

## PRIOR AUTHORIZATION POLICY

- POLICY:** Oncology (Injectable) – Bendamustine Products Prior Authorization Policy
- Belrapzo™ (bendamustine intravenous infusion – Eagle)
  - Bendeka® (bendamustine intravenous infusion – Teva)
  - Treanda® (bendamustine intravenous infusion – Cephalon)
  - Bendamustine intravenous infusion – various manufacturers

**REVIEW DATE:** 07/06/2022

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### OVERVIEW

Bendamustine, an alkylating agent, is indicated for the following uses:<sup>1-3</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** (version 4.2022 – June 9, 2022): Guidelines recommend bendamustine for the treatment of a variety B-cell lymphomas, including follicular lymphoma (grade 1 and 2), gastric mucosa-associated lymphoid tissue (MALT) lymphoma, nongastric MALT lymphoma, 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, acquired immunodeficiency syndrome (AIDS)-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™ (polatuzumab vedotin-piiq intravenous [IV] infusion), or Gazyva® (obinutuzumab IV infusion) depending on the lymphoma type and previous treatment .
- **Chronic lymphocytic leukemia/small lymphocytic lymphoma** (version 3.2022 – June 3, 2022): Guidelines recommend bendamustine, in combination with rituximab, Gazyva, or Arzerra® (ofatumumab IV infusion), for the first-line treatment of patients without del(17p)/TP53 mutation, who are ≥ 65 years of age, or younger patients with or without significant comorbidities.<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 ≥ 65 years of age, or in patients < 65 years of age with or without significant comorbidities.
- **Hematopoietic Cell Transplantation** (version 1.2022 – April 1, 2022): Guidelines 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** (version 2.2022 – February 23, 2022) and **Pediatric Hodgkin lymphoma** (version 1.2022 – April 8, 2022): Guidelines recommend bendamustine for the treatment of recurrent or refractory Hodgkin Lymphoma.<sup>4,7,11</sup> In patients ≥ 18 years of age with classic Hodgkin lymphoma, bendamustine in combination with gemcitabine and vinorelbine, or in combination with Adcetris® (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 ≥ 18 years of age with nodular lymphocyte-predominant Hodgkin lymphoma, bendamustine in combination with rituximab is

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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** (version 5.2022 – March 9, 2022): Guidelines recommend bendamustine as a treatment option for relapsed or progressive multiple myeloma.<sup>4,8</sup> Bendamustine is recommended as a single agent, or in combination with dexamethasone and Revlimid® (lenalidomide capsules) or with dexamethasone and Velcade® (bortezomib IV infusion and subcutaneous use).
- **Systemic light chain amyloidosis** (version 1.2022 – June 29, 2021): Guidelines recommend bendamustine in combination with dexamethasone for relapsed/refractory disease.<sup>4,12</sup>
- **T-cell lymphomas** (version 2.2022 – March 7, 2022): Guidelines 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** (version 3.2022 – May 2, 2022): Guidelines 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.<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 criteria (A and B):  
Note: Examples include follicular lymphoma, gastric and nongastric mucosa-associated lymphoid tissue (MALT) lymphoma, 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 criteria (A and B):  
A) Patient is  $\geq 18$  years of age; AND  
B) Bendamustine is prescribed by or in consultation with an oncologist.

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### Other Uses with Supportive Evidence

- 3. Hematopoietic Cell Transplantation.** Approve for 1 month if the patient meets ALL of the following criteria (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 criteria (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 criteria (A, B, and C):
  - A) Patient is  $\geq 18$  years of age; AND
  - B) Patient has relapsed or refractory disease; AND
  - C) Bendamustine is prescribed by or in consultation with an oncologist.
  
- 6. Systemic Light Chain Amyloidosis.** Approve for 6 months if the patient meets ALL of the following criteria (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.
  
- 7. T-Cell Lymphoma.** Approve for 6 months if the patient meets ALL of the following criteria (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.
  
- 8. Waldenstrom Macroglobulinemia/Lymphoplasmacytic Lymphoma.** Approve for 6 months if the patient meets BOTH of the following criteria (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<sup>®</sup> intravenous infusion [prescribing information]. North Wales, PA: Teva; October 2021.
2. Treanda<sup>®</sup> intravenous infusion [prescribing information]. Frazer, PA: Cephalon; June 2021.
3. Belrapzo<sup>™</sup> intravenous infusion [prescribing information]. Woodcliff Lake, NJ: Eagle Pharmaceuticals; October 2021.
4. The NCCN Drugs and Biologics Compendium. © 2022 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on June 22, 2022. Search term: bendamustine.
5. The NCCN Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Clinical Practice Guidelines in Oncology (version 3.2022 – June 3, 2022). © 2022 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on June 23, 2022.
6. The NCCN B-Cell Lymphomas Clinical Practice Guidelines in Oncology (version 4.2022 – June 9, 2022). © 2022 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on June 27, 2022.
7. The NCCN Hodgkin Lymphoma Clinical Practice Guidelines in Oncology (version 2.2022 – February 23, 2022). © 2022 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on June 23, 2022.
8. The NCCN Multiple Myeloma Clinical Practice Guidelines in Oncology (version 5.2022 – March 9, 2022). © 2022 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on June 23, 2022.
9. The NCCN T-Cell Lymphomas Clinical Practice Guidelines in Oncology (version 1.2021 – October 5, 2020). © 2020 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on July 9, 2021.
10. The NCCN Waldenstrom Macroglobulinemia/Lymphoplasmacytic Lymphoma Clinical Practice Guidelines in Oncology (version 3.2022 – May 2, 2022). © 2022 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on June 23, 2022.
11. The NCCN Pediatric Hodgkin Lymphoma Clinical Practice Guidelines in Oncology (version 1.2022 – April 8, 2022). © 2022 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on June 23, 2022.
12. The NCCN Systemic Light Chain Amyloidosis Clinical Practice Guidelines in Oncology (version 1.2022 – June 29, 2021). © 2021 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on June 23, 2022.
13. The NCCN Hematopoietic Cell Transplantation (HCT) Clinical Practice Guidelines in Oncology (version 1.2022 – April 1, 2022). © 2022 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on June 23, 2022.