CARECONTINUUM™

UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Oncology (Injectable) – Bortezomib Products Utilization Management Medical Policy
- Boruzu® (bortezomib intravenous or subcutaneous injection – Amneal Pharmaceuticals)
- Velcade® (bortezomib intravenous or subcutaneous injection – Takeda, generic)

REVIEW DATE: 11/20/2024; selected revision 12/11/2024

OVERVIEW

Bortezomib, a proteasome inhibitor, is indicated in adults with the following conditions:[1,12]
- **Mantle cell lymphoma**.
- **Multiple myeloma**.

Guidelines

Bortezomib is mentioned in several guidelines published by the National Comprehensive Cancer Network (NCCN).[2-11]
- **Acute lymphoblastic leukemia:** Guidelines for adults (version 2.2024 – July 19, 2024) and for pediatric patients (version 1.2025 – August 28, 2024) include bortezomib + chemotherapy among the other recommended regimens for relapsed or refractory disease.[3,4]
- **B-cell lymphomas:** Guidelines (version 3.2024 – August 26, 2024) recommend bortezomib as a component of VR-CAP (bortezomib/rituximab/cyclophosphamide/doxorubicin/prednisone) as a preferred less aggressive therapy option for the initial treatment of patients (induction therapy) with newly diagnosed mantle cell lymphoma.[5] Bortezomib ± rituximab is also listed as second-line and subsequent therapy for relapsed or refractory mantle cell lymphoma. For patients with relapsed or refractory multicentric Castleman's disease, bortezomib ± rituximab is listed among the treatment options.
- **Classic Hodgkin lymphoma:** Guidelines for pediatric disease (version 1.2024 – May 14, 2024) include bortezomib/ifosfamide/vinorelbine among the subsequent therapy options for relapsed or refractory disease.[7]
- **Kaposi sarcoma:** Guidelines (version 1.2025 – November 1, 2024) include bortezomib among the subsequent systemic therapy options for patients who have relapsed or refractory disease.[6]
- **Multiple myeloma:** Bortezomib features prominently in the NCCN Multiple Myeloma clinical practice guidelines (version 1.2025 – September 17, 2024).[8] Bortezomib-containing regimens are listed as preferred for primary therapy (transplant and nontransplant candidates) and previously treated disease. Bortezomib is also a component of multiple other regimens across the spectrum of disease. For maintenance therapy, bortezomib ± lenalidomide capsules (and ± dexamethasone for transplant candidates) are also listed as treatment options.
- **Systemic light chain amyloidosis:** Guidelines (version 1.2025 – September 13, 2024) list bortezomib alone or in combination with other agents for primary therapy (transplant and non-transplant candidates) and previously treated disease.[9] NCCN notes that bortezomib was well tolerated at doses up to 1.6 mg/m^2 on a once-weekly schedule and 1.3 mg/m^2 on a twice-weekly schedule. The once-weekly regimen was associated with lower neurotoxicity.
- **T-cell lymphomas:** Guidelines (version 1.2025 – November 11, 2024) recommend bortezomib (category 2A) as an alternative regimen for second-line or subsequent therapy.[11]
- **Waldenstrom's macroglobulinemia/lymphoplasmacytic lymphoma:** Guidelines (version 1.2025 – September 13, 2024) recommend bortezomib/dexamethasone/rituximab as one of the

"Other Recommended Regimens" (category 2A) for primary therapy and for previously treated disease.[10]

Dosing Information

Bortezomib (Velcade, generics) must be reconstituted prior to intravenous or subcutaneous administration.[1] Boruzu is available as a solution in a single-dose vial (3.5 mg/1.4 mL).[12] The final concentration for subcutaneous or intravenous administration is the same for Boruzu and Velcade (generics).[1,12] Dosing regimens vary and are dependent upon concomitant therapies and tolerability.[1,7,9] Additionally, dose modifications with bortezomib are recommended for the management of hematological toxicity (e.g., neutropenia, thrombocytopenia), non-hematological toxicity (e.g., Grade 3 or higher), peripheral neuropathy, and hepatic impairment. This may include reducing the dose or withholding the drug until the toxicity is resolved. See the respective Prescribing Information for more detail.

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of bortezomib. 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. Because of the specialized skills required for evaluation and diagnosis of patients treated with bortezomib, as well as the monitoring required for adverse events and long-term efficacy, approval requires bortezomib to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of bortezomib is recommended in those who meet one of the following criteria:

FDA-Approved Indications

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1. Mantle Cell Lymphoma. Approve for 1 year 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 previously tried at least one other therapy for mantle cell lymphoma; OR
Note: Examples of other therapies for mantle cell lymphoma include regimens containing a rituximab product, cytarabine, cisplatin, cyclophosphamide, doxorubicin, vincristine, or bendamustine.

ii. The medication is used in combination with at least one other agent; AND
Note: Examples of other agents used in combination with bortezomib for mantle cell lymphoma include a rituximab product, bendamustine, cyclophosphamide, and doxorubicin.

C) The medication is prescribed by or in consultation with an oncologist or a hematologist.

Dosing. Approve if the requested dosing meets BOTH of the following (A and B):

A) Each individual dose must not exceed 1.3 mg/m^2 administered intravenously or subcutaneously; AND

B) Patient receives a maximum of six infusions over a 28-day period.

2. Multiple Myeloma. Approve for 1 year 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.** The medication will be used in combination with at least one other agent; OR
    Note: Examples of other agents that may be used in combination with bortezomib include dexamethasone, cyclophosphamide, doxorubicin, Doxil (doxorubicin liposomal intravenous infusion), Revlimid (lenalidomide capsules), Thalomid (thalidomide capsules), cisplatin, etoposide, Darzalex (daratumumab intravenous infusion), Pomalyst (pomalidomide capsules), bendamustine, Empliciti (elotuzumab intravenous infusion), Farydak (panobinostat capsules).
  - **ii.** The medication is being used for maintenance therapy; AND
- **C)** The medication is prescribed by or in consultation with an oncologist or a hematologist.

Dosing. Approve if the requested dosing meets BOTH of the following (A and B):
- **A)** Each individual dose must not exceed 1.6 mg/m^2 administered intravenously or subcutaneously; AND
- **B)** Patient receives a maximum of six infusions over a 28-day period.

Other Uses with Supportive Evidence

3. Acute Lymphoblastic Leukemia. Approve for 1 year if the patient meets BOTH of the following (A and B):
- **A)** Patient has relapsed or refractory disease; AND
- **B)** The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve if the requested dosing meets BOTH of the following (A and B):
- **A)** Each individual dose must not exceed 1.6 mg/m^2 administered intravenously or subcutaneously; AND
- **B)** Patient receives a maximum of six infusions over a 28-day period.

4. Castleman's Disease. Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):
- **A)** Patient is ≥ 18 years of age; AND
- **B)** Patient has multicentric Castleman's disease; AND
- **C)** Patient has relapsed, refractory, or progressive disease; AND
- **D)** The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve if the requested dosing meets BOTH of the following (A and B):
- **A)** Each individual dose must not exceed 1.6 mg/m^2 administered intravenously or subcutaneously; AND
- **B)** Patient receives a maximum of six infusions over a 28-day period.

5. Classic Hodgkin Lymphoma. Approve for 1 year if the patient meets BOTH of the following (A and B):
- **A)** Patient has tried at least one systemic chemotherapy regimen; AND
  Note: Examples of systemic chemotherapies used in regimens for Hodgkin lymphoma include doxorubicin, bleomycin, vincristine, etoposide, and dacarbazine.
- **B)** The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve if the requested dosing meets BOTH of the following (A and B):
- **A)** Each individual dose must not exceed 1.6 mg/m^2 administered intravenously or subcutaneously; AND
- **B)** Patient receives a maximum of six infusions over a 28-day period.

6. Kaposi Sarcoma. Approve for 1 year if the patient meets ALL of the following (A, B, and C):
- **A)** Patient is ≥ 18 years of age; AND
- **B)** Patient has tried at least one systemic chemotherapy; AND
  Note: Examples of systemic chemotherapies include doxorubicin and paclitaxel.
- **C)** The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve if the requested dosing meets BOTH of the following (A and B):
- **A)** Each individual dose must not exceed 1.6 mg/m^2 administered intravenously or subcutaneously; AND
- **B)** Patient receives a maximum of three infusions over a 28-day period.

7. Systemic Light Chain Amyloidosis. Approve for 1 year 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 or a hematologist.

Dosing. Approve if the requested dosing meets BOTH of the following (A and B):
- **A)** Each individual dose must not exceed 1.6 mg/m^2 administered intravenously or subcutaneously; AND
- **B)** Patient receives a maximum of six infusions over a 28-day period.

8. T-Cell Lymphoma. Approve for 1 year if the patient meets ALL of the following (A, B, and C):
- **A)** Patient is ≥ 18 years of age; AND
- **B)** Patient has tried at least one systemic therapy; AND
  Note: Examples of systemic therapies include EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin), Adcetris (brentuximab vedotin intravenous infusion) + CHP (cyclophosphamide, doxorubicin, and prednisone), zidovudine + interferon, CHOEP (cyclophosphamide, doxorubicin, vincristine, etoposide, and prednisone), HyperCVAD (cyclophosphamide, vincristine, doxorubicin, and dexamethasone) alternating with high-dose methotrexate and cytarabine.
- **C)** The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve if the requested dosing meets BOTH of the following (A and B):
A) Each individual dose must not exceed 1.6 mg/m^2 administered intravenously or subcutaneously; AND
B) Patient receives a maximum of six infusions over a 28-day period.

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9. Waldenstrom's Macroglobulinemia/Lymphoplasmacytic Lymphoma. Approve for 1 year if the patient meets ALL of the following (A, B, and C):
A) Patient is ≥ 18 years of age; AND
B) The medication will be used in combination with rituximab and dexamethasone; AND
C) The medication is prescribed by or in consultation with an oncologist or a hematologist.

Dosing. Approve if the requested dosing meets BOTH of the following (A and B):
A) Each individual dose must not exceed 1.6 mg/m^2 administered intravenously or subcutaneously; AND
B) Patient receives a maximum of six infusions over a 28-day period.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of bortezomib 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. Velcade® subcutaneous injection or intravenous infusion [prescribing information]. Lexington, MA: Takeda; November 2021.
2. The NCCN Drugs and Biologics Compendium. © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on November 18, 2024. Search term: bortezomib.
3. The NCCN Acute Lymphoblastic Leukemia Clinical Practice Guidelines in Oncology (version 2.2024 – July 19, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on November 18, 2024.
4. The NCCN Pediatric Acute Lymphoblastic Leukemia Clinical Practice Guidelines in Oncology (version 1.2025 – August 28, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on November 18, 2024.
5. The NCCN B-Cell Lymphomas Clinical Practice Guidelines in Oncology (version 3.2024 – August 26, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed November 18, 2024.
6. The NCCN Kaposi Sarcoma Clinical Practice Guidelines in Oncology (version 1.2025 – November 1, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on November 18, 2024.
7. The NCCN Pediatric Hodgkin Lymphoma Clinical Practice Guidelines in Oncology (version 1.2024 – May 14, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on November 18, 2024.
8. The NCCN Multiple Myeloma Clinical Practice Guidelines in Oncology (version 1.2025 – September 17, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on November 18, 2024.
9. The NCCN Systemic Light Chain Amyloidosis Clinical Practice Guidelines in Oncology (version 1.2025 – September 13, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed November 18, 2024.
10. The NCCN Waldenstrom's Macroglobulinemia/Lymphoplasmacytic Lymphoma Clinical Practice Guidelines in Oncology (version 1.2025 – September 13, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed November 18, 2024.
11. The NCCN T-Cell Lymphomas Clinical Practice Guidelines in Oncology (version 1.2025 – November 11, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed November 18, 2024.
12. Boruzu® subcutaneous injection or intravenous infusion [prescribing information]. Bridgewater, NJ: Amneal Pharmaceuticals; September 2024.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	**Mantle Cell Lymphoma:** An age requirement of ≥ 18 years was added. **Multiple Myeloma:** An age requirement of ≥ 18 years was added. **Castleman's Disease:** An age requirement of ≥ 18 years was added. **Kaposi Sarcoma:** An age requirement of ≥ 18 years was added. **Systemic Light Chain Amyloidosis:** An age requirement of ≥ 18 years was added. **Waldenstrom's Macroglobulinemia/Lymphoplasmacytic Lymphoma:** An age requirement of ≥ 18 years was added. **Acute Lymphoblastic Leukemia:** The condition of approval was changed to as listed; previously listed as "Acute Lymphoblastic Lymphoma". **T-Cell Lymphoma:** Added new approval condition and criteria.	11/15/2023
Annual Revision	No criteria changes.	11/20/2024
Selected Revision	Changed policy name to "Oncology (Injectable) – Bortezomib Products". Added Boruzu, a ready-to-use injectable formulation of bortezomib to the policy.	12/11/2024