoma when all of the following criteria are met:
  - The requested drug is used in combination with polatuzumab vedotin-piiq with or without rituximab.
  - The member has received treatment with an anthracycline-based regimen (e.g., doxorubicin)
  - The member is not a candidate for transplant.
- Mantle cell lymphoma (MCL) when any of the following criteria are met:
  - The requested drug is used in combination with rituximab, or
  - The requested drug is used as a component of RBAC500 (rituximab, bendamustine, and cytarabine), or
  - The requested drug is used in combination with acalabrutinib and rituximab
- Marginal zone lymphoma
  - Nodal marginal zone lymphoma when used in combination with rituximab or obinutuzumab.
  - Gastric MALT lymphoma (extranodal marginal zone lymphoma of the stomach) when used in combination with rituximab or obinutuzumab.
  - Nongastric MALT lymphoma (extranodal marginal zone lymphoma of nongastric sites) when used in combination with rituximab or obinutuzumab.
  - Splenic marginal zone lymphoma when used in combination with rituximab or obinutuzumab.
- Post-transplant lymphoproliferative disorders (monomorphic PTLD B-cell type) when all of the following criteria are met:
  - The requested drug is used as subsequent therapy

- The member is not a candidate for transplant or the requested drug will be used as a bridging option until CAR T-cell product is available
- The requested drug will be used in combination with polatuzumab vedotin-piiq with or without rituximab

T-Cell Lymphoma

Authorization of 12 months may be granted for treatment of T-cell lymphomas with any of the following subtypes:

- Adult T-cell leukemia/lymphoma (ATLL) when all of the following criteria are met:
  - The requested drug is used as a single agent
  - The requested drug is used as subsequent therapy
- Hepatosplenic T-Cell lymphoma when all of the following criteria are met:
  - The requested drug is used as a single agent
  - The requested drug is used for refractory disease after 2 first-line therapy regimens
- Peripheral T-cell lymphoma (PTCL) [including the following subtypes: anaplastic large cell lymphoma, peripheral T-cell lymphoma not otherwise specified, angioimmunoblastic T-cell lymphoma, enteropathy associated T-cell lymphoma, monomorphic epitheliotropic intestinal T-cell lymphoma, nodal peripheral T-cell lymphoma with TFH phenotype, or follicular T-cell lymphoma] when all of the following criteria are met:
  - The requested drug is used as a single agent
  - The requested drug is used as palliative or subsequent therapy
- Breast implant associated anaplastic large cell lymphoma (ALCL) when all of the following are met:
  - The requested drug is used as a single agent
  - The requested drug is used as subsequent therapy
- T-cell prolymphocytic leukemia when used as a single agent for symptomatic disease

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

Authorization of 12 months may be granted for treatment of CLL/SLL without chromosome 17p deletion or TP53 mutation

Waldenström's Macroglobulinemia/Lymphoplasmacytic Lymphoma/Bing-Neel Syndrome

Authorization of 12 months may be granted for treatment of Waldenström's macroglobulinemia/lymphoplasmacytic lymphoma or Bing-Neel syndrome when either of the following criteria are met:

- The requested drug will be used in combination with rituximab, or
- The requested drug will be used as a single agent.

Multiple Myeloma (MM)

Authorization of 12 months may be granted for treatment of MM when all of the following criteria are met:

- The disease is relapsed or refractory and the member has tried more than 3 prior therapies, and

- The requested drug will be used in any of the following regimens:
  - In combination with lenalidomide and dexamethasone, or
  - In combination with bortezomib and dexamethasone, or
  - In combination with carfilzomib and dexamethasone, or
  - As a single agent.

Classic Hodgkin Lymphoma (cHL)

Authorization of 12 months may be granted for treatment of cHL when all of the following criteria are met:

- The requested drug will be used as subsequent therapy or palliative therapy, and
- The requested drug will be used in any of the following regimens:
  - In combination with brentuximab vedotin, or
  - In combination with gemcitabine and vinorelbine, or
  - In combination with carboplatin and etoposide, or
  - As a single agent.

Nodular Lymphocyte Predominant Hodgkin Lymphoma (NLPHL)

Authorization of 12 months may be granted for treatment of nodular lymphocyte predominant Hodgkin lymphoma when all of the following criteria are met:

- The requested drug will be used as subsequent therapy
- The requested drug will be used in combination with rituximab

Systemic Light Chain Amyloidosis

Authorization of 12 months may be granted for treatment of systemic light chain amyloidosis when all of the following criteria are met:

- The requested drug will be used in combination with dexamethasone
- The requested drug will be used to treat relapsed or refractory disease

Hematopoietic Cell Transplantation

Authorization of 12 months may be granted for use in hematopoietic cell transplantation when all of the following criteria are met:

- The requested drug will be used as conditioning for autologous transplant
- The requested drug will be used in combination with etoposide, cytarabine and melphalan

Cold Agglutinin Disease

Authorization of 12 months may be granted for treatment of cold agglutinin disease when used in combination with rituximab.

Mycosis Fungoides/Sezary Syndrome

Authorization of 12 months may be granted for treatment of mycosis fungoides/Sezary syndrome when used in combination with brentuximab vedotin.

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Continuation of Therapy

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in the coverage criteria section when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

Section 2: 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. Treanda [package insert]. Parsippany, NJ: Teva Pharmaceuticals USA, Inc.; October 2022.
2. Bendeka [package insert]. Parsippany, NJ: Teva Pharmaceuticals USA, Inc.; January 2024.
3. Belrapzo [package insert]. Woodcliff Lake, NJ; Eagle Pharmaceuticals, Inc; January 2024.
4. Vivimusta [package insert]. Princeton, NJ; Slayback Pharma LLC; December 2022.
5. Bendamustine [package insert]. Durham, NC; Accord Healthcare Inc; November 2022.
6. The NCCN Drugs & Biologics Compendium® © 2025 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed February 3, 2025.
7. IBM Micromedex® DRUGDEX® (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at https://www.micromedexsolutions.com Accessed April 8, 2024.

8. Calquence [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; January 2025.

SECTION 2

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.)