

Velcade® (bortezomib) (Intravenous/Subcutaneous)

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I. Length of Authorization ^{1,5,6,8,14,25,26,30,35-41}

Coverage will be provided for 6 months and may be renewed unless otherwise specified.

- Initial treatment for Multiple Myeloma: Coverage will be provided for a total of 9 cycles (42-days per cycle).
- Maintenance therapy in Multiple Myeloma for transplant-ineligible patients: Coverage will be provided for a total of 5 cycles (35-days per cycle).
- Maintenance therapy in Multiple Myeloma post-autologous stem cell transplant: Coverage may be renewed up to 2 years of total therapy.
- Re-treatment of Multiple Myeloma, initial treatment of Mantle Cell Lymphoma, & Adult T-Cell Leukemia/Lymphoma: Coverage will be provided for a total of 8 cycles (21-days per cycle).
- Systemic Light Chain Amyloidosis as a single agent or in combination with cyclophosphamide and/or dexamethasone: Coverage will be provided for a total of 8 cycles (35-days per cycle as a single agent; 21- or 28-days per cycle in combination with cyclophosphamide and/or dexamethasone).
- Systemic Light Chain Amyloidosis in combination with melphalan and dexamethasone: Coverage will be provided for a total of 9 cycles (21-days per cycle)
- Waldenström's Macroglobulinemia in combination with rituximab and/or dexamethasone: Coverage will be provided for a total of 6 cycles (28-days per cycle) or 8 cycles (21-days per cycle).

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- Velcade 3.5 mg powder for injection: 8 vials per 28 day supply

B. Max Units (per dose and over time) [HCPCS Unit]:

- **Multiple Myeloma (maintenance therapy for transplant ineligible patients) & Systemic Light Chain Amyloidosis:**
 - 280 billable units every 35 days
- **AIDS-Related Kaposi Sarcoma & Waldenström’s Macroglobulinemia:**
 - 280 billable units every 28 days
- **Multiple Myeloma (initial treatment):**
 - 140 billable units every 42 days
- **All Other Indications:**
 - 140 billable units every 21 days

III. Initial Approval Criteria ^{1,2}

Coverage is provided in the following conditions:

- Patient aged 18 years or older (unless otherwise specified); **AND**

Universal Criteria

- Will not be administered intrathecally; **AND**

Multiple Myeloma † ⊕ ^{1-4,6,13,15-20,24-26}

- Used in combination with a corticosteroid containing regimen as primary therapy for symptomatic disease or for relapse (re-treatment) after 6 months following primary induction therapy with the same regimen; **OR**
- Used as maintenance therapy as a single agent or in combination with lenalidomide; **AND**
 - Patient responded to primary myeloma therapy; **OR**
 - Patient responded or had stable disease following autologous stem cell transplant (*in combination with lenalidomide only*); **AND**
 - Patient has not received in excess of 2 years of maintenance therapy with a bortezomib product; **OR**
- Used as therapy for relapse or progressive disease in combination with a dexamethasone containing regimen

Mantle Cell Lymphoma † ⊕ ^{1,2,12,21-23,27}

- Used as initial therapy or after initial treatment with involved site radiation therapy alone as a component of VR-CAP (bortezomib, rituximab, cyclophosphamide, doxorubicin, and prednisone) in patients who are not candidates for high-dose therapy/autologous stem cell rescue; **OR**
- Used in patients who have received at least one prior therapy as a single agent; **OR**
- Used as second-line therapy in combination with rituximab; **AND**
 - Patient had a very good partial response to induction therapy; **OR**
 - Patient had stable disease or partial response with substantial disease after induction therapy (*excludes use as a component of VR-CAP*); **OR**
 - Patient has relapsed or progressive disease following an extended response to prior chemoimmunotherapy (*excludes use as a component of VR-CAP*)

Systemic Light Chain Amyloidosis ‡^{2,10}

- Patient has newly diagnosed OR relapsed/refractory disease; **AND**
 - Used in combination with cyclophosphamide and dexamethasone; **OR**
 - 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 ‡^{2,5,11,14,29}

- 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 ‡^{2,12}

- 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 ‡^{2,7,9}

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

Pediatric Acute Lymphoblastic Leukemia ‡^{2,8,28}

- Patient is at least 1 year of age or older: **AND**
 - Patient has relapsed or refractory Philadelphia (Ph) chromosome negative B-cell disease (B-ALL); **OR**
 - Patient has relapsed or refractory Philadelphia (Ph) chromosome positive B-cell disease (B-ALL); **AND**
 - Used in combination with dasatinib or imatinib as a component of the COG AALL07P1 regimen (bortezomib, vincristine, doxorubicin, pegaspargase, prednisone); **OR**
 - Patient has relapsed or refractory T-cell disease (T-ALL); **AND**
 - Used in combination with a corticosteroid (e.g., prednisone or dexamethasone), vincristine, doxorubicin, and pegaspargase

AIDS-Related Kaposi Sarcoma ‡^{2,41}

- Must be used as subsequent therapy in combination with antiretroviral therapy (ART); **AND**
- Patient has relapsed/refractory advanced, cutaneous, oral, visceral, or nodal disease; **AND**
- Patient has progressed on or not responded to first-line therapy; **AND**

- Patient has progressed on alternate first-line therapy

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

IV. Renewal Criteria ^{1,2,6}

Coverage can be renewed based upon the following criteria:

- Patient continues to meet universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in section III; **AND**
- Disease response with treatment as defined by 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, thrombotic microangiopathy, etc.

Maintenance therapy of multiple myeloma after autologous stem cell transplant

- Patient has not received over 2 years of therapy.

V. Dosage/Administration ^{1,5,6,8,14,25,26,30,35-41}

Indication	Dose
Multiple Myeloma – previously untreated	1.3 mg/m ² intravenously (IV)/subcutaneously (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	<u>Following primary therapy with a bortezomib-containing regimen for transplant-ineligible patients:</u> 1.6 mg/m ² IV/SC weekly (days 1, 8, 15, and 22) every 35 days for up to 5 cycles. <u>Following autologous stem cell transplant:</u> 1.3 mg/m ² IV/SC every two weeks for up to 2 years
Multiple Myeloma – re-treatment	1.3 mg/m ² IV/SC twice weekly (days 1, 4, 8, and 11) followed by a 10-day rest period (days 12-21) for up to 8 cycles
Mantle Cell Lymphoma – previously untreated	1.3 mg/m ² IV/SC in combination with rituximab, cyclophosphamide, doxorubicin, and oral prednisone for six 3-week treatment cycles. Velcade is given twice weekly (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/m ² IV/SC twice weekly (days 1, 4, 8, and 11) followed by a 10-day rest period (days 12-21). <ul style="list-style-type: none"> • For extended therapy of more than 8 cycles, Velcade 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).
Systemic Light Chain Amyloidosis	<p><u>Single agent:</u> 1.6 mg/m² IV/SC weekly (days 1, 8, 15, and 22) every 35 days for up to 8 cycles</p> <p><u>In combination with cyclophosphamide and/or dexamethasone:</u> 1.3 mg/m² IV/SC twice weekly (days 1, 4, 8, and 11) every 21 or 28 days for up to 8 cycles</p> <p><u>In combination with melphalan and dexamethasone:</u> 1.3mg/m² IV/SC twice weekly (days 1, 4, 8, and 11) every 28 days for up to 9 cycles</p>
Waldenström's macroglobulinemia	<p><u>Single agent:</u></p> <ul style="list-style-type: none"> 1.3 mg/m² IV twice weekly (days 1, 4, 8, and 11) every 21 days, until disease progression or unacceptable toxicity <p><u>In combination with rituximab and/or dexamethasone:</u></p> <ul style="list-style-type: none"> 1.3 mg/m² IV/SC twice weekly (days 1, 4, 8, and 11) every 21 days for 4 continuous cycles, followed by a 12-week rest period, then up to 4 additional cycles given every 12 weeks 1.6 mg/m² IV weekly (days 1, 8, 15, and 22) every 28 days for up to 6 cycles
Adult T-Cell Leukemia/ Lymphoma	1.3 mg/m ² IV/SC twice weekly (days 1, 4, 8, and 11) every 21 days for up to 8 cycles
AIDS-Related Kaposi Sarcoma	1.6 mg/m ² IV weekly (days 1, 8, and 15) every 28 days
All Other Indications	1.3 mg/m ² IV/SC twice weekly (days 1, 4, 8, and 11) for 2 weeks of a 21 day cycle
<p><i>Reconstituted concentration varies by route of administration:</i></p> <ul style="list-style-type: none"> 1 mg/mL intravenously 2.5 mg/mL subcutaneously 	

VI. Billing Code/Availability Information

HCPCS code:

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

NDC:

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

VII. References

- Velcade [package insert]. Cambridge, MA; Millennium Pharmaceuticals, Inc; April 2019. Accessed April 2020.
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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 April 2020.

3. Boccadoro M, Brinthen 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, Brinthen 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. Horton, T. M., Whitlock, J. A., Lu, X. , et al. Bortezomib reinduction chemotherapy in high-risk ALL in first relapse: a report from the Children's Oncology Group. *Br J Haematol* 2019;186:274-285. doi:10.1111/bjh.15919
9. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) T-Cell Lymphomas. Version 1.2020. National Comprehensive Cancer Network, 2020. 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 April 2020.
10. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Systemic Light Chain Amyloidosis. Version 1.2020. National Comprehensive Cancer Network, 2020. 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 April 2020.
11. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Waldenström’s Macroglobulinemia/Lymphoplasmacytic Lymphoma. Version 2.2020. National Comprehensive Cancer Network, 2020. 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 April 2020.
12. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) B-Cell Lymphomas. Version 1.2020. National Comprehensive Cancer Network, 2020. 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 April 2020.
 13. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Multiple Myeloma. Version 3.2020. National Comprehensive Cancer Network, 2020. 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 April 2020.
 14. Treon SP, Ioakimidis L, Soumerai JD, et al. Primary therapy of Waldenström macroglobulinemia with bortezomib, dexamethasone, and rituximab: WMCTG clinical trial 05-180. *J Clin Oncol*. 2009 Aug 10;27(23):3830-5. doi: 10.1200/JCO.2008.20.4677. Epub 2009 Jun 8.
 15. Mateos MV, Oriol A, Martínez-López J, et al. Outcomes with two different schedules of bortezomib, melphalan, and prednisone (VMP) for previously untreated multiple myeloma: matched pair analysis using long-term follow-up data from the phase 3 VISTA and PETHEMA/GEM05 trials. *Ann Hematol*. 2016 Dec;95(12):2033-2041. Epub 2016 Oct 14.
 16. San Miguel JF, Schlag R, Khuageva NK, et al. Persistent overall survival benefit and no increased risk of second malignancies with bortezomib-melphalan-prednisone versus melphalan-prednisone in patients with previously untreated multiple myeloma. *J Clin Oncol*. 2013 Feb 1;31(4):448-55. doi: 10.1200/JCO.2012.41.6180. Epub 2012 Dec 10.
 17. Harousseau JL, Palumbo A, Richardson PG, et al. Superior outcomes associated with complete response in newly diagnosed multiple myeloma patients treated with nonintensive therapy: analysis of the phase 3 VISTA study of bortezomib plus melphalan-prednisone versus melphalan-prednisone. *Blood*. 2010 Nov 11;116(19):3743-50. doi: 10.1182/blood-2010-03-275800. Epub 2010 Jul 13.
 18. San Miguel JF, Schlag R, Khuageva NK, et al. Bortezomib plus melphalan and prednisone for initial treatment of multiple myeloma. *N Engl J Med*. 2008 Aug 28;359(9):906-17. doi: 10.1056/NEJMoa0801479.
 19. Dimopoulos MA, Orłowski RZ, Facon T, et al. Retrospective matched-pairs analysis of bortezomib plus dexamethasone versus bortezomib monotherapy in relapsed multiple myeloma. *Haematologica*. 2015 Jan;100(1):100-6. doi: 10.3324/haematol.2014.112037. Epub 2014 Sep 26.
 20. Moreau P, Pylypenko H, Grosicki S, et al. Subcutaneous versus intravenous administration of bortezomib in patients with relapsed multiple myeloma: a randomised, phase 3, non-inferiority study. *Lancet Oncol*. 2011 May;12(5):431-40. doi: 10.1016/S1470-2045(11)70081-X. Epub 2011 Apr 18.

21. Robak T, Jin J, Pylypenko H, et al. Frontline bortezomib, rituximab, cyclophosphamide, doxorubicin, and prednisone (VR-CAP) versus rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP) in transplantation-ineligible patients with newly diagnosed mantle cell lymphoma: final overall survival results of a randomised, open-label, phase 3 study. *Lancet Oncol.* 2018 Nov;19(11):1449-1458. doi: 10.1016/S1470-2045(18)30685-5. Epub 2018 Oct 19.
22. Verhoef G, Robak T, Huang H, et al. Association between quality of response and outcomes in patients with newly diagnosed mantle cell lymphoma receiving VR-CAP versus R-CHOP in the phase 3 LYM-3002 study. *Haematologica.* 2017 May;102(5):895-902. doi: 10.3324/haematol.2016.152496. Epub 2017 Feb 9.
23. Robak T, Huang H, Jin J, et al. Bortezomib-based therapy for newly diagnosed mantle-cell lymphoma. *N Engl J Med.* 2015 Mar 5;372(10):944-53. doi: 10.1056/NEJMoa1412096.
24. Jagannath S, Barlogie B, Berenson J, et al. A phase 2 study of two doses of bortezomib in relapsed or refractory myeloma. *Br J Haematol.* 2004 Oct;127(2):165-72.
25. Richardson PG, Barlogie B, Berenson J, et al. A phase 2 study of bortezomib in relapsed, refractory myeloma. *N Engl J Med.* 2003 Jun 26;348(26):2609-17.
26. Petrucci MT, Giraldo P, Corradini P, et al. A prospective, international phase 2 study of bortezomib retreatment in patients with relapsed multiple myeloma. *J Haematol.* 2013 Mar;160(5):649-59. doi: 10.1111/bjh.12198. Epub 2013 Jan 7.
27. Fisher RI, Bernstein SH, Kahl BS, et al. Multicenter phase II study of bortezomib in patients with relapsed or refractory mantle cell lymphoma. *J Clin Oncol.* 2006 Oct 20;24(30):4867-74. Epub 2006 Sep 25.
28. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Pediatric Acute Lymphoblastic Leukemia. Version 2.2020. National Comprehensive Cancer Network, 2020. 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 April 2020.
29. Ghobrial IM, Xie W, Padmanabhan S, et al. Phase II trial of weekly bortezomib in combination with rituximab in untreated patients with Waldenström Macroglobulinemia. *Am J Hematol.* 2010 Sep;85(9):670-4. doi: 10.1002/ajh.21788.
30. Niesvizky R, Flinn IW, Rifkin R, et al. Community-Based Phase IIIB Trial of Three UPFRONT Bortezomib-Based Myeloma Regimens. *J Clin Oncol.* 2015 Nov 20;33(33):3921-9. doi: 10.1200/JCO.2014.58.7618.
31. Richardson PG, Sonneveld P, Schuster MW, et al. Bortezomib or high-dose dexamethasone for relapsed multiple myeloma. *N Engl J Med* 2005; 352:2487.
32. Richardson PG, Barlogie B, Berenson J, et al. Extended follow-up of a phase II trial in relapsed, refractory multiple myeloma: final time-to-event results from the SUMMIT trial. *Cancer.* 2006 Mar 15;106(6):1316-9.
33. Khan AA, Siraj F, Bhargava M, Aggarwal S. Successful treatment of multicentric Castleman's disease accompanying myeloma with bortezomib. *BMJ Case Rep.* 2012;2012:bcr2012007646. Published 2012 Dec 20. doi:10.1136/bcr-2012-007646.

34. Gasparetto C, Sanchorawala V, Snyder RM, et al. Use of melphalan (M)/dexamethasone (D)/bortezomib in AL amyloidosis. J Clin Oncol 2010; 28:Abstract 8024.
35. Venner CP, Lane T, Foard D, et al. Cyclophosphamide, bortezomib, and dexamethasone therapy in AL amyloidosis is associated with high clonal response rates and prolonged progression-free survival. Blood. 2012 May 10;119(19):4387-90. doi: 10.1182/blood-2011-10-388462.
36. Kastritis E, Wechalekar AD, Dimopoulos MA, et al. Bortezomib with or without dexamethasone in primary systemic (light chain) amyloidosis. J Clin Oncol. 2010 Feb 20;28(6):1031-7. doi: 10.1200/JCO.2009.23.8220.
37. Ishitsuka K, Utsunomiya A, Katsuya H, et al. A phase II study of bortezomib in patients with relapsed or refractory aggressive adult T-cell leukemia/lymphoma. Cancer Sci. 2015;106(9):1219-1223. doi:10.1111/cas.12735.
38. Chen CI, Kouroukis CT, White D, et al. Bortezomib is active in patients with untreated or relapsed Waldenstrom's macroglobulinemia: a phase II study of the National Cancer Institute of Canada Clinical Trials Group. J Clin Oncol. 2007 Apr 20;25(12):1570-5.
39. Palladini G, Perfetti V, Obici L, et al. Association of melphalan and high-dose dexamethasone is effective and well tolerated in patients with AL (primary) amyloidosis who are ineligible for stem cell transplantation. Blood. 2004 Apr 15;103(8):2936-8.
40. Reece DE, Sanchorawala V, Hegenbart U, et al. Weekly and twice-weekly bortezomib in patients with systemic AL amyloidosis: results of a phase 1 dose-escalation study. Blood. 2009 Aug 20;114(8):1489-97. doi: 10.1182/blood-2009-02-203398.
41. Reid EG, Suazo A, Lensing SY, et al. Pilot Trial AMC-063: Safety and Efficacy of Bortezomib in AIDS-associated Kaposi Sarcoma. Clin Cancer Res. 2020;26(3):558-565. doi:10.1158/1078-0432.CCR-19-1044.
42. National Government Services, Inc. Local Coverage Article for Bortezomib – Related to LCD L33394 (A52371). Centers for Medicare & Medicaid Services, Inc. Updated on 04/24/2020 with effective date of 05/01/2020. Accessed April 2020.
43. CGS Administrators, LLC. Local Coverage Article: Billing and Coding: Bortezomib (Velcade) -J9041 (A56891). Centers for Medicare & Medicaid Services, Inc. Updated on 09/20/2019 with effective date of 09/26/2019. Accessed April 2020.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C46.0	Kaposi's sarcoma of skin
C46.1	Kaposi's sarcoma of soft tissue
C46.2	Kaposi's sarcoma of palate
C46.3	Kaposi's sarcoma of lymph nodes
C46.4	Kaposi's sarcoma of gastrointestinal sites
C46.50	Kaposi's sarcoma of unspecified lung
C46.51	Kaposi's sarcoma of right lung
C46.52	Kaposi's sarcoma of left lung

ICD-10	ICD-10 Description
C46.7	Kaposi's sarcoma of other sites
C46.9	Kaposi's sarcoma, unspecified
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
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

ICD-10	ICD-10 Description
C90.32	Solitary plasmacytoma in relapse
C91.00	Acute lymphoblastic leukemia not having achieved remission
C91.02	Acute lymphoblastic leukemia, 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

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, Local Coverage Determinations (LCDs), and Local Coverage Articles (LCAs) 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/LCA):

Jurisdiction(s): 6, K	NCD/LCD/LCA Document (s): A52371
https://www.cms.gov/medicare-coverage-database/search/article-date-search.aspx?DocID=A52371&bc=gAAAAAAAAAAAAAA==	
Jurisdiction(s): 15	NCD/LCD/LCA Document (s): A56891
https://www.cms.gov/medicare-coverage-database/search/article-date-search.aspx?DocID=A56891&bc=gAAAAAAAAAAAAAA==	

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