Carfilzomib (Kyprolis®)

IMPORTANT REMINDER

We develop Medical Policies to provide guidance to Members and Providers. This Medical Policy relates only to the services or supplies described in it. The existence of a Medical Policy is not an authorization, certification, explanation of benefits or a contract for the service (or supply) that is referenced in the Medical Policy. For a determination of the benefits that a Member is entitled to receive under his or her health plan, the Member's health plan must be reviewed. If there is a conflict between the medical policy and a health plan or government program (e.g., TennCare), the express terms of the health plan or government program will govern.

POLICY

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

- 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.

Compendial Uses

- 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 are considered experimental/investigational and not medically necessary.

DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: Documentation of the presence of translocation t(11:14) (where applicable).

COVERAGE CRITERIA

Multiple Myeloma

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

- The member is a transplant candidate and will be using the requested medication for primary therapy of symptomatic disease in combination with:
  - Isatuximab-irfc, lenalidomide, and dexamethasone; or
  - Daratumumab, lenalidomide, and dexamethasone
- 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
- 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

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

Systemic Light Chain Amyloidosis

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)

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

CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in the coverage criteria section when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

DOSAGE AND ADMINISTRATION

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

For all indications, dosing does not exceed the following:

- If using twice weekly: 56 mg/m^2 (not to exceed 124 mg) per dose, not to exceed 6 doses per 28 days
- If using once weekly: 70 mg/m^2 (not to exceed 154 mg) per dose, not to exceed 3 doses per 28 days

APPLICABLE TENNESSEE STATE MANDATE REQUIREMENTS

BlueCross BlueShield of Tennessee's Medical Policy complies with Tennessee Code Annotated Section 56-7-2352 regarding coverage of off-label indications of Food and Drug Administration (FDA) approved drugs when the off-label use is recognized in one of the statutorily recognized standard reference compendia or in the published peer-reviewed medical literature.

ADDITIONAL INFORMATION

For appropriate chemotherapy regimens, dosage information, contraindications, precautions, warnings, and monitoring information, please refer to one of the standard reference compendia (e.g., the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) published by the National Comprehensive Cancer Network®, Drugdex Evaluations of Micromedex Solutions at Truven Health, or The American Hospital Formulary Service Drug Information).

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. http://www.nccn.org. Accessed September 24, 2024.
3. 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.

EFFECTIVE DATE 7/31/2026

ID_CHS_2025