Clinical Policy: Bortezomib (Velcade)

Reference Number: CP.PHAR.410
Effective Date: 12.11.18
Last Review Date: 02.25
Line of Business: Commercial, HIM, Medicaid

Coding Implications
Revision Log

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

Description

Bortezomib (Velcade®) is a proteasome inhibitor.

FDA Approved Indication(s)

Velcade is indicated for treatment of adult 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 health plans affiliated with Centene Corporation® 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 Velcade requests, member must use bortezomib, if available, 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*).

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

Approval duration:
Medicaid/HIM – 6 months
Commercial – 6 months or to the member's renewal date, whichever is longer

B. NCCN Recommended Uses (off-label) (must meet all)**:**

1. Diagnosis of one of the following (a-j):
   a. Kaposi sarcoma (advanced cutaneous, oral, visceral, or nodal disease) - after ≥ 2 prior lines of systemic therapy;

b. Mantle cell lymphoma (B-cell lymphoma);
c. HIV-related B-cell lymphoma;
d. Multicentric Castleman's disease (B-cell lymphoma subtype) - as subsequent therapy;
e. Systemic light chain amyloidosis;
f. Adult T-cell leukemia/lymphoma - as subsequent therapy;
g. Waldenström macroglobulinemia/lymphoplasmacytic lymphoma;
h. T-cell acute lymphoblastic leukemia (T-ALL) – for relapsed or refractory disease;
i. Pediatric acute lymphoblastic leukemia (ALL) - as subsequent therapy;
j. Pediatric Hodgkin lymphoma (HL) - as subsequent therapy in combination with ifosafamide and vinorelbine;

2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years (all indications except pediatric ALL and HL);
4. For Velcade requests, member must use bortezomib, if available, 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*).*
   **Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval duration:
Medicaid/HIM – 6 months
Commercial – 6 months or to the member's renewal date, whichever is longer

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

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

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 the requested agent for a covered indication and has received this medication for at least 30 days;

2. Member is responding positively to therapy;
3. For Velcade requests, member must use bortezomib, if available, 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*).

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

Approval duration:
Medicaid/HIM – 12 months
Commercial – 12 months or to the member's renewal date, whichever is longer

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

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.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid, 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
MCL: mantle 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. • 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.	1.3 mg/m^2

VI. Product Availability*

Single-dose vials for injection:

- Sterile lyophilized powder for reconstitution: 1 mg, 2.5 mg, 3.5 mg
- Solution: 3.5 mg/3.5 mL, 3.5 mg/1.4 mL

**The branded product, Velcade, is only available as 3.5 mg sterile lyophilized powder*

VII. References

1. Velcade Prescribing Information. Lexington, MA: Takeda Pharmaceuticals America, Inc.; August 2022. Available at: https://www.takedaoncology.com/medicines/united-states/. Accessed November 21, 2024.
2. Bortezomib Prescribing Information. Lake Forest, IL: Hospira, Inc.; December 2022. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/209191s003lbl.pdf. Accessed November 21, 2024.
3. Bortezomib Prescribing Information. Princeton, NJ: Maia Pharmaceuticals, Inc; July 2022. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/215331s000lbl.pdf Accessed November 21, 2024.
4. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed November 21, 2024.

5. National Comprehensive Cancer Network. Multiple Myeloma Version 1.2025. Available at: https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf. Accessed November 21, 2024.
6. National Comprehensive Cancer Network. Adult T-Cell Lymphomas Version 1.2025. Available at: https://www.nccn.org/professionals/physician_gls/pdf/t-cell.pdf. Accessed November 21, 2024.
7. National Comprehensive Cancer Network. Pediatric Acute Lymphoblastic Leukemia Version 1.2025. Available at: https://www.nccn.org/professionals/physician_gls/pdf/ped_all.pdf. Accessed November 21, 2024.
8. National Comprehensive Cancer Network. Acute Lymphoblastic Leukemia Version 2.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/all.pdf. Accessed November 21, 2024.
9. National Comprehensive Cancer Network. B-Cell Lymphomas Version 3.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf. Accessed November 21, 2024.

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	P&T Approval Date
1Q 2021 annual review: AIDS-related Kaposi sarcoma pediatric HL NCCN recommended uses added; references to HIM.PHAR.21 revised to HIM.PA.154; references reviewed and updated.	11.10.20	02.21
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.	11.14.21	02.22
RT4: added new 1 mg and 2.5 mg strengths of bortezomib (available generically only from Hospira); added redirection to generic bortezomib for brand Velcade requests.	05.27.22	
RT4: added new 2.5 and 3.5 mg formulations (available generically only) as solution for a single-dose injection.	08.17.22	

Reviews, Revisions, and Approvals	Date	P&T Approval Date
1Q 2023 annual review: no significant changes; references reviewed and updated. Template changes applied to other diagnoses/indications and continued therapy section. Updated HCPCS codes [J9046, J9048, J9049].	11.11.22	02.23
Added HCPCS code [J9051], removed inactive HCPCS code [J9044].	10.27.23	
1Q 2024 annual review: removed specification that 1 mg and 2.5 mg were speicially 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; references reviewed and updated.	11.20.23	02.24
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; updated "AIDS-related Kaposi Sarcoma" to "Kaposi Sarcoma" per NCCN compendium; references reviewed and updated.	10.21.24	02.25

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.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

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.