VENTURA COUNTY
HEALTH CARE PLAN

UTILIZATION REVIEW MEDICAL POLICY

POLICY: Oncology (Injectable) – Bendamustine Products Utilization Review Medical Policy
- Belrapzo™ (bendamustine injection for intravenous use – Eagle Pharmaceuticals)
- Bendeka® (bendamustine injection for intravenous use – Teva Pharmaceuticals, Inc.)
- Treanda® (bendamustine injection for intravenous use – Cephalon, Inc.)
- Bendamustine injection for intravenous use – various manufacturers

REVIEW DATE: 07/15/2020

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

B-Cell Lymphomas

The National Comprehensive Cancer Network (NCCN) guidelines for B-cell lymphomas (version 2.2020 – July 9, 2020) 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, Polivy™ (polatuzumab vedotin-piiq injection for intravenous use), or Gazyva depending on the lymphoma type and previous treatment history.

Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma

The NCCN guidelines for chronic lymphocytic leukemia/small lymphocytic lymphoma (version 4.2020 – December 20, 2019) recommend bendamustine, in combination with rituximab (e.g., Rituxan, Truxima), Gazyva® (obinutuzumab injection for intravenous [IV] use), or Arzerra® (ofatumumab injection for IV use), for the first-line treatment of patients $\geq$ 65 years of age without del(17p)/TP53 mutation, 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 $\geq$ 65 years of age, or in patients < 65 years of age with or without significant comorbidities.

Hodgkin Lymphoma

The NCCN guidelines for Hodgkin lymphoma (version 2.2020 – April 17, 2020) recommend bendamustine for the treatment of recurrent or refractory classic Hodgkin Lymphoma.[4,7] In patients $\geq$ 18 years of age, bendamustine in combination with gemcitabine and vinorelbine, or in combination with Adcetris® (brentuximab injection for IV use) 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 > 60 years of age, bendamustine is recommended as a single agent for palliative therapy of relapsed or refractory disease.

Multiple Myeloma
Bendamustine is recommended in the NCCN guidelines for multiple myeloma (version 4.2020 – May 8, 2020) 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 injection for IV and subcutaneous use).[4,12]

Primary Cutaneous Lymphomas
The NCCN guidelines for primary cutaneous lymphomas (version 2.2020 – April 10, 2020) 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]

T-Cell Lymphomas
The NCCN guidelines for T-cell lymphomas (version 1.2020 – January 6, 2020) recommend bendamustine as a single agent for the treatment of relapsed or refractory peripheral T-cell lymphomas, adult T-cell leukemia/lymphoma, and refractory hepatosplenic gamma-delta T-cell lymphoma as subsequent therapy.[4,20]

Waldenstrom Macroglobulinemia/Lymphoplasmacytic Lymphoma
Bendamustine is recommended in the NCCN guidelines for Waldenstrom macroglobulinemia/lymphoplasmacytic lymphoma (version 2.2020 – April 15, 2020) 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 indication(s). 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.

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 the following dosing regimen (A and B):
   A) Each individual dose must not exceed 120 mg/m^2 given by intravenous infusion; AND
   B) Patient receives a maximum of two doses per 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 the following dosing regimen (A and B):
A) Each individual dose must not exceed 100 mg/m^2 given by intravenous infusion; AND
B) Patient receives a maximum of two doses per 28-day cycle.

Other Uses with Supportive Evidence

3. Hodgkin Lymphoma. Approve for 6 months if the patient meets the following criteria (A, B, and C):
A) Patient is ≥ 18 years of age; AND
B) Bendamustine is used as second-line or subsequent therapy; AND
C) Bendamustine is prescribed by or in consultation with an oncologist.

Dosing. Approve the following dosing regimen (A and B):
A) Each individual dose must not exceed 120 mg/m^2; AND
B) Patient receives a maximum of two doses per 21-day or 28-day treatment cycle.[8-11]

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 the following dosing regimen (A and B):
A) Each individual dose must not exceed 150 mg/m^2; AND
B) Patient receives a maximum of two doses per 28-day cycle.[13-19]

5. T-Cell Lymphoma (Note: Examples include Peripheral T-Cell Lymphoma, Mycosis Fungoides/Sezary Syndrome, Primary Cutaneous CD30+ T-Cell Lymphoproliferative Disorders, Adult T-Cell Leukemia/Lymphoma, Hepatosplenic Gamma-Delta T-Cell Lymphoma). Approve for 6 months if bendamustine is prescribed by or in consultation with an oncologist.

Dosing. Approve the following dosing regimen (A and B):
A) Each individual dose must not exceed 120 mg/m^2; AND
B) The patient receives a maximum of two doses in each 21-day cycle.[21]

6. Waldenstrom Macroglobulinemia/Lymphoplasmacytic Lymphoma. Approve for 6 months if bendamustine is prescribed by or in consultation with an oncologist.[4,22]

Dosing. Approve the following dosing regimen (A and B):
A) Each individual dose must not exceed 90 mg/m^2; AND
B) The patient receives a maximum of two doses in each 28-day cycle.[23-25]

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® [prescribing information]. North Wales, PA: Teva Pharmaceuticals, Inc.; October 2019.
2. Treanda® [prescribing information]. Frazer, PA: Cephalon; November 2019.
3. Belrapzo™ [prescribing information]. Woodcliff Lake, NJ: Eagle Pharmaceuticals, Inc.; October 2019.
4. The NCCN Drugs and Biologics Compendium. © 2020 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on July 6, 2020. Search term: bendamustine.
5. The NCCN Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Clinical Practice Guidelines in Oncology (version 4.2020 – December 20, 2019). © 2019 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on July 6, 2020.
6. The NCCN B-Cell Lymphomas Clinical Practice Guidelines in Oncology (version 1.2020 – January 22, 2020). © 2020 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on July 6, 2020.
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20. The NCCN T-Cell Lymphomas Clinical Practice Guidelines in Oncology (version 1.2020 – January 6, 2020). © 2020 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on July 6, 2020.
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HISTORY

Type of Revision	Summary of Changes	Review Date
New policy	--	12/12/2018
Early annual revision	Added Belrapzo to the policy. Removed hematologist from criterion. Removed "Indolent" from B-Cell non Hodgkin Lymphoma condition of approval. Simplified Hodgkin Lymphoma criteria by removing information concerning combination therapy or use as a single agent. Removed "Previously Treated Relapsed or Refractory" from condition of approval and added it to the criteria. Removed criteria concerning combination therapy or use as a single agent. Revised Peripheral T-Cell Lymphoma indication to T-Cell Lymphoma and rolled Peripheral T-Cell Lymphoma, Mycosis Fungoides/Sezary Syndrome, Primary Cutaneous CD30+ T-Cell Lymphoproliferative Disorders, Adult T-Cell Leukemia/Lymphoma, and Hepatosplenic Gamma-Delta T-Cell Lymphoma all under this indication. Removed criteria concerning combination use and use as a single agent. Removed use with rituximab or as a single agent from Waldenstrom Macroglobulinemia criteria. Removed Duration of Therapy and Note to Nurse Clinician from all criteria. Removed Other Cancer Related Indications	07/17/2019
Annual revision	No criteria changes.	07/15/2020