RXADVANCE
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Clinical Policy Title:	bendamustine
Policy Number:	RxA.352
Drug(s) Applied:	Bendeka®, Treanda®
Original Policy Date:	03/06/2020
Last Review Date:	09/14/2020
Line of Business Policy Applies to:	All lines of business

Background

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

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
Bendamustine hydrochloride (Bendeka®, Treanda®)	CLL/SLL	Bendeka®: 100 mg/m^2 IV over 10 minutes on Days 1 and 2 of a 28-day cycle, up to 6 cycles Treanda®: 100 mg/m^2 IV over 30 minutes on days 1 and 2 of a 28-day cycle, up to 6 cycles	100 mg/m^2 on days 1 and 2 every 28 days
Bendamustine hydrochloride (Treanda®)	Indolent B-cell lymphoma	Bendeka®: 120 mg/m^2 IV over 10 minutes on Days 1 and 2 of a 21-day cycle, up to 8 cycles Treanda®: 120 mg/m^2 IV over 60 minutes on days 1 and 2 of a 21-day cycle, up to 8 cycles	120 mg/m^2 on days 1 and 2 every 21 days

Dosage Forms

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
Bendamustine (Treanda®): Lyophilized powder (single-dose vial): 25 mg in a 20 mL vial; 100 mg in a 20 mL vial

Clinical Policy

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

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 18 years of age or older;
4. Request meets one of the following (a or b):*
   a. Dose does not exceed (i or ii):
      I. Bendeka®: 100 mg/m^2 on Days 1 and 2 of a 28-day cycle, up to 6 cycles;
      II. Treanda®: 100 mg/m^2 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: 6 months
Medicaid: 6 months
HIM: 6 months

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 18 years of age or older;
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^2 on Days 1 and 2 of a 21-day cycle, up to 8 cycles;
ii. Treanda®: 120 mg/m^2 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: 6 months
Medicaid: 6 months
HIM: 6 months

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 18 years of age or older;
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: 6 months
Medicaid: 6 months
HIM: 6 months

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 18 years of age or older;
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: 6 months
Medicaid: 6 months
HIM: 6 months

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 18 years of age or older;
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: 6 months
Medicaid: 6 months
HIM: 6 months

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 18 years of age or older;
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: 6 months
Medicaid: 6 months
HIM: 6 months

II. Continued Therapy Approval

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

1. Currently receiving medication that has been authorized by RxAdvance , 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^2 on Days 1 and 2 of a 28-day cycle, up to 6 cycles;
         b) Treanda®: 100 mg/m^2 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^2 on Days 1 and 2 of a 21-day cycle, up to 8 cycles;
         b) Treanda®: 120 mg/m2 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: 12 months
Medicaid: 12 months
HIM: 12 months for Treanda®

III. Appendices

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.

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

CHOEP (cyclophosphamide, doxorubicin, vincristine, etoposide, prednisone)	Varies	Varies
EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin)	Varies	Varies
Examples of first-line therapy for adult T-cell leukemia/lymphoma		
CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone)	Varies	Varies
CHOEP (cyclophosphamide, doxorubicin, vincristine, etoposide, prednisone)	Varies	Varies
EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin)	Varies	Varies
HyperCVAD (cyclophosphamide, vincristine, doxorubicin, dexamethasone) alternating with high-dose methotrexate and cytarabine	Varies	Varies
Examples of primary therapy for hepatosplenic gamma-delta T-cell lymphoma		
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
Examples of primary therapy for MM		
Bortezomib/liposomal doxorubicin/dexamethasone	Varies	Varies
Carfilzomib (twice weekly)/ dexamethasone	Varies	Varies
Carfilzomib/lenalidomide/dexamethasone	Varies	Varies
Daratumumab/bortezomib /dexamethasone	Varies	Varies
Examples of chemoimmunotherapy for monomorphic PTLD (B-cell type)		
RCHOP (Rituxan® [rituximab], cyclophosphamide, doxorubicin, vincristine, prednisone)	Varies	Varies
RCEPP (Rituxan® [rituximab], cyclophosphamide, etoposide, prednisone, procarbazine)	Varies	Varies
RCVP (Rituxan® [rituximab], cyclophosphamide, vincristine, prednisone)	Varies	Varies
RCEOP (Rituxan® [rituximab], cyclophosphamide, etoposide, vincristine, prednisone)	Varies	Varies

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) 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

References

1. Bendeka® Prescribing Information. North Wales, PA: Teva Pharmaceuticals USA, Inc.; October 2019. Available at: https://www.bendeka.com/. Accessed July 31, 2020.
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3. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed August 14, 2019.
4. National Comprehensive Cancer Network. Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Version 4.2020. Available at: https://www.nccn.org. Accessed July 31, 2020.
5. National Comprehensive Cancer Network. B-cell Lymphomas Version 2.2020. Available at: https://www.nccn.org. Accessed July 31, 2020.
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8. National Comprehensive Cancer Network. Multiple Myeloma Version 4.2020. Available at: https://www.nccn.org. Accessed July 31, 2020.
9. National Comprehensive Cancer Network. Waldenstrom's Macroglobulinemia/Lymphoplasmacytic Lymphoma Version 2.2020. Available at: https://www.nccn.org. Accessed July 31, 2020.
10. Clinical Pharmacology [database online] powered by ClinicalKey. Tampa, FL: Elsevier, 2020. Accessed with subscription at: http://www.clinicalkey.com. Updated January 14, 2020. Accessed July 31, 2020.
11. Bendamustine, Lexi-Drug. Lexicomp. Wolters Kluwer Health, Inc. Riverwoods, IL. Accessed with subscription at: http://online.lexi.com. Accessed July 31, 2020

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	01/2020	03/06/2020
Policy was reviewed: 1. Policy title table was updated: Clinical Policy Title was updated to " bendamustine"; Drug(s) Applied was updated to "Bendeka®, Treanda®"; Line of Business Policy Applies to was updated to "All". 2. Clinical policy was updated: Approval duration was updated for both Initial and Continued Approval Criteria; Continued	07/31/2020	09/14/2020

Approval was rephrased to "Currently receiving medication that has been authorized by RxAdvance.. ". 3. References were updated.		