Reference number(s)
4198-A

Standard Medicare Part B Management Cyramza

Products Referenced by this Document

Drugs that are listed in the following table include both brand and generic and all dosage forms and strengths unless otherwise stated. Ove the counter (OTC) products are not included unless otherwise stated.

Brand Name	Generic Name
Cyramza	ramucirumab

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.

FDA-approved Indications[1]

Gastric Cancer

Cyramza, as a single agent or in combination with paclitaxel, is indicated for the treatment of adults with advanced or metastatic, gastric or gastro-esophageal junction (GEJ) adenocarcinoma with disease progression on or after prior fluoropyrimidine- or platinum-containing chemotherapy.

Non-Small Cell Lung Cancer (NSCLC)

- Cyramza, in combination with erlotinib, is indicated for the first-line treatment of adults 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.
- Cyramza, in combination with docetaxel, is indicated for the treatment of adults 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.

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Colorectal Cancer

Cyramza, in combination with FOLFIRI (irinotecan, folinic acid, and fluorouracil), is indicated for the treatment of adults with metastatic colorectal cancer (mCRC) with disease progression on or after prior therapy with bevacizumab, oxaliplatin, and a fluoropyrimidine.

Hepatocellular Carcinoma

Cyramza, as a single agent, is indicated for the treatment of adults with hepatocellular carcinoma (HCC) who have an alpha fetoprotein (AFP) of greater than or equal to 400 ng/mL and have been treated with sorafenib.

Compendial Uses[2-5]

- Gastric and Gastro-esophageal Junction (GEJ) Cancer
- Esophagogastric Junction (EGJ) and Esophageal Adenocarcinoma
- Non-Small Cell Lung Cancer (NSCLC)
- Colorectal Cancer
    - Anal Adenocarcinoma and Appendiceal Adenocarcinoma
- Hepatocellular Carcinoma (HCC)
- Mesothelioma
- Thymic Carcinoma
- Urothelial Carcinoma

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

Documentation

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

Coverage Criteria

Gastric, Gastro-esophageal Junction (GEJ), Esophagogastric Junction (EGJ), and Esophageal Adenocarcinoma[1,2]

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.

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Non-Small Cell Lung Cancer (NSCLC)[1,2]

Authorization of 12 months may be granted for treatment of recurrent, advanced or metastatic NSCLC when either of the following criteria is met:

- Used in combination with docetaxel as subsequent therapy.
- Used in combination with erlotinib for EGFR exon 19 deletion or exon 21 (L858R) substitution mutation positive disease as first-line therapy.

Colorectal Cancer (CRC)[1,2,4,5]

Authorization of 12 months may be granted for treatment of colorectal cancer if either of the following criteria is met:

- 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.
- Used as adjuvant treatment in combination with FOLFIRI (fluorouracil, leucovorin, and irinotecan) or irinotecan for unresectable metachronous metastases that converted to resectable disease after initial treatment.

Hepatocellular Carcinoma (HCC)[1,2]

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

Mesothelioma[2]

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

Thymic Carcinoma[2]

Authorization of 12 months may be granted for the treatment of thymic carcinoma when any of the following are met:

- Member has recurrent, advanced, or metastatic disease and the requested medication will be used as first-line therapy in combination with carboplatin and paclitaxel and continued as a single agent maintenance therapy, or
- Member has had a R1 or R2 resection and the requested medication will be used in combination with carboplatin and paclitaxel as postoperative treatment, or
- Member has surgically resectable disease, R0 resection is considered uncertain, and the requested medication will be used in combination with carboplatin and paclitaxel as preoperative treatment.

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Urothelial Carcinoma[3]

Authorization of 12 months may be granted for treatment of advanced or metastatic urothelial carcinoma when all of the following criteria is met:

- Used in combination with docetaxel.
- Disease progression within 12 months after platinum-containing chemotherapy.

Continuation of Therapy

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

NSCLC

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

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

All Other Indications

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

- The member is currently receiving therapy with the requested medication
- The requested medication is being used to treat an indication listed in the coverage criteria section
- The member is receiving benefit from therapy. Benefit is defined as:
    - No evidence of unacceptable toxicity while on the current regimen, and
    - No evidence of disease progression while on the current regimen

Summary of Evidence

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

- The prescribing information for Cyramza.
- The available compendium
    - National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium
    - Micromedex DrugDex

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    - American Hospital Formulary Service- Drug Information (AHFS-DI)
    - Lexi-Drugs
    - Clinical Pharmacology
- NCCN Guideline: Pleural mesothelioma
- NCCN Guideline: Non-small cell lung cancer
- NCCN Guideline: Hepatocellular carcinoma
- NCCN Guideline: Gastric cancer
- NCCN Guideline: Esophageal and esophagogastric junction cancers
- NCCN Guideline: Colon cancer
- NCCN Guideline: Rectal cancer
- NCCN Guideline: Anal carcinoma
- NCCN Guideline: Thymomas and thymic carcinomas

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:

- Gastric and gastro-esophageal junction (GEJ) Cancer
- Esophagogastric junction (EGJ) and esophageal adenocarcinoma
- NSCLC – recurrent, advanced
- Colorectal cancer:
    - Anal adenocarcinoma and appendiceal adenocarcinoma
    - Advanced disease
    - In combination with irinotecan
    - Adjuvant treatment
- Hepatocellular carcinoma (HCC)
- Mesothelioma
- Thymic carcinoma
- Urothelial carcinoma

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, NSCLC, colorectal cancer, anal adenocarcinoma, appendiceal adenocarcinoma, hepatocellular carcinoma, mesothelioma, and thymic carcinoma 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).

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References

1. Cyramza [package insert]. Indianapolis, IN: Eli Lilly and Company; August 2025.
2. The NCCN Drugs & Biologics Compendium® © 2026 National Comprehensive Cancer Network, Inc. Available at: https://www.nccn.org. Accessed January 5, 2026.
3. Micromedex® (electronic version). Merative, Ann Arbor, Michigan, USA. Available at: https://www.micromedexsolutions.com. Accessed January 5, 2026.
4. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Anal Carcinoma. Version 5.2025. Available at: https://www.nccn.org/professionals/physician_gls/pdf/anal.pdf. Accessed January 5, 2026.
5. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Colon Cancer. Version 5.2025. Available at: https://www.nccn.org/professionals/physician_gls/pdf/colon.pdf. Accessed January 5, 2026.

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