

## Clinical Policy: Bendamustine (Bendeka, Treanda)

Reference Number: PA.CP.PHAR.307

Effective Date: 01/18

Last Review Date: 11/17

[Coding Implications](#)

[Revision Log](#)

### Description

The intent of the criteria is to ensure that patients follow selection elements established by Pennsylvania Health and Wellness<sup>®</sup> clinical policy for bendamustine hydrochloride (Bendeka<sup>®</sup>, Treanda<sup>®</sup>).

### Policy/Criteria

It is the policy of Pennsylvania Health and Wellness<sup>®</sup> that Bendeka and Treanda are medically necessary when the following criteria are met:

#### I. Initial Approval Criteria

##### A. Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma\* (must meet all):

1. Diagnosis of chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL);
2. Member does not have either of the following:
  - a. Creatinine clearance (CrCl) < 40 mL/min;
  - b. Moderate or severe hepatic impairment (i or ii):
    - i. AST or ALT 2.5 to 10 times the upper limit of normal [ULN] and total bilirubin 1.5 to 3 times ULN;
    - ii. Total bilirubin > 3 times ULN;
3. Member has no known hypersensitivity (e.g., anaphylactic and anaphylactoid reactions) to bendamustine, polyethylene glycol 400, propylene glycol, or monothioglycerol.

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\*CLL and SLL, non-Hodgkin lymphoma (NHL) subtypes, are different manifestations of the same disease.<sup>4</sup>

**Approval duration: 3 months**

##### B. Indolent B-Cell Non-Hodgkin Lymphoma\*† (must meet all):

1. Diagnosis of indolent/low-grade B-cell non-Hodgkin lymphoma (NHL);
2. Disease progression during or within six months of treatment with rituximab or a rituximab-containing regimen;
3. Member does not have either of the following:
  - a. CrCl < 40 mL/min;
  - b. Moderate or severe hepatic impairment (i or ii):
    - i. AST or ALT 2.5 to 10 times ULN and total bilirubin 1.5 to 3 times ULN;
    - ii. Total bilirubin > 3 times ULN;
4. Member has no known hypersensitivity (e.g., anaphylactic and anaphylactoid reactions) to bendamustine, polyethylene glycol 400, propylene glycol, or monothioglycerol.

*\*See Appendix B for a complete list of B-cell lymphomas, including examples of types that may present in an indolent or low-grade fashion.*

*†NHL subtypes (including B-cell lymphomas) for which NCCN recommends bendamustine therapy are listed under section I.C. “Other diagnoses/indications”.*

**Approval duration: 3 months**

**C. Other diagnoses/indications:** Refer to PA.CP.PHAR.57 - Global Biopharm Policy.

1. The following NCCN recommended uses for Bendeka and Treanda, meeting NCCN categories 1, 2a, or 2b, are approved per the PA.CP.PHAR.57 Global Biopharm Policy:
  - a. Multiple myeloma;
  - b. Small cell lung cancer (SCLC);
  - c. Hodgkin lymphoma – classical;
  - d. Non-Hodgkin lymphoma (NHL):
    - i. B-cell lymphomas:
      - a) Follicular lymphoma;
      - b) Marginal zone lymphomas:
        - 1) Gastric MALT lymphoma;
        - 2) Non-gastric MALT lymphoma;
        - 3) Splenic marginal zone lymphoma;
      - c) Mantle cell lymphoma;
      - d) Waldenstrom’s macroglobulinemia/lymphoplasmacytic lymphoma;
      - e) Diffuse large B-cell lymphoma;
      - f) AIDS-related B-cell lymphoma;
      - g) Primary cutaneous B-cell lymphomas;
    - ii. T-cell lymphomas:
      - a) Adult T-cell leukemia/lymphoma;
      - b) Mycosis fungoides (MF)/Sezary syndrome (SS);
      - c) Peripheral T-cell lymphoma;
      - d) Primary cutaneous CD30+ T-cell lymphoproliferative disorders.

**II. Continued Approval**

**A. All Indications** (must meet all):

1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria; or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
2. No disease progression or unacceptable toxicity;
3. Member has none of the following reasons to discontinue:
  - a. Known hypersensitivity (e.g., anaphylactic and anaphylactoid reactions) to bendamustine, polyethylene glycol 400, propylene glycol, or monothioglycerol;
  - b. Grade 4 (life-threatening) infusion reactions;
  - c. CrCl < 40 mL/min;
  - d. Moderate or severe hepatic impairment (i or ii):
    - i. AST or ALT 2.5 to 10 times ULN and total bilirubin 1.5 to 3 times ULN;
    - ii. Total bilirubin > 3 times ULN.

**Approval duration: 6 months**

**B. Other diagnoses/indications (must meet 1 or 2):**

1. Currently receiving medication via Pennsylvania Health and Wellness benefit and documentation supports positive response to therapy; or the Continuity of Care policy (PA.LTSS.PHAR.01) applies; or
2. Refer to PA.CP.PHAR.57 - Global Biopharm Policy.

**Background**

*Description/Mechanism of Action:*

Bendamustine is a bifunctional mechlorethamine derivative containing a purine-like benzimidazole ring. Mechlorethamine and its derivatives form electrophilic alkyl groups. These groups form covalent bonds with electron-rich nucleophilic moieties, resulting in interstrand DNA crosslinks. The bifunctional covalent linkage can lead to cell death via several pathways. Bendamustine is active against both quiescent and dividing cells. The exact mechanism of action of bendamustine remains unknown.

*Formulations:*

- Bendeka (bendamustine hydrochloride) Injection is supplied in individual cartons of 5 mL multiple-dose vials containing 100 mg of bendamustine hydrochloride as a ready-to-dilute solution:
  - 100 mg/4 mL (25 mg/mL)
- Treanda (bendamustine hydrochloride) Injection is supplied as a 90 mg/mL solution in individual cartons as follows:
  - 45 mg/0.5 mL of solution in a single-dose vial
  - 180 mg/2 mL of solution in a single-dose vial
- Treanda (bendamustine hydrochloride) for Injection is supplied in individual cartons as follows:
  - 25 mg white to off-white lyophilized powder in a 8 mL single-dose vial
  - 100 mg white to off-white lyophilized powder in a 20 mL single-dose vial

*FDA Approved Indications:*

Bendeka and Treanda (bendamustine hydrochloride) are alkylating drugs/intravenous formulations indicated for treatment of patients with:

- Chronic lymphocytic leukemia (CLL). Efficacy relative to first line therapies other than chlorambucil has not been established.
- Indolent B-cell non-Hodgkin lymphoma (NHL) that has progressed during or within six months of treatment with rituximab or a rituximab-containing regimen.

**Appendices**

**Appendix A: Abbreviation Key**

CLL: Chronic lymphocytic leukemia  
DLBCL: Diffuse large B-cell lymphoma  
MALT: Mucosa-associated lymphoid tissue  
MF: Mycosis fungoides

MGUS: Monoclonal gammopathy of undetermined significance  
NHL: Non-Hodgkin lymphoma  
SCLC: Small cell lung cancer

SLL: Small lymphocytic lymphoma  
 SS: Sezary syndrome

ULN: Upper limit of normal  
 WHO: World Health Organization

**Appendix B: 2016 WHO Classification of Mature B-Cell Neoplasms<sup>7</sup>**

<b>Mature B-Cell Neoplasms: Types and Subtypes*</b>	
Chronic lymphocytic leukemia/small lymphocytic lymphoma	Large B-cell lymphoma with IRF4 rearrangement
Monoclonal B-cell lymphocytosis	Primary cutaneous follicle center lymphoma
B-cell prolymphocytic leukemia	Mantle cell lymphoma
Splenic marginal zone lymphoma	In situ mantle cell neoplasia
Hairy cell leukemia	Diffuse large B-cell lymphoma (DLBCL), NOS Germinal center B-cell type Activated B-cell type
Splenic B-cell lymphoma/leukemia, unclassifiable*	
Splenic diffuse red pulp small B-cell lymphoma Hairy cell leukemia-variant	
Lymphoplasmacytic lymphoma Waldenstrom macroglobulinemia	Primary DLBCL of the central nervous system (CNS)
Monoclonal gammopathy of undetermined significance (MGUS), IgM μ heavy-chain disease γ heavy-chain disease α heavy-chain disease	Primary cutaneous DLBCL, leg type
	EBV+, DLBCL, NOS
	EBV+ mucocutaneous ulcer
	DLBCL associated with chronic inflammation
Monoclonal gammopathy of undetermined significance (MGUS), IgG/A	Lymphomatoid granulomatosis
Plasma cell myeloma	Primary mediastinal (thymic) large B-cell lymphoma
Solitary plasmacytoma of bone	Intravascular large B-cell lymphoma
Extraosseous plasmacytoma	ALK+ large B-cell lymphoma
Monoclonal immunoglobulin deposition diseases	Plasmablastic lymphoma
Extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma)	Primary effusion lymphoma
Nodal marginal zone lymphoma	HHV8+ DLBCL, NOS
Pediatric nodal marginal zone lymphoma	Burkitt lymphoma
Follicular lymphoma In situ follicular neoplasia Duodenal-type follicular lymphoma	Burkitt-like lymphoma with 11q aberration
	High-grade B-cell lymphoma, with MYC and BCL2 and/or BCL6 rearrangements
	High-grade B-cell lymphoma, NOS
Pediatric-type follicular lymphoma	B-cell lymphoma, unclassifiable, with features intermediate between DLBCL and classical Hodgkin lymphoma

\*Based on clinical trials, examples of NHL B-cell lymphomas that may present with an indolent or low grade presentation include but are not limited to small lymphocytic lymphoma/B-cell

chronic lymphocytic leukemia, lymphoplasmacytic lymphoma ( $\pm$  Waldenstrom's macroglobulinemia), plasma cell myeloma/plasmacytoma, hairy cell leukemia, follicular lymphoma (grades I and II), marginal zone B-cell lymphoma, and mantle cell lymphoma.<sup>1,2,5,6</sup>

**Coding Implications**

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J9033	Injection, bendamustine HCl (Treanda), 1 mg
J9034	Injection, bendamustine HCl (Bendeka), 1 mg
J9035	Injection, bevacizumab, 10 mg

**ICD-10-CM Diagnosis Codes that Support Coverage Criteria**

ICD-10-CM Codes	Description
B20	Human immune deficiency virus (HIV) disease
C81.00	Nodular lymphocyte predominant Hodgkin lymphoma, unspecified site
C81.10	Nodular sclerosis Hodgkin lymphoma, unspecified site
C81.20	Mixed cellularity Hodgkin lymphoma
C81.30	Lymphocyte depleted Hodgkin lymphoma
C81.40	Lymphocyte-rich Hodgkin lymphoma, unspecified site
C81.70	Other Hodgkin lymphoma, unspecified site
C82.00	Follicular lymphoma grade 1, unspecified site
C82.10	Follicular lymphoma grade 2, unspecified site
C82.20	Follicular lymphoma grade 3, unspecified site
C82.30	Follicular lymphoma grade IIIa, unspecified site
C82.40	Follicular lymphoma grade IIIb, unspecified site
C82.50	Follicle center lymphoma
C82.60	Cutaneous follicle center lymphoma, unspecified site
C82.80	Other types of follicular lymphoma, unspecified site
C83.00	Small cell B-cell lymphoma, unspecified site
C83.10	Mantle cell lymphoma, unspecified site
C83.30	Diffuse large B-cell lymphoma, unspecified site
C84.00	Mycosis fungoides, unspecified site
C84.10	Sezary disease, unspecified site
C84.40	Peripheral C-cell lymphoma, not classified, unspecified site
C84.60	Anaplastic large cell lymphoma, ALK positive, unspecified site
C84.70	Anaplastic large cell lymphoma, ALK negative, unspecified site
C85.00	Other specified types of non-Hodgkin lymphoma, unspecified site
C85.90	Non-Hodgkin lymphoma, unspecified, unspecified site

ICD-10-CM Codes	Description
C88.4	Extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue (MALT-lymphoma)
C86.2	Enteropathy type (intestinal) T-cell lymphoma
C86.5	Angioimmunoblastic T-cell lymphoma
C86.6	Primary cutaneous CD30-positive T-cell proliferations
C88.0	Waldenstrom's macroglobulinemia
C90.00	Multiple myeloma not having achieved remission
C90.02	Multiple myeloma in relapse
C91.10	Chronic lymphocytic leukemia of B-cell type, not having achieve remission
C91.12	Chronic lymphocytic leukemia of B-cell type in relapse
C91.50	Adult T-cell lymphoma leukemia (HTLV-1-associated) not having achieved remission
C91.52	Adult T-cell lymphoma leukemia (HTLV-1-associated) in relapse

Reviews, Revisions, and Approvals	Date	Approval Date

**References**

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2. Treanda prescribing information. North Wales, PA: Teva Pharmaceuticals USA, Inc.; October 2016. Available at [http://www.treandahcp.com/pdf/TREANDA\\_final\\_PI.pdf](http://www.treandahcp.com/pdf/TREANDA_final_PI.pdf). Accessed January 4, 2017.
3. Bendamustine hydrochloride. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at NCCN.org. Accessed January 4, 2017.
4. Chronic lymphocytic leukemia/small lymphocytic lymphoma (Version 1.2017). In: National Comprehensive Cancer Network Guidelines. Available at NCCN.org. Accessed January 4, 2017.
5. B-cell lymphomas (Version 1.2017). In: National Comprehensive Cancer Network Guidelines. Available at NCCN.org. Accessed January 4, 2017.
6. Freedman AS, Friedberg JW. Classification of the hematopoietic neoplasms. In: UpToDate, Waltham, MA: Walters Kluwer Health; 2016. Available at UpToDate.com. Accessed January 4, 2017.
7. Swerdlow SH, Campo E, Pileri SA, et al. The 2016 revision of the World Health Organization classification of lymphoid neoplasms. *Blood*. 2016; 127: 2375-2390.