

Kyprolis[®] (carfilzomib) (Intravenous)

Document Number: IC-0157

Last Review Date: 03/02/2023 Date of Origin: 02/07/2013 Dates Reviewed: 12/2013, 02/2014, 06/2014, 09/2014, 12/2014, 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, 12/2020, 03/2021, 06/2021, 09/2021, 12/2021, 03/2022, 06/2022, 09/2022, 12/2022, 03/2023

I. Length of Authorization ^{1,5,21,27,32,36}

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

<u>Multiple Myeloma</u>

- Combination therapy with lenalidomide and dexamethasone is limited to eighteen (18) 28day treatment cycles.
- Combination therapy with daratumumab, lenalidomide, and dexamethasone is limited to eight (8) 28-day treatment cycles.
- Combination therapy with lenalidomide as maintenance therapy is limited to a maximum of 2 years of treatment.

Waldenström's Macroglobulinemia/Lymphoplasmacytic Lymphoma

• Combination therapy with rituximab and dexamethasone (CaRD regimen) is limited to six (6) 21-day induction treatment cycles and eight (8) 56-day maintenance treatment cycles.

II. Dosing Limits

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

- Kyprolis 10 mg single-dose vial: 2 vials per 28-day cycle
- Kyprolis 30 mg single-dose vial: 1 vial per 28-day cycle
- Kyprolis 60 mg single-dose vial: 12 vials per 28-day cycle
- B. Max Units (per dose and over time) [HCPCS Unit]:
 - Multiple Myeloma
 - o 720 billable units (720 mg) every 28 days

Systemic Light Chain Amyloidosis

 $\circ~$ 360 billable units (360 mg) every 28 days

Publication of this policy on this website is an authorized use of proprietary and copyrighted information created in collaboration with Magellan Rx Management. This policy may not be reproduced or distributed without the express written permission of Magellan Rx Management. © 2023 Magellan Rx Management



Waldenström's Macroglobulinemia/Lymphoplasmacytic Lymphoma

o 320 billable units (320 mg) every 21 days

III. Initial Approval Criteria¹

Coverage is provided in the following conditions:

• Patient is at least 18 years of age; AND

Multiple Myeloma $\dagger \ddagger \Phi^{1,2,10,11,13}$

- Used as primary therapy for symptomatic disease; AND
 - Used in combination with daratumumab, lenalidomide, and dexamethasone *(transplant candidates ONLY);* **OR**
 - \circ Used in combination with lenalidomide and dexamethasone; OR
 - Used in combination with dexamethasone and cyclophosphamide; OR
- Used for disease relapse after 6 months following primary induction therapy with the same regimen; **AND**
 - \circ Used in combination with lenalidomide and dexamethasone; OR
 - Used in combination with dexamethasone and cyclophosphamide; OR
- Used for late relapse or progressive disease (>3 prior therapies); AND
 - \circ Used in combination with bendamustine and dexamethasone; OR
- Used for previously treated relapsed, progressive, or refractory disease; AND
 - Used as a single agent **†**; **OR**
 - \circ $\;$ Used in combination with one of the following regimens:
 - Dexamethasone with or without lenalidomide **†**
 - Dexamethasone and daratumumab †
 - Dexamethasone and daratumumab and hyaluronidase-fihj *
 - Dexamethasone and cyclophosphamide with or without thalidomide
 - Dexamethasone and isatuximab-irfc †
 - Dexamethasone and selinexor
 - Dexamethasone and pomalidomide; **OR**
- Used as maintenance therapy for symptomatic disease in transplant candidates; AND
 - Used in combination with lenalidomide; AND
 - Used after response to primary myeloma therapy; **OR**
 - Used for response or stable disease following an autologous hematopoietic cell transplant (HCT); OR
 - Used for response or stable disease following a tandem autologous or allogeneic HCT for high risk* patients



*High-risk as defined by the Revised International Staging System for Multiple Myeloma is the presence of del(17p) and/or translocation t(4;14) and/or translocation t(14;16). This is not an all-inclusive list. Refer to the NCCN Multiple Myeloma Guidelines for additional risk factors.

Waldenström's Macroglobulinemia/Lymphoplasmacytic Lymphoma ‡ 2,5,18

- Used in combination with rituximab and dexamethas one (CaRD regimen); $\ensuremath{\textbf{AND}}$
 - Used as primary therapy; **OR**
 - Used for relapsed disease; AND
 - CaRD regimen was previously used as primary therapy; AND
 - Patient had a prolonged response (i.e., 24 months) to CaRD therapy

Systemic Light Chain Amyloidosis \$ 2,30,31

- Patient has relapsed or refractory non-cardiac disease; AND
 - Used as a single agent; OR
 - \circ Used in combination with dexamethasone

au FDA Approved Indication(s); au Compendia Approved Indication(s); au Orphan Drug

IV. Renewal Criteria ^{1,2}

Coverage may be renewed based upon the following criteria:

- Patient continues to meet the 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. Examples of unacceptable toxicity include: cardiac toxicity (e.g., CHF, pulmonary edema, decreased ejection fraction, cardiomyopathy, myocardial ischemia, myocardial infarction, etc.), pulmonary toxicity (e.g., acute respiratory distress syndrome [ARDS], acute respiratory failure, etc.), pulmonary hypertension, dyspnea, severe infusion-related reactions, tumor lysis syndrome (TLS), thrombocytopenia, hepatic toxicity/failure, thrombotic microangiopathy (e.g., thrombotic thrombocytopenic purpura/hemolytic uremic syndrome [TTP/HUS], etc.), acute renal failure, severe hypertension, posterior reversible encephalopathy syndrome (PRES), venous thromboembolic events (e.g., deep venous thrombosis, pulmonary embolism, etc.), hemorrhage, progressive multifocal leukoencephalopathy (PML), etc.; AND

Multiple Myeloma 1,27,32,36

• Combination therapy with lenalidomide and dexamethasone may be renewed up to a maximum of eighteen (18) 28-day treatment cycles.



- Combination therapy with daratumumab, lenalidomide, and dexamethasone may be renewed up to a maximum of eight (8) 28-day treatment cycles.
- Combination therapy with lenalidomide as maintenance therapy may be renewed up to a maximum of 2 years of therapy

Waldenström's Macroglobulinemia/Lymphoplasmacytic Lymphoma 5,21

• Combination therapy with rituximab and dexamethasone (CaRD regimen) may be renewed up to a maximum of six (6) 21-day induction treatment cycles and eight (8) 56-day maintenance treatment cycles.

V. Dosage/Administration ^{1,5,7,9,12,20-22,24-28,30,32-36}

Indication	Dose	
Multiple Myeloma (primary therapy OR disease relapse ≥6 months following primary induction therapy with the same regimen)	 Combination with daratumumab, lenalidomide and dexamethasone 20/56 regimen: Cycle 1: 20 mg/m² on day 1; if tolerated, increase to 56 mg/m² on days 8 and 15 of a 28 day treatment cycle Cycles 2 through 8: 56 mg/m² on days 1, 8, and 15 of a 28 day treatment cycle Combination with lenalidomide and dexamethasone 20/36 regimen: Cycle 1: 20 mg/m² on days 1 and 2; if tolerated, increase to 36 mg/m² days 8, 9, 15, and 16 of a 28 day treatment cycle Cycles 2 through 8: 36 mg/m² days 1, 2, 8, 9, 15, and 16 of a 28 day treatment cycle Cycles 9 through 18: 36 mg/m² days 1, 2, 15, and 16 of a 28 day treatment cycle Cycles 9 through 18: 36 mg/m² days 1, 2, 15, and 16 of a 28 day treatment cycle Combination with cyclophosphamide and dexamethasone 20/36 regimen: Cycle 1: 20 mg/m² on days 1 and 2; if tolerated, increase to 36 mg/m² days 8, 9, 15, and 16 of a 28 day treatment cycle Cycle 1: 20 mg/m² on days 1 and 2; if tolerated, increase to 36 mg/m² days 8, 9, 15, and 16 of a 28 day treatment cycle Cycle 1: 20 mg/m² on days 1 and 2; if tolerated, increase to 36 mg/m² days 8, 9, 15, and 16 of a 28 day treatment cycle Cycle 2 through 9: 36 mg/m² days 1, 2, 8, 9, 15, and 16 of a 28 day treatment cycle Cycle 10 and beyond: 36 mg/m² on days 1, 2, 15, and 16 of a 28 day treatment cycle; continue until disease progression or unacceptable toxicity 20/70 regimen: Cycle 1: 20 mg/m² on day 1; if tolerated, increase to 70 mg/m² days 8 and 15 of a 28 day treatment cycle Cycle 1: 20 mg/m² on day 1, 8, and 15 of a 28 day treatment cycle; continue until disease progression or unacceptable toxicity 	
Multiple Myeloma (relapsed, progressive, or refractory disease)	 Single agent 20/27 regimen: Cycle 1: 20 mg/m² on days 1 and 2; if tolerated, increase to 27 mg/m² on days 8, 9, 15, and 16 of a 28-day treatment cycle Cycles 2 through 12: 27 mg/m² on days 1, 2, 8, 9, 15, and 16 of a 28-day treatment cycle Cycle 13 and beyond: 27 mg/m² on days 1, 2, 15, and 16 of a 28-day treatment cycle; continue until disease progression or unacceptable toxicity 20/56 regimen: Cycle 1: 20 mg/m² on days 1 and 2; if tolerated, increase to 56 mg/m² on days 8, 9, 15, and 16 of a 28-day treatment cycle. Cycles 2 through 12: 56 mg/m² on days 1, 2, 8, 9, 15, and 16 of a 28-day treatment cycle 	



 Cycle 13 and beyond: 56 mg/m² on days 1, 2, 15, and 16 of a 28-day treatment cycle; continue until disease progression or unacceptable toxicity 		
Combination with lenalidomide and dexamethasone (KRd)		
20/27 regimen:		
 Cycle 1: 20 mg/m² on days 1 and 2; if tolerated, increase to 27 mg/m² on days 8, 9, 15, and 16 of a 28-day treatment cycle 		
 Cycles 2 through 12: 27 mg/m² on days 1, 2, 8, 9, 15, and 16 of a 28-day treatment cycle Cycles 13 through 18: 27 mg/m² on days 1, 2, 15, and 16 of a 28-day treatment cycle; beginning with cycle 19, lenalidomide and dexamethasone may be continued (until disease progression or unacceptable toxicity) without carfilzomib 		
<u>Combination with dexamethasone (Kd)</u>		
20/56 regimen:		
 Cycle 1: 20 mg/m² on days 1 and 2; if tolerated, increase to 56 mg/m² on days 8, 9, 15, and 16 of a 28-day treatment cycle 		
 Cycle 2 and beyond: 56 mg/m² on days 1, 2, 8, 9, 15, and 16 of a 28-day treatment cycle; continue until disease progression or unacceptable toxicity 		
20/70 regimen: - Cycle 1: 20 mg/m ² on day 1; if tolerated, increase to 70 mg/m ² on day 8 and 15 of a 28-day treatment cycle		
 Cycle 1: 20 mg/m² on day 1; it tolerated, increase to 70 mg/m² on day 8 and 15 of a 28 day treatment cycle; continue until disease progression or unacceptable toxicity 		
Combination with daratumumab (or daratumumab and hyaluronidase-fihj) and		
dexamethasone (DKd)		
20/56 regimen:		
 Cycle 1: 20 mg/m² on days 1 and 2; if tolerated, increase to 56 mg/m² on days 8, 9, 15 and 16 of a 28-day treatment cycle 		
 Cycle 2 and beyond: 56 mg/m² on days 1, 2, 8, 9, 15, and 16 of a 28-day treatment cycle; continue until disease progression or unacceptable toxicity 		
20/70 regimen:		
 Cycle 1: 20 mg/m² on day 1; if tolerated, increase to 70 mg/m² on day 8 and 15 of a 28-day treatment cycle Cycle 2 and beyond: 70 mg/m² on days 1, 8, and 15 of a 28-day treatment cycle; continue until disease progression or unacceptable toxicity 		
Combination with cyclophosphamide, thalidomide, and dexamethasone		
20/36 regimen:		
 Cycle 1: 20 mg/m² on days 1 and 2; if tolerated, increase to 36 mg/m² days 8, 9, 15, and 16 of a 28-day treatment cycle Cycle 2 and beyond: 36 mg/m² days 1, 2, 8, 9, 15, and 16 of a 28-day treatment cycle; continue until 		
disease progression or unacceptable toxicity		
<u>Combination with cyclophosphamide and dexamethasone</u> 20/36 regimen:		
 Induction Cycle 1: 20 mg/m² on days 1 and 2; if tolerated, increase to 36 mg/m² days 8, 9, 15, and 16 of a 28-day treatment cycle 		
 Cycles 2 through 6: 36 mg/m² days 1, 2, 8, 9, 15, and 16 of a 28-day treatment cycle Maintenance 		
 Cycles 7 through 12: 36 mg/m² on days 1, 2, 15, and 16 of a 28-day treatment cycle 		
 Cycle 13 and beyond: 36 mg/m² on days 1 and 2 of a 28-day treatment cycle; continue until disease progression or unacceptable toxicity 		
<u>Combination with isatuximab-irfc and dexamethasone (Isa-Kd)</u>		



	20/56 regimen:
	 Cycle 1: 20 mg/m² on days 1 and 2; if tolerated, increase to 56 mg/m² on days 8, 9, 15 and 16 of a 28-day
	 treatment cycle Cycle 2 and beyond: 56 mg/m² on days 1, 2, 8, 9, 15, and 16 of a 28-day treatment cycle; continue until disease progression or unacceptable toxicity
	Combination with selinexor and dexamethasone
	20/56 regimen:
	 Cycle 1: 20 mg/m² on day 1; if tolerated, increase to 56 mg/m² on days 8 and 15 of a 28-day treatment cycle Cycle 2 and beyond: 56 mg/m² on days 1, 8, and 15 of a 28-day treatment cycle; continue until disease progression or unacceptable toxicity
	Combination with pomalidomide and dexamethasone
	20/27 regimen:
	 Cycle 1: 20 mg/m² on days 1 and 2; if tolerated, increase to 27 mg/m² on days 8, 9, 15, and 16 of a 28-day treatment cycle Cycles 2 through 6: 27 mg/m² on days 1, 2, 8, 9, 15, and 16 of a 28-day treatment cycle Cycle 7 and beyond: 27 mg/m² on days 1, 2, 15, and 16 of a 28-day treatment cycle; continue until disease progression or unacceptable toxicity
	 NOTE: If disease progression occurs while on maintenance dosing, resume full dosing of 27 mg/m² on days 1, 2, 8, 9, 15, and 16 of a 28-day treatment cycle 20/36 regimen:
	 Cycle 1: 20 mg/m² on days 1 and 2; if tolerated, increase to 36 mg/m² days 8, 9, 15, and 16 of a 28-day treatment cycle
	 Cycles 2 through 8: 36 mg/m² days 1, 2, 8, 9, 15, and 16 of a 28-day treatment cycle Cycle 9 and beyond: 36 mg/m² days 1, 2, 15, and 16 of a 28-day treatment cycle; continue until disease progression or unacceptable toxicity
Multiple Myeloma	Combination with bendamustine and dexamethasone
(late relapse or	20/27 regimen:
progressive disease)	 Cycle 1: 20 mg/m² on days 1 and 2; if tolerated, increase to 27 mg/m² on days 8, 9, 15, and 16 of a 28-day treatment cycle Cycles 2 through 8: 27 mg/m² on days 1, 2, 8, 9, 15, and 16 of a 28-day treatment cycle Cycle 9 and beyond: 27 mg/m² on days 1, 2, 15, and 16 of a 28-day treatment cycle; continue until disease progression or unacceptable toxicity
Multiple Myeloma	Combination with lenalidomide
(maintenance therapy)	 36 mg/m² days 1, 2, 15, and 16 of a 28-day treatment cycle for up to 2 years NOTE: lenalidomide may be continued until disease progression or unacceptable toxicity without carfilzomib
Waldenström's	<u>CaRD regimen (carfilzomib, rituximab, dexamethasone)</u>
Macroglobulinemia/	Induction
Lymphoplasmacytic Lymphoma	 Cycle 1: 20 mg/m² on days 1, 2, 8 and 9 of a 21-day treatment cycle Cycles 2 through 6: 36 mg/m² on days 1, 2, 8 and 9 of a 21-day treatment; begin maintenance 8 weeks later
	Maintenance - 36 mg/m ² on days 1 and 2 every 8 weeks for 8 cycles
Systemic Light	Single agent or combination with dexamethasone
Chain Amyloidosis	 Cycle 1: 20 mg/m² on day 1; if tolerated, increase to 27 mg/m² days 8 and 15 of a 28-day treatment cycle Cycle 2 and beyond: up to 56 mg/m² days 1, 8, and 15 of a 28-day treatment cycle
adjustments do not i	with body surface area (BSA) of 2.2 m ² or less, calculate the Kyprolis dose using actual BSA. Dose need to be made for weight changes of 20% or less. For patients with a BSA greater than 2.2 m ² , his dose using a BSA of 2.2 m ² .

KYPROLIS[®] (carfilzomib) Prior Auth Criteria

Proprietary Information. Restricted Access – Do not disseminate or copy without approval. ©2023, Magellan Rx Management

VI. Billing Code/Availability Information

HCPCS Code:

• J9047 – Injection, carfilzomib, 1 mg; 1mg = 1 billable unit

NDC(s):

- Kyprolis 10 mg single-dose vial for injection: 76075-0103-xx
- Kyprolis 30 mg single-dose vial for injection: 76075-0102-xx
- Kyprolis 60 mg single-dose vial for injection: 76075-0101-xx

VII. References

- 1. Kyprolis [package insert]. Thousand Oaks, CA; Onyx Pharmaceuticals, Inc.; June 2022. Accessed February 2023.
- 2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for Carfilzomib. National Comprehensive Cancer Network, 2023. 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 February 2023.
- BGM Durie, J-L Harousseau, J S Miguel, et al on behalf of the International Myeloma Working Group. International uniform response criteria for multiple myeloma. Leukemia. Sep; 20(9):1467-73.
- 4. Dimopoulos MA, Kastritis E, Owen RG, et al. Treatment recommendations for patients with Waldenström's macroglobulinemia (WM) and related disorders: IWWM-7 consensus. Blood. 2014; 124(9):1404–1411.
- 5. Treon SP, Tripsas CK, Meid K, et al. Carfilzomib, rituximab, and dexamethasone (CaRD) treatment offers a neuropathy-sparing approach for treating Waldenström's macroglobulinemia. Blood. 2014;124(4):503-510.
- 6. UpToDate. Hudson (OH): Lexicomp Inc.: Carfilzomib: Drug information. Topic 86042 Version 135.0, 2018 Accessed November 2018.
- 7. Shah JJ, Stadtmauer EA, Abonour R, et al. Carfilzomib, pomalidomide and dexamethasone for relapsed or refractory myeloma. Blood 2015; 126: 2284-2290.
- 8. Berdeja JG, Hart LL, Mace JR, et al. Phase I/II study of the combination of panobinostat and carfilzomib in patient s with relapsed/refractory multiple myeloma. Haematologica 2015; 100: 670-676.
- Bringhen S, Petrucci MT, Larocca A, et al. Carfilzomib, cyclophosphamide, and dexamethasone in patients with newly diagnosed multiple myeloma: a multicenter, phase 2 study. Blood. 2014 Jul 3;124(1):63-9.
- 10. Moreau P, Mateos MV, Berenson JR, et al. Once weekly versus twice weekly carfilzomib dosing in patients with relapsed and refractory multiple myeloma (A.R.R.O.W.): interim analysis results of a randomised, phase 3 study. Lancet Oncol 2018;19(7):953-964.



- Chari A, Martinez-Lopez J, Mateos MV, et al. Daratumumab plus carfilzomib and dexamethasone in patients with relapsed or refractory multiple myeloma. Blood 2019. Aug 1;134(5):421-431. doi: 10.1182/blood.2019000722. Epub 2019 May 21.
- 12. Mikhael JR, Reeder CB, Libby EN, et al. Phase Ib/II trial of CYKLONE (cyclophosphamide, carfilzomib, thalidomide and dexamethasone) for newly diagnosed myeloma. Br J Haematol. 2015 Apr; 169(2): 219–227. Published online 2015 Feb 13.
- Stewart AK, Rajkumar SV, Dimopoulos MA, et al. Carfilzomib, lenalidomide, and dexamethasone for relapsed multiple myeloma. N Engl J Med. 2015 Jan 8;372(2):142-52. doi: 10.1056/NEJMoa1411321. Epub 2014 Dec 6.
- 14. Dimopoulos MA, Moreau P, Palumbo A, et al. Carfilzomib and dexamethasone versus bortezomib and dexamethasone for patients with relapsed or refractory multiple myeloma (ENDEAVOR): a randomised, phase 3, open-label, multicentre study. Lancet Oncol. 2016 Jan;17(1):27-38. doi: 10.1016/S1470-2045(15)00464-7. Epub 2015 Dec 5.
- 15. Papadopoulos KP, Siegel DS, Vesole DH, et al. Phase I study of 30-minute infusion of carfilzomib as single agent or in combination with low-dose dexamethasone in patients with relapsed and/or refractory multiple myeloma. J Clin Oncol. 2015 Mar 1;33(7):732-9. doi: 10.1200/JCO.2013.52.3522. Epub 2014 Sep 15.
- 16. Siegel DS, Martin T, Wang M, et al. A phase 2 study of single-agent carfilzomib (PX-171-003-A1) in patients with relapsed and refractory multiple myeloma. Blood. 2012 Oct 4;120(14):2817-25. doi: 10.1182/blood-2012-05-425934. Epub 2012 Jul 25.
- 17. Vij R, Wang M, Kaufman JL, et al. An open-label, single-arm, phase 2 (PX-171-004) study of single-agent carfilzomib in bortezomib-naive patients with relapsed and/or refractory multiple myeloma. Blood. 2012 Jun 14;119(24):5661-70. doi: 10.1182/blood-2012-03-414359. Epub 2012 May 3.
- 18. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Waldenström Macroglobulinemia/Lymphoplasmacytic Lymphoma, Version 1.2023. National Comprehensive Cancer Network, 2023. 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 Guidelines, go online to NCCN.org. Accessed February 2023.
- 19. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines[®]) for Multiple Myeloma, Version 3.2023. National Comprehensive Cancer Network, 2023. 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 Guidelines, go online to NCCN.org. Accessed February 2023.
- 20. Rosenbaum CA, Stephens LA, Kukreti V, et al. Phase 1/2 study of carfilzomib, pomalidomide, and dexamethasone (KPd) in patients (Pts) with relapsed/refractory multiple myeloma (RRMM): A Multiple Myeloma Research Consortium multicenter study.



DOI: 10.1200/JCO.2016.34.15_suppl.8007 *Journal of Clinical Oncology* 34, no. 15_suppl (May 20, 2016) 8007-8007.

- 21. Meid K, Dubeau T, Severns P, et al. Long-Term Follow-up of a Prospective Clinical Trial of Carfilzomib, Rituximab and Dexamethasone (CaRD) in Waldenstrom's Macroglobulinemia. Blood 2017; 130:2772-2772.
- 22. Yong K, Brown S, Hinsley S, et al. Carfilzomib, cyclophosphamide and dexamethasone is well tolerated in patients with relapsed/refractory multiple myeloma who have received one prior regimen. 2015; 126:1840.
- 23. Dimopoulos M, Quach H, Mateos MV, et al. Carfilzomib, dexamethasone, and daratumumab versus carfilzomib and dexamethasone for patients with relapsed or refractory multiple myeloma (CANDOR): results from a randomised, multicentre, open-label, phase 3 study. Lancet. 2020;396(10245):186-197.
- 24. Jakubowiak AJ, Dytfeld D, Griffith KA, et al. A phase 1/2 study of carfilzomib in combination with lenalidomide and low-dose dexamethasone as a frontline treatment for multiple myeloma. Blood. 2012 Aug 30;120(9):1801-9.
- 25. Korde N, Zingone A, Kwok M, et al. Phase II Clinical and Correlative Study of Carfilzomib, Lenalidomide, and Dexamethasone (CRd) in Newly Diagnosed Multiple Myeloma (MM) Patients. Blood. 2012 Nov 12;120(21):732.
- 26. Korde N, Zingone A, Kwok ML, et al. Phase II Clinical and Correlative Study Of Carfilzomib, Lenalidomide, and Dexamethasone Followed By Lenalidomide Extended Dosing (CRD-R) Induces High Rates Of MRD Negativity In Newly Diagnosed Multiple Myeloma (MM) Patients. Blood. 2013 Nov 15;122(21):538.
- 27. Zimmerman T, Raje NS, Reece D, et al. Final Results of a Phase 2 Trial of Extended Treatment (tx) with Carfilzomib (CFZ), Lenalidomide (LEN), and Dexamethasone (KRd) Plus Autologous Stem Cell Transplantation (ASCT) in Newly Diagnosed Multiple Myeloma (NDMM). Blood. 2016 Dec 2;128(22):675.
- 28. Yong K, Hinsley S, De Tute, RM, et al. Maintenance with Carfilzomib Following Carfilzomib, Cyclophosphamide and Dexamethasone at First Relapse or Primary Refractory Multiple Myeloma (MM) on the Phase 2 Muk Five Study: Effect on Minimal Residual Disease. Blood. 2018 Nov 29;132(1):802.
- 29. Moreau P, Dimopoulos MA, Yong K, et al. Isatuximab plus carfilzomib/dexamethasone versus carfilzomib/dexamethasone in patients with relapsed/refractory multiple myeloma: IKEMA Phase III study design. Future Oncol. 2020 Jan;16(2):4347-4358. doi: 10.2217/fon-2019-0431.
- 30. Manwani R, Mahmood S, Sachchithanantham S, et al. Carfilzomib is an effective upfront treatment in AL amyloidosis patients with peripheral and autonomic neuropathy. Br J Haematol 2019 Dec;187(5):638-641.doi: 10.1111/bjh.16122. Epub 2019 Aug 6.
- 31. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines[®]) for Systemic Light Chain Amyloidosis, Version 2.2023. National Comprehensive Cancer Network, 2023. 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 Guidelines, go online to NCCN.org. Accessed February 2023.

- 32. Landren O, Hulcrantz M, Diamond B, et al. Safety and Effectiveness of Weekly Carfilzomib, Lenalidomide, Dexamethasone, and Daratumumab Combination Therapy for Patients With Newly Diagnosed Multiple Myeloma: The MANHATTAN Nonrandomized Clinical Trial. JAMA Oncol. 2021 Jun 1;7(6):862-868. doi: 10.1001/jamaoncol.2021.0611.
- 33. Bringhen S, D'Agostino M, De Paoli L, et al. Phase 1/2 study of weekly carfilzomib, cyclophosphamide, dexamethasone in newly diagnosed transplant-ineligible myeloma. Leukemia. 2018 Apr;32(4):979-985. doi: 10.1038/leu.2017.327.
- 34. Gasparetto C, Lipe B, Tuchman S, et al. Once weekly selinexor, carfilzomib, and dexamethasone (SKd) in patients with relapsed/refractory multiple myeloma (MM). DOI: 10.1200/JCO.2020.38.15_suppl.8530 Journal of Clinical Oncology 38, no. 15_suppl (May 20, 2020) 8530-8530.
- 35. Gay F, Günther A, Offidani M, et al. Carfilzomib, bendamustine, and dexamethasone in patients with advanced multiple myeloma: The EMN09 phase 1/2 study of the European Myeloma Network. Cancer. 2021 Sep 15;127(18):3413-3421. doi: 10.1002/cncr.33647
- 36. Gay F, Musto P, Scalabrini D, et al. Carfilzomib with cyclophosphamide and dexamethasone or lenalidomide and dexamethasone plus autologous transplantation or carfilzomib plus lenalidomide and dexamethasone, followed by maintenance with carfilzomib plus lenalidomide or lenalidomide alone for patients with newly diagnosed multiple myeloma (FORTE): a randomized, open-label, phase 2 trial. Lancet Oncol. 2021 Dec;22(12):1705-1720. doi: 10.1016/S1470-2045(21)00535-0. Epub 2021 Nov 11.
- 37. Moreau P, Dimopoulos MA, Mikhael J, et al.; IKEMA study group. Isatuximab, carfilzomib, and dexamethasone in relapsed multiple myeloma (IKEMA): a multicentre, open-label, randomised phase 3 trial. Lancet. 2021 Jun 19;397(10292):2361-2371. doi: 10.1016/S0140-6736(21)00592-4.

ICD-10	ICD-10 Description	
C88.0	Waldenström macroglobulinemia	
C90.00	Multiple myeloma not having achieved remission	
C90.02	Multiple myeloma in relapse	
C90.10	Plasma cell leukemia not having achieved remission	
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	

Appendix 1 – Covered Diagnosis Codes



ICD-10	ICD-10 Description	
E85.3	Secondary systemic amyloidosis	
E85.4	Organ-limited amyloidosis	
E85.81	Light chain (AL) amyloidosis	
E85.89	Other amyloidosis	
E85.9	Amyloidosis, unspecified	
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: 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): N/A

	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	КҮ, ОН	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 <u>https://ocrportal.hhs.gov/ocr/portal/lobby.jsf</u>, 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 ban nói Tiếng Việt, có các dịch vụ hỗ trợ ngôn ngữ miễn phí dành cho ban. Goi 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). ໂປດຊາບ: ຖ້າວ່າ ທ່ານເວົ້າພາສາ ລາວ, ການບໍລິການຊ່ວຍເຫຼືອດ້ານພາສາ, ໂດຍບໍ່ເສັຽຄ່າ, ແມ່ນມີພ້ອມໃຫ້ທ່ານ. ໂທຣ 1.800.940.5049 (TTY: 763.847.4013). ማስታወሻ: የሚናንሩት ቋንቋ አማርኛ ከሆነ የትርጉም እርዳታ ድርጅቶች፣ በነጻ ሊያግዝዎት ተዘጋጀተዋል፡ ወደ ሚከተለው ቁጥር ይደውሉ 1.800.940.5049 (መስጣት ለተሳናቸው: 763 847 4013). ဟ်သူဉ်ဟ်သး– နမ့်၊ကတိ၊ ကညီ ကျိဉ်အယိ, နမၤန္ခ၊ ကျိဉ်အတါမၢစၢးလ၊ တလက်ဘူဉ်လက်စ္၊ နီတမံးဘဉ်သူနှဉ်လီး. 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 ដោយមិនកិតឈូល 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 1.800.940.504 (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 <u>https://ocrportal.hhs.gov/ocr/portal/lobby.jsf</u>, 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 ban nói Tiếng Việt, có các dịch vụ hỗ trợ ngôn ngữ miễn phí dành cho ban. Goi 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). ໂປດຊາບ: ຖ້າວ່າ ທ່ານເວົ້າພາສາ ລາວ, ການບໍລິການຊ່ວຍເຫຼືອດ້ານພາສາ, ໂດຍບໍ່ເສັຽຄ່າ, ແມ່ນມີພ້ອມໃຫ້ທ່ານ. ໂທຣ 1.800.940.5049 (TTY: 763.847.4013). ማስታወሻ: የሚናንሩት ቋንቋ አማርኛ ከሆነ የትርጉም እርዳታ ድርጅቶች፣ በነጻ ሊያግዝዎት ተዘጋጀተዋል፡ ወደ ሚከተለው ቁጥር ይደውሉ 1.800.940.5049 (መስጣት ለተሳናቸው: 763 847 4013). ဟ်သူဉ်ဟ်သး– နမ့်၊ကတိ၊ ကညီ ကျိဉ်အယိ, နမၤန္ခ၊ ကျိဉ်အတါမၢစၢးလ၊ တလက်ဘူဉ်လက်စ္၊ နီတမံးဘဉ်သူနှဉ်လီး. 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 ដោយមិនកិតឈូល 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 1.800.940.504 (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).