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.

Plan: PA Health & Wellness	**Submission Date: 11/01/2021**
Policy Number: PA.CP.PHAR.307	**Effective Date: 01/2018** **Revision Date: 10/2021**
Policy Name: Bendamustine (Belrapzo, Bendeka, Treanda)	

Type of Submission – Check all that apply:

- ☐ **New Policy**
- ✓ **Revised Policy***
- ☐ **Annual Review - No Revisions**
- ☐ **Statewide PDL -** *Select this box when submitting policies for Statewide PDL implementation and when submitting policies for drug classes included on the Statewide PDL.*

***All revisions to the policy must be highlighted using track changes throughout the document.**

Please provide any changes or clarifying information for the policy below:

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

Name of Authorized Individual (Please type or print): **Venkateswara R. Davuluri, MD**	**Signature of Authorized Individual:**

Clinical Policy: Bendamustine (Belrapzo, Bendeka, Treanda)

Reference Number: PA.CP.PHAR.307
Effective Date: 01/18
Last Review Date: 10/2021

Coding Implications
Revision Log

Description
Bendamustine hydrochloride (Belrapzo®, Bendeka®, Treanda®) 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 Pennsylvania Health and Wellness® 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 ≥ 18 years;
4. Prescribed in combination with rituximab, Arzerra®, or Gazyva®;
5. Request meets one of the following (a or b):
   a. Dose does not exceed 100 mg/m^2 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 ≥ 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^2 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. Primary cutaneous lymphomas (i or ii):
      i. Primary cutaneous CD30+ T-cell lymphoproliferative disorder (*as subsequent therapy*)*: primary cutaneous anaplastic large cell lymphoma (ALCL);
      ii. Mycosis fungoides (MF)/Sezary syndrome (SS);
   e. 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*);*
   f. Waldenstrom's macroglobulinemia (i.e., lymphoplasmacytic lymphoma)

   **See Appendix B - prior authorization may be required for prior therapies*
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 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*).*

   **Prescribed regimen must be FDA-approved or recommended by NCCN*

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 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; 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^2 on Days 1 and 2 of a 28-day cycle, up to 6 cycles;
      ii. Non-Hodgkin indolent B-cell lymphoma: 120 mg/m^2 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 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.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 lymphoma
CLL: chronic lymphocytic leukemia
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
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
Examples of primary therapies (NCCN)		
DLBCL		
RCHOP (Rituxan® [rituximab], cyclophosphamide, doxorubicin, vincristine, prednisone)	Varies	Varies
EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin) + Rituxan® (rituximab)	Varies	Varies
AIDS-related B-cell lymphoma		
EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin) + Rituxan® (rituximab)	Varies	Varies
CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) + Rituxan® (rituximab)	Varies	Varies
PTCL		
CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone)	Varies	Varies
EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin)	Varies	Varies
ATLL		
CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone)	Varies	Varies
HyperCVAD (cyclophosphamide, vincristine, doxorubicin, dexamethasone) alternating with high-dose methotrexate and cytarabine	Varies	Varies
HSTCL		
DHAP (dexamethasone, cisplatin, cytarabine)	Varies	Varies
ICE (ifosfamide, carboplatin, etoposide)	Varies	Varies
MM		
Bortezomib/liposomal doxorubicin/dexamethasone	Varies	Varies
Carfilzomib/lenalidomide/dexamethasone	Varies	Varies
Daratumumab/bortezomib /dexamethasone	Varies	Varies
Monomorphic PTLD (B-cell type)		
RCHOP (Rituxan® [rituximab], cyclophosphamide, doxorubicin, vincristine, prednisone)	Varies	Varies
RCEPP (Rituxan® [rituximab], cyclophosphamide, etoposide, prednisone, procarbazine)	Varies	Varies

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) 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*	Bendeka: 100 mg/m^2 IV over 10 minutes on Days 1 and 2 of a 28-day cycle, up to 6 cycles Belrapzo, Treanda: 100 mg/m^2 IV over 30 minutes on days 1 and 2 of a 28-day cycle, up to 6 cycles	See regimen
Indolent B-cell lymphoma*	Bendeka: 120 mg/m^2 IV over 10 minutes on Days 1 and 2 of a 21-day cycle, up to 8 cycles Belrapzo, Treanda: 120 mg/m^2 IV over 60 minutes on days 1 and 2 of a 21-day cycle, up to 8 cycles	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; November 2020. Available at: www.belrapzo.com. Accessed July 15, 2021.
2. Bendeka Prescribing Information. North Wales, PA: Teva Pharmaceuticals USA, Inc.; November 2020. Available at: http://www.bendeka.com/. Accessed July 13, 2021.
3. Treanda Prescribing Information. North Wales, PA: Teva Pharmaceuticals USA, Inc.; July 2021. Available at: http://treandahcp.com/. Accessed July 13, 2021.
4. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed June 28, 2021.
5. National Comprehensive Cancer Network. Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Version 4.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/cll.pdf. Accessed July 13, 2021.

6. National Comprehensive Cancer Network. B-cell Lymphomas Version 4.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf. Accessed July 13, 2021.
7. National Comprehensive Cancer Network. Hodgkin Lymphoma Version 4.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/hodgkins.pdf. Accessed July 13, 2021.
8. National Comprehensive Cancer Network. Multiple Myeloma Version 7.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf. Accessed July 13, 2021.
9. National Comprehensive Cancer Network. Primary Cutaneous Lymphomas Version 2.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/primary_cutaneous.pdf. Accessed July 13, 2021.
10. National Comprehensive Cancer Network. T-cell Lymphomas Version 1.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/t-cell.pdf. Accessed July 13, 2021.
11. National Comprehensive Cancer Network. Waldenstrom Macroglobulinemia/Lymphoplasmacytic Lymphoma Version 1.2022. Available at: https://www.nccn.org/professionals/physician_gls/pdf/waldenstroms.pdf. Accessed July 13, 2021.

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.	07/18	
4Q 2019 annual review: No changes per Statewide PDL implementation 01-01-2020	10/30/19	
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 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.	10/2020	

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	