Reference number(s)
4470-A

STANDARD MEDICARE PART B MANAGEMENT

KYPROLIS (carfilzomib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

Relapsed or Refractory Multiple Myeloma

1. Kyprolis is indicated for the treatment of adult patients with relapsed or refractory multiple myeloma who have received one to three lines of therapy in combination with:
   i. Lenalidomide and dexamethasone; or
   ii. Dexamethasone; or
   iii. Daratumumab and dexamethasone; or
   iv. Daratumumab and hyaluronidase-fihj and dexamethasone; or
   v. Isatuximab and dexamethasone.
2. Kyprolis is indicated as a single agent for the treatment of adult patients with relapsed or refractory multiple myeloma who have received one or more lines of therapy.

B. Compendial Uses

1. Multiple Myeloma
2. Waldenström macroglobulinemia/lymphoplasmacytic lymphoma
3. Systemic light chain amyloidosis

All other indications will be assessed on an individual basis. Submissions for indications other than those enumerated in this policy should be accompanied by supporting evidence from Medicare approved compendia.

II. CRITERIA FOR INITIAL APPROVAL

A. Multiple Myeloma

Authorization of 12 months may be granted for treatment of multiple myeloma when the requested medication will used in any of the following regimens:

1. In combination with dexamethasone when the member has relapsed, refractory, or progressive disease
2. In combination with cyclophosphamide and dexamethasone
3. In combination with lenalidomide and dexamethasone
4. In combination with daratumumab, lenalidomide and dexamethasone
5. In combination with daratumumab and dexamethasone or daratumumab and hyaluronidase-fihj and dexamethasone when the member has relapsed, refractory, or progressive disease

6. In combination with pomalidomide and dexamethasone when the member has relapsed or progressive disease
7. In combination with cyclophosphamide, thalidomide, and dexamethasone when the member has relapsed or progressive disease
8. In combination with isatuximab-irfc and dexamethasone when the member has relapsed, refractory, or progressive disease
9. In combination with selinexor and dexamethasone when the member has relapsed or progressive disease
10. In combination with lenalidomide as maintenance therapy for symptomatic disease
11. In combination with bendamustine and dexamethasone when the member has received more than 3 prior therapies and has relapsed or progressive disease
12. In combination with thalidomide and dexamethasone in transplant-eligible patients with newly diagnosed multiple myeloma
13. In combination with melphalan and prednisone for transplant-ineligible patients with newly diagnosed multiple myeloma
14. As a single agent when the member has received one or more lines of therapy

B. Waldenstrom Macroglobulinemia/Lymphoplasmacytic Lymphoma
Authorization of 12 months may be granted for treatment of Waldenström macroglobulinemia/lymphoplasmacytic lymphoma.

C. Systemic Light Chain Amyloidosis
Authorization of 12 months may be granted for treatment of relapsed or refractory systemic light chain amyloidosis.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must be currently receiving therapy with the requested agent.

Authorization for 12 months may be granted when all of the following criteria are met:
A. The member is currently receiving therapy with the requested medication
B. The requested medication is being used to treat an indication enumerated in Section II
C. The member is receiving benefit from therapy. Benefit is defined as:
   1. No evidence of unacceptable toxicity while on the current regimen, and
   2. No evidence of disease progression while on the current regimen

IV. SUMMARY OF EVIDENCE

The contents of this policy were created after examining the following resources:
1. The prescribing information for Kyprolis.
2. The available compendium
   a. National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium
   b. Micromedex DrugDex
   c. American Hospital Formulary Service- Drug Information (AHFS-DI)
   d. Lexi-Drugs
   e. Clinical Pharmacology
3. NCCN Guideline: Waldenstrom macroglobulinemia/Lymphoplasmacytic lymphoma
4. NCCN Guideline: Systemic light chain amyloidosis

5. NCCN Guideline: Multiple myeloma

After reviewing the information in the above resources, the FDA-approved indications listed in the prescribing information for Kyprolis are covered in addition to the following:

A. Waldenstrom macroglobulinemia/Lymphoplasmacytic lymphoma
B. Systemic light chain amyloidosis

V. EXPLANATION OF RATIONALE

Support for FDA-approved indications can be found in the manufacturer's prescribing information.

Support for using Kyprolis to treat Waldenstrom macroglobulinemia/lymphoplasmacytic lymphoma can be found in the NCCN Drugs and Biologics Compendium. Use of information in the NCCN Drugs and Biologics Compendium for off-label use of drugs and biologicals in an anti-cancer chemotherapeutic regimen is supported by the Medicare Benefit Policy Manual, Chapter 15, section 50.4.5 (Off-Label Use of Drugs and Biologicals in an Anti-Cancer Chemotherapeutic Regimen). Kyprolis can be used as a component of CaRD (carfilzomib, rituximab, and dexamethasone) regimen as either primary therapy or for relapse if previously used as primary therapy that was well tolerated and elicited a prolonged response.

Support for using Kyprolis to treat systemic light chain amyloidosis can be found in the NCCN Drugs and Biologics Compendium. Use of information in the NCCN Drugs and Biologics Compendium for off-label use of drugs and biologicals in an anti-cancer chemotherapeutic regimen is supported by the Medicare Benefit Policy Manual, Chapter 15, section 50.4.5 (Off-Label Use of Drugs and Biologicals in an Anti-Cancer Chemotherapeutic Regimen). Kyprolis can be used as treatment for relapsed/refractory non-cardiac disease as either a single agent or in combination with dexamethasone.

Support for using Kyprolis to treat multiple myeloma in combination with agents not listed in the prescribing information can be found in the NCCN Drugs and Biologics Compendium and the Micromedex DrugDex database. Use of information in the NCCN Drugs and Biologics Compendium and the DrugDex database for off-label use of drugs and biologicals in an anti-cancer chemotherapeutic regimen is supported by the Medicare Benefit Policy Manual, Chapter 15, section 50.4.5 (Off-Label Use of Drugs and Biologicals in an Anti-Cancer Chemotherapeutic Regimen).

VI. REFERENCES

1. Kyprolis [package insert]. Thousand Oaks, CA: Onyx Pharmaceuticals, Inc.; June 2022.
2. The NCCN Drugs & Biologics Compendium® © 2022 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed September 21, 2022.
3. DRUGDEX® System (electronic version). Micromedex Truven Health Analytics, Greenwood Village, Colorado, USA. Available at: http://www.micromedexsolutions.com. Accessed September 21, 2022.
4. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Multiple Myeloma. Version 1.2023. https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf. Accessed September 21, 2022.