Clinical Policy: Bortezomib (Boruzu, Velcade)

Reference Number: PA.CP.PHAR.410
Effective Date: 01/2019
Last Review Date: 01/2026

Description
Bortezomib (Boruzu®,Velcade®) is a proteasome inhibitor.

Boruzu and Velcade are indicated for treatment of patients with:
- multiple myeloma (MM)
- mantle cell lymphoma (MCL)

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

It is the policy of PA Health & Wellness® that bortezomib is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Multiple Myeloma and Mantle Cell Lymphoma (must meet all)**:**

1. Diagnosis of one of the following (a or b):
   a. MM;
   b. MCL (B-cell lymphoma subtype);
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
4. For Boruzu and Velcade requests, member must use bortezomib, unless contraindicated or clinically significant adverse effects are experienced;
5. Request meets one of the following (a or b):
   a. Dose does not exceed 1.3 mg/m^2;
   b. 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. NCCN Recommended Uses (off-label) (must meet all)**:**

1. Diagnosis of one of the following (a-j):
   a. Kaposi sarcoma that is one of the following (i or ii):
      i. Relapsed or refractory disease that is T1, extensive T0 cutaneous, or nodal - after ≥ 2 prior lines of systemic therapy;
      ii. Kaposi-sarcoma associated herpesvirus-associated inflammatory cytokine syndrome (KICS), in combination with rituximab;
   b. HIV-related B-cell lymphoma;
   c. Multicentric Castleman's disease (B-cell lymphoma subtype) - as subsequent therapy for relapsed, refractory, or progressive disease;
   d. Systemic light chain amyloidosis;
   e. Adult T-cell leukemia/lymphoma;

f. Waldenström macroglobulinemia/lymphoplasmacytic lymphoma;
g. T-cell acute lymphoblastic leukemia (T-ALL)-for relapsed or refractory disease;
h. Pediatric acute lymphoblastic leukemia (ALL);
i. Pediatric Hodgkin lymphoma (HL) - as subsequent therapy in combination with ifosafamide and vinorelbine;
j. Other category 1, 2A, or 2B NCCN-recommended uses not listed;

2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years (all indications except pediatric ALL and HL);
4. For Boruzu and Velcade requests, member must use bortezomib, unless contraindicated or clinically significant adverse effects are experienced;
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*).

Approval duration: 12 months

C. 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): PA.CP.PMN.53.

II. Continued Therapy

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

1. Currently receiving medication via PA Health &Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care policy (PA.PHARM.01) applies;
2. Member is responding positively to therapy;
3. For Boruzu and Velcade requests, member must use bortezomib, unless contraindicated or clinically significant adverse effects are experienced;
4. If request is for a dose increase, request meets one of the following (a or b):
   a. New dose does not exceed 1.3 mg/m^2;
   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 PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies.
   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): PA.CP.PMN.53.

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 – PA.CP.PMN.53 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

ALL: acute lymphoblastic leukemia
FDA: Food and Drug Administration
HL: Hodgkin lymphoma
KICS: Kaposi-sarcoma associated herpesvirus (KSHV)-associated inflammatory cytokine syndrome
MCL: mantel cell lymphoma
MM: multiple myeloma
NCCN: National Comprehensive Cancer Network
T-ALL: T-cell acute lymphoblastic leukemia

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s):
  - Patients with hypersensitivity (not including local reactions) to bortezomib, boron, or mannitol, including anaphylactic reactions
  - Contraindicated for intrathecal administration
- Boxed warning(s): none reported

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
MM	• First-line therapy: 1.3 mg/m^2 as a 3 to 5 second bolus IV injection or SC injection in combination with PO melphalan and PO prednisone for nine 6-week treatment cycles. • Relapse*: 1.3 mg/m^2 as a 3 to 5 second bolus IV injection or SC injection as a single agent or in combination with dexamethasone for up to eight 3-week cycles. For therapy beyond eight cycles, see PI for additional dosing options. *If relapse occurs ≥ 6 months after a previous response to Velcade, treatment may be restarted at the last tolerated dose.	1.3 mg/m^2
MCL	• First-line therapy: 1.3 mg/m^2 as a 3 to 5 second bolus IV injection or SC injection in combination with IV rituximab, cyclophosphamide, doxorubicin and PO prednisone (VcR-CAP) for up to six 3-week treatment cycles, plus two additional cycles if a positive response.	1.3 mg/m^2

Indication	Dosing Regimen	Maximum Dose
	• Relapse: 1.3 mg/m^2 as a 3 to 5 second bolus IV injection or SC injection for up to eight 3-week treatment cycles. Therapy may extend beyond eight cycles.	

VI. Product Availability

Drug Name	Availability
bortezomib (Boruzu)	Single-dose vial for injection: 3.5 mg/1.4 mL **The branded product, Boruzu, is only available as a sterile solution*
bortezomib (Velcade)	Single-dose vial for injection: 3.5 mg **The branded product, Velcade, is only available as 3.5 mg sterile lyophilized powder*
bortezomib	Single-dose vials for injection: • Sterile lyophilized powder for reconstitution: 1 mg, 2.5 mg, 3.5 mg • Solution: 3.5 mg/1.4 mL

VII. References

1. Velcade Prescribing Information. Lexington, MA: Takeda Pharmaceuticals America, Inc.; August 2022. Available at: https://www.takedaoncology.com/medicines/united-states/. Accessed October 27, 2025.
2. Boruzu Prescribing Information. Bridgewater, NJ: Amneal Pharmaceuticals LLC: July 2025. Available at: https://boruzu.us/. Accessed October 27, 2025.
3. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed December 2, 2025.
4. National Comprehensive Cancer Network. Multiple Myeloma Version 4.2026. Available at: https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf. Accessed December 2, 2025.
5. National Comprehensive Cancer Network. Adult T-Cell Lymphomas Version 2.2025. Available at: https://www.nccn.org/professionals/physician_gls/pdf/t-cell.pdf. Accessed December 2, 2025.
6. National Comprehensive Cancer Network. Pediatric Acute Lymphoblastic Leukemia Version 1.2026. Available at: https://www.nccn.org/professionals/physician_gls/pdf/ped_all.pdf. Accessed December 2, 2025.
7. National Comprehensive Cancer Network. Acute Lymphoblastic Leukemia Version 2.2025. Available at: https://www.nccn.org/professionals/physician_gls/pdf/all.pdf. Accessed December 2, 2025.
8. National Comprehensive Cancer Network. B-Cell Lymphomas Version 3.2025. Available at: https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf. Accessed December 2, 2025.

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
J9041	Injection, bortezomib (Velcade), 0.1 mg
J9046	Injection, bortezomib, (dr. reddy's), not therapeutically equivalent to J9041, 0.1 mg
J9048	Injection, bortezomib (fresenius kabi), not therapeutically equivalent to J9041, 0.1 mg
J9049	Injection, bortezomib (hospira), not therapeutically equivalent to J9041, 0.1 mg
J9051	Injection, bortezomib (maia), not therapeutically equivalent to J9041, 0.1 mg

Reviews, Revisions, and Approvals	Date
Policy created.	01/2019
1Q 2020 annual review: references reviewed and updated.	01/2020
1Q 2021 annual review: AIDS-related Kaposi sarcoma pediatric HL NCCN recommended uses added; references reviewed and updated.	01/2021
1Q 2022 annual review: removed requirement for Velcade to be prescribed in combination with HIV therapy for Kaposi sarcoma indication per NCCN; added T-ALL indication per NCCN; references reviewed and updated.	01/2022
1Q 2023 annual review; added new 1mg and 2.5mg strengths of bortezomib (available generically only from Hospira); added redirection to generic bortezomib for brand Velcade requests. Added also new 2.5 and 3.5mg formulations (available generically only) as solution for a single-dose injection. Added verbiage directing to the use of generic bortezomib unless contraindicated or clinically significant adverse effects are experienced	01/2023
1Q 2024 annual review: removed specification that 1 mg and 2.5 mg were specifically indicated after 1 prior therapy per PI update; revised product availability for solutions from 2.5 mg/mL to 3.5 mg/3.5mL per PI; Added HCPCS code [J9051], removed inactive HCPCS code [J9044]; references reviewed and updated.	01/2024
1Q 2025 annual review: for NCCN recommended uses (off-label) initial criteria: added mantle cell lymphoma (B-cell lymphoma) and HIV-related B-cell lymphoma as supported by NCCN compendium; references reviewed and updated.	01/2025
RT4: added new formulation Boruzu; removed "if available" from generic bortezomib redirection as it is currently available. 1Q 2026 annual review: for off-label indications per NCCN: added KICS indication, added disease qualifiers for Castleman disease and Kaposi sarcoma, and removed requirement for use as subsequent therapy for pediatric ALL; revised initial approval durations from 6 months to 12 months; references reviewed and updated.	01/2026