Kyprolis® (carfilzomib)

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I. Length of Authorization

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

II. Dosing Limits

A. Quantity Limit (max daily dose) [Pharmacy Benefit]:

- 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) [Medical Benefit]:

- **Multiple Myeloma**
  - 720 billable units every 28 days
- **Waldenström's Macroglobulinemia/Lymphoplasmacytic Lymphoma**
  - 320 billable units every 21 days

III. Initial Approval Criteria

Coverage is provided in the following conditions:

- Patient is at least 18 years old; **AND**

Multiple Myeloma †

- Used as primary chemotherapy or for disease relapse after 6 months following primary chemotherapy with this same regimen in patients with active (symptomatic) disease; **AND**
  - Used in combination with lenalidomide and dexamethasone; **OR**
  - Used in combination with dexamethasone and cyclophosphamide in NON stem-cell transplant candidates
- Used for previously treated myeloma for disease relapse or for progressive or refractory disease; **AND**
  - Used as a single agent for subsequent therapy †; **OR**
  - In combination with dexamethasone with or without lenalidomide †; **OR**
  - In combinations with dexamethasone and cyclophosphamide; **OR**

- 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**
- In combination with pomalidomide and dexamethasone; **AND**
  - Patient has received at least 2 prior therapies, including a proteasome inhibitor [i.e., bortezomib, carfilzomib, etc] and an immunomodulatory agent [i.e., lenalidomide, thalidomide, etc.]; **AND**
  - Patient has progressed on or within 60 days of completion of the last therapy

Waldenström's Macroglobulinemia/Lymphoplasmacytic Lymphoma ‡

- Must be used in combination with rituximab and dexamethasone (CaRD regimen); **AND**
  - Used as primary therapy; **OR**
  - Used for relapsed disease; **AND**
    - This regimen was used as primary therapy; **AND**
    - Patient achieved a response that lasted for at least 24 months

† FDA Approved Indication(s); ‡ Compendia Approved Indication(s)

IV. Renewal Criteria

Coverage can be renewed based upon the following criteria:

- Patient continues to meet the criteria in section III; **AND**
- Stabilization of disease and/or absence of progression of disease; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include the following: cardiac toxicity, pulmonary toxicity, pulmonary hypertension, dyspnea, infusion reactions, tumor lysis syndrome, thrombocytopenia, hepatic toxicity/failure, thrombotic microangiopathy (TTP/HUS), acute renal failure, severe hypertension, posterior reversible encephalopathy syndrome (PRES), venous thromboembolic events, hemorrhage, etc.

V. Dosage/Administration

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 to 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 to 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 to 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 and beyond: 27 mg/m² on days 1, 2, 8, 9, 15, and 16 of a 28-day treatment cycle. 20/45 regimen (*combination with panobinostat and dexamethasone*): – 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. – Cycles 2 and beyond: 45 mg/m² on days 1, 2, 8, 9, 15, and 16 of a 28-day treatment cycle. 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 to 9: 70 mg/m² on days 1, 8, and 15 of a 28-day treatment cycle; dexamethasone is given on days 1,8, 15 and 22 – Cycle 10 and beyond: 70 mg/m² on days 1, 8, and 15 of a 28-day treatment cycle; dexamethasone is given on days 1, 8 and 15 as well; continue until disease progression or unacceptable toxicity. 20/36 regimen (*combination with cyclophosphamide and dexamethasone*): – Cycle 1: 20 mg/m² on days 1 and 2; 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
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. – Cycle 2-6: 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 m^2, calculate the dose based upon a body surface area of 2.2 m^2.	

VI. Billing Code/Availability Information

Jcode:

- 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; September 2018. Accessed November 2018.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for Carfilzomib. National Comprehensive Cancer Network, 2018. 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 August 2018.
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. 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.
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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.
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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.

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) and Local Coverage Determinations (LCDs) 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): 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	KY, OH	CGS Administrators, LLC