VENTURA COUNTY
HEALTH CARE PLAN

UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Oncology (Injectable) – Bendamustine Products Utilization Management Medical Policy
- Belrapzo™ (bendamustine intravenous infusion – Eagle Pharmaceuticals)
- Bendeka® (bendamustine intravenous infusion – Teva)
- Treanda® (bendamustine intravenous infusion – Cephalon)
- Bendamustine intravenous infusion – various manufacturers

REVIEW DATE: 07/14/2021

OVERVIEW

Bendamustine, an alkylating agent, is indicated for the treatment of patients with:
- **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.[1-3]

Guidelines

Bendamustine is addressed in National Comprehensive Cancer Network (NCCN) guidelines:
- **B-cell lymphomas** (version 4.2021 – May 5, 2021): Guidelines recommend bendamustine for the treatment of a variety B-cell lymphomas, including follicular lymphoma (grade 1 and 2), gastric MALT lymphoma, nongastric MALT lymphoma, nodal marginal zone lymphoma, splenic marginal zone lymphoma, histologic transformation of marginal zone lymphoma 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.[4,6] 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 history.
- **Chronic lymphocytic leukemia/small lymphocytic lymphoma** (version 4.2021 – April 29, 2021): 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.[4,5] 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.
- **Hodgkin lymphoma** (version 4.2021 – April 20, 2021) and **Pediatric Hodgkin lymphoma** (version 3.2021 – March 18, 2021): Guidelines recommend bendamustine for the treatment of recurrent or refractory Hodgkin Lymphoma.[4,7,27] 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 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 7.2021 – April 26, 2021): Guidelines recommend bendamustine as a treatment option for relapsed or progressive multiple myeloma. 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).[4,12]
- **Primary cutaneous lymphomas** (version 2.2021 – March 4, 2021): Guidelines recommend bendamustine for the systemic treatment of mycosis fungoides/Sezary syndrome with or without skin-directed or radiation therapy, and as a single agent for the treatment of relapsed/refractory primary cutaneous CD30+ T-cell lymphoproliferative disorders.[4,26]
- **Systemic light chain amyloidosis** (version 1.2022 – June 29, 2021): Guidelines recommend bendamustine in combination with dexamethasone for relapsed/refractory disease.[4,28]
- **T-cell lymphomas** (version 1.2021 – October 5, 2020): 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.[4,20]
- **Waldenstrom macroglobulinemia/lymphoplasmacytic lymphoma** (version 1.2022 – June 24, 2021): 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.[4,22]

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of bendamustine. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indications. Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). 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 bendamustine is prescribed by or in consultation with an oncologist.

   Dosing. Approve up to 120 mg/m^2 administered by intravenous infusion no more frequently than twice in each 21-day cycle.

2. **Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma.** Approve for 6 months if bendamustine is prescribed by or in consultation with an oncologist.

   Dosing. Approve up to 100 mg/m^2 administered by intravenous infusion no more frequently than twice in each 28-day cycle.

Other Uses with Supportive Evidence

3. **Hodgkin Lymphoma.** Approve for 6 months if the patient meets 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.

   Dosing. Approve up to 120 mg/m^2 administered by intravenous infusion no more frequently than twice in each 21-day or 28-day treatment cycle.

4. **Multiple Myeloma.** Approve for 6 months if the patient meets the following criteria (A and B):
   A) Patient has relapsed or refractory disease; AND
   B) Bendamustine is prescribed by or in consultation with an oncologist.

   Dosing. Approve up to 150 mg/m^2 administered by intravenous infusion no more frequently than twice in each 28-day cycle.

5. **Systemic Light Chain Amyloidosis.** Approve for 6 months if the patient meets the following criteria (A, B, and C):
   A) Patient has relapsed or refractory disease; AND
   B) Bendamustine is used in combination with dexamethasone; AND
   C) Bendamustine is prescribed by or in consultation with an oncologist.

   Dosing. Approve up to 100 mg/m^2 administered by intravenous infusion no more frequently than twice in each 28-day cycle.

6. **T-Cell Lymphoma.** Approve for 6 months if bendamustine is prescribed by or in consultation with an oncologist.
   Note: Examples include Peripheral T-Cell Lymphoma, Mycosis Fungoides/Sezary Syndrome, Primary Cutaneous CD30+ T-Cell Lymphoproliferative Disorders, breast implant-associated anaplastic large cell lymphoma, Adult T-Cell Leukemia/Lymphoma, Hepatosplenic T-Cell Lymphoma.

   Dosing. Approve up to 120 mg/m^2 administered by intravenous infusion no more frequently than twice in each 21-day cycle.

7. **Waldenstrom Macroglobulinemia/Lymphoplasmacytic Lymphoma.** Approve for 6 months if bendamustine is prescribed by or in consultation with an oncologist.

Dosing. Approve up to 90 mg/m^2 administered by intravenous infusion no more frequently than twice in each 28-day cycle.

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

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2. Treanda® [prescribing information]. Frazer, PA: Cephalon; June 2021.
3. Belrapzo™ [prescribing information]. Woodcliff Lake, NJ: Eagle Pharmaceuticals; October 2019.
4. The NCCN Drugs and Biologics Compendium. © 2021 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on July 9, 2021. Search term: bendamustine.
5. The NCCN Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Clinical Practice Guidelines in Oncology (version 4.2021 – April 29, 2021). © 2021 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on July 9, 2021.
6. The NCCN B-Cell Lymphomas Clinical Practice Guidelines in Oncology (version 4.2021 – May 5, 2021). © 2021 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on July 9, 2021.
7. The NCCN Hodgkin Lymphoma Clinical Practice Guidelines in Oncology (version 4.2021 – April 20, 2021). © 2021 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on July 9, 2021.
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20. 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.
21. Damaj G, Gressin R, Bouabdallah K, et al. Results from a prospective, open-label, Phase II trial of bendamustine in refractory or relapsed T-cell lymphomas: the BENTLY trial. *J Clin Oncol*. 2013;31:104-110.
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HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	07/15/2020
Annual Revision	**Hodgkin Lymphoma.** The criterion that the patient is ≥ 18 years of age was removed. **Systemic Light Chain Amyloidosis.** New criteria were added for this condition of approval. **T-Cell Lymphoma.** Added breast implant-associated anaplastic large cell lymphoma as an additional example and removed gamma-delta from hepatosplenic gamma-delta T-cell lymphoma in the Note.	07/14/2021