

**Clinical Policy: Bendamustine (Bendeka, Treanda)**

Reference Number: CP.PHAR.307

Effective Date: 02.01.17

Last Review Date: 11.19

Line of Business: Commercial, Medicaid, HIM\*, HIM-Medical Benefit

[Coding Implications](#)[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

**Description**

Bendamustine hydrochloride (Bendeka<sup>®</sup>, Treanda<sup>®</sup>) is an alkylating drug.

*\*For Health Insurance Marketplace (HIM), if request is through pharmacy benefit, Bendeka is non-formulary and cannot be approved using these criteria; refer to the formulary exception policy, HIM.PA.103.*

**FDA Approved Indication(s)**

Bendeka and Treanda are indicated for the treatment of patients with:

- Chronic lymphocytic leukemia (CLL); Efficacy relative to first line therapies other than chlorambucil has not been established
- Indolent B-cell non-Hodgkin lymphoma (NHL) that has progressed during or within six months of treatment with rituximab or a rituximab-containing regimen

**Policy/Criteria**

*Provider must submit documentation (such as office chart notes and lab results or other clinical information) supporting that member has met all approval criteria.*

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

**I. Initial Approval Criteria****A. Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (must meet all):**

1. Diagnosis of chronic lymphocytic leukemia (CLL) (i.e., small lymphocytic lymphoma [SLL]);
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age  $\geq$  18 years;
4. Request meets one of the following (a or b):\*
  - a. Dose does not exceed (i or ii):
    - i. Bendeka: 100 mg/m<sup>2</sup> on Days 1 and 2 of a 28-day cycle, up to 6 cycles;
    - ii. Treanda: 100 mg/m<sup>2</sup> 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*).

*\*Prescribed regimen must be FDA-approved or recommended by NCCN*

**Approval duration:**

**Commercial/Medicaid** – 6 months

**HIM** – 6 months for Treanda (*refer to HIM.PA.103 for Bendeka if pharmacy benefit*)

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

1. One of the following diagnoses (a through j):
  - 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;
  - c. Gastric MALT lymphoma;
  - d. Nongastric MALT lymphoma;
  - e. Nodal marginal zone lymphoma;
  - f. Splenic marginal zone lymphoma;
  - g. Mantle cell lymphoma;
  - h. Diffuse large B-cell lymphoma;
  - i. AIDS-related B-cell lymphoma;
  - j. Monomorphic post-transplant lymphoproliferative disorder (PTLD) (B-cell type);
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age  $\geq$  18 years;
4. If the member has a diagnosis of diffuse large B-cell lymphoma, AIDS-related B-cell lymphoma, or monomorphic PTLD (B-cell type), member has used appropriate prior therapy (*see Appendix B for examples*);
5. Request meets one of the following (a or b):\*
  - a. Dose does not exceed (i or ii):
    - i. Bendeka: 120 mg/m<sup>2</sup> on Days 1 and 2 of a 21-day cycle, up to 8 cycles;
    - ii. Treanda: 120 mg/m<sup>2</sup> 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*).

\*Prescribed regimen must be FDA-approved or recommended by NCCN

**Approval duration:**

**Commercial/Medicaid** – 6 months

**HIM** – 6 months for Treanda (*refer to HIM.PA.103 for Bendeka if pharmacy benefit*)

**C. Non-Hodgkin T-Cell Lymphomas (off-label) (must meet all):**

1. One of the following diagnoses (a, b, c, d, or e):
  - a. Peripheral T-cell lymphoma (PTCL);
  - b. Mycosis fungoides (MF)/Sezary syndrome (SS);
  - c. Primary cutaneous CD30+ T-cell lymphoproliferative disorders;
  - d. Adult T-cell leukemia/lymphoma;
  - e. Hepatosplenic gamma-delta T-cell lymphoma;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age  $\geq$  18 years;
4. If the member has a diagnosis of PTCL or adult T-cell leukemia/lymphoma, member has used appropriate prior therapy (*see Appendix B for examples*);
5. If member has a diagnosis of primary cutaneous CD30+ T-cell lymphoproliferative disorders, medication is prescribed as a single-agent therapy for relapsed/refractory disease;
6. If member has a diagnosis of hepatosplenic gamma-delta T-cell lymphoma, medication is prescribed as a single-agent therapy for refractory disease after 2 primary therapies (*see Appendix B for examples*);

7. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).\*

*\*Prescribed regimen must be FDA-approved or recommended by NCCN*

**Approval duration:**

**Commercial/Medicaid** – 6 months

**HIM** – 6 months for Treanda (*refer to HIM.PA.103 for Bendeka if pharmacy benefit*)

**D. Hodgkin Lymphoma (off-label) (must meet all):**

1. Diagnosis of classical Hodgkin lymphoma (HL);
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age  $\geq$  18 years;
4. Disease is relapsed or refractory;
5. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).\*

*\*Prescribed regimen must be FDA-approved or recommended by NCCN*

**Approval duration:**

**Commercial/Medicaid** – 6 months

**HIM** – 6 months for Treanda (*refer to HIM.PA.103 for Bendeka if pharmacy benefit*)

**E. Multiple Myeloma (off-label) (must meet all):**

1. Diagnosis of multiple myeloma (MM);
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age  $\geq$  18 years;
4. Member has used appropriate prior therapy (*see Appendix B for examples*);
5. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).\*

*\*Prescribed regimen must be FDA-approved or recommended by NCCN*

**Approval duration:**

**Commercial/Medicaid** – 6 months

**HIM** – 6 months for Treanda (*refer to HIM.PA.103 for Bendeka if pharmacy benefit*)

**F. Waldenstrom's Macroglobulinemia/Lymphoplasmacytic Lymphoma (off-label) (must meet all):**

1. Diagnosis of Waldenstrom's macroglobulinemia (i.e., lymphoplasmacytic lymphoma);
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age  $\geq$  18 years;
4. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).\*

*\*Prescribed regimen must be FDA-approved or recommended by NCCN*

**Approval duration:**

**Commercial/Medicaid** – 6 months

**HIM** – 6 months for Treanda (*refer to HIM.PA.103 for Bendeka if pharmacy benefit*)

**G. Other diagnoses/indications**

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid and HIM-Medical Benefit.

**II. Continued Therapy**

**A. All Indications in Section I (must meet all):**

1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Bendeka or Treanda for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. If request is for a dose increase, request meets (a or b):\*
  - a. New dose does not exceed (i or ii):
    - i. CLL/SLL:
      - a) Bendeka: 100 mg/m<sup>2</sup> on Days 1 and 2 of a 28-day cycle, up to 6 cycles;
      - b) Treanda: 100 mg/m<sup>2</sup> Days 1 and 2 of a 28-day cycle, up to 6 cycles;
    - ii. Non-Hodgkin indolent B-cell lymphoma:
      - a) Bendeka: 120 mg/m<sup>2</sup> on Days 1 and 2 of a 21-day cycle, up to 8 cycles;
      - b) Treanda: 120 mg/m<sup>2</sup> 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*).

*\*Prescribed regimen must be FDA-approved or recommended by NCCN*

**Approval duration:**

**Commercial/Medicaid** – 12 months

**HIM** – 12 months for Treanda (*refer to HIM.PA.103 for Bendeka if pharmacy benefit*)

**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 the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid and HIM-Medical Benefit.

**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 policies – CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid and HIM-Medical Benefit or evidence of coverage documents.

**IV. Appendices/General Information**

*Appendix A: Abbreviation/Acronym Key*

CLL: chronic lymphocytic leukemia

FDA: Food and Drug Administration

HL: Hodgkin lymphoma  
MF: mycosis fungoides  
MM: multiple myeloma  
NCCN: National Comprehensive Cancer Network  
NHL: non-Hodgkin lymphoma

PTCL: peripheral T-cell lymphoma  
PTLD: post-transplant lymphoproliferative disorder  
SLL: small lymphocytic lymphoma  
SS: Sezary syndrome

*Appendix B: Therapeutic Alternatives*

*This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.*

<b>Drug Name</b>	<b>Dosing Regimen</b>	<b>Dose Limit/ Maximum Dose</b>
<b>Examples of first-line therapy for diffuse large B-cell lymphoma</b>		
RCHOP (Rituxan <sup>®</sup> [rituximab], cyclophosphamide, doxorubicin, vincristine, prednisone)	Varies	Varies
EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin) + Rituxan <sup>®</sup> (rituximab)	Varies	Varies
RCEPP (Rituxan <sup>®</sup> [rituximab], cyclophosphamide, etoposide, prednisone, procarbazine)	Varies	Varies
RCDOPE (Rituxan <sup>®</sup> [rituximab], cyclophosphamide, liposomal doxorubicin, vincristine, prednisone)	Varies	Varies
RGCVP (Rituxan <sup>®</sup> [rituximab], gemcitabine, cyclophosphamide, vincristine, prednisolone)	Varies	Varies
<b>Examples of first-line therapy for AIDS-related B-cell lymphomas</b>		
EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin) + Rituxan <sup>®</sup> (rituximab)	Varies	Varies
CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) + Rituxan <sup>®</sup> (rituximab)	Varies	Varies
<b>Examples of first-line therapy for PTCL</b>		
CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone)	Varies	Varies
CHOEP (cyclophosphamide, doxorubicin, vincristine, etoposide, prednisone)	Varies	Varies
EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin)	Varies	Varies
<b>Examples of first-line therapy for adult T-cell leukemia/lymphoma</b>		
CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone)	Varies	Varies
CHOEP (cyclophosphamide, doxorubicin, vincristine, etoposide, prednisone)	Varies	Varies
EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin)	Varies	Varies

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
HyperCVAD (cyclophosphamide, vincristine, doxorubicin, dexamethasone) alternating with high-dose methotrexate and cytarabine	Varies	Varies
<b>Examples of primary therapy for hepatosplenic gamma-delta T-cell lymphoma</b>		
CHOEP (cyclophosphamide, doxorubicin, vincristine, etoposide, prednisone)	Varies	Varies
DHAP (dexamethasone, cisplatin, cytarabine)	Varies	Varies
EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin)	Varies	Varies
ICE (ifosfamide, carboplatin, etoposide)	Varies	Varies
IVAC (ifosfamide, etoposide, cytarabine)	Varies	Varies
<b>Examples of primary therapy for MM</b>		
Bortezomib/liposomal doxorubicin/dexamethasone	Varies	Varies
Carfilzomib (twice weekly)/ dexamethasone	Varies	Varies
Carfilzomib/lenalidomide/dexamethasone	Varies	Varies
Daratumumab/bortezomib /dexamethasone	Varies	Varies
<b>Examples of chemoimmunotherapy for monomorphic PTL (B-cell type)</b>		
RCHOP (Rituxan <sup>®</sup> [rituximab], cyclophosphamide, doxorubicin, vincristine, prednisone)	Varies	Varies
RCEPP (Rituxan <sup>®</sup> [rituximab], cyclophosphamide, etoposide, prednisone, procarbazine)	Varies	Varies
RCVP (Rituxan <sup>®</sup> [rituximab], cyclophosphamide, vincristine, prednisone)	Varies	Varies
RCEOP (Rituxan <sup>®</sup> [rituximab], cyclophosphamide, etoposide, vincristine, prednisone)	Varies	Varies

Therapeutic alternatives are listed as Brand name<sup>®</sup> (generic) when the drug is available by brand name only and generic (Brand name<sup>®</sup>) when the drug is available by both brand and generic.

*Appendix C: Contraindications/Boxed Warnings*

- Contraindication(s):
  - Bendeka: patients with a history of a hypersensitivity reaction to bendamustine, polyethylene glycol 400, propylene glycol, or monothioglycerol
  - Treanda: patients with a history of a hypersensitivity reaction to bendamustine
- Boxed warning(s): none reported

**V. Dosage and Administration**

Indication	Dosing Regimen	Maximum Dose
CLL/SLL*	Bendeka: 100 mg/m <sup>2</sup> IV over 10 minutes on Days 1 and 2 of a 28-day cycle, up to 6 cycles	See regimen

Indication	Dosing Regimen	Maximum Dose
	Treanda: 100 mg/m <sup>2</sup> IV over 30 minutes on days 1 and 2 of a 28-day cycle, up to 6 cycles	
Indolent B-cell lymphoma*	Bendeka: 120 mg/m <sup>2</sup> IV over 10 minutes on Days 1 and 2 of a 21-day cycle, up to 8 cycles  Treanda: 120 mg/m <sup>2</sup> IV 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

Drug Name	Availability
Bendamustine (Bendeka)	Solution (multiple-dose vial): 100 mg/4 mL
Bendamustine (Treanda)	Solution (single-dose vial): 45 mg/0.5 mL; 180 mg/2 mL Lyophilized powder (single-dose vial): 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.; July 2018. Available at: <http://www.bendeka.com/>. Accessed August 14, 2019.
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**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
4Q 2018 annual review: HIM-Medical Benefit added; summarized NCCN and FDA-approved uses for improved clarity; added age requirement and specialist involvement in care; added PTLD (category 2A recommendation) as a covered indication per NCCN compendium; updated continued therapy section to include language for continuity of care; references reviewed and updated.	07.17.18	11.18
Added Commercial line of business to policy.	10.08.19	
4Q 2018 annual review: added HIM* line of business for Treanda based on formulary status; added additional therapeutic alternatives to Appendix B with NCCN category 1: MM; added hepatosplenic gamma-delta T-cell lymphoma to non-Hodgkin T-cell lymphomas (off-label) uses and related therapeutic alternatives to Appendix B; references reviewed and updated.	08.14.19	11.19

**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.

**For Health Insurance Marketplace members**, when applicable, this policy applies only when the prescribed agent is on your health plan approved formulary. Request for non-formulary drugs must be reviewed using the non-formulary policy; HIM.PA.103.

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