

Medical Policy Manual **Approved Rev: Do Not Implement until 9/30/26**

Ramucirumab (Cyramza®)

IMPORTANT REMINDER

We develop Medical Policies to provide guidance to Members and Providers. This Medical Policy relates only to the services or supplies described in it. The existence of a Medical Policy is not an authorization, certification, explanation of benefits or a contract for the service (or supply) that is referenced in the Medical Policy. For a determination of the benefits that a Member is entitled to receive under his or her health plan, the Member's health plan must be reviewed. If there is a conflict between the medical policy and a health plan or government program (e.g., TennCare), the express terms of the health plan or government program will govern.

POLICY

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

- 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 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.
 - Cyramza, in combination with erlotinib, is indicated for the first-line treatment of **adults** with metastatic NSCLC whose tumors have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 (L858R) substitution mutations.
- 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

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

All other indications are considered experimental/investigational and not medically necessary.



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DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: 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

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.

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:

- 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)

Authorization of 12 months may be granted for treatment of advanced or metastatic colorectal cancer, including anal adenocarcinoma and appendiceal adenocarcinoma, in combination with FOLFIRI (irinotecan, folinic acid, and 5-fluorouracil) or irinotecan.

Hepatocellular Carcinoma (HCC)

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

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

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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CONTINUATION OF THERAPY

NSCLC

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for NSCLC when either of the following criteria is met:

- There is 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

All Other Indications

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in the Coverage Criteria section when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

MEDICATION QUANTITY LIMITS

Drug Name	Diagnosis	Maximum Dosing Regimen
Cyramza (Ramucirumab)	Colorectal Cancer, including Appendiceal Adenocarcinoma and Anal Adenocarcinoma	Route of Administration: Intravenous 8mg/kg every 2 weeks
Cyramza (Ramucirumab)	Esophageal, Gastric or Gastroesophageal Junction Adenocarcinoma	Route of Administration: Intravenous 8mg/kg every 2 weeks
Cyramza (Ramucirumab)	Hepatocellular Carcinoma	Route of Administration: Intravenous 8mg/kg every 2 weeks
Cyramza (Ramucirumab)	Mesothelioma (Pleural, Pericardial, or Tunica Vaginalis Testis)	Route of Administration: Intravenous 10mg/kg every 3 weeks
Cyramza (Ramucirumab)	Non-Small Cell Lung Cancer	Route of Administration: Intravenous 10mg/kg every 2 weeks
Cyramza (Ramucirumab)	Thymic Carcinoma	Route of Administration: Intravenous 10mg/kg every 3 weeks

APPLICABLE TENNESSEE STATE MANDATE REQUIREMENTS

BlueCross BlueShield of Tennessee's Medical Policy complies with Tennessee Code Annotated Section 56-7-2352 regarding coverage of off-label indications of Food and Drug Administration (FDA) approved drugs when the off-label use is recognized in one of the statutorily recognized standard reference compendia or in the published peer-reviewed medical literature.

ADDITIONAL INFORMATION

For appropriate chemotherapy regimens, dosage information, contraindications, precautions, warnings, and monitoring information, please refer to one of the standard reference compendia (e.g., the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) published by the National Comprehensive Cancer Network®, Drugdex Evaluations of Micromedex Solutions at Truven Health, or The American Hospital Formulary Service Drug Information).



BlueCross BlueShield
of Tennessee

Policy

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REFERENCES

1. Cymaza [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. 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**.
4. **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.**

EFFECTIVE DATE

9/30/2026

ID_CHS_2026