Kyprolis® (carfilzomib)
(Intravenous)

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I. Length of Authorization [1,5,21,27,32,36]

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

Multiple Myeloma

- Combination therapy with lenalidomide and dexamethasone is limited to eighteen (18) 28-day 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**
  - 720 billable units (720 mg) every 28 days
- **Systemic Light Chain Amyloidosis**
  - 480 billable units (480 mg) every 28 days

- **Waldenström's Macroglobulinemia/Lymphoplasmacytic Lymphoma**
  - 320 billable units (320 mg) every 21 days

III. Initial Approval Criteria [1]

Coverage is provided in the following conditions:

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

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

- Used as primary therapy for symptomatic disease; **AND**
  - Used in combination with daratumumab, 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 late relapse or progressive disease (>3 prior therapies); **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 †
    - 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 ‡ [2,5,18,21]

- 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**
    - Patient had a prolonged response (i.e., 24 months) to CaRD therapy

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

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

† FDA Approved Indication(s); ‡ Compendia Approved Indication(s); Φ 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 [1,5,7,9,12,20-22,24-28,30,32-36,38]

Indication	Dose*
Multiple Myeloma (primary therapy OR disease relapse ≥6 months following primary induction therapy with the same regimen)	<u>Combination with daratumumab, lenalidomide and dexamethasone (Dara-KRd)</u> 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 <u>Combination with lenalidomide and dexamethasone (KRd)</u> 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 <u>Combination with cyclophosphamide and dexamethasone (KCd)</u> 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 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 – Cycles 2 through 9: 70 mg/m² days 1, 8, and 15 of a 28-day treatment cycle – Cycle 10 and beyond: 70 mg/m² on days 1 and 15 of a 28-day treatment cycle; continue until disease progression or unacceptable toxicity
Multiple Myeloma (relapsed, progressive, or refractory disease)	<u>Single agent</u> 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 Combination with dexamethasone (Kd) 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 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 Combination with cyclophosphamide and dexamethasone (KCd) 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 Combination with isatuximab-irfc and dexamethasone (Isa-Kd)

	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 <u>Combination with selinexor and dexamethasone (XKd)</u> 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 <u>Combination with pomalidomide and dexamethasone(KPd)</u> 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 (late relapse or progressive disease)	<u>Combination with bendamustine and dexamethasone</u> 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 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 (maintenance therapy)	<u>Combination with lenalidomide</u> – 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 Macroglobulinemia/ Lymphoplasmacytic Lymphoma	<u>CaRD regimen (carfilzomib, rituximab, dexamethasone)</u> Induction – 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/m² 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/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 <u>20/36 regimen</u>

	– Cycle 1: 20 mg/m² on days 1 and 2; if tolerated, increase to 36 mg/m² days 8, 9, 15, 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 and beyond: 36mg/m² days 1, 2, 15, and 16 of a 28-day treatment cycle
***Note**: For patients with body surface area (BSA) of 2.2 m² 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 patients with a BSA greater than 2.2 m², calculate the Kyprolis dose using a BSA of 2.2 m².*	

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

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Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C88.0	Waldenström macroglobulinemia

ICD-10	ICD-10 Description
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
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)

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
15	KY, OH	CGS Administrators, LLC