POLICY: Oncology (Injectable) – Kyprolis Utilization Management Medical Policy

- Kyprolis (carfilzomib intravenous infusion – Amgen/Onyx)

EFFECTIVE DATE: 1/1/2021
LAST REVISION DATE: 09/16/2024

COVERAGE CRITERIA FOR: All Aspirus Medicare Plans

OVERVIEW

Kyprolis, a proteasome inhibitor, is approved for **multiple myeloma** in the following situations:[1]

- for relapsed or refractory disease, in combination with: dexamethasome ± 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.
- for 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:** The NCCN guidelines (version 3.2024 – March 8, 2024) recommend multiple therapeutic regimens that may be used for primary therapy and previously treated multiple myeloma.[3] For transplant candidates, Kyprolis/lenalidomide/dexamethasone is recommended as a "Preferred" regimen for primary treatment (category 2A), and Kyprolis/cyclophosphamide/dexamethasone is among the regimens that are useful in certain circumstances (category 2A). Additionally, Kyprolis/Darzalex/lenalidomide/dexamethasone (category 2A) is listed as useful in certain circumstances as primary therapy for transplant candidates. Kyprolis/lenalidomide is recommended as maintenance therapy under "Useful in Certain Circumstances" (category 2A). For previously treated multiple myeloma, Kyprolis/lenalidomide/dexamethasone is listed under "Other Recommended Regimens" (category 2A) for primary therapy in non-transplant candidates. In this setting, Kyprolis/cyclophosphamide/dexamethasone is recommended under "Useful in Certain Circumstances" (category 2A). Multiple "Preferred" regimens are listed for relapsed/refractory disease (after 1 to 3 prior therapies), including Kyprolis/lenalidomide/dexamethasone, Kyprolis/Sarclisa/dexamethasone, and Kyprolis/Darzalex/dexamethasone (all category 1). Kyprolis/Pomalyst® (pomalidomide

capsules)/dexamethasone is also recommended in this setting (category 2A). Additionally, there are multiple Kyprolis-containing regimens recommended as "Other Recommended Regimens" or "Useful in Certain Circumstances" for relapsed/refractory disease.

- **Systemic Light Chain Amyloidosis:** The NCCN guidelines (version 2.2024 – December 12, 2023) recommend Kyprolis + dexamethasone (category 2A) under "Other Recommended Regimens" for primary therapy in patients with significant neuropathy.[6] The guidelines also list Kyprolis ± dexamethasone as a therapy for previously treated disease, for patients with non-cardiac amyloidosis. Of note, cardiac toxicity and hypertension are among the Warnings listed for Kyprolis.[1]
- **Waldenstrom's Macroglobulinemia/Lymphoplasmacytic Lymphoma:** In NCCN guidelines (version 2.2024 – December 5, 2023), Kyprolis/rituximab/dexamethasone (category 2A) is listed among "Other Recommended Regimens" for primary treatment of Waldenstrom's Macroglobulinemia/lymphoplasmacytic lymphoma.[4]

Dosing Information

For multiple myeloma, the dosing regimen is individualized. Refer to the Appendix for more specific dosing regimens recommended in the prescribing information. 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's 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 Rituxan® (rituximab intravenous infusion) and dexamethasone for patients with Waldenstrom's 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 lenalidomide or cyclophosphamide and dexamethasone; OR
     - **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 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 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 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.

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 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 2022.
2. The NCCN Drugs and Biologics Compendium. © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on April 17, 2024. Search term: carfilzomib.
3. The NCCN Multiple Myeloma Clinical Practice Guidelines in Oncology (version 3.2024 – March 8, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on April 17, 2024.
4. The NCCN Waldenstrom's Macroglobulinemia/Lymphoplasmacytic Lymphoma Clinical Practice Guidelines in Oncology (version 2.2024 – December 5, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on April 18, 2024.
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 2.2024 – December 12, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on April 17, 2024.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	**Multiple Myeloma:** In reference to Kyprolis combination therapy, added "or cyclophosphamide". Also, in reference to one prior regimen, added "cyclophosphamide" in the Note as an example.	04/12/2023
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
Aspirus P&T Review	Policy reviewed and approved by Aspirus P&T committee. Annual review process	09/16/2024

APPENDIX

Table 1. Approved Kyprolis Dosing When Administered with Dexamethasone.*

Kyprolis Regimen	Cycle 1								
	Day 1	**Day 2**	**Days 3-7**	**Day 8**	**Day 9**	**Days 10-14**	**Day 15**	**Day 16**	**Days 17-28**
Kyprolis once weekly regimen	20 mg/m^2	--	--	70 mg/m^2	--	--	70 mg/m^2	--	--
Kyprolis twice weekly regimen	20 mg/m^2	20 mg/m^2	--	56 mg/m^2	56 mg/m^2	--	56 mg/m^2	56 mg/m^2	--
Kyprolis Regimen	**Cycles 2 through 9**								
Kyprolis once weekly regimen	70 mg/m^2	--	--	70 mg/m^2	--	--	70 mg/m^2	--	--
Kyprolis twice weekly regimen	56 mg/m^2	56 mg/m^2	--	56 mg/m^2	56 mg/m^2	--	56 mg/m^2	56 mg/m^2	--
Kyprolis Regimen	**Cycles 10 and later**								
Kyprolis once weekly regimen	70 mg/m^2	--	--	70 mg/m^2	--	--	70 mg/m^2	--	--
Kyprolis twice weekly regimen	56 mg/m^2	56 mg/m^2	--	56 mg/m^2	56 mg/m^2	--	56 mg/m^2	56 mg/m^2	--

* Refer to the Kyprolis prescribing information for recommended dose modifications based on toxicity and for dosing schedule for concomitant dexamethasone.

Table 2. Approved Kyprolis Dosing When Administered with Revlimid and Dexamethasone.*

Kyprolis Regimen	Cycle 1								
	Day 1	**Day 2**	**Days 3-7**	**Day 8**	**Day 9**	**Days 10-14**	**Day 15**	**Day 16**	**Days 17-28**
Kyprolis twice weekly regimen	20 mg/m^2	20 mg/m^2	--	27 mg/m^2	27 mg/m^2	--	27 mg/m^2	27 mg/m^2	--
Kyprolis Regimen	**Cycles 2 through 12**								
Kyprolis once weekly regimen	27 mg/m^2	27 mg/m^2	--	27 mg/m^2	27 mg/m^2	--	27 mg/m^2	27 mg/m^2	--
Kyprolis Regimen	**Cycles 13 and later^**								
Kyprolis once weekly regimen	27 mg/m^2	27 mg/m^2	--	--	--	--	27 mg/m^2	27 mg/m^2	--

* Refer to the Kyprolis prescribing information for recommended dose modifications based on toxicity and for dosing schedule for Revlimid and dexamethasone.
^ Kyprolis is administered through Cycle 18.

Table 3. Approved Kyprolis Dosing When Administered as Monotherapy.*

Kyprolis Regimen	Cycle 1								
	Day 1	**Day 2**	**Days 3-7**	**Day 8**	**Day 9**	**Days 10-14**	**Day 15**	**Day 16**	**Days 17-28**
Kyprolis 20/27 mg/m^2 regimen	20 mg/m^2	20 mg/m^2	--	27 mg/m^2	27 mg/m^2	--	27 mg/m^2	27 mg/m^2	--
Kyprolis 20/56 mg/m^2 regimen	20 mg/m^2	20 mg/m^2	--	56 mg/m^2	56 mg/m^2	--	56 mg/m^2	56 mg/m^2	--
Kyprolis Regimen	**Cycles 2 through 12**								
Kyprolis 20/27 mg/m^2 regimen	27 mg/m^2	27 mg/m^2	--	27 mg/m^2	27 mg/m^2	--	27 mg/m^2	27 mg/m^2	--
Kyprolis 20/56 mg/m^2 regimen	56 mg/m^2	56 mg/m^2	--	56 mg/m^2	56 mg/m^2	--	56 mg/m^2	56 mg/m^2	--
Kyprolis Regimen	**Cycles 13 and later**								

Kyprolis 20/27 mg/m^2 regimen	27 mg/m^2	27 mg/m^2	--	--	--	--	27 mg/m^2	27 mg/m^2	--
Kyprolis 20/56 mg/m^2 regimen	56 mg/m^2	56 mg/m^2	--	56 mg/m^2	56 mg/m^2	--	56 mg/m^2	56 mg/m^2	--

* Refer to the Kyprolis prescribing information for recommended dose modifications based on toxicity.

Table 4. Approved Kyprolis Dosing When Administered in Combination with Darzalex Intravenous or Darzalex Faspro or Sarclisa (20/56 regimen only) and Dexamethasone.[1*]

Kyprolis Regimen	**Cycle 1**								
	Day 1	**Day 2**	**Days 3-7**	**Day 8**	**Day 9**	**Days 10-14**	**Day 15**	**Day 16**	**Days 17-28**
Kyprolis 20/56 regimen	20 mg/m^2	20 mg/m^2	--	56 mg/m^2	56 mg/m^2	--	56 mg/m^2	56 mg/m^2	--
Kyprolis 20/70 mg/m^2 regimen	20 mg/m^2	--	--	70 mg/m^2	--	--	70 mg/m^2	--	--
Kyprolis Regimen	**Cycle 2 and later**								
Kyprolis 20/56 regimen	56 mg/m^2	56 mg/m^2	--	56 mg/m^2	56 mg/m^2	--	56 mg/m^2	56 mg/m^2	--
Kyprolis 20/70 mg/m^2 regimen	70 mg/m^2	--	--	70 mg/m^2	--	--	70 mg/m^2	--	--

* Refer to the Kyprolis prescribing information for recommended dose modifications based on toxicity.