Cyramza

Description

Cyramza (ramucirumab)

Background
Cyramza (ramucirumab) is a single-agent treatment or combination for patients with advanced or metastatic gastric cancer, gastroesophageal junction cancer or metastatic non-small cell lung cancer (NSCLC). Gastroesophageal junction cancer occurs where the esophagus joins the stomach. Cyramza is also indicated in combination with patients with non-small cell lung cancer and colorectal cancer. 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 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 gastroesophageal junction adenocarcinoma with disease progression on or after prior fluoropyrimidine-or platinum-containing chemotherapy.

2. **Non-Small Cell Lung Cancer** - 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.

Cyramza has a boxed warning for increased risk of hemorrhage, including severe and sometimes fatal hemorrhagic events. Permanently discontinue Cyramza in patients who experience severe bleeding (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).

**Related policies**
Alecensa, Avastin, Erbitux, Gilotrif, Herceptin, Iressa, Keytruda, Lonsurf, Mekinist, Opdivo, Portrazza, Stivarga, Tafinlar, Tagrisso, Tykerb, Xalkori, Vectibix, Zaltrap, Zykadia
This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Cyramza may be considered medically necessary in patients 18 years of age or older for the treatment of advanced or metastatic gastric cancer, gastro-esophageal junction adenocarcinoma, metastatic non-small cell lung cancer (NSCLC), or metastatic colorectal cancer if the conditions indicated below are met.

Cyramza may be considered investigational for patients less than 18 years of age and for all other indications.

Prior-Approval Requirements

**Age**
18 years of age or older

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

1. Advanced or metastatic gastric cancer
2. Gastro-esophageal junction adenocarcinoma

AND ALL of the following:
   a. Usage as a single agent (monotherapy) or combination therapy with paclitaxel
   b. Patient has received prior chemotherapy containing fluoropyrimidine or platinum and experienced disease progression on or after therapy

3. Metastatic non-small cell lung cancer (NSCLC)
   a. Combination therapy with docetaxel
   b. Patient has received prior chemotherapy containing platinum and experienced disease progression on or after therapy
   c. Patients with EGFR or ALK genomic tumor mutations:
      i. Disease progression AFTER at least one prior therapy

4. Metastatic colorectal cancer
   a. Combination therapy with Folfiri
   b. Patient has received prior chemotherapy containing
bevacizumab, oxaliplatin, or a fluoropyrimidine and experienced
disease progression on or after therapy

AND the following:
1. Confirmation that patient does not have the following and if condition
develops, therapy will be discontinued:
   a. Hemorrhage or any severe bleeding event
   b. Arterial thromboembolic events (ATEs)

Prior – Approval Renewal Requirements

Age
18 years of age or older

Diagnoses
Patient must have ONE of the following:

1. Advanced or metastatic gastric cancer
2. Gastro-esophageal junction adenocarcinoma
3. Metastatic non-small cell lung cancer (NSCLC)
4. Metastatic colorectal cancer

AND ALL of the following:
1. Patient has not experienced disease progression or unacceptable
toxicity
2. Confirmation that patient does not have the following and if condition
develops, therapy will be discontinued:
   a. Hemorrhage or any severe bleeding event
   b. Arterial thromboembolic events (ATEs)

Policy Guidelines

Pre - PA Allowance
None

Prior - Approval Limits
Duration 12 months
Summary
Cyramza is a single-agent or in combination treatment for patients with advanced or metastatic gastric cancer, gastroesophageal junction that specifically binds to the vascular endothelial growth factor receptors. Cyramza is also indicated 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. Cyramza is also indicated in combination with Folfiri, for the treatment of metastatic colorectal cancer with disease progression on or after prior therapy. Cyramza specifically binds VEGF Receptor 2 and blocks binding of VEGFR ligands, VEGF-A, VEGF-C, and VEGF-D. As a result, ramucirumab inhibits ligand-stimulated activation of VEGF Receptor 2, thereby inhibiting ligand-induced proliferation, and migration of human endothelial cells. 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

Policy History
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<tr>
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<tr>
<td>May 2014</td>
<td>New Policy Addition</td>
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<tr>
<td>September 2014</td>
<td>Annual review</td>
</tr>
<tr>
<td>January 2015</td>
<td>Addition of metastatic non-small cell lung cancer (NSCLC)</td>
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<td>March 2015</td>
<td>Annual editorial review and reference update</td>
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Section: Prescription Drugs  Effective Date: October 1, 2017
Subsection: Antineoplastic Agents  Original Policy Date: May 30, 2014
Subject: Cyramza  Page: 6 of 6

May 2015  Addition of Metastatic Colorectal Cancer
December 2015  Annual review
March 2016  Annual editorial review
             Policy number change from 5.04.44
June 2016  Annual editorial review and reference update
June 2017  Annual editorial review and reference update
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Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on September 15, 2017 and is effective on October 1, 2017.