CARECONTINUUM™

UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Oncology (Injectable – Proteasome Inhibitor) – Kyprolis Utilization Management Medical Policy
- Kyprolis® (carfilzomib intravenous infusion – Amgen/Onyx)

REVIEW DATE: 04/15/2026

OVERVIEW

Kyprolis, a proteasome inhibitor, is approved for **multiple myeloma** in the following situations:[1]
- Relapsed or refractory disease, in combination with dexamethasone ± lenalidomide, Darzalex® (daratumumab intravenous infusion)/dexamethasone, Darzalex Faspro® (daratumumab and hyaluronidase-fihj subcutaneous injection)/dexamethasone, or with Sarclisa® (isatuximab-irfc intravenous infusion)/dexamethasone in adults who have received one to three lines of previous therapy.
- Relapsed or refractory disease, as a single agent in adults who have received one or more lines of therapy.

Guidelines

Kyprolis is discussed in guidelines from the National Comprehensive Cancer Network (NCCN).[2]
- **Multiple Myeloma:** NCCN guidelines (version 5.2026 – January 9, 2026) recommend multiple therapeutic regimens that may be used for primary therapy and previously treated multiple myeloma.[3] Kyprolis in combination with other agents is recommended for primary therapy, maintenance therapy, and relapsed or refractory disease.
- **Systemic Light Chain Amyloidosis:** NCCN guidelines (version 2.2025 – March 12, 2025) recommend Kyprolis + dexamethasone (category 2A) as "Useful in Certain Circumstances" for primary therapy in patients with significant neuropathy.[6] The guidelines also list Kyprolis ± dexamethasone as a therapy for previously treated disease and for patients with non-cardiac amyloidosis. Of note, cardiac toxicity and hypertension are among the Warnings listed for Kyprolis.[1]
- **Waldenstrom Macroglobulinemia/Lymphoplasmacytic Lymphoma:** NCCN guidelines (version 2.2026 – March 3, 2026) recommend Kyprolis/rituximab/dexamethasone among "other recommended regimens" for primary treatment or for relapse if previously used as primary treatment (category 2A).[4]

Dosing Information

For multiple myeloma, the dosing regimen is individualized. Dose modifications of Kyprolis are recommended for the management of hematological toxicity (e.g., neutropenia, thrombocytopenia), renal toxicity, other non-hematological toxicity, and hepatic impairment. This may include reducing the dose (to a minimum of 15 mg/m^2) or withholding the drug until the toxicity is resolved. In some cases, treatment is continued until disease progression or unacceptable toxicity. Therapy is individualized with careful consideration of the risks and benefits of continued treatment. In Waldenstrom macroglobulinemia, limited dosing is available; however, safety has been established for the FDA-approved dosing of Kyprolis. In a small Phase II study, Kyprolis was administered with rituximab and dexamethasone for patients with Waldenstrom macroglobulinemia.[5] During Cycle 1, the dose of Kyprolis was 20 mg/m^2. During Cycles 2 through 6, the dose of Kyprolis was 36 mg/m^2 on Days 1, 2, 8, and 9 of each 21-day cycle. This was

followed by maintenance dosing (8 weeks later) with Kyprolis at a dose of 36 mg/m^2 on Days 1 and 2 every 8 weeks for 8 cycles.

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of Kyprolis. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indications. Extended approvals are allowed if the patient continues to meet the criteria and dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with Kyprolis, as well as the monitoring required for adverse events and long-term efficacy, approval requires Kyprolis to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Kyprolis is recommended in those who meet one of the following criteria:

FDA-Approved Indication

1. **Multiple Myeloma**. Approve for 1 year if the patient meets ALL of the following (A, B, and C):
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** Patient meets ONE of the following (i or ii):
     - **i.** Kyprolis will be used in combination with at least TWO other medications; OR
       Note: Examples of medications that may be used in combination with Kyprolis include dexamethasone, lenalidomide, cyclophosphamide, Darzalex (daratumumab intravenous infusion), Darzalex Faspro (daratumumab and hyaluronidase-fihj subcutaneous injection), or Sarclisa (isatuximab-irfc intravenous infusion).
     - **ii.** Patient has tried at least ONE prior regimen for multiple myeloma; AND
       Note: Examples include bortezomib, lenalidomide, cyclophosphamide, Darzalex (daratumumab intravenous infusion), Ninlaro (ixazomib capsules).
   - **C)** The medication is prescribed by or in consultation with an oncologist or a hematologist.

   Dosing. Approve if the requested dosing meets BOTH of the following (A and B):
   - **A)** Each single dose must not exceed 70 mg/m^2; AND
   - **B)** Patient receives a maximum of six infusions per 28-day treatment cycle.

Other Uses with Supportive Evidence

2. **Systemic Light Chain Amyloidosis.** Approve for 1 year if the patient meets ALL of the following (A, B, and C):
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** Patient meets ONE of the following (i or ii):
     - **i.** The medication will be used in combination with dexamethasone for newly diagnosed disease; OR
     - **ii.** The patient meets BOTH of the following (a and b):

a) The patient has non-cardiac amyloidosis; AND
b) Patient has received at least one other regimen for this condition; AND
Note: Examples of agents used in other regimens include Darzalex (daratumumab intravenous infusion), Darzalex Faspro (daratumumab and hyaluronidase-fihj subcutaneous injection), bortezomib, lenalidomide, cyclophosphamide, and melphalan.

C) The medication is prescribed by or in consultation with an oncologist or a hematologist.

Dosing. Approve if the requested dosing meets BOTH of the following (A and B):
A) Each single dose must not exceed 70 mg/m^2; AND
B) Patient receives a maximum of six infusions per 28-day treatment cycle.

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3. Waldenstrom's Macroglobulinemia/Lymphoplasmacytic Lymphoma. Approve for 1 year if the patient meets ALL of the following (A, B, and C):
A) Patient is ≥ 18 years of age; AND
B) The medication will be used in combination with a rituximab product and dexamethasone; AND
C) The medication is prescribed by or in consultation with an oncologist or a hematologist.

Dosing. Approve if the requested dosing meets BOTH of the following (A and B):
A) Each single dose must not exceed 70 mg/m^2; AND
B) Patient receives a maximum of six infusions per 28-day treatment cycle.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Kyprolis is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Kyprolis® intravenous infusion [prescribing information]. Onyx/Amgen: Thousand Oaks, CA; June 2025.
2. The NCCN Drugs and Biologics Compendium. © 2026 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on April 10, 2026. Search term: carfilzomib.
3. The NCCN Multiple Myeloma Clinical Practice Guidelines in Oncology (version 5.2026 – January 9, 2026). © 2026 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on April 10, 2026.
4. The NCCN Waldenstrom Macroglobulinemia/Lymphoplasmacytic Lymphoma Clinical Practice Guidelines in Oncology (version 2.2026 – March 3, 2026). © 2026 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on April 10, 2026.
5. Treon SP, Tripsas CK, Meid K, et al. Carfilzomib, rituximab, and dexamethasone (CaRD) treatment offers a neuropathy-sparing approach for treating Waldenström's macroglobulinemia. *Blood*. 2014;124(4):503-510.
6. The NCCN Systemic Light Chain Amyloidosis Clinical Practice Guidelines in Oncology (version 2.2026 – March 16, 2026). © 2026 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on April 10, 2026.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	**Light Chain Amyloidosis:** Added qualifier "Systemic" to the condition name, to match guideline nomenclature. Added criterion that the medication is used for newly diagnosed disease in combination with dexamethasone.	04/24/2024
Update	04/11/2025: No criteria changes. The policy name was changed from "Oncology (Injectable) - Kyprolis UM Medical Policy" to "Oncology (Injectable - Proteasome Inhibitor) - Kyprolis UM Medical Policy"	N/A
Annual Revision	No criteria changes.	04/16/2025
Annual Revision	**Multiple Myeloma:** The option for approval which stated, "Kyprolis will be used in combination with lenalidomide or cyclophosphamide and dexamethasone" was updated to "Kyprolis will be used in combination with at least two other medications." A Note was added for examples of medications that may be used in combination with Kyprolis. **Systemic Light Chain Amyloidosis:** Darzalex (daratumumab intravenous infusion), Darzalex Faspro (daratumumab and hyaluronidase-fihj subcutaneous injection) were added to the Note of examples of agents used in other regimens.	04/15/2026