Reference number(s)
4198-A

STANDARD MEDICARE PART B MANAGEMENT

CYRAMZA (ramucirumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

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 (GEJ) adenocarcinoma with disease progression on or after prior fluoropyrimidine- or platinum-containing chemotherapy.

2. Non-Small Cell Lung Cancer (NSCLC)
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 NSCLC with disease progression on or after platinum-based chemotherapy. Patients with epidermal growth factor receptor (EGFR) or anaplastic lymphoma kinase (ALK) genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving Cyramza.

3. Colorectal Cancer
Cyramza, in combination with FOLFIRI (irinotecan, folinic acid, and fluorouracil), is indicated for the treatment of patients with metastatic colorectal cancer (mCRC) 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.

B. Compendial Uses

1. Esophageal adenocarcinoma
2. Gastric, gastro-esophageal junction (GEJ), esophagogastric junction (EGJ) cancer – not surgical candidates, recurrent disease, in combination with irinotecan with or without fluorouracil
3. Colorectal cancer:
    a. Anal adenocarcinoma and appendiceal adenocarcinoma
    b. Advanced disease
    c. In combination with irinotecan
    d. Adjuvant treatment
4. NSCLC - recurrent, advanced
5. Urothelial carcinoma
6. Mesothelioma

All other indications will be assessed on an individual basis. Submissions for indications other than those enumerated in this policy should be accompanied by supporting evidence from Medicare approved compendia.

II. DOCUMENTATION

Submission of the following information must be available, upon request for initial approval: EGFR mutation testing results and alpha fetoprotein (AFP) level results (where applicable).

III. CRITERIA FOR INITIAL APPROVAL

A. Gastric, Gastro-esophageal Junction (GEJ), Esophagogastric Junction (EGJ), and Esophageal Adenocarcinoma
Authorization of 12 months may be granted for treatment of gastric, gastro-esophageal junction (GEJ), esophagogastric junction (EGJ), and esophageal adenocarcinoma for members who are not surgical candidates or who have unresectable locally advanced, recurrent or metastatic disease, when used as subsequent therapy as a single agent, in combination with paclitaxel, or in combination with irinotecan with or without fluorouracil.

B. Non-Small Cell Lung Cancer (NSCLC)
Authorization of 12 months may be granted for treatment of recurrent, advanced or metastatic NSCLC when either of the following criteria is met:
1. Used in combination with docetaxel as subsequent therapy.
2. Used in combination with erlotinib for EGFR exon 19 deletion or exon 21 (L858R) substitution mutation positive disease.

C. Colorectal Cancer (CRC)
Authorization of 12 months may be granted for treatment colorectal cancer if either of the following criteria is met:
1. Used for advanced or metastatic colorectal cancer, including anal adenocarcinoma and appendiceal adenocarcinoma, in combination with FOLFIRI (irinotecan, folinic acid, and 5-fluorouracil) or irinotecan.
2. Used as adjuvant treatment in combination with FOLFIRI (fluorouracil, leucovorin, and irinotecan) or irinotecan for unresectable metachronous metastases that converted to resectable disease after primary treatment.

D. Hepatocellular Carcinoma (HCC)
Authorization of 12 months may be granted for subsequent treatment of progressive hepatocellular carcinoma as a single agent in patients who have an alpha fetoprotein (AFP) of greater than or equal to 400 ng/mL.

E. Urothelial Carcinoma
Authorization of 12 months may be granted for treatment of advanced or metastatic urothelial carcinoma when all of the following criteria is met:
1. Used in combination with docetaxel.
2. Disease progression within 12 months after platinum-containing chemotherapy.

F. Mesothelioma

Authorization of 12 months may be granted for the subsequent treatment of pleural mesothelioma, pericardial mesothelioma, or tunica vaginalis testis mesothelioma when used in combination with gemcitabine.

IV. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must be currently receiving therapy with the requested agent.

A. NSCLC

Authorization of 12 months may be granted when all of the following criteria are met:

1. The member is currently receiving therapy with the requested medication
2. The requested medication is being used to treat non-small cell lung cancer
3. The member is receiving benefit from therapy. Benefit is defined as:
    a. No evidence of unacceptable toxicity or disease progression while on the current regimen, or
    b. Disease is T790M negative and there is no evidence of unacceptable toxicity while on the current regimen

B. All other indications

Authorization for 12 months may be granted when all of the following criteria are met:

1. The member is currently receiving therapy with the requested medication
2. The requested medication is being used to treat an indication enumerated in Section III
3. The member is receiving benefit from therapy. Benefit is defined as:
    a. No evidence of unacceptable toxicity while on the current regimen, and
    b. No evidence of disease progression while on the current regimen

V. SUMMARY OF EVIDENCE

The contents of this policy were created after examining the following resources:

1. The prescribing information for Cyramza.
2. The available compendium
    a. National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium
    b. Micromedex DrugDex
    c. American Hospital Formulary Service- Drug Information (AHFS-DI)
    d. Lexi-Drugs
    e. Clinical Pharmacology
3. NCCN Guideline: Pleural mesothelioma
4. NCCN Guideline: Non-small cell lung cancer
5. NCCN Guideline: Hepatocellular carcinoma
6. NCCN Guideline: Gastric cancer
7. NCCN Guideline: Esophageal and esophagogastric junction cancers
8. NCCN Guideline: Colon cancer
9. NCCN Guideline: Rectal cancer
10. NCCN Guideline: Anal carcinoma

After reviewing the information in the above resources, the FDA-approved indications listed in the prescribing information for Cyramza are covered in addition to the following:

1. Esophageal adenocarcinoma
2. Gastric, gastro-esophageal junction (GEJ), esophagogastric junction (EGJ) cancer – not surgical candidates, recurrent disease, in combination with irinotecan with or without fluorouracil

3. Colorectal cancer:
    a. Anal adenocarcinoma and appendiceal adenocarcinoma
    b. Advanced disease
    c. In combination with irinotecan
    d. Adjuvant treatment
4. NSCLC - recurrent, advanced
5. Urothelial carcinoma
6. Mesothelioma

VI. EXPLANATION OF RATIONALE

Support for FDA-approved indications can be found in the manufacturer's prescribing information.

Support for using Cyramza to treat esophageal adenocarcinoma, gastric, GEJ, and EGJ cancers, colorectal cancer, anal adenocarcinoma, appendiceal adenocarcinoma, NSCLC, and mesothelioma can be found in the NCCN Drugs and Biologics Compendium. Use of information in the NCCN Drugs and Biologics Compendium for off-label use of drugs and biologicals in an anti-cancer chemotherapeutic regimen is supported by the Medicare Benefit Policy Manual, Chapter 15, section 50.4.5 (Off-Label Use of Drugs and Biologicals in an Anti-Cancer Chemotherapeutic Regimen).

Support for using Cyramza to treat urothelial carcinoma can be found in the Micromedex DrugDex database. Use of information in the DrugDex database for off-label use of drugs and biologicals in an anti-cancer chemotherapeutic regimen is supported by the Medicare Benefit Policy Manual, Chapter 15, section 50.4.5 (Off-Label Use of Drugs and Biologicals in an Anti-Cancer Chemotherapeutic Regimen).

VII. REFERENCES

1. Cyramza [package insert]. Indianapolis, IN: Eli Lilly and Company; March 2022.
2. The NCCN Drugs & Biologics Compendium® © 2023 National Comprehensive Cancer Network, Inc. Available at: https://www.nccn.org. Accessed January 4, 2023.
3. IBM Micromedex® DRUGDEX® (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed January 4, 2023.
4. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Anal Carcinoma. Version 2.2022. https://www.nccn.org/professionals/physician_gls/pdf/anal.pdf. Accessed January 4, 2023.