Kyprolis® (carfilzomib)
(Intravenous)

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I. Length of Authorization [1,5,12,22,23]

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

* *Combination therapy with lenalidomide and dexamethasone as subsequent treatment in multiple myeloma is limited to eighteen (18) 28-day treatment cycles.*
* *Combination therapy with cyclophosphamide, thalidomide, and dexamethasone as subsequent treatment in multiple myeloma is limited to twelve (12) 28-day treatment cycles.*
* *Treatment of Waldenström's Macroglobulinemia/ Lymphoplasmacytic Lymphoma 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 30 mg powder for injection: 1 vial per 28 day supply
- Kyprolis 60 mg powder for injection: 12 vials per 28 day supply

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

- **Multiple Myeloma**
  - 720 billable units every 28 days
- **Waldenström's 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 [1-3,6-17,19,22]

- Used as primary therapy or for disease relapse after 6 months following primary induction therapy with the same regimen in patients with active (symptomatic) disease; **AND**
    - Used in combination with lenalidomide and dexamethasone; **OR**
    - Used in combination with dexamethasone and cyclophosphamide; **OR**
- Used for previously treated myeloma for disease relapse or for 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 cyclophosphamide with or without thalidomide; **OR**
    - Used in combination with panobinostat; **AND**
        - Patient has received at least 2 prior regimens, including bortezomib and an immunomodulatory agent [i.e., lenalidomide, thalidomide, etc.]; **OR**
    - Used in combination with pomalidomide and dexamethasone; **AND**
        - Patient has received at least 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'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 achieved a response from CaRD that lasted for at least 24 months

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

IV. Renewal Criteria[1,2,6]

Coverage can be renewed based upon the following criteria:

- Patient continues to meet 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, pulmonary toxicity, 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, hemorrhage, progressive multifocal leukoencephalopathy (PML), etc.

V. Dosage/Administration[1,5,7-9,11,12,20,21,22]

Indication	Dose
Multiple Myeloma	20/27 regimen (*single agent*): – 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 (*single agent*): – 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 20/27 regimen (*combination with lenalidomide and dexamethasone*): – 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 to 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 20/27 regimen (*combination with pomalidomide and dexamethasone*): – 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; continue until disease progression or unacceptable toxicity – 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 (*combination with pomalidomide and dexamethasone*): – 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 20/45 regimen (*combination with panobinostat):* – Cycle 1: 20 mg/m² on days 1 and 2; if tolerated, increase to 45 mg/m² on days 8, 9, 15, and 16 of a 28-day treatment cycle – Cycle 2 and beyond: 45 mg/m² on days 1, 2, 8, 9, 15, and 16 of a 28-day treatment cycle; continue until disease progression or unacceptable toxicity 20/56 regimen (*combination with dexamethasone*): – 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 (*combination with dexamethasone*): – 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 20/36 regimen for **NEWLY DIAGNOSED** disease (*combination with cyclophosphamide and dexamethasone*): – 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 20/36 regimen for **RELAPSED/REFRACTORY** disease (*combination with cyclophosphamide and dexamethasone*): • 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 – Cycles 13 and beyond: 36 mg/m² on days 1 and 2 of a 28-day treatment cycle; continue until disease progression or unacceptable toxicity 20/56 regimen (*combination with daratumumab and dexamethasone):* – 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 (*combination with daratumumab and dexamethasone):* – 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 *20/36 regimen (combination with cyclophosphamide, thalidomide, and dexamethasone):* – 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 4: 36 mg/m² days 1, 2, 8, 9, 15, and 16 of a 28-day treatment cycle – Patients who achieve stable disease or better may continue treatment for up to 8 additional cycles
Waldenström's Macroglobulinemia/ Lymphoplasmacytic Lymphoma	CaRD regimen (carfilzomib, rituximab, dexamethasone) • 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
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 m², calculate the dose based upon a body surface area of 2.2 m².	

VI. Billing Code/Availability Information

HCPCS code:

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

NDC:

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

VII. References

1. Kyprolis [package insert]. Thousand Oaks, CA; Onyx Pharmaceuticals Inc; August 2020. Accessed August 2020.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for Carfilzomib. National Comprehensive Cancer Network, 2020. 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 July 2020.
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19. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Multiple Myeloma Version 4.2020. National Comprehensive Cancer Network, 2020. 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 July 2020.
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Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C83.00	Small cell B-cell lymphoma, unspecified site
C83.01	Small cell B-cell lymphoma, lymph nodes of head, face and neck
C83.02	Small cell B-cell lymphoma, intrathoracic lymph nodes
C83.03	Small cell B-cell lymphoma, intra-abdominal lymph nodes
C83.04	Small cell B-cell lymphoma, lymph nodes of axilla and upper limb
C83.05	Small cell B-cell lymphoma, lymph nodes of inguinal region and lower limb
C83.06	Small cell B-cell lymphoma, intrapelvic lymph nodes
C83.07	Small cell B-cell lymphoma, spleen
C83.08	Small cell B-cell lymphoma, lymph nodes of multiple sites
C83.09	Small cell B-cell lymphoma, extranodal and solid organ sites
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
Z85.72	Personal history of non-Hodgkin lymphomas
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: http://www.cms.gov/medicare-coverage-database/search/advanced-search.aspx. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA):

Jurisdiction(s): J & M	**NCD/LCD/Article Document (s):** A56141
https://www.cms.gov/medicare-coverage-database/search/article-date-search.aspx?DocID=A56141&bc=gAAAAAAAAAAAAA	

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC