BlueCross BlueShield Federal Employee Program

KYPROLIS (carfilzomib)

RATIONALE FOR INCLUSION IN PA PROGRAM

Background

Kyprolis (carfilzomib) is an antineoplastic agent for the treatment of multiple myeloma. Kyprolis works by inhibiting proteasome activity in blood and tissue, thereby delaying tumor growth of multiple myeloma, hematologic, and solid tumors (1).

Regulatory Status

FDA-approved indications: Kyprolis (carfilzomib) is a proteasome inhibitor indicated: (1-2)

1. For the treatment of adult patients with relapsed or refractory multiple myeloma who have received one to three lines of therapy in combination with:
    a. Lenalidomide and dexamethasone; or
    b. Dexamethasone; or
    c. Daratumumab and dexamethasone; or
    d. Daratumumab and hyaluronidase-fihj and dexamethasone, or
    e. Isatuximab-irfc and dexamethasone
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 Kyprolis. Death due to cardiac arrest has occurred within a day of Kyprolis administration. 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 Kyprolis in combination with lenalidomide and dexamethasone; with dexamethasone; or with daratumumab and 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 (PRES)
14. Progressive Multifocal Leukoencephalopathy (PML)
15. Renal toxicity

Off-Label Use: (2)

The National Comprehensive Cancer Network (NCCN) Guidelines supports the off-label use of Kyprolis in the treatment of:

- 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, or for relapse if previously used as primary therapy that was well tolerated and elicited a prolonged response.

Infusion-related 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 infusion-related 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 can cause fetal harm. Female patients of reproductive potential should be advised to use effective contraception during treatment with Kyprolis and for at least 6 months following the final dose. Male patients with female partners of reproductive potential should be advised to use effective contraception during treatment with Kyprolis and for 3 months following the final dose (1).

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

Summary

Kyprolis (carfilzomib) is an antineoplastic agent for the treatment of multiple myeloma. Kyprolis

works by inhibiting proteasome activity in blood and tissue, thereby delaying tumor growth of multiple myeloma, hematologic, and solid tumors. Kyprolis has warnings for cardiac toxicities, acute renal failure, tumor lysis syndrome, pulmonary toxicity, hypertension, venous thrombosis, infusion-related reactions, hemorrhage, thrombocytopenia, hepatic toxicity and hepatic failure, thrombotic microangiopathy, posterior reversible encephalopathy syndrome, progressive multifocal leukoencephalopathy and embryo-fetal toxicity. The safety and effectiveness of Kyprolis have not been established in pediatric patients (1).

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

References

1. Kyprolis [package insert]. Thousand Oaks, CA: Onyx Pharmaceuticals, Inc.; June 2022.
2. Sarclisa [package insert]. Bridgewater, NJ: Sanofi-aventis U.S. LLC; November 2023.
3. NCCN Drugs & Biologics Compendium® Carfilzomib 2025. National Comprehensive Cancer Network, Inc. Accessed on January 13, 2025.
4. NCCN Clinical Practice Guidelines in Oncology® Multiple Myeloma (Version 1.2025). National Comprehensive Cancer Network, Inc. September 2024. Accessed on January 13, 2025.