

## PRIOR AUTHORIZATION POLICY

**POLICY:** Oncology (Injectable) – Bendamustine Products Prior Authorization Policy

- Belrapzo<sup>®</sup> (bendamustine intravenous infusion – Eagle)
- Bendeka<sup>®</sup> (bendamustine intravenous infusion – Teva)
- Treanda<sup>®</sup> (bendamustine intravenous infusion – Cephalon)
- Vivimusta<sup>®</sup> (bendamustine intravenous infusion – Slayback, Latina)
- Bendamustine intravenous infusion – various manufacturers

**REVIEW DATE:** 07/17/2024

---

### OVERVIEW

Bendamustine, an alkylating agent, is indicated for the following uses:<sup>1-3,14</sup>

- **B-cell non-Hodgkin lymphoma, indolent**, that has progressed during or within 6 months of treatment with rituximab or a rituximab containing regimen.
- **Chronic lymphocytic leukemia**. Efficacy compared to first-line agents other than chlorambucil has not been established.

### Guidelines

Bendamustine is addressed in National Comprehensive Cancer Network guidelines:

- **B-Cell Lymphomas:** Guidelines (version 2.2024 – April 30, 2024) recommend bendamustine for the treatment of a variety B-cell lymphomas, including follicular lymphoma (grade 1 and 2), gastric extranodal marginal zone lymphoma of the stomach, extranodal marginal zone lymphoma of nongastric sites, nodal marginal zone lymphoma, splenic marginal zone lymphoma, histologic transformation of indolent lymphomas to diffuse large B-cell lymphoma (DLBCL), mantle cell lymphoma, DLBCL, high-grade B-cell lymphoma, human immunodeficiency virus (HIV)-related B-cell lymphoma, and post-transplant lymphoproliferative disorders.<sup>4,6</sup> Bendamustine is recommended as monotherapy, or in combination with rituximab (e.g., Rituxan, biosimilars), Polivy<sup>™</sup> (polatuzumab vedotin-piiq intravenous [IV] infusion), or Gazyva<sup>®</sup> (obinutuzumab IV infusion) depending on the lymphoma type and previous treatment .
- **Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma:** Guidelines (version 3.2024 – March 26, 2024) recommend bendamustine, in combination with rituximab or Gazyva, for the first-line treatment of patients without del(17p)/TP53 mutation, who have indications for treatment (not recommended for frail patients).<sup>4,5</sup> Bendamustine in combination with rituximab is recommended for the treatment of relapsed or refractory disease without del(17p)/TP53 mutation in patients with indications for treatment (not recommended for frail patients).
- **Hematopoietic Cell Transplantation:** Guidelines (version 1.2024 – April 26, 2024) recommend bendamustine in combination with etoposide, cytarabine, and melphalan as a conditioning regimen for autologous transplantation for patients with non-Hodgkin lymphoma without central nervous system disease, or Hodgkin lymphoma.<sup>4,13</sup>
- **Hodgkin Lymphoma and Pediatric Hodgkin Lymphoma:** Guidelines for Hodgkin lymphoma (version 3.2024 – March 18, 2024) and pediatric Hodgkin lymphoma (version 1.2024 – May 14, 2024) recommend bendamustine for the treatment of recurrent or refractory Hodgkin lymphoma.<sup>4,7,11</sup> In patients  $\geq 18$  years of age with classic Hodgkin lymphoma, bendamustine in combination with gemcitabine and vinorelbine, or in combination with Adcetris<sup>®</sup> (brentuximab IV infusion) is recommended for second-line or subsequent therapy (if not previously used), or in combination with carboplatin and etoposide for third-line or subsequent therapy, or as a single agent for subsequent therapy. In patients  $\geq 18$  years of age with nodular lymphocyte-predominant

07/17/2024

© 2024. All Rights Reserved.

This document is confidential and proprietary. Unauthorized use and distribution are prohibited.

Hodgkin lymphoma, bendamustine in combination with rituximab is recommended for the subsequent treatment of progressive, relapsed, or refractory disease. In patients > 60 years of age, bendamustine is recommended as a single agent for palliative therapy of relapsed or refractory disease. For heavily pretreated pediatric patients with Hodgkin lymphoma, bendamustine in combination with Adcetris is recommended for re-induction or subsequent treatment of relapsed or refractory disease.

- **Multiple Myeloma:** Guidelines (version 4.2024 – April 26, 2024) recommend bendamustine as a treatment option for late relapsed or progressive multiple myeloma (patient has received > 3 prior therapies).<sup>4,8</sup> Bendamustine is recommended as a single agent, or in combination with dexamethasone and lenalidomide, with dexamethasone and bortezomib, or with dexamethasone and Kyprolis® (carfilzomib intravenous infusion).
- **Primary Cutaneous Lymphomas:** Guidelines (version 2.2024 – May 6, 2024) recommend bendamustine in combination with Adcetris for the primary treatment of CD30+ mycosis fungoides stage IVA2 and mycosis fungoides/Sezary syndrome stage IVB visceral disease, or generalized cutaneous or extracutaneous lesions with large cell transformation.<sup>4,15</sup> Bendamustine in combination with Adcetris is also recommended for the subsequent treatment of stage IIB to Stage IV mycosis fungoides.
- **Systemic Light Chain Amyloidosis:** Guidelines (version 2.2024 – December 12, 2023) recommend bendamustine in combination with dexamethasone for relapsed/refractory disease.<sup>4,12</sup>
- **T-Cell Lymphomas:** Guidelines (version 4.2024 – May 28, 2024) recommend bendamustine as a single agent for the treatment of relapsed or refractory peripheral T-cell lymphomas, breast implant-associated anaplastic large cell lymphoma, adult T-cell leukemia/lymphoma, and refractory hepatosplenic T-cell lymphoma as subsequent therapy.<sup>4,9</sup>
- **Waldenstrom Macroglobulinemia/Lymphoplasmacytic Lymphoma:** Guidelines (version 2.2024 – December 5, 2023) recommend bendamustine as a single agent or in combination with rituximab for primary treatment, for the treatment of previously treated disease that did not respond, or for progressive or relapsed disease, or symptomatic Bing-Neel syndrome.<sup>4,10</sup>

## POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of bendamustine. All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. Because of the specialized skills required for evaluation and diagnosis of patients treated with bendamustine as well as the monitoring required for adverse events and long-term efficacy, approval requires bendamustine to be prescribed by or in consultation with a physician who specializes in the condition being treated.

**Automation:** None.

## RECOMMENDED AUTHORIZATION CRITERIA

Coverage of bendamustine is recommended in those who meet one of the following criteria:

### FDA-Approved Indications

1. **B-Cell Non-Hodgkin Lymphoma.** Approve for 6 months if the patient meets BOTH of the following (A and B):

Note: Examples include follicular lymphoma, extranodal marginal zone lymphoma of the stomach, extranodal marginal zone lymphoma of nongastric sites, nodal marginal zone lymphoma, splenic

marginal zone lymphoma, histologic transformation of indolent lymphomas to diffuse large B-cell lymphoma (DLBCL), DLBCL, and high-grade B-cell lymphoma.

A) Patient is  $\geq 18$  years of age; AND

B) Bendamustine is prescribed by or in consultation with an oncologist.

2. **Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma.** Approve for 6 months if the patient meets BOTH of the following (A and B):

A) Patient is  $\geq 18$  years of age; AND

B) Bendamustine is prescribed by or in consultation with an oncologist.

### Other Uses with Supportive Evidence

3. **Hematopoietic Cell Transplantation.** Approve for 1 month if the patient meets ALL of the following (A, B, and C):

A) Bendamustine is used as conditioning prior to autologous hematopoietic cell transplantation; AND

B) Patient has ONE of the following conditions (i or ii):

i. Non-Hodgkin lymphoma without central nervous system disease; OR

ii. Hodgkin lymphoma; AND

C) Bendamustine is prescribed by or in consultation with an oncologist or a physician who specializes in hematopoietic cell transplantation.

4. **Hodgkin Lymphoma.** Approve for 6 months if the patient meets BOTH of the following (A and B):

A) Bendamustine is used as second-line or subsequent therapy; AND

B) Bendamustine is prescribed by or in consultation with an oncologist.

5. **Multiple Myeloma.** Approve for 6 months if the patient meets ALL of the following (A, B, and C):

A) Patient is  $\geq 18$  years of age; AND

B) Patient has been treated with more than 3 prior regimens; AND

C) Bendamustine is prescribed by or in consultation with an oncologist.

6. **Mycosis Fungoides/Sezary Syndrome.** Approve for 6 months if the patient meets ALL of the following (A, B, and C):

A) Patient is  $\geq 18$  years of age; AND

B) Bendamustine is used in combination with Adcetris (brentuximab intravenous infusion); AND

C) Bendamustine is prescribed by or in consultation with an oncologist.

7. **Systemic Light Chain Amyloidosis.** Approve for 6 months if the patient meets ALL of the following (A, B, C, and D):

A) Patient is  $\geq 18$  years of age; AND

B) Patient has relapsed or refractory disease; AND

C) Bendamustine is used in combination with dexamethasone; AND

D) Bendamustine is prescribed by or in consultation with an oncologist.

8. **T-Cell Lymphoma.** Approve for 6 months if the patient meets ALL of the following (A, B, and C):

Note: Examples include peripheral T-cell lymphoma, breast implant-associated anaplastic large cell lymphoma, adult T-cell leukemia/lymphoma, hepatosplenic T-cell lymphoma.

A) Patient is  $\geq 18$  years of age; AND

B) Bendamustine is used as a single agent; AND

C) Bendamustine is prescribed by or in consultation with an oncologist.

- 9. Waldenstrom Macroglobulinemia/Lymphoplasmacytic Lymphoma.** Approve for 6 months if the patient meets BOTH of the following (A and B):
- A)** Patient is  $\geq 18$  years of age; AND
  - B)** Bendamustine is prescribed by or in consultation with an oncologist.

#### CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of bendamustine is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

#### REFERENCES

1. Bendeka® intravenous infusion [prescribing information]. North Wales, PA: Teva; January 2024.
2. Treanda® intravenous infusion [prescribing information]. Frazer, PA: Cephalon; October 2022.
3. Belrapzo™ intravenous infusion [prescribing information]. Woodcliff Lake, NJ: Eagle Pharmaceuticals; January 2024.
4. The NCCN Drugs and Biologics Compendium. © 2024 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on July 9, 2024. Search term: bendamustine.
5. The NCCN Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Clinical Practice Guidelines in Oncology (version 3.2024 – March 26, 2024). © 2024 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on July 9, 2024.
6. The NCCN B-Cell Lymphomas Clinical Practice Guidelines in Oncology (version 2.2024 – April 30, 2024). © 2024 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on July 9, 2024.
7. The NCCN Hodgkin Lymphoma Clinical Practice Guidelines in Oncology (version 3.2024 – March 18, 2023). © 2023 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on July 9, 2024.
8. The NCCN Multiple Myeloma Clinical Practice Guidelines in Oncology (version 4.2024 – April 26, 2024). © 2024 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on July 9, 2024.
9. The NCCN T-Cell Lymphomas Clinical Practice Guidelines in Oncology (version 4.2024 – May 28, 2024). © 2024 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on July 9, 2024.
10. The NCCN Waldenstrom Macroglobulinemia/Lymphoplasmacytic Lymphoma Clinical Practice Guidelines in Oncology (version 2.2024 – December 5, 2023). © 2023 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on July 9, 2024.
11. The NCCN Pediatric Hodgkin Lymphoma Clinical Practice Guidelines in Oncology (version 1.2024 – May 14, 2024). © 2024 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on July 9, 2024.
12. The NCCN Systemic Light Chain Amyloidosis Clinical Practice Guidelines in Oncology (version 2.2024 – December 12, 2023). © 2023 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on July 9, 2024.
13. The NCCN Hematopoietic Cell Transplantation (HCT) Clinical Practice Guidelines in Oncology (version 1.2024 – April 26, 2024). © 2024 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on July 9, 2024.
14. Vivimusta® intravenous infusion [prescribing information]. Princeton, NJ: Slayback and Sermoneta, Italy: Latina Pharma; February 2024.
15. The NCCN Primary Cutaneous Lymphomas Clinical Practice Guidelines in Oncology (version 2.2024 – May 6, 2024). © 2024 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on July 9, 2024.

