Clinical Policy: Bendamustine (Bendeka, Treanda)

Reference Number: CP.PHAR.307
Effective Date: 02.01.17
Last Review Date: 11.17
Line of Business: Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Bendamustine hydrochloride (Bendeka®, Treanda®) is an alkylating drug.

FDA Approved Indication(s)

- Chronic lymphocytic leukemia (CLL)
  - Bendeka and Treanda are indicated for the treatment of patients with chronic lymphocytic leukemia. Efficacy relative to first line therapies other than chlorambucil has not been established.
- Non-Hodgkin lymphoma (NHL)
  - Bendeka and Treanda are indicated for the treatment of patients with indolent B-cell non-Hodgkin lymphoma that has progressed during or within six months of treatment with rituximab or a rituximab-containing regimen.

Policy/Criteria

Provider must submit documentation (which may include office chart notes and lab results) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Beleodaq and Treanda are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Non-Hodgkin Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (must meet all)**:**

1. Diagnosis of chronic lymphocytic leukemia (CLL) (i.e., small lymphocytic lymphoma [SLL]);
2. Age ≥ 18 years;
3. Meets (a or b):
   a. FDA approved use:
      i. CLL/SLL;
   b. NCCN recommended use (i or ii):
      i. First-line therapy with or without rituximab for CLL/SLL without del(17p)/TP53 mutation if ≥ 65 years of age or if younger with or without significant comorbidities;
      ii. Therapy for relapsed or refractory disease without del(17p)/TP53 mutation (a or b):

a) As a single agent or in combination with rituximab;
b) In combination with rituximab and either idelalisib or ibrutinib;

4. Request meets one of the following (a or b):
   a. Dose does not exceed (i or ii):
      i. Bendeka: 100 mg/m^2 administered intravenously over 10 minutes on Days 1 and 2 of a 28-day cycle, up to 6 cycles;
      ii. Treanda: 100 mg/m^2 infused intravenously over 30 minutes on days 1 and 2 of a 28-day cycle, up to 6 cycles;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 6 months

B. Non-Hodgkin B-Cell Lymphomas (must meet all)**:**
1. Age ≥ 18 years;
2. One of the following diagnoses (a through i):
   a. Indolent B-cell non-Hodgkin lymphoma:
      i. FDA approved use:
         a) Indolent B-cell non-Hodgkin lymphoma that has progressed during or within six months of treatment with rituximab or a rituximab-containing regimen;
   b. Follicular lymphoma:
      i. NCCN recommended use (a or b):
         a) First-line therapy in combination with rituximab or obinutuzumab for stage I (bulky), contiguous stage II (bulky), non-contiguous stage II disease, or with stage III or IV disease;
         b) Second-line or subsequent therapy as a single agent or in combination with rituximab or obinutuzumab for refractory or progressive disease;
   c. Gastric MALT lymphoma:
      i. NCCN recommended use (a, b or c):
         a) First-line therapy in combination with rituximab for stage IV disease;
         b) Additional therapy in combination with rituximab for stage IE-IIE disease;
         c) Second-line or subsequent therapy for recurrent or progressive disease in combination with rituximab or obinutuzumab;
   d. Nongastric MALT lymphoma:
      i. NCCN recommended use - categories 1 and 2A (a or b):
         a) First-line therapy in combination with rituximab for stage IV disease or recurrent stage I-II disease;
         b) Second-line or subsequent therapy for refractory or progressive disease in combination with rituximab or obinutuzumab;
   e. Nodal marginal zone lymphoma:
      i. NCCN recommended use (a or b):
         a) First-line therapy in combination with rituximab for stage III or IV disease;
         b) Second-line or subsequent therapy for refractory or progressive disease in combination with rituximab or obinutuzumab;

f. Splenic marginal zone lymphoma:
   i. NCCN recommended use (a or b):
      a) First-line therapy in combination with rituximab for progressive disease following initial treatment for splenomegaly;
      b) Second-line or subsequent therapy for refractory or progressive disease in combination with rituximab or obinutuzumab;
g. Mantle cell lymphoma;
   i. NCCN recommended use:
      a) Stage I-II disease, aggressive stage II bulky, III, or IV disease, or symptomatic indolent stage II bulky, III, or IV disease as (1 or 2):
         1) Less aggressive induction therapy with rituximab;
         2) Second line therapy with or without rituximab to achieve complete response after partial response to induction therapy or for relapsed, refractory or progressive disease;
h. Diffuse large B-cell lymphoma:
   i. NCCN recommended use (a or b):
      a) Second-line or subsequent therapy with or without rituximab for relapsed or refractory disease in noncandidates for high-dose therapy;
      b) Second-line or subsequent therapy with or without rituximab for relapsed or refractory primary cutaneous diffuse large B-cell lymphoma, leg type in noncandidates for high-dose therapy;
i. AIDS-related B-cell lymphoma:
   i. NCCN recommended use:
      a) Second-line or subsequent therapy with or without rituximab for relapse of AIDS-related diffuse large B-cell lymphoma, primary effusion lymphoma, and HHV8-positive diffuse large B-cell lymphoma, not otherwise specified (NOS) in noncandidates for high-dose therapy;

3. Request meets one of the following (a or b):
   a. Dose does not exceed (i or ii):
      i. Bendeka: 120 mg/m^2 administered intravenously over 10 minutes on Days 1 and 2 of a 21-day cycle, up to 8 cycles;
      ii. Treanda: 120 mg/m^2 infused intravenously over 60 minutes on days 1 and 2 of a 21-day cycle, up to 8 cycles;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 6 months

C. Non-Hodgkin Primary Cutaneous B-Cell Lymphomas (must meet all)**:**
1. Diagnosis of primary cutaneous B-cell lymphoma;
2. Age ≥ 18 years of age;
3. NCCN recommended use (a or b):
   a. In combination with rituximab for primary cutaneous marginal zone or follicle center lymphoma as (i, ii or iii):
      i. First-line therapy for generalized extracutaneous disease;
      ii. Therapy for very extensive or refractory generalized T3 cutaneous disease;

iii. Second-line or subsequent therapy for refractory or progressive generalized extracutaneous disease;

b. For primary cutaneous marginal zone or follicle center lymphoma as therapy for very extensive or refractory generalized T3 cutaneous disease or as second-line or subsequent therapy for refractory or progressive generalized extracutaneous disease in combination with obinutuzumab;

4. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 6 months

D. Non-Hodgkin T-Cell Lymphomas (must meet all)**:**

1. Age ≥ 18 years of age;
2. Diagnosis of one of the following:
   a. Peripheral T-cell lymphoma (PTCL):
      i. NCCN recommended use:
         a) Second-line or subsequent therapy for relapsed or refractory angioimmunoblastic T-cell lymphoma, PTCL not otherwise specified, anaplastic large cell lymphoma, enteropathy-associated T-cell lymphoma, or monomorphic epitheliotropic intestinal T-cell lymphoma;
   b. Mycosis fungoides (MF)/Sezary syndrome (SS):
      i. NCCN recommended use:
         a) Single-agent therapy for tumors with aggressive growth rate for (1 or 2):
            1) Stage IB-IIA MF with histologic evidence of folliculotropic or large cell transformation or stage IIB with generalized tumor lesions, with or without skin-directed therapy;
            2) Stage IV non-Sezary or visceral disease ;
   c. Primary cutaneous CD30+ T-cell lymphoproliferative disorders:
      i. NCCN recommended use:
         a) Single-agent therapy for primary cutaneous anaplastic large cell lymphoma (ALCL) with multifocal lesions or cutaneous ALCL with regional nodes (excludes systemic ALCL) as (1 or 2):
            1) Primary treatment;
            2) Therapy for relapsed or refractory disease;
   d. Adult T-cell leukemia/lymphoma:
      i. NCCN recommended use:
         a) Second-line therapy as a single agent for nonresponders to first-line therapy for acute disease or lymphoma or as subsequent therapy after high dose therapy/autologous stem cell rescue (HDT/ASCR);
3. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 6 months

E. Hodgkin Lymphoma (must meet all)**:**

1. Diagnosis of classical Hodgkin lymphoma (HL);
2. Age ≥ 18 years of age;

3. NCCN recommended:
   a. As additional therapy as a single agent for refractory disease if Deauville 4-5 or for relapsed disease;
   b. Symptom management as a single agent for relapsed or refractory disease in older adults (age > 60);
4. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 6 months

F. Multiple Myeloma (must meet all)**:**
1. Diagnosis of multiple myeloma (MM);
2. Age ≥ 18 years of age;
3. NCCN recommended use:
   a. Therapy for previously treated myeloma for disease relapse or for progressive or refractory disease (i, ii or iii):
      i. As a single agent;
      ii. In combination with lenalidomide and dexamethasone;
      iii. In combination with bortezomib and dexamethasone;
4. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 6 months

G. Waldenstrom's Macroglobulinemia/Lymphoplasmacytic Lymphoma (must meet all)**:**
1. Diagnosis of Waldenstrom's macroglobulinemia (i.e., lymphoplasmacytic lymphoma);
2. Age ≥ 18 years of age;
3. NCCN recommended use:
   a. With or without rituximab as (i or ii):
      i. Primary therapy;
      ii. Therapy for previously treated disease that does not respond to primary therapy or for progressive or relapsed disease
4. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 6 months

H. Other diagnoses/indications
1. Refer to CP.PHAR.57 for specialty if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**
1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy (e.g., no disease progression or unacceptable toxicity);

3. If request is for a dose increase, request meets (a or b):
   a. New dose does not exceed (i or ii):
      i. Non-Hodgkin CLL/SLL:
         a) Bendeka: 100 mg/m^2 administered intravenously over 10 minutes on Days 1 and 2 of a 28-day cycle, up to 6 cycles;
         b) Treanda: 100 mg/m^2 infused intravenously over 30 minutes on days 1 and 2 of a 28-day cycle, up to 6 cycles;
      ii. Non-Hodgkin indolent B-cell lymphoma:
         a) Bendeka: 120 mg/m2 administered intravenously over 10 minutes on Days 1 and 2 of a 21-day cycle, up to 8 cycles;
         b) Treanda: 120 mg/m2 infused intravenously over 60 minutes on days 1 and 2 of a 21-day cycle, up to 8 cycles;
   b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to CP.PHAR.57 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy – CP.PHAR.57 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

ALCL: anaplastic large cell lymphoma
CLL: chronic lymphocytic leukemia
FDA: Food and Drug Administration
HDT/ASCR: high dose therapy/autologous stem cell rescue
HL: Hodgkin lymphoma
MF: mycosis fungoides
MM: multiple myeloma
NCCN: National Comprehensive Cancer Network
NHL: non-Hodgkin lymphoma
PTCL: peripheral T-cell lymphoma
SCLC: small cell lung cancer
SLL: small lymphocytic lymphoma
SS: Sezary syndrome

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
CLL/SLL*	Bendeka: 100 mg/m2 administered intravenously over 10 minutes on Days 1 and 2 of a 28-day cycle, up to 6 cycles;	See regimen

	Treanda: 100 mg/m2 infused intravenously over 30 minutes on days 1 and 2 of a 28-day cycle, up to 6 cycles;	
Indolent B-cell lymphoma*	Bendeka: 120 mg/m2 administered intravenously over 10 minutes on Days 1 and 2 of a 21-day cycle, up to 8 cycles; Treanda: 120 mg/m2 infused intravenously over 60 minutes on days 1 and 2 of a 21-day cycle, up to 8 cycles;	See regimen

**Non-Hodgkin lymphomas*

VI. Product Availability

Bendeka: Multiple-dose vial

- Solution: 100 mg/4 mL

Treanda: Single-dose vial

- Solution: 45 mg/0.5 mL; 180 mg/2 mL
- Lyophilized powder: 25 mg in a 20 mL vial; 100 mg in a 20 mL vial

VII. References

1. Bendeka Prescribing Information. North Wales, PA: Teva Pharmaceuticals USA, Inc.; February 2017. Available at: http://bendeka.com/Pdf/PrescribingInformation.PDF. Accessed August 2017.
2. Treanda Prescribing Information. North Wales, PA: Teva Pharmaceuticals USA, Inc.; October 2016. Available at: http://www.treandahcp.com/pdf/TREANDA_final_PI.pdf. Accessed August 2017.
3. Bendamustine. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at nccn.org. Accessed August 2017.
4. Chronic lymphocytic leukemia/small lymphocytic lymphoma (Version 2.2017). In: National Comprehensive Cancer Network Guidelines. Available at nccn.org. Accessed August 2017.
5. B-cell lymphomas (Version 3.2017). In: National Comprehensive Cancer Network Guidelines. Available at nccn.org. Accessed August 2017.
6. Primary cutaneous B-cell lymphomas (Version 2.2017). In: National Comprehensive Cancer Network Guidelines. Available at nccn.org. Accessed August 2017.
7. T-cell lymphomas (Version 2.2017). In: National Comprehensive Cancer Network Guidelines. Available at nccn.org. Accessed August 2017.
8. Peripheral T-cell lymphoma (Version 2.2017). In: National Comprehensive Cancer Network Guidelines. Available at nccn.org. Accessed August 2017.
9. Hodgkin lymphoma (Version 1.2017). In: National Comprehensive Cancer Network Guidelines. Available at nccn.org. Accessed August 2017.
10. Multiple myeloma (Version 3.2017). In: National Comprehensive Cancer Network Guidelines. Available at nccn.org. Accessed August 2017.
11. Waldenstrom's macroglobulinemia/lymphoplasmacytic lymphoma (Version 1.2017). In: National Comprehensive Cancer Network Guidelines. Available at nccn.org. Accessed August 2017.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J9033	Injection, bendamustine HCl (Treanda), 1 mg
J9034	Injection, bendamustine HCl (Bendeka), 1 mg

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy split from CP.PHAR.182 Excellus Oncology.	01.01.17	02.17
Age and dosing added Safety information removed. NCCN recommended uses added separately. Removed HCPCS code for bevacizumab. Removed ICD-10-CM codes.	09.05.17	11.17

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan

retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.