CLINICAL GUIDELINES FOR MEDICAL NECESSITY

MEDICAL ONCOLOGY

Carfilzomib (Kyprolis®)

Version: 1.0

EFFECTIVE DATE: 1/1/2024

NantHealth® | Eviti®

Please note the following:

Carfilzomib (Kyprolis®)

Note: For Medicare members/enrollees, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs, and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Please refer to the CMS website at http://www.cms.gov for additional information.

Note: For Medicaid members/enrollees, circumstances when state Medicaid coverage provisions conflict with the coverage provisions within this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

Carfilzomib (Kyprolis): Discussion

Carfilzomib is a proteosome inhibitor. It is a modified epoxyketone, a therapeutic agent for the treatment of cancer, that selectively targets the proteasome enzymes within the cell. It irreversibly binds to the active sites of the 20S proteasome, as well as the core component within the 26S proteasome. By selectively and irreversibly inhibiting these proteasomes, carfilzomib can delay proliferation and induce apoptosis of malignant plasma cells. [1]

Carfilzomib is approved by the Food and Drug Administration (FDA):

1. For the treatment of adult patients with relapsed or refractory multiple myeloma who have received one to three lines of therapy in combination with:
    a) Lenalidomide and dexamethasone; OR
    b) Dexamethasone; OR
    c) Daratumumab and dexamethasone; OR
    d) Daratumumab and hyaluronidase-fihj and dexamethasone; OR
    e) Isatuximab and dexamethasone.

2. As a single agent for the treatment of patients with relapsed or refractory multiple myeloma who have received one or more lines of therapy. [2]

The National Comprehensive Cancer Network (NCCN) endorses Carfilzomib in the following cancer types: multiple myeloma, system light chain amyloidosis, Waldenström macroglobulinemia/lymphoplasmacytic lymphoma. [3,4,5.]

Carfilzomib: Definitions

- **Apoptosis** – A set of physical, often visible, features that are associated with the demise of an individual cell. One purpose of apoptosis is to eliminate cells that contain potentially dangerous mutations. If a cell's apoptosis function is not working properly, the cell can grow and divide uncontrollably and ultimately create a tumor.

- **Food and Drug Administration (FDA)** – The FDA is responsible for protecting the public health by assuring the safety, efficacy, and security of human and veterinary drugs, biological products, medical devices, our nation's food supply, cosmetics, and products that emit radiation.
- **National Comprehensive Cancer Network (NCCN) -** An alliance of thirty-two leading cancer centers devoted to patient care, research, and education. The NCCN guidelines are utilized for Radiation Therapy and Medical Oncology standards. NCCN consensus clinical standards are periodically updated and NantHealth, Inc. reviews these and updates its policies within a timely manner.

Carfilzomib: Policy

Carfilzomib will be considered for coverage when the following criteria are met:

Multiple Myeloma

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND
3. Primary therapy for symptomatic multiple myeloma for transplant candidates in combination with daratumumab, lenalidomide, and dexamethasone; OR
4. Primary therapy for symptomatic multiple myeloma or for disease relapse after 6 months following primary induction therapy with the same regimen in combination with
    a) Dexamethasone and lenalidomide (preferred regimen when used in transplant candidates as primary therapy and in the relapse setting; other recommended regimen when used in non-transplant candidates as primary therapy)
    b) Dexamethasone and cyclophosphamide; treatment option for patients with renal insufficiency and/or peripheral neuropathy) (other recommended regimen when used in the relapse setting); OR
5. Maintenance therapy for symptomatic multiple myeloma in combination with lenalidomide for transplant candidates (dual maintenance recommended for high-risk disease)
    a) After a response to primary myeloma therapy
    b) For response or stable disease following an autologous hematopoietic cell transplant (HCT)
    c) For response or stable disease following a tandem autologous or allogeneic HCT for high-risk patients under certain circumstances; OR
6. Therapy for previously treated multiple myeloma for relapse or progressive disease in combination with:
    a) Dexamethasone and lenalidomide if bortezomib-refractory
    b) Daratumumab and dexamethasone
    c) Isatuximab-irfc and dexamethasone
    d) Pomalidomide and dexamethasone
    e) Dexamethasone and cyclophosphamide
    f) Dexamethasone given twice weekly

g) Dexamethasone, cyclophosphamide, and thalidomide
h) Dexamethasone given weekly
i) Selinexor and dexamethasone; OR

7. Therapy for previously treated multiple myeloma for late relapse or progressive disease (>3 prior therapies) in combination with bendamustine, and dexamethasone.[3]

Systemic Light Chain Amyloidosis

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND
3. Treatment for relapsed/refractory non-cardiac disease
   a) As a single agent
   b) In combination with dexamethasone [4]

Waldenström Macroglobulinemia/ Lymphoplasmacytic Lymphoma

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND
3. Used as a component of CaRD (carfilzomib, rituximab, and dexamethasone) regimen
   a) As primary therapy
   b) Consider for relapse if previously used as primary therapy that was well tolerated and elicited a prolonged response.[5]

Note: Coverage of amivantamab-vmjw will be provided for an FDA-approved indication or National Comprehensive Cancer Network (NCCN) guidelines when it is a Category 1, 2A, or 2B recommendation OR when all criteria are met.

Authorization Period and Renewal Criteria

1. Initial Authorization Period: 12 months
2. Renewal Criteria: No evidence of disease progression or unacceptable toxicity
3. Renewal Authorization Period: 12 months

Carfilzomib: References

1. Carfilzomib (Kyprolis): A Novel Proteasome Inhibitor for Relapsed And/or Refractory Multiple Myeloma. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4849338. Accessed May 18, 2023.
2. Carfilzomib (Kyprolis) Package Insert. https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/202714s034lbl.pdf. Accessed May 18, 2023.
3. National Comprehensive Cancer Network Guidelines. Multiple Myeloma (Version 3.2023). https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf. Accessed May 18, 2023.
4. National Comprehensive Cancer Network Guidelines. Systemic Light Chain Amyloidosis (Version 2.2023). https://www.nccn.org/professionals/physician_gls/pdf/amyloidosis.pdf. Accessed May 18, 2023.
5. National Comprehensive Cancer Network Guidelines. Waldenström Macroglobulinemia/ Lymphoplasmacytic Lymphoma (Version 1.2023). https://www.nccn.org/professionals/physician_gls/pdf/waldenstroms.pdf. Accessed May 18, 2023.

Carfilzomib Coding (CPT®, ICD 10 and HCPCS) *

*Procedure codes appearing in medical policy documents are only included as a general reference. This list may not be all-inclusive and is subject to updates. In addition, the codes listed are not a guarantee of payment.

CODE	DESCRIPTION
C88.0	Waldenström Macroglobulinemia
C90.00	Multiple Myeloma
E85.81	Light Chain (AL) Amyloidosis
J9047	Carfilzomib (Kyprolis)

Carfilzomib: Revision and Review History

No.	Description	Date(s)
1	Original Effective Date:	1/1/2024
2	Policy Review Dates:	5/18/2023
3	Policy Revision Dates:	
4	Department Owner:	Medical Affairs
5	NH Advisory Committee Approval Dates:	8/21/2023
6	Revision Changes:	