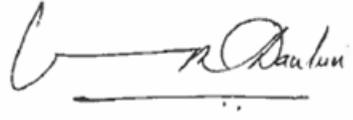


**Prior Authorization Review Panel**

**CHC-MCO Policy Submission**

A separate copy of this form must accompany each policy submitted for review.  
Policies submitted without this form will not be considered for review.

<b>Plan: PA Health &amp; Wellness</b>	<b>Submission Date: 11/01/2022</b>
<b>Policy Number: PA.CP.PHAR.307</b>	<b>Effective Date: 01/2018</b> <b>Revision Date: 10/2022</b>
<b>Policy Name: Bendamustine (Belrapzo, Bendeka, Treanda)</b>	
<p><b>Type of Submission – <u>Check all that apply:</u></b></p> <p> <input type="checkbox"/> New Policy  <input checked="" type="checkbox"/> Revised Policy*  <input type="checkbox"/> Annual Review - No Revisions  <input type="checkbox"/> Statewide PDL - <i>Select this box when submitting policies for Statewide PDL implementation and when submitting policies for drug classes included on the Statewide PDL.</i> </p>	
<p><b>*All revisions to the policy <u>must</u> be highlighted using track changes throughout the document.</b></p> <p><b>Please provide any changes or clarifying information for the policy below:</b></p> <p>4Q 2022 annual review: added SLCA and hematopoietic cell transplantation under NCCN recommended use given category 2A recommendation; removed primary cutaneous lymphomas as use is no longer supported by NCCN primary cutaneous lymphoma guideline; references reviewed and updated.</p>	
<p><b>Name of Authorized Individual (Please type or print):</b></p> <p>Venkateswara R. Davuluri, MD</p>	<p><b>Signature of Authorized Individual:</b></p> 

## Clinical Policy: Bendamustine (Belrapzo, Bendeka, Treanda)

Reference Number: PA.CP.PHAR.307

Effective Date: 01/2018

Last Review Date: 10/2022

[Coding Implications](#)  
[Revision Log](#)

### Description

Bendamustine hydrochloride (Belrapzo<sup>®</sup>, Bendeka<sup>®</sup>, Treanda<sup>®</sup>) is an alkylating drug.

### FDA Approved Indication(s)

Belrapzo, Bendeka, and Treanda are indicated for the 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

### Policy/Criteria

It is the policy of PA Health & Wellness<sup>®</sup> that Belrapzo, 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) (i.e., small lymphocytic lymphoma [SLL]);
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age  $\geq$  18 years;
4. Prescribed in combination with rituximab, Arzerra<sup>®</sup>, or Gazyva<sup>®</sup>;
5. Request meets one of the following (a or b):
  - a. Dose does not exceed 100 mg/m<sup>2</sup> on Days 1 and 2 of a 28-day cycle, up to 6 cycles;
  - b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Approval duration: 6 months**

##### B. Non-Hodgkin B-Cell Lymphomas (must meet all):

1. One of the following diagnoses (a through j):
  - a. Indolent B-cell non-Hodgkin lymphoma that has progressed during or within six months of treatment with rituximab or a rituximab-containing regimen;
  - b. Follicular lymphoma;
  - c. Gastric MALT lymphoma;
  - d. Nongastric MALT lymphoma;
  - e. Nodal marginal zone lymphoma;
  - f. Splenic marginal zone lymphoma;
  - g. Mantle cell lymphoma;
  - h. Diffuse large B-cell lymphoma(DLBCL) (*as subsequent therapy*);\*
  - i. AIDS-related B-cell lymphoma (*as subsequent therapy*);\*

- j. Monomorphic post-transplant lymphoproliferative disorder (PTLD) (B-cell type) (*as subsequent therapy*);\*
  - k. High-grade B-cell lymphomas: not otherwise specified or with translocations of MYC and BCL2 and/or BCL6 (double/triple hit lymphoma) (*as subsequent therapy*);\*
- \*See Appendix B - prior authorization may be required for prior therapies*
- 2. Prescribed by or in consultation with an oncologist or hematologist;
  - 3. Age  $\geq$  18 years;
  - 4. For nodal/splenic marginal zone lymphoma or gastric/nongastric MALT lymphoma, prescribed in combination with rituximab or Gazyva;
  - 5. For mantle cell lymphoma, prescribed in combination with rituximab;
  - 6. Request meets one of the following (a or b):
    - a. Dose does not exceed 120 mg/m<sup>2</sup> on Days 1 and 2 of a 21-day cycle, up to 8 cycles;
    - b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Approval duration: 6 months**

**C. NCCN Recommended Uses (off-label) (must meet all):**

- 1. Diagnosis of one of the following (a, b, c, d, e, or f):
    - a. Classic or nodular lymphocyte-predominant Hodgkin lymphoma (HL) (*as subsequent therapy*);\*
    - b. Pediatric HL (*as re-induction or subsequent therapy*);\*
    - c. Multiple myeloma (MM);
    - d. T-cell lymphomas (i, ii, or iii):
      - i. Hepatosplenic T-cell lymphoma (HSTCL) (*as subsequent therapy*);\*
      - ii. Adult T-cell leukemia/lymphoma (ATLL) (*as subsequent therapy*);\*
      - iii. Peripheral T-cell lymphoma (PTCL) (*as subsequent therapy*)\*:  
relapsed/refractory ALCL, 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 T-follicular helper (TFH) phenotype, or follicular T-cell lymphoma;
      - iv. Breast-implant associated ALCL (*as subsequent therapy*);\*
    - e. Waldenstrom's macroglobulinemia (i.e., lymphoplasmacytic lymphoma)
    - f. Systemic light chain amyloidosis (SLCA) in combination with dexamethasone (*as subsequent therapy*);\*
    - g. Hematopoietic cell transplantation in combination with etoposide, cytarabine, and melphalan for NHL without central nervous system (CNS) disease or for HL;
- \*See Appendix B - prior authorization may be required for prior therapies*
- 2. Prescribed by or in consultation with an oncologist or hematologist;
  - 3. Age  $\geq$  18 years, unless diagnosis is pediatric HL;
  - 4. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Approval duration: 6 months**

**D. Other diagnoses/indications**

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

**II. Continued Approval**

**A. All Indications in Section I (must meet all):**

1. Currently receiving medication via PA Health & Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care policy (PA.LTSS.PHAR.01) applies; Member is responding positively to therapy;
2. Member is responding positively to therapy;
3. If request is for a dose increase, request meets (a or b):
  - a. New dose does not exceed (i or ii):
    - i. CLL/SLL: 100 mg/m<sup>2</sup> on Days 1 and 2 of a 28-day cycle, up to 6 cycles;
    - ii. Non-Hodgkin indolent B-cell lymphoma: 120 mg/m<sup>2</sup> on Days 1 and 2 of a 21-day cycle, up to 8 cycles;
  - b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Approval duration: 12 months**

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

1. Currently receiving medication via PA Health & 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.PMN.53

**III. Diagnoses/Indications for which coverage is NOT authorized:**

- A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – PA.CP.PMN.53 for Medicaid or evidence of coverage documents.

**IV. Appendices/General Information**

*Appendix A: Abbreviation/Acronym Key*

ALCL: anaplastic large cell lymphoma  
ATLL: adult T-cell leukemia/lymphoma  
CLL: chronic lymphocytic leukemia  
CNS: central nervous system  
DLBCL: diffuse large B-cell lymphoma  
FDA: Food and Drug Administration  
HL: Hodgkin lymphoma  
HSTCL: hepatosplenic gamma-delta T-cell lymphoma  
MF: mycosis fungoides

MM: multiple myeloma  
NCCN: National Comprehensive Cancer Network  
NHL: non-Hodgkin lymphoma  
PTCL: peripheral T-cell lymphoma  
PTLD: post-transplant lymphoproliferative disorder  
SLCA: systemic light chain amyloidosis  
SLL: small lymphocytic lymphoma  
SS: Sezary syndrome

*Appendix B: Therapeutic Alternatives*

*This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.*

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
<b>Examples of primary therapies (NCCN)</b>		
<b>DLBCL</b>		
RCHOP (Rituxan® [rituximab], cyclophosphamide, doxorubicin, vincristine, prednisone)	Varies	Varies
EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin) + Rituxan® (rituximab)	Varies	Varies
<b>AIDS-related B-cell lymphoma</b>		
EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin) + Rituxan® (rituximab)	Varies	Varies
CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) + Rituxan® (rituximab)	Varies	Varies
<b>PTCL</b>		
CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone)	Varies	Varies
EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin)	Varies	Varies
<b>ATLL</b>		
CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone)	Varies	Varies
HyperCVAD (cyclophosphamide, vincristine, doxorubicin, dexamethasone) alternating with high-dose methotrexate and cytarabine	Varies	Varies
<b>HSTCL</b>		
DHAP (dexamethasone, cisplatin, cytarabine)	Varies	Varies
ICE (ifosfamide, carboplatin, etoposide)	Varies	Varies
<b>MM</b>		
Bortezomib/liposomal doxorubicin/dexamethasone	Varies	Varies
Carfilzomib/lenalidomide/dexamethasone	Varies	Varies
Daratumumab/bortezomib /dexamethasone	Varies	Varies
<b>Monomorphic PTLD (B-cell type)</b>		
RCHOP (Rituxan® [rituximab], cyclophosphamide, doxorubicin, vincristine, prednisone)	Varies	Varies
RCEPP (Rituxan® [rituximab], cyclophosphamide, etoposide, prednisone, procarbazine)	Varies	Varies
<b>SLCA</b>		

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Daratumumab and hyaluronidase-fihj/bortezomib/cyclophosphamide/dexamethasone	Varies	Varies

Therapeutic alternatives are listed as Brand name<sup>®</sup> (generic) when the drug is available by brand name only and generic (Brand name<sup>®</sup>) when the drug is available by both brand and generic.

*Appendix C: Contraindications/Boxed Warnings*

- Contraindication(s):
  - Belrapzo, Bendeka: patients with a history of a hypersensitivity reaction to bendamustine, polyethylene glycol 400, propylene glycol, or monothioglycerol
  - Treanda: patients with a history of a hypersensitivity reaction to bendamustine
- Boxed warning(s): none reported

**V. Dosage and Administration**

Indication	Dosing Regimen	Maximum Dose
CLL/SLL*	<p>Bendeka: 100 mg/m<sup>2</sup> IV over 10 minutes on Days 1 and 2 of a 28-day cycle, up to 6 cycles</p> <p>Belrapzo, Treanda: 100 mg/m<sup>2</sup> IV over 30 minutes on days 1 and 2 of a 28-day cycle, up to 6 cycles</p>	See regimen
Indolent B-cell lymphoma*	<p>Bendeka: 120 mg/m<sup>2</sup> IV over 10 minutes on Days 1 and 2 of a 21-day cycle, up to 8 cycles</p> <p>Belrapzo, Treanda: 120 mg/m<sup>2</sup> IV over 60 minutes on days 1 and 2 of a 21-day cycle, up to 8 cycles</p>	See regimen

\*Non-Hodgkin lymphomas

**VI. Product Availability**

Drug Name	Availability
Bendamustine (Belrapzo, Bendeka)	Solution (multiple-dose vial): 100 mg/4 mL
Bendamustine (Treanda)	Solution (single-dose vial): 45 mg/0.5 mL; 180 mg/2 mL Lyophilized powder (single-dose vial): 25 mg in a 20 mL vial; 100 mg in a 20 mL vial

**VII. References**

1. Belrapzo Prescribing Information. Woodcliff Lake, NJ: Eagle Pharmaceuticals, Inc; June 2022. Available at: [www.belrapzo.com](http://www.belrapzo.com). Accessed June 24, 2022.
2. Bendeka Prescribing Information. North Wales, PA: Teva Pharmaceuticals USA, Inc.; October 2021. Available at: <http://www.bendeka.com/>. Accessed June 24, 2022

3. Treanda Prescribing Information. North Wales, PA: Teva Pharmaceuticals USA, Inc.; June 2021. Available at: <http://treandahcp.com/>. Accessed June 24, 2022
4. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: [http://www.nccn.org/professionals/drug\\_compendium](http://www.nccn.org/professionals/drug_compendium). Accessed June 24, 2022
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10. National Comprehensive Cancer Network. Waldenstrom Macroglobulinemia/Lymphoplasmacytic Lymphoma Version 3.2022. Available at: [https://www.nccn.org/professionals/physician\\_gls/pdf/waldenstroms.pdf](https://www.nccn.org/professionals/physician_gls/pdf/waldenstroms.pdf). Accessed June 24, 2022.

**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
J9036	Injection, bendamustine HCl, (Belrapzo), 1 mg

Reviews, Revisions, and Approvals	Date	Approval Date
4Q 2018 annual review: summarized NCCN and FDA-approved uses for improved clarity; added specialist involvement in care; added PTLD (category 2A recommendation) as a covered indication per NCCN compendium; updated continued therapy section to include language for continuity of care; references reviewed and updated.	07/2018	
4Q 2019 annual review: No changes per Statewide PDL implementation 01-01-2020	10/2019	
4Q 2020 annual review: off-label criteria sets combined into one - additional criteria limited to subsequent therapy requirement; added additional therapeutic alternatives to Appendix B with NCCN	10/2020	

## CLINICAL POLICY

### Bendamustine



category 1: MM; added hepatosplenic gamma-delta T-cell lymphoma to non-Hodgkin T-cell lymphomas (off-label) uses and related therapeutic alternatives to Appendix B; appendix B prior therapy examples truncated; references reviewed and updated.		
4Q 2021 annual review: added Belrapzo; per NCCN category 2A recommendations: added requirements for combination use for CLL, MALT lymphoma, and marginal zone lymphoma; clarified types of PTCLs; removed gamma delta requirement from HSTCL; added off-label indications of breast-implant ALCL, nodular lymphocyte-predominant HL, pediatric HL, and high-grade B-cell lymphomas; for off-label indications, revised age requirement to allow bypass if diagnosis is pediatric HL; references reviewed and updated.	10/2021	
4Q 2022 annual review: added SLCA and hematopoietic cell transplantation under NCCN recommended use given category 2A recommendation; removed primary cutaneous lymphomas as use is no longer supported by NCCN primary cutaneous lymphoma guideline; references reviewed and updated.	10/2022	