Velcade® (bortezomib)
(Intravenous/Subcutaneous)

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I. Length of Authorization

Coverage will be provided for 6 months and may be renewed. For use as maintenance therapy in multiple myeloma, coverage may be renewed up to 2 years of total therapy.

II. Dosing Limits

A. Quantity Limit (max daily dose) [Pharmacy Benefit]:

– Velcade 3.5 mg powder for injection: 4 vials per 14 day supply

B. Max Units (per dose and over time) [Medical Benefit]:

- Multiple Myeloma – Maintenance Therapy Only
  - 140 billable units every 14 days
- All Other Indications
  - 140 billable units every 21 days

III. Initial Approval Criteria

Coverage is provided in the following conditions:

- Patient aged 18 years or older; AND

Multiple myeloma †

- Used as primary therapy for active (symptomatic) disease or for relapse after 6 months following primary induction therapy; OR
- Used as maintenance therapy as a single agent; OR
- Used as therapy for relapse or progressive disease

Mantle cell lymphoma †

- Used as initial therapy in transplant ineligible patients as a component of VR-CAP (bortezomib, rituximab, cyclophosphamide, doxorubicin, and prednisone); OR
- Used as second-line therapy for extended response to prior chemoimmunotherapy as a single agent or in combination with rituximab

Systemic Light Chain Amyloidosis ‡

- Patient is newly diagnosed; AND
    - Used in combination with cyclophosphamide and dexamethasone; OR
    - Used as a single agent; OR
    - Used in combination with dexamethasone with or without melphalan; OR
- Patient has relapsed or refractory disease§; AND
    - Used as a single agent; OR
    - Used in combination with dexamethasone with or without melphalan

§Consider repeating initial therapy if relapse-free for several years

Waldenström's macroglobulinemia/Lymphoplasmacytic Lymphoma ‡

- Used in combination with dexamethasone and rituximab; OR
- Used as a single agent or in combination with rituximab; OR
- Used in combination with dexamethasone

Multicentric Castleman's Disease ‡

- Must be used as subsequent therapy; AND
- Patient has progressed following treatment for relapsed/refractory or progressive disease; AND
- Used as a single agent or in combination with rituximab

Adult T-Cell Leukemia/Lymphoma ‡

- Must be used as a single agent for non-responders to first-line therapy for acute disease or lymphoma

† FDA Approved Indication(s); ‡ Compendia recommended indication(s)

IV. Renewal Criteria

Coverage can be renewed based upon the following criteria:

- Patient continues to meet the criteria identified in section III; AND
- Tumor response with stabilization of disease or decrease in size of tumor or tumor spread; AND

- Absence of unacceptable toxicity from the drug. Example of unacceptable toxicity include: peripheral neuropathy, hypotension, cardiac toxicity, pulmonary toxicity, posterior reversible encephalopathy syndrome, gastrointestinal toxicity, thrombocytopenia, neutropenia, tumor lysis syndrome, hepatic toxicity, etc.
- For maintenance therapy of multiple myeloma: patient has not received over 2 years of therapy.

V. Dosage/Administration

Indication	Dose
Multiple myeloma - previously untreated	1.3 mg/m² IV/SC in combination with oral melphalan and oral prednisone for nine 6-week treatment cycles. In cycles 1-4, Velcade is given twice weekly (days 1, 4, 8, 11, 22, 25, 29, and 32). In cycles 5-9, Velcade is given once weekly (days 1, 8, 22, and 29).
Multiple myeloma – maintenance therapy	1.3 mg/m² IV/SC every two weeks for up to 2 years
Mantle Cell Lymphoma – previously untreated	1.3 mg/m² IV/SC in combination with rituximab, cyclophosphamide, doxorubicin, and oral prednisone for six 3-week cycles. Velcade is given twice weekly for two weeks (Days 1, 4, 8, and 11) followed by a 10-day rest period on Days 12-21. For patients with a response first documented at cycle 6, two additional cycles are recommended.
Multiple myeloma & Mantle Cell Lymphoma- relapsed	1.3 mg/m² IV/SC twice weekly x 4 doses (days 1, 4, 8, and 11) followed by a 10-day rest period (days 12-21). • For extended therapy of more than 8 cycles, bortezomib may be administered on the standard schedule or, for relapsed multiple myeloma, on a maintenance schedule of once weekly for 4 weeks (days 1, 8, 15, and 22), followed by a 13-day rest period (days 23 to 35)
Waldenström's macroglobulinemia	• 1.3 mg/m² IV/SC twice weekly for 2 weeks (days 1, 4, 8, and 11) in a 21 day cycle • In combination with rituximab alone: 1.6mg/m² days 1, 8, and 15 of a 28 day cycle
All Other Indications	1.3 mg/m² IV/SC twice weekly (days 1, 4, 8, and 11) for 2 weeks of a 21 day cycle

VI. Billing Code/Availability Information

Jcode:

- J9041– Injection, bortezomib (velcade), 0.1 mg; 1 billable unit = 0.1 mg

NDC(s):

- Velcade 3.5 mg single-use vial powder for injection: 63020-0049-xx

VII. References

1. Velcade [package insert]. Cambridge, MA; Millennium Pharmaceuticals, Inc; June 2017. Accessed January 2019.

2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for Bortezomib. National Comprehensive Cancer Network, 2019. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed January 2019.
3. Boccadoro M, Bringhen S, Gaidano G, et al, "Bortezomib, Melphalan, Prednisone, and Thalidomide (VMPT) Followed by Maintenance With Bortezomib and Thalidomide (VT) for Initial Treatment of Elderly Multiple Myeloma Patients," J Clin Oncol, 2010, 28(7s):8013 [abstract 8013 from 2010 ASCO Annual Meeting].
4. Palumbo A, Bringhen S, Rossi D, et al, "Bortezomib, Melphalan, Prednisone and Thalidomide (VMPT) Followed by Maintenance With Bortezomib and Thalidomide for Initial Treatment of Elderly Multiple Myeloma Patients," Blood, 2009, 114(22):128 [abstract 128 from ASH 2009 Annual Meeting].
5. Ghobrial IM, Hong F, Padmanabhan S, et al, "Phase II Trial of Weekly Bortezomib in Combination With Rituximab in Relapsed or Relapsed and Refractory Waldenstrom Macroglobulinemia," J Clin Oncol, 2010, 28(8):1422-8.
6. Sonneveld P, Schmidt-Wolf IG, van der Holt B, et al. Bortezomib induction and maintenance treatment in patients with newly diagnosed multiple myeloma: results of the randomized phase III HOVON-65/ GMMG-HD4 trial. J Clin Oncol. 2012 Aug 20;30(24):2946-55. doi: 10.1200/JCO.2011.39.6820. Epub 2012 Jul 16.
7. Zinzani PL, Musuraca G, Tani M, et al. Phase II trial of proteasome inhibitor bortezomib in patients with relapsed or refractory cutaneous T-cell lymphoma. J Clin Oncol 2007;25:4293-4297.
8. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) T-Cell Lymphomas. Version 2.2019. National Comprehensive Cancer Network, 2019. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed January 2019.
9. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Systemic Light Chain Amyloidosis. Version 1.2019. National Comprehensive Cancer Network, 2019. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed January 2019.
10. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Waldenström's Macroglobulinemia/Lymphoplasmacytic Lymphoma. Version

2.2019. National Comprehensive Cancer Network, 2019. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed January 2019.

11. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) B-Cell Lymphomas. Version 1.2019. National Comprehensive Cancer Network, 2019. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed January 2019.
12. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Multiple Myeloma. Version 2.2019. National Comprehensive Cancer Network, 2019. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed January 2019.
13. First Coast Service Options, Inc. Local Coverage Determination (LCD): Bortezomib (Velcade®) (L33273) Centers for Medicare & Medicare Services, Inc. Updated on 12/19/2018 with effective date of 1/1/2019. Accessed January 2019.
14. National Government Services, Inc. Local Coverage Article for Bortezomib – Related to LCD L33394 (A52371). Centers for Medicare & Medicaid Services, Inc. Updated on 01/04/2019 with effective date of 1/1/2019. Accessed January 2019.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C83.00	Small cell B-cell lymphoma, unspecified site
C83.01	Small cell B-cell lymphoma, lymph nodes of head, face and neck
C83.02	Small cell B-cell lymphoma, intrathoracic lymph nodes
C83.03	small cell B-cell lymphoma, intra-abdominal lymph nodes
C83.04	Small cell B-cell lymphoma, lymph nodes of axilla and upper limb
C83.05	Small cell B-cell lymphoma, lymph nodes of inguinal region and lower limb
C83.06	Small cell B-cell lymphoma, intrapelvic lymph nodes
C83.07	Small cell B-cell lymphoma, spleen
C83.08	Small cell B-cell lymphoma, lymph nodes of multiple sites
C83.09	Small cell B-cell lymphoma, extranodal and solid organ sites
C83.10	Mantle cell lymphoma, unspecified site

ICD-10	ICD-10 Description
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
C88.0	Waldenstrom macroglobulinemia
C90.00	Multiple myeloma not having achieved remission
C90.01	Multiple myeloma in remission
C90.02	Multiple myeloma, in relapse
C90.10	Plasma cell leukemia not having achieved remission
C90.11	Plasma cell leukemia in remission
C90.12	Plasma cell leukemia in relapse
C90.20	Extramedullary plasmacytoma not having achieved remission
C90.21	Extramedullary plasmacytoma in remission
C90.22	Extramedullary plasmacytoma in relapse
C90.30	Solitary plasmacytoma not having achieved remission
C90.31	Solitary plasmacytoma in remission
C90.32	Solitary plasmacytoma in relapse
C91.50	Adult T-cell lymphoma/leukemia (HTLV-1-associated) not having achieved remission
C91.52	Adult T-cell lymphoma/leukemia (HTLV-1-associated), in relapse
D36.0	Benign neoplasm of lymph nodes
D47.Z2	Castleman disease
E85.81	Light chain (AL) amyloidosis
E85.89	Other amyloidosis
E85.9	Amyloidosis, unspecified
R59.0	Localized enlarged lymph nodes
R59.1	Generalized enlarged lymph nodes
R59.9	Enlarged lymph nodes, unspecified
Z85.72	Personal history of non-Hodgkin lymphomas
Z85.79	Personal history of other malignant neoplasms of lymphoid, hematopoietic and related tissues

Dual coding requirements:

- Codes Z85.72 & Z85.79 are secondary codes and must be billed in conjunction with a primary code

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD) and Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. They can be found at: http://www.cms.gov/medicare-coverage-database/search/advanced-search.aspx. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD):

Jurisdiction(s): N	NCD/LCD Document (s): L33273
https://www.cms.gov/medicare-coverage-database/search/lcd-date-search.aspx?DocID=L33273&bc=gAAAAAAAAAAAAA==	

Jurisdiction(s): 6, K	NCD/LCD Document (s): A52371
https://www.cms.gov/medicare-coverage-database/search/article-date-search.aspx?DocID=A52371&bc=gAAAAAAAAAAAAA==	

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC