## Kyporlis

### Description

**Kyporlis (carfilzomib)**

**Background**

Kyporlis (carfilzomib) is an antineoplastic agent for the treatment of multiple myeloma in combination with dexamethasone or lenalidomide plus dexamethasone for the treatment of patients with relapsed or refractory multiple myeloma who have received one to three lines of therapy, or as a single agent for the treatment of patients with relapsed or refractory multiple myeloma who have received one or more lines of therapy. Kyporlis works by inhibiting proteasome activity in blood and tissue and delayed tumor growth of multiple myeloma, hematologic, and solid tumors (1).

**Regulatory Status**

FDA-approved indication: Kyporlis (carfilzomib) is a proteasome inhibitor indicated for the treatment: (1)

1. In combination with dexamethasone or with lenalidomide plus dexamethasone for the treatment of patients with relapsed or refractory multiple myeloma who have received one to three lines of therapy

2. As a single agent for the treatment of patients with relapsed or refractory multiple myeloma who have received one or more lines of therapy

Cardiac adverse reactions, including heart failure and ischemia, have occurred following administration of Kyporlis. Death due to cardiac arrest has occurred within a day of Kyporlis administration. Cardiac failure events were reported in 7% of patients. Monitor for cardiac complications and manage promptly. Venous thromboembolic events (including deep venous
thrombosis and pulmonary embolism) have been observed with Kyprolis. Thromboprophylaxis is recommended for patients being treated with the combination of Kyprolis with dexamethasone or with lenalidomide plus dexamethasone. Kyprolis in combination with melphalan and prednisone is not indicated for transplant-ineligible patients with newly diagnosed multiple myeloma (1).

Kyprolis should be withheld or interrupted in patients with the following conditions, until the condition has been resolved or returned to baseline: (1)
1. Pulmonary arterial hypertension (PAH)
2. Pulmonary Toxicity, including Acute Respiratory Distress Syndrome, Acute Respiratory Failure, and Acute Diffuse Infiltrative Pulmonary Disease
3. Hypertension Including Hypertensive Crisis
4. Hemorrhage
5. Cardiac failure
6. Ischemia
7. Dyspnea
8. Tumor lysis syndrome (TLS)
9. Neutropenia
10. Thrombocytopenia
11. Hepatic toxicity and hepatic failure
12. Thrombotic Microangiopathy
13. Posterior Reversible Encephalopathy Syndrome
14. Renal toxicity

Off Label Use:
The NCCN Panel has included newer agents, such as Kyprolis, as therapy options for (2,3):
1. Waldenström’s macroglobulinemia/lymphoplasmacytic lymphoma as a neuropathy-sparing treatment option. Kyprolis must be used in combination with rituximab and dexamethasone (CaRD) regimen as primary therapy, and for relapse ≥24 months if used as primary therapy (2)

Infusion reactions can occur immediately following or up to 24 hours after administration of Kyprolis. Dexamethasone should be administered prior to Kyprolis to reduce the incidence and severity of reactions. Prior to receiving Kyprolis, patients must be well hydrated to reduce the risk of renal toxicity and of tumor lysis syndrome (TLS) (1).
Kyprolis carries a pregnancy category D status. Females of reproductive potential should be advised to avoid becoming pregnant while being treated, as Kyprolis has been shown to cause fetal harm (1).

The safety and effectiveness of Kyprolis have not been established in pediatric patients (1).

**Related policies**
Ninlaro, Velcade

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**Policy**

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Kyprolis may be considered **medically necessary** in patients 18 years of age or older for the treatment of patients with multiple myeloma or Waldenstrom's macroglobulinemia/lymphoplasmacytic lymphoma and when the conditions below are met.

Kyprolis is considered **investigational** for patients that are less than 18 years of age and for all other indications.

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**Prior-Approval Requirements**

**Age**
18 years of age or older

**Diagnoses**

Patient must have **ONE** of the following:

1. Relapsed or refractory multiple myeloma (MM)

   **AND ONE** of the following:

   a. In combination with dexamethasone or with lenalidomide plus dexamethasone
      a. Must have received one to three lines of multiple myeloma therapy
   b. As a single agent in patients who have received one or more lines of multiple myeloma therapy
2. Waldenström’s macroglobulinemia/lymphoplasmacytic lymphoma
   a. Used in combination with rituximab and dexamethasone

Prior – Approval Renewal Requirements

Age
18 years of age or older

Diagnoses

Patient must have ONE of the following:

1. Relapsed or refractory multiple myeloma (MM)

   AND ONE of the following:
   a. In combination with dexamethasone or with lenalidomide plus dexamethasone
   b. Used as a single agent

2. Waldenström’s macroglobulinemia/lymphoplasmacytic lymphoma
   a. Used in combination with rituximab and dexamethasone

   AND ALL of the following:
   a. Patient must NOT have any disease progression

Policy Guidelines

Pre - PA Allowance
None

Prior - Approval Limits

Duration 12 months

Prior – Approval Renewal Limits

Duration 12 months

Rationale

Summary
Kyprolis (carfilzomib) is a proteasome inhibitor indicated for treatment of patients with multiple myeloma who will be using in combination with dexamethasone or with lenalidomide plus dexamethasone in patients who have received one prior multiple myeloma therapy or as a single agent in patients who have received one prior multiple myeloma therapy. Dexamethasone should be administered prior to Kyprolis to reduce the incidence and severity of infusion reactions (1).

Prior approval is required to ensure the safe, clinically appropriate and cost effective use of Kyprolis while maintaining optimal therapeutic outcomes.

References

Policy History
<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
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<tbody>
<tr>
<td>October 2012</td>
<td>New Addition</td>
</tr>
<tr>
<td>December 2012</td>
<td>Annual editorial review and update</td>
</tr>
<tr>
<td>March 2014</td>
<td>Annual review</td>
</tr>
<tr>
<td>June 2015</td>
<td>Annual editorial review and reference update</td>
</tr>
<tr>
<td>January 2016</td>
<td>Addition of use in combination with dexamethasone or with lenalidomide plus dexamethasone in patient who have received one prior multiple myeloma therapy or as a single agent in patients who have received one prior multiple myeloma therapy and a new indication of Waldenstrom’s macroglobulinemia/lymphoplasmacytic lymphoma when used in combination with rituximab and dexamethasone. Removal of the requirement of patients who have received at least two prior therapies including Velcade (bortezomib) and an immunomodulator agent and have demonstrated disease progression on or within 60 days of completion of the last therapy</td>
</tr>
<tr>
<td>June 2016</td>
<td>Policy changed from 5.04.24 to 5.21.24</td>
</tr>
<tr>
<td>September 2016</td>
<td>Annual editorial review and reference update</td>
</tr>
<tr>
<td>June 2017</td>
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<tr>
<td></td>
<td>Annual review and reference update</td>
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June 2018  Annual review and reference update
          Update of criteria to match verbiage in package insert for the diagnosis of multiple myeloma
June 2019  Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on June 20, 2019 and is effective on July 1, 2019.