

Bortezomib

Velcade®; Bortezomib§ (Intravenous/Subcutaneous)

Document Number: IC-0137

Last Review Date: 12/01/2022

Date of Origin: 11/28/2011

Dates Reviewed: 12/2011, 03/2012, 06/2012, 09/2012, 12/2012, 03/2013, 06/2013, 09/2013, 12/2013, 03/2014, 06/2014, 09/2014, 12/2014, 03/2015, 05/2015, 08/2015, 11/2015, 02/2016, 05/2016, 08/2016, 11/2016, 02/2017, 05/2017, 08/2017, 11/2017, 02/2018, 05/2018, 09/2018, 12/2018, 03/2019, 06/2019, 09/2019, 12/2019, 03/2020, 06/2020, 09/2020, 03/2021, 03/2022, 12/2022

I. Length of Authorization ^{1-7,49}

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

- Pediatric Hodgkin Lymphoma: Coverage will be provided for a total of 4 cycles (21-days per cycle).

II. Dosing Limits

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

- 3.5 mg powder for injection single-dose vial: 8 vials per 28-day supply

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

- **Multiple Myeloma & Systemic Light Chain Amyloidosis:**
 - 280 billable units every 35 days
- **Kaposi Sarcoma & Waldenström's Macroglobulinemia:**
 - 210 billable units every 28 days
- **Pediatric Hodgkin Lymphoma:**
 - 105 billable units every 21 days
- **All Other Indications:**
 - 140 billable units every 21 days

III. Initial Approval Criteria ¹⁻⁶

Coverage is provided in the following conditions:

- Patient is at least 18 years of age (unless otherwise specified); **AND**

Universal Criteria ¹⁻⁶

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

Multiple Myeloma † Φ 1-9,11,18,20-25,29-31,35-37,47,48

Mantle Cell Lymphoma – B-Cell Lymphoma † Φ 1-7,17,26-28,32

- Used as induction or additional therapy in combination with rituximab; **OR**
- Used as subsequent therapy as a single agent or in combination with rituximab

Systemic Light Chain Amyloidosis ‡ 7,15,39-41,44,45,50,51

- Used in one of the following treatment settings:
 - Newly diagnosed disease
 - Repeat initial therapy if relapse-free for several years
 - Relapsed or refractory disease; **AND**
- Used in combination with dexamethasone; **OR**
- Used as a single agent

Waldenström's Macroglobulinemia/Lymphoplasmacytic Lymphoma (WM/LPL) ‡ 7,10,16,19,34,43

- Used in combination with dexamethasone and rituximab

Multicentric Castleman's Disease – B-Cell Lymphoma ‡ 7,17,38

- Used as subsequent therapy; **AND**
- Used as a single agent or in combination with rituximab

Adult T-Cell Leukemia/Lymphoma ‡ 7,12,14,42

- Used as a single agent; **AND**
- Used as subsequent therapy

Adult* Acute Lymphoblastic Leukemia (ALL) ‡ 7,13

- Used in combination with chemotherapy; **AND**
- Patient has relapsed/refractory Philadelphia (Ph) chromosome negative T-cell disease (T-ALL)

**NCCN recommendations for ALL may be applicable to adolescent and young adult (AYA) patients within the age range of 15-39 years.*

Pediatric Acute Lymphoblastic Leukemia (ALL) ‡ 7,13,33

- Patient is at least 1 year of age^{**}; **AND**
- Patient has relapsed or refractory disease; **AND**
- Used as a component of vincristine, doxorubicin, pegaspargase based regimen; **AND**
 - Patient has B-cell disease; **AND**
 - Patient has Philadelphia (Ph) chromosome negative disease; **OR**
 - Patient has Philadelphia (Ph) chromosome positive disease and also used in combination with dasatinib or imatinib; **OR**
 - Patient has T-cell disease (T-ALL)

***NCCN recommendations for Pediatric ALL may be applicable to certain adolescent and young adult (AYA) patients up to 30 years of age.*

Kaposi Sarcoma †^{7,46}

- Used as subsequent therapy for relapsed or refractory disease; **AND**
- Patient has advanced cutaneous, oral, visceral, or nodal disease; **AND**
 - Used as a single-agent in patients without human immunodeficiency virus (HIV); **OR**
 - Used in combination with antiretroviral therapy (ART) for patients with HIV

Pediatric Hodgkin Lymphoma †^{7,49}

- Patient age is ≤ 18 years of age^{***}; **AND**
- Used for relapsed or refractory disease in combination with ifosfamide and vinorelbine

****Pediatric Hodgkin Lymphoma patients may include certain adolescent and young adult (AYA) patients up to 39 years of age.*

† FDA Approved Indication(s); ‡ Compendia recommended indication(s); Φ 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 (PRES), gastrointestinal toxicity, thrombocytopenia, neutropenia, tumor lysis syndrome, hepatic toxicity, thrombotic microangiopathy, etc.

V. Dosage/Administration¹⁻⁵¹

Indication	Dose
Multiple Myeloma; Systemic Light Chain Amyloidosis	Up to 1.6 mg/m ² intravenously (IV)/subcutaneously (SC) as four doses per cycle every 35 days until disease progression or unacceptable toxicity.
Waldenström's Macroglobulinemia; Kaposi Sarcoma	Up to 1.6 mg/m ² IV/SC as three doses per cycle every 28 days until disease progression or unacceptable toxicity.
Pediatric Hodgkin Lymphoma	1.2 mg/m ² IV/SC on days 1, 4, and 8 every 21 days for up to 4 cycles
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

BORTEZOMIB (Velcade®, Bortezomib) Prior Auth Criteria

Proprietary Information. Restricted Access – Do not disseminate or copy without approval.

©2022, Magellan Rx Management

VI. Billing Code/Availability Information

Product Formulation	Drug	Manufacturer	Approval	HCPCS Code	Route	NDC
Bortezomib powder for injection	Velcade 3.5 mg powder for inj. SDV *	Takeda	NDA/ANDA	J9041	IV/SC	63020-0049-xx
	Bortezomib 3.5 mg powder for inj. §	Dr. Reddy's	NDA	J9046	IV	43598-0865-xx
	Bortezomib 3.5 mg powder for inj. §	Fresenius	NDA	<ul style="list-style-type: none">J9048 (eff 1/1/23)J9044 (term 12/31/22)	IV	63323-0721-xx
	Bortezomib 1 mg powder for inj. § Bortezomib 2.5 mg powder for inj. §	Hospira	NDA	J9049	IV/SC	00409-1704-xx 00409-1703-xx
Bortezomib Solution for injection	Bortezomib 2.5 mg/1 mL inj. SDV § Bortezomib 3.5 mg/1.4 mL inj. SDV §	Accord H., Inc	NDA	J9999/ C9399	IV	16729-0564-xx 16729-0565-xx
	Bortezomib 3.5 mg/3.5 mL inj. SDV § Bortezomib 3.5 mg/1.4 mL inj. SDV §	Maia Pharma			IV	70511-0161-xx 70511-0162-xx
*Multiple manufacturers produce ANDA generics						
§ Bortezomib was approved by the FDA as a 505(b)(2) NDA of the innovator product, Velcade (bortezomib). These products are not rated as therapeutically equivalent to their reference listed drug in the Food and Drug Administration's (FDA) Orange Book, and are therefore considered single source products based on the statutory definition of "single source drug" in section 1847A(c)(6) of the Act.						
https://www.cms.gov/files/document/2022-hcpcs-application-summary-quarter-3-2022-drugs-and-biologicals-updated-11012022.pdf						
J9041	Injection, bortezomib, 0.1 mg					
J9044	Injection, bortezomib, not otherwise specified, 0.1 mg (terms 12/31/2022)					
J9046	Injection, bortezomib, (dr. reddy's), not therapeutically equivalent to J9041, 0.1 mg (Effective on 1/1/2023)					
J9048	Injection, bortezomib (fresenius kabi), not therapeutically equivalent to J9041, 0.1 mg (Effective on 1/1/2023)					
J9049	Injection, bortezomib (hospira), not therapeutically equivalent to J9041, 0.1 mg (Effective on 1/1/2023)					
J9999	Not otherwise classified, antineoplastic drugs					
C9399	Unclassified drugs or biologicals					

VII. References

1. Velcade [package insert]. Cambridge, MA; Millennium Pharmaceuticals, Inc; November 2021. Accessed November 2022.
2. Bortezomib [package insert]. Lake Zurich, IL; Fresenius Kabi, Inc; September 2021. Accessed November 2022.
3. Bortezomib [package insert]. Visakhapatnam, India; Dr. Reddy's Laboratories, Inc; February 2022. Accessed November 2022.
4. Bortezomib [package insert]. Lake Forest, IL; Hospira, Inc; May 2022. Accessed November 2022.
5. Bortezomib [package insert]. Princeton, NJ; MAIA Pharm., Inc; July 2022. Accessed November 2022.
6. Bortezomib [package insert]. Durham, NC; Accord Healthcare, Inc; July 2022. Accessed November 2022.

BORTEZOMIB (Velcade®, Bortezomib) Prior Auth Criteria

Proprietary Information. Restricted Access – Do not disseminate or copy without approval.

©2022, Magellan Rx Management

7. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for Bortezomib. National Comprehensive Cancer Network, 2022. 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 November 2022.
8. 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].
9. 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].
10. 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.
11. 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.
12. 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.
13. 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
14. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) T-Cell Lymphomas. Version 2.2022. National Comprehensive Cancer Network, 2022. 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 November 2022.
15. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Systemic Light Chain Amyloidosis. Version 1.2023. National Comprehensive Cancer Network, 2022. 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 November 2022.

16. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Waldenström's Macroglobulinemia/Lymphoplasmacytic Lymphoma. Version 1.2023. National Comprehensive Cancer Network, 2022. 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 November 2022.
17. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) B-Cell Lymphomas. Version 5.2022. National Comprehensive Cancer Network, 2022. 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 November 2022.
18. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Multiple Myeloma. Version 2.2023. National Comprehensive Cancer Network, 2022. 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 November 2022.
19. 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.
20. 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.
21. 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.
22. 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.
23. 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.
24. Dimopoulos MA, Orlowski 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.
25. 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.
 26. 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.
 27. 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.
 28. 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.
 29. 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.
 30. 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.
 31. 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.
 32. 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.
 33. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Pediatric Acute Lymphoblastic Leukemia. Version 1.2023. National Comprehensive Cancer Network, 2022. 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 November 2022.
 34. 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.
 35. 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.
 36. Richardson PG, Sonneveld P, Schuster MW, et al. Bortezomib or high-dose dexamethasone for relapsed multiple myeloma. *N Engl J Med* 2005; 352:2487.

37. 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.
38. 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.
39. 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.
40. 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.
41. Kastiris 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.
42. 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.
43. 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.
44. 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.
45. 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.
46. 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.
47. Zhang S, Kulkarni AA, Xu B, et al. Bortezomib-based consolidation or maintenance therapy for multiple myeloma: a meta-analysis. *Blood Cancer J*. 2020;10(3):33. Published 2020 Mar 6. doi:10.1038/s41408-020-0298-1.
48. Palumbo A, Bringhen S, Larocca A, et al. Bortezomib-melphalan-prednisone-thalidomide followed by maintenance with bortezomib-thalidomide compared with bortezomib-melphalan-prednisone for initial treatment of multiple myeloma: updated follow-up and improved survival. *J Clin Oncol*. 2014 Mar 1;32(7):634-40. doi: 10.1200/JCO.2013.52.0023.
49. Horton TM, Drachtman RA, Chen L, et al. A phase 2 study of bortezomib in combination with ifosfamide/vinorelbine in paediatric patients and young adults with refractory/recurrent Hodgkin lymphoma: a Children's Oncology Group study. *Br J Haematol*. 2015;170(1):118-122. doi:10.1111/bjh.13388.
50. Palladini G, Kastiris E, Maurer M, et al Daratumumab plus CyBorD for patients with newly diagnosed AL amyloidosis: safety run-in results of ANDROMEDA. *Blood* 2020 Jul 2;136(1):71-80. doi: 10.1182/blood.2019004460.

51. Kastritis E, Dialoupi I, Gavriatopoulou M, et al. Primary treatment of light-chain amyloidosis with bortezomib, lenalidomide, and dexamethasone. *Blood Adv.* 2019;3(20):3002-3009. doi:10.1182/bloodadvances.2019000147.
52. National Government Services, Inc. Local Coverage Article for Bortezomib – Related to LCD L33394 (A52371). Centers for Medicare & Medicaid Services, Inc. Updated on 09/09/2022 with effective date of 10/01/2022. Accessed November 2022.

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
C46.7	Kaposi's sarcoma of other sites
C46.9	Kaposi's sarcoma, unspecified
C81.10	Nodular sclerosis Hodgkin lymphoma, unspecified site
C81.11	Nodular sclerosis Hodgkin lymphoma, lymph nodes of head, face, and neck
C81.12	Nodular sclerosis Hodgkin lymphoma, intrathoracic lymph nodes
C81.13	Nodular sclerosis Hodgkin lymphoma, intra-abdominal lymph nodes
C81.14	Nodular sclerosis Hodgkin lymphoma, lymph nodes of axilla and upper limb
C81.15	Nodular sclerosis Hodgkin lymphoma, lymph nodes of inguinal region and lower limb
C81.16	Nodular sclerosis Hodgkin lymphoma, intrapelvic lymph nodes
C81.17	Nodular sclerosis Hodgkin lymphoma, spleen
C81.18	Nodular sclerosis Hodgkin lymphoma, lymph nodes of multiple sites
C81.19	Nodular sclerosis Hodgkin lymphoma, extranodal and solid organ sites
C81.20	Mixed cellularity Hodgkin lymphoma, unspecified site
C81.21	Mixed cellularity Hodgkin lymphoma, lymph nodes of head, face, and neck
C81.22	Mixed cellularity Hodgkin lymphoma, intrathoracic lymph nodes
C81.23	Mixed cellularity Hodgkin lymphoma, intra-abdominal lymph nodes
C81.24	Mixed cellularity Hodgkin lymphoma, lymph nodes of axilla and upper limb
C81.25	Mixed cellularity Hodgkin lymphoma, lymph nodes of inguinal region and lower limb
C81.26	Mixed cellularity Hodgkin lymphoma, intrapelvic lymph nodes

ICD-10	ICD-10 Description
C81.27	Mixed cellularity Hodgkin lymphoma, spleen
C81.28	Mixed cellularity Hodgkin lymphoma, lymph nodes of multiple sites
C81.29	Mixed cellularity Hodgkin lymphoma, extranodal and solid organ sites
C81.30	Lymphocyte depleted Hodgkin lymphoma, unspecified site
C81.31	Lymphocyte depleted Hodgkin lymphoma, lymph nodes of head, face, and neck
C81.32	Lymphocyte depleted Hodgkin lymphoma, intrathoracic lymph nodes
C81.33	Lymphocyte depleted Hodgkin lymphoma, intra-abdominal lymph nodes
C81.34	Lymphocyte depleted Hodgkin lymphoma, lymph nodes of axilla and upper limb
C81.35	Lymphocyte depleted Hodgkin lymphoma, lymph nodes of inguinal region and lower limb
C81.36	Lymphocyte depleted Hodgkin lymphoma, intrapelvic lymph nodes
C81.37	Lymphocyte depleted Hodgkin lymphoma, spleen
C81.38	Lymphocyte depleted Hodgkin lymphoma, lymph nodes of multiple sites
C81.39	Lymphocyte depleted Hodgkin lymphoma, extranodal and solid organ sites
C81.40	Lymphocyte-rich Hodgkin lymphoma, unspecified site
C81.41	Lymphocyte-rich Hodgkin lymphoma, lymph nodes of head, face, and neck
C81.42	Lymphocyte-rich Hodgkin lymphoma, intrathoracic lymph nodes
C81.43	Lymphocyte-rich Hodgkin lymphoma, intra-abdominal lymph nodes
C81.44	Lymphocyte-rich Hodgkin lymphoma, lymph nodes of axilla and upper limb
C81.45	Lymphocyte-rich Hodgkin lymphoma, lymph nodes of inguinal region and lower limb
C81.46	Lymphocyte-rich Hodgkin lymphoma, intrapelvic lymph nodes
C81.47	Lymphocyte-rich Hodgkin lymphoma, spleen
C81.48	Lymphocyte-rich Hodgkin lymphoma, lymph nodes of multiple sites
C81.49	Lymphocyte-rich Hodgkin lymphoma, extranodal and solid organ sites
C81.70	Other Hodgkin lymphoma unspecified site
C81.71	Other Hodgkin lymphoma lymph nodes of head, face, and neck
C81.72	Other Hodgkin lymphoma intrathoracic lymph nodes
C81.73	Other Hodgkin lymphoma intra-abdominal lymph nodes
C81.74	Other Hodgkin lymphoma lymph nodes of axilla and upper limb
C81.75	Other Hodgkin lymphoma lymph nodes of inguinal region and lower limb
C81.76	Other Hodgkin lymphoma intrapelvic lymph nodes
C81.77	Other Hodgkin lymphoma spleen
C81.78	Other Hodgkin lymphoma lymph nodes of multiple sites
C81.79	Other Hodgkin lymphoma extranodal and solid organ sites
C81.90	Hodgkin lymphoma, unspecified, unspecified site

ICD-10	ICD-10 Description
C81.91	Hodgkin lymphoma, unspecified, lymph nodes of head, face, and neck
C81.92	Hodgkin lymphoma, unspecified, intrathoracic lymph nodes
C81.93	Hodgkin lymphoma, unspecified, intra-abdominal lymph nodes
C81.94	Hodgkin lymphoma, unspecified, lymph nodes of axilla and upper limb
C81.95	Hodgkin lymphoma, unspecified, lymph nodes of inguinal region and lower limb
C81.96	Hodgkin lymphoma, unspecified, intrapelvic lymph nodes
C81.97	Hodgkin lymphoma, unspecified, spleen
C81.98	Hodgkin lymphoma, unspecified, lymph nodes of multiple sites
C81.99	Hodgkin 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
C83.50	Lymphoblastic (diffuse) lymphoma, unspecified site
C83.51	Lymphoblastic (diffuse) lymphoma, lymph nodes of head, face, and neck
C83.52	Lymphoblastic (diffuse) lymphoma, intrathoracic lymph nodes
C83.53	Lymphoblastic (diffuse) lymphoma, intra-abdominal lymph nodes
C83.54	Lymphoblastic (diffuse) lymphoma, lymph nodes of axilla and upper limb
C83.55	Lymphoblastic (diffuse) lymphoma, lymph nodes of inguinal region and lower limb
C83.56	Lymphoblastic (diffuse) lymphoma, intrapelvic lymph nodes
C83.57	Lymphoblastic (diffuse) lymphoma, spleen
C83.58	Lymphoblastic (diffuse) lymphoma, lymph nodes of multiple sites
C83.59	Lymphoblastic (diffuse) 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

ICD-10	ICD-10 Description
C90.12	Plasma cell leukemia in relapse
C90.20	Extramedullary plasmacytoma not having achieved remission
C90.22	Extramedullary plasmacytoma in relapse
C90.30	Solitary plasmacytoma not having achieved remission
C90.32	Solitary plasmacytoma in relapse
C91.00	Acute lymphoblastic leukemia not having achieved remission
C91.01	Acute lymphoblastic leukemia, in 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
D47.9	Neoplasm of uncertain behavior of lymphoid, hematopoietic and related tissue, unspecified
D47.Z2	Castleman disease
D47.Z9	Other specified neoplasms of uncertain behavior of lymphoid, hematopoietic and related tissue
E31.9	Polyglandular dysfunction, unspecified
E85.3	Secondary systemic amyloidosis
E85.4	Organ-limited amyloidosis
E85.81	Light chain (AL) amyloidosis
E85.89	Other amyloidosis
E85.9	Amyloidosis, unspecified
G62.9	Polyneuropathy, unspecified
G90.0	Idiopathic peripheral autonomic neuropathy
L98.9	Disorder of the skin and subcutaneous tissue, unspecified
Z85.71	Personal history of Hodgkin Lymphoma

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: <https://www.cms.gov/medicare-coverage-database/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/view/article.aspx?articleid=52371&ver=48&keyword=&keywordType=starts&areaId=all&docType=6,3,5,1,F,P&contractOption=all&hcpcsOption=code&hcpcsStartCode=j9044&hcpcsEndCode=j9044&sortBy=title&bc=1	

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

PreferredOne Community Health Plan Nondiscrimination Notice

PreferredOne Community Health Plan (“PCHP”) complies with applicable Federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability, or sex. PCHP does not exclude people or treat them differently because of race, color, national origin, age, disability, or sex.

PCHP:

Provides free aids and services to people with disabilities to communicate effectively with us, such as:

- Qualified sign language interpreters
- Written information in other formats (large print, audio, accessible electronic formats, other formats)

Provides free language services to people whose primary language is not English, such as:

- Qualified interpreters
- Information written in other languages

If you need these services, contact a Grievance Specialist.

If you believe that PCHP has failed to provide these services or discriminated in another way on the basis of race, color, national origin, age, disability, or sex, you can file a grievance with:

Grievance Specialist
PreferredOne Community Health Plan
PO Box 59052
Minneapolis, MN 55459-0052
Phone: 1.800.940.5049 (TTY: 763.847.4013)
Fax: 763.847.4010
customerservice@preferredone.com

You can file a grievance in person or by mail, fax, or email. If you need help filing a grievance, a Grievance Specialist is available to help you.

You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights, electronically through the Office for Civil Rights Complaint Portal, available at <https://ocrportal.hhs.gov/ocr/portal/lobby.jsf>, or by mail or phone at:

U.S. Department of Health and Human Services
200 Independence Avenue, SW
Room 509F, HHH Building
Washington, D.C. 20201
1-800-368-1019, 800-537-7697 (TDD)

Complaint forms are available at <http://www.hhs.gov/ocr/office/file/index.html>.

Language Assistance Services

ATTENTION: If you do not speak English, language assistance services, free of charge, are available to you. Call 1.800.940.5049 (TTY: 763.847.4013).

ATENCIÓN: si habla español, tiene a su disposición servicios gratuitos de asistencia lingüística. Llame al 1.800.940.5049 (TTY: 763.847.4013).

LUS CEEV: Yog tias koj hais lus Hmoob, cov kev pab txog lus, muaj kev pab dawb rau koj. Hu rau 1.800.940.5049 (TTY: 763.847.4013).

XIYYEEFFANNAA: Afaan dubbattu Oroomiffa, taiaajiila qarqaarsa afaanii, kanfaltiidhaan ala, ni argama. Bilbilaa 1.800.940.5049 (TTY: 763.847.4013).

CHÚ Ý: Nếu bạn nói Tiếng Việt, có các dịch vụ hỗ trợ ngôn ngữ miễn phí dành cho bạn. Gọi số 1.800.940.5049 (TTY: 763.847.4013).

注意：如果您使用繁體中文，您可以免費獲得語言援助服務。請致電 1.800.940.5049 (TTY: 763.847.4013)。

ВНИМАНИЕ: Если вы говорите на русском языке, то вам доступны бесплатные услуги перевода. Звоните 1.800.940.5049 (телетайп: 763.847.4013).

ໂບດຊາບ: ຖ້າວ່າທ່ານເວົ້າພາສາລາວ, ການບໍລິການຊ່ວຍເຫຼືອດ້ານພາສາ, ໂດຍບໍ່ເສຍຄ່າ, ແມ່ນມີພ້ອມໃຫ້ທ່ານ. ໂທ 1.800.940.5049 (TTY: 763.847.4013).

ማስታወሻ: የሚናገሩት ቋንቋ አማርኛ ከሆነ የትርጉም እርዳታ ድርጅቶች፣ በነጻ ሊያግዝዎት ተዘጋጅተዋል፡ ወደ ሚከተለው ቁጥር ይደውሉ 1.800.940.5049 (መስማት ለተሳናቸው፡ 763.847.4013) .

ဟ်သ့ဟ်သး- နမၤကတိၤ ကသီၤ ကျိၣ်အယိၤ, နမၤန့ၣ် ကျိၣ်အတၢ်မၤစၢၤလၢ တလၢကၢၣ်လၢကၢၣ်စၢၤ နီၣ်တမံၤဘၣ်သ့န့ၣ်လီၤ. ကိး 1.800.940.5049 (TTY: 763.847.4013).

ACHTUNG: Wenn Sie Deutsch sprechen, stehen Ihnen kostenlos sprachliche Hilfsdienstleistungen zur Verfügung. Rufnummer: 1.800.940.5049 (TTY: 763.847.4013).

ប្រយ័ត្ន៖ បើសិនជាអ្នកនិយាយ ភាសាខ្មែរ, សេវាជំនួយផ្នែកភាសា ដោយមិនគិតល្បួល គឺអាចមានសំរាប់បំរើអ្នក។ ចរ ទូរស័ព្ទ 1.800.940.5049 (TTY: 763.847.4013)។

ملحوظة: إذا كنت تتحدث اذكر اللغة، فإن خدمات المساعدة اللغوية تتوافر لك بالمجان. اتصل برقم 1.800.940.5049 (رقم هاتف الصم والبكم: 763.847.4013).

ATTENTION : Si vous parlez français, des services d'aide linguistique vous sont proposés gratuitement. Appelez le 1.800.940.5049 (TTY: 763.847.4013).

주의: 한국어를 사용하시는 경우, 언어 지원 서비스를 무료로 이용하실 수 있습니다. 1.800.940.5049 (TTY: 763.847.4013), 번으로 전화해 주십시오.

PAUNAWA: Kung nagsasalita ka ng Tagalog, maaari kang gumamit ng mga serbisyo ng tulong sa wika nang walang bayad. Tumawag sa 1.800.940.5049 (TTY: 763.847.4013).

PreferredOne Insurance Company Nondiscrimination Notice

PreferredOne Insurance Company ("PIC") complies with applicable Federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability, or sex. PIC does not exclude people or treat them differently because of race, color, national origin, age, disability, or sex.

PIC:

Provides free aids and services to people with disabilities to communicate effectively with us, such as:

- Qualified sign language interpreters
- Written information in other formats (large print, audio, accessible electronic formats, other formats)

Provides free language services to people whose primary language is not English, such as:

- Qualified interpreters
- Information written in other languages

If you need these services, contact a Grievance Specialist.

If you believe that PIC has failed to provide these services or discriminated in another way on the basis of race, color, national origin, age, disability, or sex, you can file a grievance with:

Grievance Specialist
PreferredOne Insurance Company
PO Box 59212
Minneapolis, MN 55459-0212
Phone: 1.800.940.5049 (TTY: 763.847.4013)
Fax: 763.847.4010
customerservice@preferredone.com

You can file a grievance in person or by mail, fax, or email. If you need help filing a grievance, a Grievance Specialist is available to help you.

You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights, electronically through the Office for Civil Rights Complaint Portal, available at <https://ocrportal.hhs.gov/ocr/portal/lobby.jsf>, or by mail or phone at:

U.S. Department of Health and Human Services
200 Independence Avenue, SW
Room 509F, HHH Building
Washington, D.C. 20201
1-800-368-1019, 800-537-7697 (TDD)

Complaint forms are available at <http://www.hhs.gov/ocr/office/file/index.html>.

Language Assistance Services

ATTENTION: If you do not speak English, language assistance services, free of charge, are available to you. Call 1.800.940.5049 (TTY: 763.847.4013).

ATENCIÓN: si habla español, tiene a su disposición servicios gratuitos de asistencia lingüística. Llame al 1.800.940.5049 (TTY: 763.847.4013).

LUS CEEV: Yog tias koj hais lus Hmoob, cov kev pab txog lus, muaj kev pab dawb rau koj. Hu rau 1.800.940.5049 (TTY: 763.847.4013).

XIYYEEFFANNAA: Afaan dubbattu Oroomiffa, tajaajila gargaarsa afaanii, kanfaltiidhaan ala, ni argama. Bilbilaa 1.800.940.5049 (TTY: 763.847.4013).

CHÚ Ý: Nếu bạn nói Tiếng Việt, có các dịch vụ hỗ trợ ngôn ngữ miễn phí dành cho bạn. Gọi số 1.800.940.5049 (TTY: 763.847.4013).

注意：如果您使用繁體中文，您可以免費獲得語言援助服務。請致電 1.800.940.5049 (TTY: 763.847.4013)。

ВНИМАНИЕ: Если вы говорите на русском языке, то вам доступны бесплатные услуги перевода. Звоните 1.800.940.5049 (телетайп: 763.847.4013).

ໂບດຊາບ: ຖ້າວ່າທ່ານເວົ້າພາສາລາວ, ການບໍລິການຊ່ວຍເຫຼືອຕໍ່ພາສາ, ໂດຍບໍ່ເສຍຄ່າ, ແມ່ນມີພ້ອມໃຫ້ທ່ານ. ໂທ 1.800.940.5049 (TTY: 763.847.4013).

ማስታወሻ: የሚናገሩት ቋንቋ አማርኛ ከሆነ የትርጉም እርዳታ ድርጅቶች፣ በነጻ ሊያግዝዎት ተዘጋጅተዋል፡ ወደ ሚከተለው ቁጥር ይደውሉ 1.800.940.5049 (መስማት ለተሳናቸው፡ 763.847.4013) .

ဟ်သျှာ်ဟ်သး- နမံကတိ၊ ကညိ ကျိာ်အယံ၊ နမံကျိာ်အတိမၤစၢၤလၢ တလၢာ်ဘျၣ်လၢာ်စၢၤ နီတမံၤဘျၣ်သန့လီၤ. ကိ: 1.800.940.5049 (TTY: 763.847.4013).

ACHTUNG: Wenn Sie Deutsch sprechen, stehen Ihnen kostenlos sprachliche Hilfsdienstleistungen zur Verfügung. Rufnummer: 1.800.940.5049 (TTY: 763.847.4013).

ប្រយ័ត្ន៖ បើសិនជាអ្នកនិយាយ ភាសាខ្មែរ, សេវាជំនួយផ្នែកភាសា ដោយមិនគិតល្បួល គឺអាចមានសំរាប់បំរើអ្នក។ ចូរ ទូរស័ព្ទ 1.800.940.5049 (TTY: 763.847.4013)។

ملحوظة: إذا كنت تتحدث اذكر اللغة، فإن خدمات المساعدة اللغوية تتوافر لك بالمجان. اتصل برقم 1.800.940.5049 (رقم هاتف الصم والبكم: 763.847.4013).

ATTENTION : Si vous parlez français, des services d'aide linguistique vous sont proposés gratuitement. Appelez le 1.800.940.5049 (TTY: 763.847.4013).

주의: 한국어를 사용하시는 경우, 언어 지원 서비스를 무료로 이용하실 수 있습니다. 1.800.940.5049 (TTY: 763.847.4013), 번으로 전화해 주십시오.

PAUNAWA: Kung nagsasalita ka ng Tagalog, maaari kang gumamit ng mga serbisyo ng tulong sa wika nang walang bayad. Tumawag sa 1.800.940.5049 (TTY: 763.847.4013).