Kyprolis® (carfilzomib)
(Intravenous)

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I. Length of Authorization [1,5,12,21,27]

Coverage will be provided for 6 months and may be renewed.

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.

Waldenström Macroglobulinemia/Lymphoplasmacytic Lymphoma

- Treatment is limited to six (6) 21-day induction therapy treatment cycles and eight (8) 56-day maintenance therapy 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 every 28 days
- **Waldenström Macroglobulinemia/Lymphoplasmacytic Lymphoma**
  - 320 billable units 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 [1,2,10,11,13-17,19,23,32,2e,4e,8e,10e,34e,37e-39e]

- 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 previously treated relapsed, progressive, or refractory disease; **AND**
    - Used as a single agent **†**; **OR**
    - Used in combination with dexamethasone with or without lenalidomide **†**; **OR**
    - Used in combination with dexamethasone and daratumumab **†**; **OR**
    - Used in combination with dexamethasone and daratumumab and hyaluronidase-fihj **†**; **OR**
    - Used in combination with dexamethasone and cyclophosphamide; **OR**
    - Used in combination with dexamethasone and isatuximab-irfc; **OR**
    - Used in combination with dexamethasone and selinexor; **OR**
    - Used in combination with pomalidomide and dexamethasone; **AND**
        - Patient has received at least two (2) prior therapies, including a proteasome inhibitor (i.e., bortezomib, etc.) and an immunomodulatory agent (i.e., lenalidomide, thalidomide, etc.); **AND**
        - Disease has progressed on or within 60 days of completion of the last therapy

Waldenström Macroglobulinemia/Lymphoplasmacytic Lymphoma ‡ [2,5,18,27e-31e,33e,43e]

- Used in combination with rituximab and dexamethasone (CaRD regimen); **AND**
    - Used as primary therapy

Preferred therapies and recommendations are determined by review of clinical evidence. NCCN category of recommendation is taken into account as a component of this review. Regimens deemed equally efficacious (i.e., those having the same NCCN categorization) are considered to be therapeutically equivalent.

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

IV. Renewal Criteria [1,2,6]

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 (including CHF, pulmonary edema, decreased ejection fraction), pulmonary toxicity (including acute respiratory distress syndrome (ARDS), acute respiratory failure), pulmonary hypertension, dyspnea, severe infusion related reactions, tumor lysis syndrome (TLS), thrombocytopenia, hepatic toxicity/failure, thrombotic microangiopathy (including thrombotic thrombocytopenic purpura/hemolytic uremic syndrome [TTP/HUS]), acute renal failure, severe hypertension, posterior reversible encephalopathy syndrome (PRES), venous thromboembolic events (including deep venous thrombosis, pulmonary embolism), hemorrhage, progressive multifocal leukoencephalopathy (PML), etc.; **AND**

Multiple Myeloma [1,12,27]

- 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.

Waldenström Macroglobulinemia/Lymphoplasmacytic Lymphoma [5,21]

- May be renewed up to a maximum of six (6) 21-day induction therapy treatment cycles and eight (8) 56-day maintenance therapy treatment cycles.

V. Dosage/Administration [1,5,7,9,12,20-22,24-30,32-34]

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 (20/56 regimen)</u> – 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 <u>Combination with lenalidomide and dexamethasone (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 – Cycles 9 through 18: 36 mg/m^2 days 1, 2, 15, and 16 of a 28-day treatment cycle <u>Combination with cyclophosphamide and dexamethasone</u>

	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 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 20/70 regimen: – 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 until disease progression or unacceptable toxicity
Multiple Myeloma (relapsed, progressive, or refractory disease)	<u>Single agent</u> 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 <u>Combination with lenalidomide and dexamethasone (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 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 <u>Combination with dexamethasone</u> 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 <u>Combination with daratumumab (or daratumumab and hyaluronidase-fihj) and dexamethasone</u> 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 and dexamethasone (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 (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 (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 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
Waldenström Macroglobulinemia/ Lymphoplasmacytic Lymphoma	CaRD regimen (carfilzomib, rituximab, dexamethasone) 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; 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	Single agent or combination with dexamethasone – 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 – Cycles 2 and beyond: Up to 56 mg/m^2 days 1, 8, and 15 of a 28-day treatment cycle
Note: Calculate the Kyprolis dose using the patient's actual body surface area at baseline. In patients with a body surface area greater than 2.2 m^2, calculate the dose based upon a body surface area 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 (STANDARD)

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Appendix 1 – Covered Diagnosis Codes

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
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.

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC