Reference number(s)
4470-A

Standard Medicare Part B Management Kyprolis

Products Referenced by this Document

Drugs that are listed in the following table include both brand and generic and all dosage forms and strengths unless otherwise stated. Over-the-counter (OTC) products are not included unless otherwise stated.

Brand Name	Generic Name
Kyprolis	carfilzomib

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.

FDA-Approved Indications[1]

Relapsed or Refractory Multiple Myeloma

- 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:
  - Lenalidomide and dexamethasone; or
  - Dexamethasone; or
  - Daratumumab and dexamethasone; or
  - Daratumumab and hyaluronidase-fihj and dexamethasone; or
  - Isatuximab and dexamethasone.
- 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.

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Compendial Uses[2-4]

- Multiple Myeloma
- Waldenström macroglobulinemia/lymphoplasmacytic lymphoma
- Systemic light chain amyloidosis
- POEMS (polyneuropathy, organomegaly, endocrinopathy, monoclonal protein, skin changes) Syndrome
- Plasma cell-related Monoclonal Immunoglobulin Deposition Disease (MIDD)
- Plasma cell-related Monoclonal Gammopathy of Renal Significance (MGRS)

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

Documentation

The following documentation must be available, upon request, for all submissions: Documentation of testing or laboratory results confirming presence of translocation t(11:14), where applicable.

Coverage Criteria

Multiple Myeloma[1-4]

Authorization of 12 months may be granted for treatment of multiple myeloma when any of the following criteria are met:

- The member will be using the requested medication for primary therapy of symptomatic disease in combination with isatuximab-irfc, lenalidomide, and dexamethasone
- The member is transplant-eligible and will be using the requested medication for newly diagnosed multiple myeloma in combination with:
    - Daratumumab, lenalidomide, and dexamethasone; or
    - Thalidomide and dexamethasone
- The member is transplant-ineligible and will be using the requested medication for newly diagnosed multiple myeloma in combination with melphalan and prednisone
- The member has previously received one or more lines of therapy and will be using the requested medication as a single agent
- The member has relapsed or refractory disease and has previously received at least three prior lines of therapy and will be using the requested medication in combination with bendamustine and dexamethasone

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- The member has relapsed or progressive disease and translocation t(11:14) and will be using the requested medication in combination with venetoclax and dexamethasone
- The member has relapsed, refractory, or progressive disease and will be using the requested medication in combination with:
    - Cyclophosphamide, thalidomide, and dexamethasone; or
    - Pomalidomide and dexamethasone; or
    - Pomalidomide, daratumumab, and dexamethasone; or
    - Daratumumab and dexamethasone; or
    - Daratumumab and hyaluronidase-fihj and dexamethasone; or
    - Isatuximab-irfc and dexamethasone; or
    - Selinexor and dexamethasone; or
    - Dexamethasone
- The member will be using the requested medication in combination with:
    - Lenalidomide and dexamethasone; or
    - Cyclophosphamide and dexamethasone
- The member is a transplant candidate and will be using the requested medication for maintenance therapy of symptomatic disease in combination with lenalidomide

Waldenstrom Macroglobulinemia/Lymphoplasmacytic Lymphoma[2]

Authorization of 12 months may be granted for treatment of Waldenström macroglobulinemia/lymphoplasmacytic lymphoma in combination with rituximab and dexamethasone.

Systemic Light Chain Amyloidosis[2]

Authorization of 12 months may be granted for treatment of systemic light chain amyloidosis when either of the following criteria are met:

- The requested medication will be used as a single agent to treat relapsed/refractory non-cardiac disease
- The requested medication will be used in combination with dexamethasone

POEMS (polyneuropathy, organomegaly, endocrinopathy, monoclonal protein, skin changes) Syndrome, plasma cell-related Monoclonal Immunoglobulin Deposition Disease (MIDD), and plasma cell-related Monoclonal Gammopathy of Renal Significance (MGRS)[2,4]

Authorization of 12 months may be granted for treatment of POEMS syndrome, plasma cell-related MIDD, and plasma cell-related MGRS.

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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:

- The member is currently receiving therapy with the requested medication
- The requested medication is being used to treat an indication in the coverage criteria section
- The member is receiving benefit from therapy. Benefit is defined as:
    - No evidence of unacceptable toxicity while on the current regimen, and
    - No evidence of disease progression while on the current regimen

Summary of Evidence

The contents of this document were created after examining the following resources:

- The prescribing information for Kyprolis.
- The available compendium
    - National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium
    - Micromedex DrugDex
    - American Hospital Formulary Service- Drug Information (AHFS-DI)
    - Lexi-Drugs
    - Clinical Pharmacology
- NCCN Guideline: Waldenstrom macroglobulinemia/Lymphoplasmacytic lymphoma
- NCCN Guideline: Systemic light chain amyloidosis
- 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:

- Waldenstrom macroglobulinemia/Lymphoplasmacytic lymphoma
- Systemic light chain amyloidosis
- POEMS syndrome, plasma cell-related MIDD, and plasma cell-related MGRS

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

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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, and as treatment for newly diagnosed disease 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).

Support for using Kyprolis to treat POEMS syndrome, plasma cell-related MIDD, and plasma cell-related MGRS 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).

References

1. Kyprolis [package insert]. Thousand Oaks, CA: Onyx Pharmaceuticals, Inc.; June 2025.
2. The NCCN Drugs & Biologics Compendium® © 2025 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed September 24, 2025.
3. DRUGDEX® System (electronic version). Micromedex Truven Health Analytics, Greenwood Village, Colorado, USA. Available at: http://www.micromedexsolutions.com. Accessed September 29, 2025.
4. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Multiple Myeloma. Version 2.2026. https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf. Accessed September 25, 2025.

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