Kyprolis® (carfilzomib)
(Intravenous)

Document Number: IC-0157

Last Review Date: 05/05/2026
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, 06/2023, 09/2023, 12/2023, 03/2024, 05/2024, 05/2025, 05/2026

I. Length of Authorization [1,5,21,32,36,43]

- Initial: Prior authorization validity will be provided initially for 6 months (180 days).
- Renewal: Prior authorization validity may be renewed every 6 months (180 days) thereafter, unless otherwise specified.
  - Prior authorization validity may be renewed for up to a maximum of 32 weeks (8 cycles) of therapy for the following:
    - ❖ Primary therapy in Multiple Myeloma for transplant candidates in combination with daratumumab/daratumumab and hyaluronidase, lenalidomide, and dexamethasone.
  - Prior authorization validity may be renewed for up to a maximum of 40 weeks (10 cycles) of therapy for the following:
    - ❖ Primary therapy in Multiple Myeloma for transplant candidates in combination with isatuximab, lenalidomide, and dexamethasone.
  - Prior authorization validity may be renewed for up to a maximum of 104 weeks (26 cycles) of therapy for the following:
    - ❖ Maintenance therapy in Multiple Myeloma for transplant candidates in combination with isatuximab and lenalidomide.
  - Prior authorization validity may be renewed for up to a maximum of 2 years of therapy for the following:
    - ❖ Maintenance therapy in Multiple Myeloma for transplant candidates in combination with lenalidomide.
  - Prior authorization validity may be renewed for up to a maximum of 64 weeks (8 cycles) of therapy for the following:
    - ❖ Maintenance therapy in Waldenström Macroglobulinemia/Lymphoplasmacytic Lymphoma in combination with rituximab and dexamethasone (CaRD regimen).

II. Dosing Limits

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

- **Multiple Myeloma**

© 2026 Prime Therapeutics Management, LLC
Proprietary & Confidential.

- 720 billable units (720 mg) every 28 days
- **Systemic Light Chain Amyloidosis**
  - 480 billable units (480 mg) every 28 days
- **Waldenström Macroglobulinemia/Lymphoplasmacytic Lymphoma**
  - 320 billable units (320 mg) every 21 days

III. Initial Approval Criteria [1]

Prior authorization validity is provided in the following conditions:

- Member is at least 18 years of age; **AND**

Multiple Myeloma* † ‡ Φ [1,2,7,9-11,13-17,19,20,22-29,32-37,39]

- Used as primary therapy for symptomatic disease; **AND**
  - Used in combination with daratumumab/daratumumab and hyaluronidase, lenalidomide, and dexamethasone *(transplant candidates ONLY);* **OR**
  - Used in combination with isatuximab, lenalidomide, and dexamethasone *(transplant candidates ONLY);* **OR**
  - 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**
  - Used in combination with lenalidomide and dexamethasone; **OR**
  - Used in combination with dexamethasone and cyclophosphamide; **OR**
- Used for relapsed or refractory disease after 3 prior lines of therapy; **AND**
  - Used in combination with bendamustine and dexamethasone; **OR**
- Used for previously treated relapsed, progressive, or refractory disease; **AND**
  - Used as a single agent **†**; **OR**
  - Used in combination with one of the following regimens:
    - Dexamethasone with or without lenalidomide **†**
    - Dexamethasone and daratumumab/daratumumab and hyaluronidase **†**
    - Dexamethasone and cyclophosphamide with or without thalidomide
    - Dexamethasone and isatuximab **†**
    - Dexamethasone and selinexor
    - Dexamethasone and pomalidomide with or without daratumumab/daratumumab and hyaluronidase
    - Dexamethasone and venetoclax (*members with t(11:14) ONLY*); **OR**
- Used as maintenance therapy for symptomatic disease in transplant candidates; **AND**

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

©2026 Prime Therapeutics Management, LLC

- 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 members; **OR**
- Used in combination with lenalidomide and isatuximab following primary therapy with isatuximab, lenalidomide, and dexamethasone; **OR**

- Used for the management of POEMS (polyneuropathy, organomegaly, endocrinopathy, monoclonal protein, skin changes) syndrome; **AND**
  - Used in combination with dexamethasone as a replacement for bortezomib

***The regimens listed for the treatment of Multiple Myeloma may also be used for the treatment of Polyneuropathy, Organomegaly, Endocrinopathy, Monoclonal protein, Skin changes (POEMS), Monoclonal Immunoglobulin Deposition Disease (MIDD), and plasma cell-related Monoclonal Gammopathy of Renal Significance (MGRS)*

Waldenström Macroglobulinemia/Lymphoplasmacytic Lymphoma ‡ [2,5,18,21]

- Used in combination with rituximab and dexamethasone (CaRD regimen); **AND**
  - Used as primary therapy; **OR**
  - Used for relapsed disease; **AND**
    - CaRD regimen was previously used as primary therapy; **AND**
    - Member had a prolonged response (i.e., 24 months) to CaRD therapy

Systemic Light Chain Amyloidosis ‡ [2,30,31,38]

- Member has newly diagnosed disease; **AND**
  - Used in combination with dexamethasone; **AND**
  - Member has significant neuropathy; **OR**
- Member has relapsed or refractory disease; **AND**
  - Member has non-cardiac disease; **AND**
    - Used as a single agent; **OR**
    - Used in combination with dexamethasone; **OR**
  - Member has significant neuropathy; **AND**
    - Used as repeat of initial therapy if relapse-free for several years; **AND**
    - Used in combination with dexamethasone

† FDA Approved Indication(s); ‡ Compendia Recommended Indication(s); Φ Orphan Drug

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

©2026 Prime Therapeutics Management, LLC

IV. Renewal Criteria [1,2]

Prior authorization validity can be renewed based upon the following criteria:

- Member 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**
- Duration of authorization has not been exceeded *(refer to Section I)*; **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.

V. Dosage/Administration [1,5,7,9,12,20-22,24-28,30,32-36,38-43]

Indication	Dose*
Multiple Myeloma (primary therapy OR disease relapse ≥6 months following primary induction therapy with the same regimen)	<u>Combination with lenalidomide and dexamethasone (KRd)</u> <u>20/36 regimen:</u> – Cycle 1: 20 mg/m^2 on days 1 and 2; if tolerated, increase to 36 mg/m^2 days 8, 9, 15, and 16 of a 28-day treatment cycle – Cycles 2 through 8: 36 mg/m^2 days 1, 2, 8, 9, 15, and 16 of a 28-day treatment cycle *May proceed to maintenance therapy in combination with lenalidomide for up to 2 years (see maintenance dosing section in table below).* <u>Combination with cyclophosphamide and dexamethasone (KCd)</u> <u>20/36 regimen:</u> – Cycle 1: 20 mg/m^2 on days 1 and 2; if tolerated, increase to 36 mg/m^2 days 8, 9, 15, and 16 of a 28-day treatment cycle – Cycles 2 through 9: 36 mg/m^2 days 1, 2, 8, 9, 15, and 16 of a 28-day treatment cycle – Cycle 10 and beyond: 36 mg/m^2 on days 1, 2, 15, and 16 of a 28-day treatment cycle; continue until disease progression or unacceptable toxicity <u>20/70 regimen:</u> – Cycle 1: 20 mg/m^2 on day 1; if tolerated, increase to 70 mg/m^2 days 8 and 15 of a 28-day treatment cycle – Cycles 2 through 9: 70 mg/m^2 days 1, 8, and 15 of a 28-day treatment cycle – Cycle 10 and beyond: 70 mg/m^2 on days 1 and 15 of a 28-day treatment cycle; continue

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

©2026 Prime Therapeutics Management, LLC

	until disease progression or unacceptable toxicity
Multiple Myeloma (primary therapy-transplant candidates only)	Combination with daratumumab/daratumumab and hyaluronidase, lenalidomide and dexamethasone (Dara-KRd) 20/56 regimen: – Cycle 1: 20 mg/m^2 on day 1; if tolerated, increase to 56 mg/m^2 on days 8 and 15 of a 28-day treatment cycle – Cycles 2 through 8: 56 mg/m^2 on days 1, 8, and 15 of a 28-day treatment cycle Combination with isatuximab, lenalidomide, and dexamethasone (Isa-KRd) 20/56 regimen: – Cycle 1: 20 mg/m^2 on day 1; if tolerated, increase to 56 mg/m^2 on days 8 and 15 of a 28-day treatment cycle – Cycles 2 through 10: 56 mg/m^2 on days 1, 8, and 15 of a 28-day treatment cycle *May proceed to maintenance therapy in combination with isatuximab and lenalidomide for up to 26 maintenance cycles (see maintenance dosing section in table below)*
Multiple Myeloma (relapsed, progressive, or refractory disease)	Single agent 20/27 regimen: – Cycle 1: 20 mg/m^2 on days 1 and 2; if tolerated, increase to 27 mg/m^2 on days 8, 9, 15, and 16 of a 28-day treatment cycle – Cycles 2 through 12: 27 mg/m^2 on days 1, 2, 8, 9, 15, and 16 of a 28-day treatment cycle – Cycle 13 and beyond: 27 mg/m^2 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/m^2 on days 1 and 2; if tolerated, increase to 56 mg/m^2 on days 8, 9, 15, and 16 of a 28-day treatment cycle. – Cycles 2 through 12: 56 mg/m^2 on days 1, 2, 8, 9, 15, and 16 of a 28-day treatment cycle – Cycle 13 and beyond: 56 mg/m^2 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/m^2 on days 1 and 2; if tolerated, increase to 27 mg/m^2 on days 8, 9, 15, and 16 of a 28-day treatment cycle – Cycles 2 through 12: 27 mg/m^2 on days 1, 2, 8, 9, 15, and 16 of a 28-day treatment cycle – Cycles 13 through 18: 27 mg/m^2 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 Combination with dexamethasone (Kd) 20/56 regimen: – Cycle 1: 20 mg/m^2 on days 1 and 2; if tolerated, increase to 56 mg/m^2 on days 8, 9, 15,

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

©2026 Prime Therapeutics Management, LLC

	and 16 of a 28-day treatment cycle – Cycle 2 and beyond: 56 mg/m^2 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 2 and beyond: 70 mg/m^2 on days 1, 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/m^2 on days 1 and 2; if tolerated, increase to 56 mg/m^2 on days 8, 9, 15 and 16 of a 28-day treatment cycle – Cycle 2 and beyond: 56 mg/m^2 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 2 and beyond: 70 mg/m^2 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/m^2 on days 1 and 2; if tolerated, increase to 36 mg/m^2 days 8, 9, 15, and 16 of a 28-day treatment cycle – Cycle 2 and beyond: 36 mg/m^2 days 1, 2, 8, 9, 15, and 16 of a 28-day treatment cycle; continue until disease progression or unacceptable toxicity Combination with cyclophosphamide and dexamethasone (KCd) 20/36 regimen: Induction – Cycle 1: 20 mg/m^2 on days 1 and 2; if tolerated, increase to 36 mg/m^2 days 8, 9, 15, and 16 of a 28-day treatment cycle – Cycles 2 through 6: 36 mg/m^2 days 1, 2, 8, 9, 15, and 16 of a 28-day treatment cycle Maintenance – Cycles 7 through 12: 36 mg/m^2 on days 1, 2, 15, and 16 of a 28-day treatment cycle – Cycle 13 and beyond: 36 mg/m^2 on days 1 and 2 of a 28-day treatment cycle; continue until disease progression or unacceptable toxicity Combination with isatuximab-irfc and dexamethasone (Isa-Kd) 20/56 regimen: – Cycle 1: 20 mg/m^2 on days 1 and 2; if tolerated, increase to 56 mg/m^2 on days 8, 9, 15 and 16 of a 28-day treatment cycle – Cycle 2 and beyond: 56 mg/m^2 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 (XKd)

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

©2026 Prime Therapeutics Management, LLC

	20/56 regimen: – Cycle 1: 20 mg/m^2 on day 1; if tolerated, increase to 56 mg/m^2 on days 8 and 15 of a 28-day treatment cycle – Cycle 2 and beyond: 56 mg/m^2 on days 1, 8, and 15 of a 28-day treatment cycle; continue until disease progression or unacceptable toxicity Combination with pomalidomide and dexamethasone (KPd) 20/27 regimen: – Cycle 1: 20 mg/m^2 on days 1 and 2; if tolerated, increase to 27 mg/m^2 on days 8, 9, 15, and 16 of a 28-day treatment cycle – Cycles 2 through 6: 27 mg/m^2 on days 1, 2, 8, 9, 15, and 16 of a 28-day treatment cycle – Cycle 7 and beyond: 27 mg/m^2 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/m^2 on days 1, 2, 8, 9, 15, and 16 of a 28-day treatment cycle 20/36 regimen: – Cycle 1: 20 mg/m^2 on days 1 and 2; if tolerated, increase to 36 mg/m^2 days 8, 9, 15, and 16 of a 28-day treatment cycle – Cycles 2 through 8: 36 mg/m^2 days 1, 2, 8, 9, 15, and 16 of a 28-day treatment cycle – Cycle 9 and beyond: 36 mg/m^2 days 1, 2, 15, and 16 of a 28-day treatment cycle; continue until disease progression or unacceptable toxicity Combination with pomalidomide, daratumumab/daratumumab and hyaluronidase, and dexamethasone: 20/27 regimen: – Cycle 1: 20 mg/m^2 on days 1 and 2; if tolerated, increase to 27 mg/m^2 on days 8, 9, 15, and 16 of a 28-day treatment cycle – Cycles 2 through 8: 27 mg/m^2 on days 1, 2, 8, 9, 15, and 16 of a 28-day treatment cycle – Cycle 9 and beyond: 27 mg/m^2 on days 1, 2, 15, and 16 of a 28-day treatment cycle; continue until disease progression or unacceptable toxicity Combination with venetoclax and dexamethasone 20/27 regimen: – Cycle 1: 20 mg/m^2 on days 1 and 2; if tolerated, increase to 27 mg/m^2 on days 8, 9, 15, and 16 of a 28-day treatment cycle – Cycles 2 through 12: 27 mg/m^2 on days 1, 2, 8, 9, 15, and 16 of a 28-day treatment cycle – Cycle 13 and beyond: 27 mg/m^2 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/m^2 on days 1 and 2; if tolerated, increase to 56 mg/m^2 on days 8, 9, 15, and 16 of a 28-day treatment cycle – Cycle 2 and beyond: 56 mg/m^2 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:

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

©2026 Prime Therapeutics Management, LLC

	– 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 2 and beyond: 70 mg/m^2 on days 1, 8, and 15 of a 28-day treatment cycle; continue until disease progression or unacceptable toxicity
Multiple Myeloma (relapsed or refractory disease after 3 prior therapies)	<u>Combination with bendamustine and dexamethasone</u> <u>20/27 regimen:</u> – Cycle 1: 20 mg/m^2 on days 1 and 2; if tolerated, increase to 27 mg/m^2 on days 8, 9, 15, and 16 of a 28-day treatment cycle – Cycles 2 through 8: 27 mg/m^2 on days 1, 2, 8, 9, 15, and 16 of a 28-day treatment cycle – Cycle 9 and beyond: 27 mg/m^2 on days 1, 2, 15, and 16 of a 28-day treatment cycle; continue until disease progression or unacceptable toxicity
Multiple Myeloma (maintenance therapy for symptomatic disease in transplant candidates)	<u>Combination with lenalidomide</u> – 36 mg/m^2 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 <u>Combination with lenalidomide and isatuximab (Isa-KR)</u> – 56 mg/m^2 days 1 and 15 of a 28-day treatment cycle for up to 26 cycles
Multiple Myeloma (management of POEMS)	<u>Combination with dexamethasone (Kd)</u> <u>20/56 regimen:</u> – Cycle 1: 20 mg/m^2 on days 1 and 2; if tolerated, increase to 56 mg/m^2 on days 8, 9, 15, and 16 of a 28-day treatment cycle – Cycle 2 and beyond: 56 mg/m^2 on days 1, 2, 8, 9, 15, and 16 of a 28-day treatment cycle; continue until disease progression or unacceptable toxicity <u>20/70 regimen:</u> – 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 2 and beyond: 70 mg/m^2 on days 1, 8, and 15 of a 28-day treatment cycle; continue until disease progression or unacceptable toxicity
Waldenström Macroglobulinemia/ Lymphoplasmacytic Lymphoma	<u>CaRD regimen (carfilzomib, rituximab, dexamethasone)</u> Induction – Cycle 1: 20 mg/m^2 on days 1, 2, 8 and 9 of a 21-day treatment cycle – Cycles 2 through 6: 36 mg/m^2 on days 1, 2, 8 and 9 of a 21-day treatment cycle; begin maintenance 8 weeks later Maintenance – 36 mg/m^2 on days 1 and 2 every 8 weeks for 8 cycles
Systemic Light Chain Amyloidosis	<u>Single agent or combination with dexamethasone</u> <u>20/27/56 regimen:</u> – Cycle 1: 20 mg/m^2 on day 1; if tolerated, increase to 27 mg/m^2 days 8 and 15 of a 28-day treatment cycle – Cycle 2 and beyond: up to 56 mg/m^2 days 1, 8, and 15 of a 28-day treatment cycle <u>20/36 regimen:</u>

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

©2026 Prime Therapeutics Management, LLC

	– Cycle 1: 20 mg/m^2 on days 1 and 2; if tolerated, increase to 36 mg/m^2 days 8, 9, 15, 16 of a 28-day treatment cycle – Cycles 2 through 8: 36 mg/m^2 days 1, 2, 8, 9, 15, and 16 of a 28-day treatment cycle – Cycles 9 and beyond: 36mg/m^2 days 1, 2, 15, and 16 of a 28-day treatment cycle
***Note**: For members with body surface area (BSA) of 2.2 m^2 or less, calculate the Kyprolis dose using actual BSA. Dose adjustments do not need to be made for weight changes of 20% or less. For members with a BSA greater than 2.2 m^2, calculate the Kyprolis dose using a BSA of 2.2 m^2.*	

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 2025. Accessed March 2026.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for Carfilzomib. National Comprehensive Cancer Network, 2026. 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 March 2026.
3. 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. 2006 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 270.0, 2024 Accessed March 2026.
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 patients with relapsed/refractory multiple myeloma. Haematologica 2015; 100: 670-676.

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

©2026 Prime Therapeutics Management, LLC

9. 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.
11. 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.
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 2.2026. National Comprehensive Cancer Network, 2026. 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 March 2026.
19. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Multiple Myeloma, Version 5.2026. National Comprehensive Cancer Network, 2026. 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 April 2026.

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

©2026 Prime Therapeutics Management, LLC

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 2.2026. National Comprehensive

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

©2026 Prime Therapeutics Management, LLC

Cancer Network, 2026. 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 March 2026.

32. Landgren 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.
38. Cohen AD, Landau H, Scott EC, et al. Safety and efficacy of carfilzomib (CFZ) in previously-treated systemic light-chain (AL) amyloidosis. Blood 2016;128:645-645. Doi: 10.1182/blood.V128.22.645.645.
39. Costa LJ, Davies FE, Monohan GP, et al. Phase 2 study of venetoclax plus carfilzomib and dexamethasone in patients with relapsed/refractory multiple myeloma. Blood Adv. 2021 Oct 12;5(19):3748-3759. doi: 10.1182/bloodadvances.2020004146.
40. Jasielec JK, Kubicki T, Raje N, et al. Carfilzomib, lenalidomide, and dexamethasone plus transplant in newly diagnosed multiple myeloma. Blood 2020;136:2513-2523.
41. Yong KL, Hinsley S, Auner HW, et al. Carfilzomib or bortezomib in combination with cyclophosphamide and dexamethasone followed by carfilzomib maintenance for patients with multiple myeloma after one prior therapy: results from a multicenter, phase II, randomized, controlled trial (MUK*five*). Haematologica. 2021 Oct 1;106(10):2694-2706. doi: 10.3324/haematol.2021.278399.

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

©2026 Prime Therapeutics Management, LLC

42. Derman BA, Zonder J, Reece D, et al. Phase 1/2 study of carfilzomib, pomalidomide, and dexamethasone with and without daratumumab in relapsed multiple myeloma. Blood Adv. 2023 Oct 10;7(19):5703-5712. doi: 10.1182/bloodadvances.2022008866.
43. Leypoldt LB, Tichy D, Besemer B, et al. Isatuximab, Carfilzomib, Lenalidomide, and Dexamethasone for the Treatment of High-Risk Newly Diagnosed Multiple Myeloma. *J Clin Oncol*. 2024;42(1):26-37.

Appendix A – Non-Quantitative Treatment Limitations (NQTL) Factor Checklist

Non-quantitative treatment limitations (NQTLs) refer to the methods, guidelines, standards of evidence, or other conditions that can restrict how long or to what extent benefits are provided under a health plan. These may include things like utilization review or prior authorization. The utilization management NQTL applies comparably, and not more stringently, to mental health/substance use disorder (MH/SUD) Medical Benefit Prescription Drugs and medical/surgical (M/S) Medical Benefit Prescription Drugs. The table below lists the factors that were considered in designing and applying prior authorization to this drug/drug group, and a summary of the conclusions that Prime's assessment led to for each.

Factor	Conclusion
Indication	Yes: Consider for PA
Safety and efficacy	No: PA not a priority
Potential for misuse/abuse	No: PA not a priority
Cost of drug	Yes: Consider for PA

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C88.0	Waldenström macroglobulinemia
C90.00	Multiple myeloma not having achieved remission
C90.01	Multiple myeloma in remission
C90.02	Multiple myeloma in relapse
C90.10	Plasma cell leukemia not having achieved remission
C90.11	Plasma cell leukemia in remission
C90.12	Plasma cell leukemia in relapse
C90.20	Extramedullary plasmacytoma not having achieved remission
C90.21	Extramedullary plasmacytoma in remission
C90.22	Extramedullary plasmacytoma in relapse
C90.30	Solitary plasmacytoma not having achieved remission
C90.31	Solitary plasmacytoma in remission
C90.32	Solitary plasmacytoma in relapse
D47.9	Neoplasm of uncertain behavior of lymphoid, hematopoietic and related tissue, unspecified
D47.Z9	Other specified neoplasms of uncertain behavior of lymphoid, hematopoietic and related tissue

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

©2026 Prime Therapeutics Management, LLC

ICD-10	ICD-10 Description
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
G90.9	Disorder of the autonomic nervous system, unspecified
L98.9	Disorder of the skin and subcutaneous tissue, unspecified
Z85.79	Personal history of other malignant neoplasms of lymphoid, hematopoietic and related tissues

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

The preceding information is intended for non-Medicare coverage determinations. 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 Determinations (NCDs) and/or Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. Local Coverage Articles (LCAs) may also exist for claims payment purposes or to clarify benefit eligibility under Part B for drugs which may be self-administered. The following link may be used to search for NCD, LCD, or LCA documents: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications, including any preceding information, may be applied 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
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC

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

©2026 Prime Therapeutics Management, LLC

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

©2026 Prime Therapeutics Management, LLC