BlueCross BlueShield Federal Employee Program

Cyramza
(ramucirumab)

RATIONALE FOR INCLUSION IN PA PROGRAM

Background

Cyramza (ramucirumab) is a single-agent treatment or combination for patients with advanced or metastatic gastric cancer, gastroesophageal junction cancer, metastatic non-small cell lung cancer (NSCLC), colorectal cancer, or hepatocellular carcinoma. Some of these tumors create proteins called vascular endothelial growth factors (VEGF). These proteins attach to the receptors of blood vessel cells causing new blood vessels to form around the tumors, enabling growth. Cyramza blocks VEGF proteins from linking to the blood vessels helping to inhibit tumor growth by slowing new blood vessel formation and the blood supply that feeds tumors (1).

Regulatory Status

FDA-approved indications: Cyramza is a human vascular endothelial growth factor receptor 2 (VEGFR2) antagonist indicated for the treatment of: (1)

1. **Gastric Cancer** - Cyramza as a single agent, or in combination with paclitaxel, is indicated for the treatment of patients with advanced or metastatic, gastric or gastro-esophageal junction adenocarcinoma with disease progression on or after prior fluoropyrimidine-or platinum-containing chemotherapy.
2. **Non-Small Cell Lung Cancer**
    a. Cyramza, in combination with erlotinib, is indicated for the first-line treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 (L858R) substitution mutations.
    b. Cyramza, in combination with docetaxel, is indicated for the treatment of patients with metastatic non-small cell lung cancer (NSCLC) with disease progression on or after platinum-based chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving Cyramza.
3. **Metastatic Colorectal Cancer** - Cyramza, in combination with FOLFIRI, for the treatment of metastatic colorectal cancer with disease progression on or after prior therapy with bevacizumab, oxaliplatin, and a fluoropyrimidine.

4. **Hepatocellular Carcinoma** - Cyramza, as a single agent, is indicated for the treatment of patients with hepatocellular carcinoma (HCC) who have an alpha fetoprotein (AFP) of ≥400 ng/mL and have been treated with sorafenib.

Cyramza has warnings for increased risk of hemorrhage, including severe and sometimes fatal hemorrhagic events. Permanently discontinue Cyramza in patients who experience severe bleeding. Cyramza warnings also include gastrointestinal perforation and impaired wound healing. If either of these adverse effects occur, Cyramza should be discontinued (1).

Cyramza has an increased incidence of severe hypertension in patients receiving it. Hypertension should be controlled prior to initiating treatment. Monitor blood pressure every two weeks or more frequently as indicated during treatment. Temporarily suspend Cyramza for severe hypertension until medically controlled. Permanently discontinue Cyramza if medically significant hypertension cannot be controlled with antihypertensive therapy or in patients with hypertensive crisis or hypertensive encephalopathy (1).

Cyramza is an antiangiogenic therapy that can increase the risk of gastrointestinal perforation, a potentially fatal event. Permanently discontinue Cyramza in patients who experience a gastrointestinal perforation (1).

Reversible Posterior Leukoencephalopathy Syndrome (RPLS) has been reported. Confirm the diagnosis of RPLS with MRI and discontinue Cyramza in patients who develop RPLS. Symptoms may resolve or improve within days, although some patients with RPLS can experience ongoing neurologic sequelae or death (1).

Monitor patients during the infusion for signs and symptoms of infusion related reactions (IRR) in a setting with available resuscitation equipment. Immediately and permanently discontinue Cyramza for Grade 3 or 4 IRRs (1).

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

Summary

Cyramza (ramucirumab) is a single-agent treatment or combination for patients with advanced or

metastatic gastric cancer, gastroesophageal junction cancer, metastatic non-small cell lung cancer (NSCLC), colorectal cancer, or hepatocellular carcinoma. Some of these tumors create proteins called vascular endothelial growth factors (VEGF). These proteins attach to the receptors of blood vessel cells causing new blood vessels to form around the tumors, enabling growth. Cyramza blocks VEGF proteins from linking to the blood vessels helping to inhibit tumor growth by slowing new blood vessel formation and the blood supply that feeds tumors. The safety and effectiveness of Cyramza in patients under 18 years of age have not been established (1).

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

References

1. Cyramza [package insert]. Indianapolis, IN: Eli Lilly and Co.; March 2022.
2. NCCN Drugs & Biologics Compendium® Ramucirumab 2025. National Comprehensive Cancer Network, Inc. Accessed on January 24, 2025.

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