New Century Health

Drug Policy:

Kyprolis™ (carfilzomib)

POLICY NUMBER UM ONC_1224	SUBJECT Kyprolis™ (carfilzomib)		DEPT/PROGRAM UM Dept	PAGE 1 of 4
DATES COMMITTEE REVIEWED 10/03/12, 12/11/13, 03/11/15, 03/27/15, 05/24/16, 03/04/17, 03/14/18, 03/13/19, 12/11/19, 03/11/20, 04/08/20, 08/12/20, 09/09/20, 02/10/21, 04/14/21, 11/15/21, 01/12/22, 03/09/22, 05/11/22, 07/13/22, 11/09/22, 03/08/23, 05/10/23, 08/09/23	APPROVAL DATE August 9, 2023	EFFECTIVE DATE August 25, 2023	COMMITTEE APPROVAL DATES 10/03/12, 12/11/13, 03/11/15, 03/27/15, 05/24/16, 03/04/17, 03/14/18, 03/13/19, 12/11/19, 03/11/20, 04/08/20, 08/12/20, 09/09/20, 02/10/21, 04/14/21, 11/15/21, 01/12/22, 03/09/22, 05/11/22, 07/13/22, 11/09/22, 03/08/23, 05/10/23, 08/09/23	
PRIMARY BUSINESS OWNER: UM		COMMITTEE/BOARD APPROVAL Utilization Management Committee		
NCQA STANDARDS UM 2		ADDITIONAL AREAS OF IMPACT		
CMS REQUIREMENTS	STATE/FEDERAL REQUIREMENTS		APPLICABLE LINES OF BUSINESS Commercial, Exchange, Medicaid	

I. PURPOSE

To define and describe the accepted indications for Kyprolis (carfilzomib) usage in the treatment of cancer, including FDA approved indications, and off-label indications.

New Century Health (NCH) is responsible for processing all medication requests from network ordering providers. Medications not authorized by NCH may be deemed as not approvable and therefore not reimbursable.

The use of this drug must be supported by one of the following: FDA-approved product labeling, CMS-approved compendia, National Comprehensive Cancer Network (NCCN), American Society of Clinical Oncology (ASCO) clinical guidelines, or peer-reviewed literature that meets the requirements of the CMS Medicare Benefit Policy Manual Chapter 15.

II. INDICATIONS FOR USE/INCLUSION CRITERIA

A. Continuation requests for a not-approvable medication shall be exempt from this NCH policy provided:

1. The requested medication was used within the last year, AND
2. The member has not experienced disease progression and/or no intolerance to the requested medication, AND

3. Additional medication(s) are not being added to the continuation request.

B. Multiple Myeloma (MM)

1. NOTE 1: Kyprolis(carfilzomib)-based regimens (e.g., KRd) are not supported by NCH Policyfor newly diagnosed, transplant ineligible multiple myeloma. This policy position is based on the results of the ENDURANCE trial which showed equivalent outcomes and increased cardiotoxicity for Kyprolis (carfilzomib) + Revlimid (lenalidomide) + Dexamethasone, compared to Velcade (bortezomib) + Revlimid (lenalidomide) + Dexamethasone. Please refer to NCH alternative agents/regimens recommended by NCH, including but not limited to regimens available at http://pathways.newcenturyhealth.com.
2. NOTE 2: [Daratumumab + Kyprolis (carfilzomib) + Revlimid (lenalidomide) + Dexamethasone] is not supported by NCH Policy for newly diagnosed, transplant eligible multiple myeloma. This policy position is based on the lack of Level 1 evidence (randomized trials and/or meta-analyses) to show superior outcomes and/or lower toxicities with the above regimen compared to the NCH recommended regimen of [Daratumumab + Velcade (bortezomib) + Revlimid (lenalidomide) + Dexamethasone]. Please refer to NCH alternative agents/regimens recommended by NCH, including but not limited to regimens available at http://pathways.newcenturyhealth.com.
3. For relapsed or refractory disease, Kyprolis (carfilzomib) may be used in ANY ONE of the following:
    a. In combination with dexamethasone
    b. In combination with lenalidomide +/- steroid
    c. In combination with cyclophosphamide +/- steroid
    d. In combination with daratumumab +/- steroid
    e. In combination with pomalidomide +/- steroid if the member has failed 2 prior regimens or lines of therapy that include one proteasome inhibitor (e.g., bortezomib, ixazomib, carfilzomib) & one immunomodulatory agent (e.g., lenalidomide, thalidomide).

III. EXCLUSION CRITERIA

A. Member has disease progression while taking Kyprolis (carfilzomib).

B. Dosing exceeds single dose limit of Kyprolis (carfilzomib) 56 mg/m^2 twice weekly or 70 mg/m^2 once weekly.

C. Investigational use of Kyprolis (carfilzomib) with an off-label indication that is not sufficient in evidence or is not generally accepted by the medical community. Sufficient evidence that is not supported by CMS recognized compendia or acceptable peer reviewed literature is defined as any of the following:

1. Whether the clinical characteristics of the patient and the cancer are adequately represented in the published evidence.
2. Whether the administered chemotherapy/biologic therapy/immune therapy/targeted therapy/other oncologic therapy regimen is adequately represented in the published evidence.
3. Whether the reported study outcomes represent clinically meaningful outcomes experienced by patients. Generally, the definitions of Clinically Meaningful outcomes are those recommended by ASCO, e.g., Hazard Ratio of less than 0.80 and the recommended survival benefit for OS and PFS should be at least 3 months.
4. Whether the experimental design, considering the drugs and conditions under investigation, is appropriate to address the investigative question. (For example, in some clinical studies, it

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may be unnecessary or not feasible to use randomization, double blind trials, placebos, or crossover).

5. That non-randomized clinical trials with a significant number of subjects may be a basis for supportive clinical evidence for determining accepted uses of drugs.
6. That case reports are generally considered uncontrolled and anecdotal information and do not provide adequate supportive clinical evidence for determining accepted uses of drugs.
7. That abstracts (including meeting abstracts) without the full article from the approved peer-reviewed journals lack supporting clinical evidence for determining accepted uses of drugs.

IV. MEDICATION MANAGEMENT

A. Please refer to the FDA label/package insert for details regarding these topics.

V. APPROVAL AUTHORITY

A. Review – Utilization Management Department

B. Final Approval – Utilization Management Committee

VI. ATTACHMENTS

A. None

VII. REFERENCES

A. Kumar SK, et al. Carfilzomib or bortezomib in combination with lenalidomide and dexamethasone for patients with newly diagnosed multiple myeloma without intention for immediate autologous stem-cell transplantation (ENDURANCE): a multicenter, open-label, phase 3, randomized, controlled trial. Lancet Oncol. 2020 Oct;21(10):1317-1330.

B. Dimopoulos MA, et al. ENDEAVOR Trial. Carfilzomib and dexamethasone versus bortezomib and dexamethasone for patients with relapsed or refractory multiple myeloma (ENDEAVOR): a randomized, phase 3, open-label, multicenter study. Lancet Oncol. 2016 Jan;17(1):27-38.

C. Usmani SZ, et al. Carfilzomib, dexamethasone, and daratumumab versus carfilzomib and dexamethasone for patients with relapsed or refractory multiple myeloma (CANDOR): updated outcomes from a randomised, multicentre, open-label, phase 3 study. Lancet Oncol. 2022 Jan;23(1):65-76.

D. Kyprolis prescribing information. ONYX Pharmaceuticals, Inc. South San Francisco, CA 2020.

E. Clinical Pharmacology Elsevier Gold Standard 2023.

F. Micromedex® Healthcare Series: Micromedex Drugdex Ann Arbor, Michigan 2023.

G. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium 2023.

H. AHFS Drug Information. American Society of Health-Systems Pharmacists or Wolters Kluwer Lexi-Drugs. Bethesda, MD 2023.

I. Ellis LM, et al. American Society of Clinical Oncology perspective: Raising the bar for clinical trials by defining clinically meaningful outcomes. J Clin Oncol. 2014 Apr 20;32(12):1277-80.

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J. Medicare Benefit Policy Manual Chapter 15 Covered Medical and Other Health Services: https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/bp102c15.pdf.

K. NCQA UM 2023 Standards and Elements.

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