UTILIZATION MANAGEMENT MEDICAL POLICY

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

REVIEW DATE: 07/16/2025

OVERVIEW

Bendamustine, an alkylating agent, is indicated for the following uses:[1-3,31]

- **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 (NCCN) guidelines:

- **B-Cell Lymphomas:** Guidelines (version 2.2025 – February 10, 2025) recommend bendamustine for the treatment of a variety B-cell lymphomas, including follicular lymphoma (grade 1 and 2), 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.[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:** Guidelines (version 3.2025 – April 2, 2025) 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).[4,5] 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 2.2025 – June 3, 2025) 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.[4,30]
- **Hodgkin Lymphoma** and **Pediatric Hodgkin Lymphoma:** Guidelines for Hodgkin lymphoma (version 2.2025 – January 30, 2025) and pediatric Hodgkin lymphoma (version 2.2025 – June 9,, 2025) recommend bendamustine for the treatment of recurrent or refractory Hodgkin lymphoma.[4,7,26] 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:** Guidelines (version 1.2026 – June 24, 2025) recommend bendamustine as a treatment option for late relapsed or progressive multiple myeloma (patient has received > 3 prior therapies).[4,12] 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).
- **Systemic Light Chain Amyloidosis:** Guidelines (version 1.2026 – June 11, 2025) recommend bendamustine in combination with dexamethasone for relapsed/refractory disease.[4,27]
- **T-Cell Lymphomas**: Guidelines (version 2.2025 – May 28, 2025) 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**: Guidelines (version 1.2026 – June 24, 2025) 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, for progressive or relapsed disease, or symptomatic Bing-Neel syndrome.[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

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1. B-Cell Non-Hodgkin Lymphoma. Approve for 6 months if the patient meets ALL of the following (A, B, and C):
Note: Examples include follicular lymphoma, marginal zone lymphoma, mantle cell lymphoma, diffuse large B-cell lymphoma (DLBCL), histologic transformation of indolent lymphomas to diffuse large B-cell lymphoma (DLBCL), high-grade B-cell lymphoma, HIV-Related B-Cell Lymphomas, and Post-Transplant Lymphoproliferative Disorders.
A) Patient is ≥ 18 years of age; AND
B) Patient meets ONE of the following (i or ii):

i. Patient has follicular lymphoma, marginal zone lymphoma, or mantle cell lymphoma; OR
ii. Patient meets BOTH of the following (a and b):
a) Patient has diffuse large B-cell lymphoma (DLBCL), histologic transformation of indolent lymphomas to diffuse large B-cell lymphoma (DLBCL), high-grade B-cell lymphoma, HIV-related B-cell lymphoma, or post-transplant lymphoproliferative disorder; AND
b) The medication is used as second-line or subsequent therapy; AND

C) The medication 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 treatment cycle.

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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 ≥ 18 years of age; AND
B) The medication 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 treatment cycle.

Other Uses with Supportive Evidence

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3. Hematopoietic Cell Transplantation. Approve for 1 month if the patient meets ALL of the following (A, B, C, and D):
A) The medication 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) The medication is used in combination with etoposide, cytarabine, and melphalan.
D) The medication is prescribed by or in consultation with an oncologist or a physician who specializes in hematopoietic cell transplantation.

Dosing. Approve up to 200 mg/m^2 administered by intravenous infusion no more frequently than twice prior to autologous hematopoietic cell transplantation.

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4. Hodgkin Lymphoma. Approve for 6 months if the patient meets BOTH of the following (A and B):
A) The medication is used as second-line or subsequent therapy; AND
B) The medication 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.

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5. Multiple Myeloma. Approve for 6 months if the patient meets ALL of the following (A, B, and C):
A) Patient is ≥ 18 years of age; AND
B) Patient meets ONE of the following (i or ii):
i. Patient has been treated with at least 3 prior regimens; OR
ii. Patient meets BOTH of the following (a and b):

a) Patient has central nervous disease; AND
b) The medication is used as part of a multimodality therapy; AND
Note: Examples of multimodality therapies include radiation and systemic therapy.

C) The medication 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 treatment cycle.

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

A) Patient is ≥ 18 years of age; AND
B) Patient has relapsed or refractory disease; AND
C) The medication is used in combination with dexamethasone; AND
D) The medication 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 treatment cycle.

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7. T-Cell Lymphoma. Approve for 6 months if the patient meets ALL of the following (A, B, and C):
Note: Examples of T-cell lymphoma include peripheral T-cell lymphoma not otherwise specified, enteropathy-associated T-cell lymphoma, monomorphic epitheliotropic intestinal T-cell lymphoma, angioimmunoblastic T-cell lymphoma, nodal peripheral T-cell lymphoma, follicular helper T-cell lymphoma, follicular T-cell lymphoma, anaplastic large cell lymphoma, breast implant-associated anaplastic large cell lymphoma, T-cell prolymphocytic leukemia, adult T-cell leukemia/lymphoma, hepatosplenic T-cell lymphoma, and CD30+ peripheral T-cell lymphoma.

A) Patient is ≥ 18 years of age; AND
B) Patient meets ONE of the following (i, ii, or iii):

i. Patient has peripheral T-cell lymphoma not otherwise specified, enteropathy-associated T-cell lymphoma, monomorphic epitheliotropic intestinal T-cell lymphoma, angioimmunoblastic T-cell lymphoma, nodal peripheral T-cell lymphoma, follicular helper T-cell lymphoma, follicular T-cell lymphoma, or anaplastic large cell lymphoma; OR

ii. Patient meets BOTH of the following (a and b):
a) Patient has CD30+ peripheral T-cell lymphoma, breast implant-associated anaplastic large cell lymphoma, T-cell prolymphocytic leukemia, or adult T-cell leukemia/lymphoma; AND
b) The medication is used as second-line or subsequent therapy; OR

iii. Patient meets BOTH of the following (a and b):
a) Patient has hepatosplenic T-cell lymphoma; AND
b) The medication is used as subsequent therapy after two systemic regimens; AND
Note: Examples of systemic regimens include ICE (ifosfamide, carboplatin, etoposide), DHAP (dexamethasone, cytarabine, cisplatin), DHAX (dexamethasone, cytarabine, oxaliplatin),IVAC(ifosfamide, etoposide, cytarabine

C) The medication 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 treatment cycle.

8. **Waldenstrom Macroglobulinemia/Lymphoplasmacytic Lymphoma.** Approve for 6 months if the patient meets BOTH of the following (A and B):
   A) Patient is ≥ 18 years of age; AND
   B) The medication 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 treatment 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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3. Belrapzo® intravenous infusion [prescribing information]. Woodcliff Lake, NJ: Eagle Pharmaceuticals; January 2024.
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6. The NCCN B-Cell Lymphomas Clinical Practice Guidelines in Oncology (version 2.2025 – February 10, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on June 27, 2025.
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HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	**B-Cell Non-Hodgkin Lymphoma:** Gastric and nongastric mucosa-associated lymphoid tissue (MALT) lymphoma was removed from the Note. Extranodal marginal zone lymphoma of the stomach and extranodal marginal zone lymphoma of nongastric sites were added to the Note. **Multiple Myeloma:** Relapsed or refractory disease was removed as a requirement. Patient has been treated with more than 3 prior regimens added as a new requirement.	07/12/2023
Annual Revision	**Vivimusta:** Added Vivimusta to list of bendamustine products; the same criteria apply as those for the other bendamustine products. **Mycosis Fungoides/Sezary Syndrome:** New condition of approval was added.	07/17/2024
Annual Revision	**B-Cell Non-Hodgkin Lymphoma:** Added a requirement that the medication is used as second-line or subsequent therapy for diffuse large B-cell lymphoma, histologic transformation of indolent lymphomas to diffuse large B-cell lymphoma, high-grade B-cell lymphoma, HIV-related B-cell lymphoma, and post-transplant lymphoproliferative disorder. **Hematopoietic Cell Transplantation:** Added a requirement that the medication is used in combination with etoposide, cytarabine, and melphalan. **Multiple Myeloma:** Changed the requirement from "more than three prior regimens" to "at least three prior regimens.". Added another option for approval, which includes that the patient has central nervous disease and the medication is used as part of a multimodal therapy. **Mycosis Fungoides/Sezary Syndrome:** Removed as a condition of approval. **T-Cell Lymphoma**: Added a requirement that the medication is used as second-line or subsequent therapy for CD30+ peripheral T-cell lymphoma, breast implant-associated anaplastic large cell lymphoma, T-cell prolymphocytic leukemia, or adult T-cell leukemia/lymphoma. Added a requirement that the medication is used as subsequent therapy after two systemic regimens for hepatosplenic T-cell lymphoma. Removed the requirement that Bendamustine is used as a single agent.	07/16/2025