# Clinical Policy: Bortezomib (Velcade)

Reference Number: ERX.SPA.310
Effective Date: 03.01.19
Last Review Date: 02.22
Line of Business: Commercial, Medicaid

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)*

**The 1 mg and 2.5 mg strengths are indicated specifically for patients who have received at least 1 prior therapy.*

**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.*

*Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.*

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Velcade 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: 6 months**

**B. NCCN Recommended Uses (off-label)** (must meet all)**:**
1. Diagnosis of one of the following (a-h):
   a. AIDS-related Kaposi sarcoma (advanced cutaneous, oral, visceral, or nodal disease) - after ≥ 2 prior lines of systemic therapy;
   b. Multicentric Castleman's disease (B-cell lymphoma subtype) - as subsequent therapy;
   c. Systemic light chain amyloidosis;
   d. Adult T-cell leukemia/lymphoma - as subsequent therapy;
   e. Waldenström macroglobulinemia/lymphoplasmacytic lymphoma;
   f. T-cell acute lymphoblastic leukemia (T-ALL) – for relapsed or refractory disease;
   g. Pediatric acute lymphoblastic leukemia (ALL) - as subsequent therapy;

h. 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: 6 months**

**C. Other diagnoses/indications**

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

**II. Continued Therapy**

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

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions, 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: 12 months**

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

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   **Approval duration: Duration of request or 6 months (whichever is less)**; or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

**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 – ERX.PA.01 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.<br>• 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.<br>**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.<br>• 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-use vials: 1 mg, 2.5 mg, and 3.5 mg of bortezomib as sterile lyophilized white to off-white powder for reconstitution

## VII. References

1. Velcade Prescribing Information. Cambridge, MA: Millennium Pharmaceuticals, Inc.; November 2021. Available at: https://www.velcade.com/files/pdfs/VELCADE_PRESCRIBING_INFORMATION.pdf Accessed May 27, 2022.
2. Bortezomib Prescribing Information. Lake Forest, IL: Hospira, Inc.; May 2022. Available at https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/209191s000lbl.pdf. Accessed May 27, 2022.
3. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed May 27, 2022.
4. National Comprehensive Cancer Network. T-Cell Lymphomas Version 1.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/t-cell.pdf. Accessed November 14, 2021.
5. National Comprehensive Cancer Network. Pediatric Acute Lymphoblastic Leukemia Version 1.2022. Available at: https://www.nccn.org/professionals/physician_gls/pdf/ped_all.pdf. Accessed November 14, 2021.
6. National Comprehensive Cancer Network. Acute Lymphoblastic Leukemia Version 2.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/all.pdf. Accessed November 14, 2021.

| Reviews, Revisions, and Approvals | Date | P&T Approval Date |
|---|---|---|
| Policy created. | 12.11.18 | 02.19 |
| 1Q 2020 annual review: no significant changes; references reviewed and updated. | 11.19.19 | 02.20 |
| 1Q 2021 annual review: AIDS-related Kaposi sarcoma pediatric HL NCCN recommended uses added; references reviewed and updated. | 11.10.20 | 02.21 |

| Reviews, Revisions, and Approvals | Date | P&T Approval Date |
|---|---|---|
| 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 strength of bortezomib (available generically only from Hospira); added redirection to generic bortezomib for brand Velcade requests. | 05.27.22 | |

**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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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.