

| CLINICAL MEDICATION POLICY | |
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| Policy Name: | Velcade® (bortezomib) |
| Policy Number: | MP-047-MD-DE |
| Responsible Department(s): | Medical Management; Clinical Pharmacy |
| Provider Notice Date: | 01/15/2018 |
| Issue Date: | 02/15/2018 |
| Effective Date: | 02/15/2018 |
| Annual Approval Date: | 12/15/2018 |
| Revision Date: | N/A |
| Products: | Highmark Health Options Medicaid |
| Application: | All participating hospitals and providers |
| Page Number(s): | 1 of 7 |

DISCLAIMER

Highmark Health Options medical policy is intended to serve only as a general reference resource regarding coverage for the services described. This policy does not constitute medical advice and is not intended to govern or otherwise influence medical decisions.

POLICY STATEMENT

Highmark Health Options may provide coverage under the medical-surgical benefits of the Company's Medicaid products for medically necessary intravenous infusions or subcutaneous administrations of VELCADE (bortezomib).

This policy is designed to address medical necessity guidelines that are appropriate for the majority of individuals with a particular disease, illness or condition. Each person's unique clinical circumstances warrant individual consideration, based upon review of applicable medical records.

The qualifications of the policy will meet the standards of the National Committee for Quality Assurance (NCQA) and the Delaware Department of Health and Social Services (DHSS) and all applicable state and federal regulations.

DEFINITIONS

VELCADE (bortezomib) – A targeted chemotherapy drug in a class of medicines called proteasome inhibitors that perform activities that block or slow down the actions of proteasomes, to delay tumor growth and influence tumor cell death.

Multiple Myeloma (MM) – A cancer that forms in a type of white blood cell (plasma cell) in the bone marrow. Plasma cells help fight infections by making antibodies that recognize and attack germs. In patients with myeloma, the plasma cells form abnormal antibodies, which can damage the bone, bone marrow, and other organs.

VMP – A chemotherapy treatment for multiple myeloma. There are three drugs used within this treatment, including: bortezomib, melphalan, and prednisone.

VMPT-VT (bortezomib, melphalan, prednisone, thalidomide; bortezomib, thalidomide).

Mantle Cell Lymphoma (MCL) – A cancer that forms in the lymph nodes. The cancer cells arise from the outer rim or “mantle” of lymphoid cells that surrounds a lymphoid follicle.

VcR-CAP (bortezomib, rituximab, cyclophosphamide, doxorubicin, and oral prednisone) – the chemotherapy regimen used for mantle cell lymphoma.

PROCEDURES

1. Velcade (bortezomib) is considered medically necessary as an intravenous infusion or subcutaneous injection when the member meets the following criteria:
 - A. Multiple myeloma
 - 1) The member is aged 18 years or older; AND
 - 2) The prescribing physician must be a hematologist or oncologist; AND
 - 3) Member received a prophylaxis for herpes zoster with acyclovir (notated in chart documentation); AND
 - 4) The member’s platelets and ANC lab values should be monitored before the start of treatment and at the beginning of each cycle; AND
 - 5) The dose should not exceed 1.3 mg/m² for a maximum of 54 weeks; OR
 - 6) The drug will be used as part of a VMPT-VT regimen in previously untreated member; AND
 - a) The dose should not exceed 1.3 mg/m² for a maximum of four weeks during the induction phase; AND
 - b) The dose should not exceed 1.3 mg/m² for a maximum of two years during the VT maintenance phase; OR
 - 7) The drug will be used in combination with dexamethasone with or without doxorubicin, thalidomide, lenalidomide, or cyclophosphamide as a primary therapy in transplant-eligible or ineligible members; AND
 - 8) The dose should not exceed 1.3 mg/m²; OR
 - 9) The drug will be used as second-line therapy after disease progression on induction therapy; AND

- 10) The dose should not exceed 1.3 mg/m²;
- 11) May restart at last tolerated dose twice weekly every three weeks for a maximum of eight cycles if relapsed at least six months after previous bortezomib therapy; AND
- 12) May administer alone or with dexamethasone;
OR
- 13) The drug will be used as subsequent therapy in combination with panobinostat and dexamethasone when the member received at least two previous lines of therapy;
AND
- 14) Previous therapy included an immunomodulator and bortezomib

B. Mantle cell lymphoma

- 1) The member is aged 18 years or older; AND
- 2) The prescribing physician must be a hematologist or oncologist; AND
- 3) Member received a prophylaxis for herpes zoster with acyclovir (notated in chart documentation); AND
- 4) Platelets, ANC, hemoglobin should be monitored at the beginning of each cycle; AND
- 5) The drug will be used as part of a VcR-CAP regimen in previously untreated members;
AND
- 6) The dose should not exceed 1.3 mg/m² for a total of 18 weeks;
OR
- 7) The drug will be used as second-line therapy after disease progression on induction therapy; AND
- 8) The dose should not exceed 1.3 mg/m²

2. Contraindications

Velcade is contraindicated in patients with hypersensitivity to bortezomib, boron, or mannitol, including anaphylactic reactions.

Velcade is contraindicated for intrathecal administration.

3. When the Velcade services are not covered

Velcade is not covered for conditions other than those listed above because scientific evidence has not been established. Therefore, services will be considered not medically necessary.

Coverage may be provided for any non-FDA labeled indication or a medically accepted indication that is supported by nationally recognized pharmacy compendia or peer-reviewed medical literature for treatment of the diagnosis for which it is prescribed and will be reviewed on a case-by-case basis to determine medical necessity.

When criteria are not met, the request will be forwarded to a Medical Director for review. The physician reviewer must override criteria when, in their professional judgment, the requested medication is medically necessary.

4. Post-payment Audit Statement

The medical record must include documentation that reflects the medical necessity criteria and is subject to audit by Highmark Health Options at any time pursuant to the terms of your provider agreement.

5. Place of Service

The place of service for the administration of Velcade is outpatient.

GOVERNING BODIES APPROVAL

On May 14, 2003, the FDA approved VELCADE® for the treatment of refractory or relapsed multiple myeloma. VELCADE® is the first drug in a new class of anticancer agents known as proteasome inhibitors to be approved.

In 2005, VELCADE® was approved for the treatment of patients with multiple myeloma who had received at least one prior therapy.

On December 8, 2006, the FDA approved VELCADE® for the treatment of patients with mantle cell lymphoma who have received at least one prior therapy.

On June 20, 2008, the FDA approved VELCADE® for the treatment of patients with untreated multiple myeloma.

On October 10, 2014, the FDA approved VELCADE® for use in previously untreated patients with mantle cell lymphoma. VELCADE® is the first treatment in the United States to be approved for use in previously untreated patients with mantle cell lymphoma.

CODING REQUIREMENTS

Covered Procedure Codes

| HCPCS Code | Description |
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| J9041 | Injection, bortezomib, 0.1 mg |

Covered Diagnosis Codes

| ICD-10 Codes | Description |
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| C82.00 | Follicular lymphoma grade I, unspecified site |
| C82.01 | Follicular lymphoma grade I, lymph nodes of head, face, and neck |
| C82.02 | Follicular lymphoma grade I, intrathoracic lymph nodes |
| C82.03 | Follicular lymphoma grade I, intra-abdominal lymph nodes |
| C82.04 | Follicular lymphoma grade I, lymph nodes of axilla and upper limb |
| C82.05 | Follicular lymphoma grade I, lymph nodes of inguinal region and lower limb |
| C82.06 | Follicular lymphoma grade I, intrapelvic lymph nodes |
| C82.07 | Follicular lymphoma grade I, spleen |
| C82.08 | Follicular lymphoma grade I, lymph nodes of multiple sites |
| C82.09 | Follicular lymphoma grade I, extranodal and solid organ sites |
| C82.10 | Follicular lymphoma grade II, unspecified site |
| C82.11 | Follicular lymphoma grade II, lymph nodes of head, face, and neck |
| C82.12 | Follicular lymphoma grade II, intrathoracic lymph nodes |
| C82.13 | Follicular lymphoma grade II, intra-abdominal lymph nodes |
| C82.14 | Follicular lymphoma grade II, lymph nodes of axilla and upper limb |

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| C82.15 | Follicular lymphoma grade II, lymph nodes of inguinal region and lower limb |
| C82.16 | Follicular lymphoma grade II, intrapelvic lymph nodes |
| C82.17 | Follicular lymphoma grade II, spleen |
| C82.18 | Follicular lymphoma grade II, lymph nodes of multiple sites |
| C82.19 | Follicular lymphoma grade II, extranodal and solid organ sites |
| C82.20 | Follicular lymphoma grade III, unspecified site |
| C82.21 | Follicular lymphoma grade III, lymph nodes of head, face, and neck |
| C82.22 | Follicular lymphoma grade III, intrathoracic lymph nodes |
| C82.23 | Follicular lymphoma grade III, intra-abdominal lymph nodes |
| C82.24 | Follicular lymphoma grade III, lymph nodes of axilla and upper limb |
| C82.25 | Follicular lymphoma grade III, lymph nodes of inguinal region and lower limb |
| C82.26 | Follicular lymphoma grade III, intrapelvic lymph nodes |
| C82.27 | Follicular lymphoma grade III, spleen |
| C82.28 | Follicular lymphoma grade III, lymph nodes of multiple sites |
| C82.29 | Follicular lymphoma grade III, extranodal and solid organ sites |
| C82.30 | Follicular lymphoma grade IIIa, unspecified site |
| C82.31 | Follicular lymphoma grade IIIa, lymph nodes of head, face, and neck |
| C82.32 | Follicular lymphoma grade IIIa, intrathoracic lymph nodes |
| C82.33 | Follicular lymphoma grade IIIa, intra-abdominal lymph nodes |
| C82.34 | Follicular lymphoma grade IIIa, lymph nodes of axilla and upper limb |
| C82.35 | Follicular lymphoma grade IIIa, lymph nodes of inguinal region and lower limb |
| C82.36 | Follicular lymphoma grade IIIa, intrapelvic lymph nodes |
| C82.37 | Follicular lymphoma grade IIIa, spleen |
| C82.38 | Follicular lymphoma grade IIIa, lymph nodes of multiple sites |
| C82.39 | Follicular lymphoma grade IIIa, extranodal and solid organ sites |
| C82.40 | Follicular lymphoma grade IIIb, unspecified site |
| C82.41 | Follicular lymphoma grade IIIb, lymph nodes of head, face, and neck |
| C82.42 | Follicular lymphoma grade IIIb, intrathoracic lymph nodes |
| C82.43 | Follicular lymphoma grade IIIb, intra-abdominal lymph nodes |
| C82.44 | Follicular lymphoma grade IIIb, lymph nodes of axilla and upper limb |
| C82.45 | Follicular lymphoma grade IIIb, lymph nodes of inguinal region and lower limb |
| C82.46 | Follicular lymphoma grade IIIb, intrapelvic lymph nodes |
| C82.47 | Follicular lymphoma grade IIIb, spleen |
| C82.48 | Follicular lymphoma grade IIIb, lymph nodes of multiple sites |
| C82.49 | Follicular lymphoma grade IIIb, extranodal and solid organ sites |
| C82.50 | Diffuse follicle center lymphoma, unspecified site |
| C82.51 | Diffuse follicle center lymphoma, lymph nodes of head, face, and neck |
| C82.52 | Diffuse follicle center lymphoma, intrathoracic lymph nodes |
| C82.53 | Diffuse follicle center lymphoma, intra-abdominal lymph nodes |
| C82.54 | Diffuse follicle center lymphoma, lymph nodes of axilla and upper limb |
| C82.55 | Diffuse follicle center lymphoma, lymph nodes of inguinal region and lower limb |
| C82.56 | Diffuse follicle center lymphoma, intrapelvic lymph nodes |
| C82.57 | Diffuse follicle center lymphoma, spleen |

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| C82.58 | Diffuse follicle center lymphoma, lymph nodes of multiple sites |
| C82.59 | Diffuse follicle center lymphoma, extranodal and solid organ sites |
| C82.80 | Other types of follicular lymphoma, unspecified site |
| C82.81 | Other types of follicular lymphoma, lymph nodes of head, face, and neck |
| C82.82 | Other types of follicular lymphoma, intrathoracic lymph nodes |
| C82.83 | Other types of follicular lymphoma, intra-abdominal lymph nodes |
| C82.84 | Other types of follicular lymphoma, lymph nodes of axilla and upper limb |
| C82.85 | Other types of follicular lymphoma, lymph nodes of inguinal region and lower limb |
| C82.86 | Other types of follicular lymphoma, intrapelvic lymph nodes |
| C82.87 | Other types of follicular lymphoma, spleen |
| C82.88 | Other types of follicular lymphoma, lymph nodes of multiple sites |
| C82.89 | Other types of follicular lymphoma, extranodal and solid organ sites |
| C82.90 | Follicular lymphoma, unspecified site |
| C82.91 | Follicular lymphoma, unspecified, lymph nodes of head, face, and neck |
| C82.92 | Follicular lymphoma, unspecified, intrathoracic lymph nodes |
| C82.93 | Follicular lymphoma, unspecified, intra-abdominal lymph nodes |
| C82.94 | Follicular lymphoma, unspecified, lymph nodes of axilla and upper limb |
| C82.95 | Follicular lymphoma, unspecified, lymph nodes of inguinal region and lower limb |
| C82.96 | Follicular lymphoma, unspecified, intrapelvic lymph nodes |
| C82.97 | Follicular lymphoma, unspecified, spleen |
| C82.98 | Follicular lymphoma, unspecified, lymph nodes of multiple sites |
| C82.99 | Follicular lymphoma, unspecified, extranodal and solid organ sites |
| C83.10 | Mantle cell lymphoma, unspecified site |
| C83.11 | Mantle cell lymphoma, lymph nodes of head, face, and neck |
| C83.12 | Mantle cell lymphoma, intrathoracic lymph nodes |
| C83.13 | Mantle cell lymphoma, intra-abdominal lymph nodes |
| C83.14 | Mantle cell lymphoma, lymph nodes of axilla and upper limb |
| C83.15 | Mantle cell lymphoma, lymph nodes of inguinal region and lower limb |
| C83.16 | Mantle cell lymphoma, intrapelvic lymph nodes |
| C83.17 | Mantle cell lymphoma, spleen |
| C83.18 | Mantle cell lymphoma, lymph nodes of multiple sites |
| C83.19 | Mantle cell lymphoma, extranodal and solid organ sites |
| C90.00 | Multiple myeloma not having achieved remission |
| C90.01 | Multiple myeloma in remission |
| C90.02 | Multiple myeloma in relapse |

REIMBURSEMENT

Participating facilities will be reimbursed per their Highmark Health Options contract.

POLICY SOURCE(S)

VELCADE® (bortezomib) [package insert]. Cambridge, MA: Millennium Pharms; 09/2015. Accessed on 01/05/2017 and retrieved from: <http://www.velcade.com/>.

Bortezomib. In: Micromedex 2.0 online. Ann Arbor (MI): Truven Health Analytics; [2016; accessed 12/14/16].

Richardson P, Sonneveld P, Schuster M, et al. Bortezomib or high-dose dexamethasone for relapsed multiple myeloma. N Engl J Med. 2005; 352: 2487-2498 Accessed on 01/05/2017 and retrieved from: <http://www.ncbi.nlm.nih.gov/pubmed/15958804>.

National Comprehensive Cancer Network® NCCN Clinical Practice Guidelines in Oncology™. Accessed on 12/28/2016 and available at: <http://www.nccn.org/index.asp>.

- NCCN Guidelines Version 3.2017: Multiple Myeloma
- NCCN Guidelines Version 1.2017: B-cell Lymphomas

Understanding FARYDK® (panobinostat) capsules. North Hollywood, CA: International Myeloma Foundation; 2016. Accessed on 01/05/2017 and retrieved from <https://www.myeloma.org/sites/default/files/images/publications/UnderstandingPDF/u-farydak.pdf>.

Policy History

| Date | Activity |
|-------------|--------------------------|
| 03/20/2017 | Initial policy developed |
| 12/12/2017 | QI/UM Committee approval |
| 02/15/2018 | Provider effective date |