# Medical Policy:

## Cyramza® (ramucirumab) Intravenous

| POLICY NUMBER | LAST REVIEW | ORIGIN DATE |
|---|---|---|
| MG.MM.PH.48 | March 20, 2024 | |



The treating physician or primary care provider must submit to EmblemHealth, or ConnectiCare, as applicable (hereinafter jointly referred to as "EmblemHealth"), the clinical evidence that the member meets the criteria for the treatment or surgical procedure. Without this documentation and information, EmblemHealth will not be able to properly review the request preauthorization or post-payment review. The clinical review criteria expressed below reflects how EmblemHealth determines whether certain services or supplies are medically necessary. This clinical policy is not intended to pre-empt the judgment of the reviewing medical director or dictate to health care providers how to practice medicine. Health care providers are expected to exercise their medical judgment in rendering appropriate care. Health care providers are expected to exercise their medical judgment in rendering appropriate care.

EmblemHealth established the clinical review criteria based upon a review of currently available clinical information (including clinical outcome studies in the peer reviewed published medical literature, regulatory status of the technology, evidence-based guidelines of public health and health research agencies, evidence-based guidelines and positions of leading national health professional organizations, views of physicians practicing in relevant clinical areas, and other relevant factors). EmblemHealth expressly reserves the right to revise these conclusions as clinical information changes and welcomes further relevant information. Each benefit program defines which services are covered. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered and/or paid for by EmblemHealth, as some programs exclude coverage for services or supplies that EmblemHealth considers medically necessary.

If there is a discrepancy between this guideline and a member's benefits program, the benefits program will govern. Identification of selected brand names of devices, tests and procedures in a medical coverage policy is for reference only and is not an endorsement of any one device, test or procedure over another. In addition, coverage may be mandated by applicable legal requirements of a state, the Federal Government or the Centers for Medicare & Medicaid Services (CMS) for Medicare and Medicaid members. All coding and web site links are accurate at time of publication.

EmblemHealth may also use tools developed by third parties, such as the MCG™ Care Guidelines, to assist us in administering health benefits. The MCG™ Care Guidelines are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice. EmblemHealth Services Company, LLC, has adopted this policy in providing management, administrative and other services to EmblemHealth Plan, Inc., EmblemHealth Insurance Company, EmblemHealth Services Company, LLC, and Health Insurance Plan of Greater New York (HIP) related to health benefit plans offered by these entities. ConnectiCare, an EmblemHealth company, has also adopted this policy. All of the aforementioned entities are affiliated companies under common control of EmblemHealth Inc.

## Definition

Cyramza (ramucirumab) is a vascular endothelial growth factor (VEGF) receptor 2 antagonist that inhibits ligand-stimulated activation of the VEGF receptor 2, ligand-induced proliferation, and migration of human endothelial cells. Unlike all clinically approved angiogenesis inhibitors, the fully human monoclonal antibody ramucirumab, specifically inhibits VEGFR-2.

## Length of Authorization

Coverage will be provided for six months and may be renewed.

## Dosing Limits [Medical Benefit]

**Max Units (per dose and over time):**

Gastric/Esophageal/Esophagogastric Junction Cancers, Colorectal Cancer and HCC: 180 billable units every 14 days

NSCLC: 240 billable units every 14 days

## Guideline

### I. INITIAL CRITERIA

Cyramza (ramucirumab) may be considered medically necessary for the following diagnosis when all of the following criteria are met:

1. **Gastric, Esophageal and Gastro-esophageal Junction Cancers, initiation:**
   A. Patient is 18 years of age or older; **AND**
   B. Patient has advanced or metastatic disease; **AND**
   C. Used as a single agent **OR** in combination with paclitaxel **OR** used in combination with irinotecan; **AND**
   D. Must be used as subsequent therapy, progressing after treatment with fluoropyrimidine- or platinum-containing chemotherapy

2. **Non-small cell lung cancer, initiation:**
   A. Patient is 18 years of age or older; **AND**
   B. Patient meets **ONE** of the following criteria (i or ii):
      i. Cyramza will be used as first-line therapy; **AND**
         a. Patient has epidermal growth factor receptor (EGFR) exon 19 deletion or L858R mutation positive disease; **AND**
         b. Cyramza will be used in combination with erlotinib; **OR**
      ii. Cyramza will be used as subsequent therapy; **AND**
         a. Cyramza will be used in combination with docetaxel intravenous infusion; **AND**
         b. Patient has received targeted drug therapy if the patient's tumor is positive for a targetable mutation
         *Note: Examples of targetable mutations include sensitizing epidermal growth factor receptor mutation, anaplastic lymphoma kinase fusions*

3. **Colorectal cancer, initiation**
   A. Patient is 18 years of age or older; **AND**
   B. Patient's disease is metastatic; **AND**
   C. Cyramza is being used in combination with FOLFIRI (irinotecan, folinic acid, and 5-fluorouracil) **OR** irinotecan for metastatic disease that progressed on or after therapy with bevacizumab, oxaliplatin and a fluoropyrimidine

4. **Hepatocellular carcinoma:**
   A. Patient is 18 years of age or older; **AND**
   B. Cyramza is being used as a single agent; **AND**
   C. Patient has an alpha fetoprotein of $\geq$ 400 ng/mL; **AND**
   D. Patient has Child-Pugh Class A disease; **AND**
   E. Patient has been previously treated with sorafenib

### II. Renewal Criteria

Coverage for Cyramza (ramucirumab) may be **renewed** when the following criteria are met:

A. Disease response; **AND**
B. Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include the following: hemorrhage, arterial thrombotic events, uncontrollable hypertension, infusion-related reactions, severe proteinuria (>3g/24h), gastrointestinal perforation, wound healing complications, etc.

### Limitations/Exclusions

1. Ramucirumab is considered investigational and may not be considered medically necessary for the

following conditions: bladder cancer, breast cancer, chondrosarcoma, genitourinary tumor, fallopian tube cancer, head and neck cancer, malignant pleural diseases, melanoma, ovarian cancer, peritoneal carcinoma, prostate cancer, renal cell carcinoma, soft tissue sarcoma.

### Dosing/Administration

| Indication | Dose |
|---|---|
| **Colorectal Cancer, Gastric/Esophageal/ Esophagogastric Junction Cancers, Hepatocellular Carcinoma** | Administer 8 mg/kg intravenously every 14 days until disease progression or unacceptable toxicity |
| **Non-Small Cell Lung Cancer** | In combination with docetaxel:<br>Administer 10 mg/kg intravenously every 21 days until disease progression or unacceptable toxicity<br>In combination with erlotinib:<br>Administer 10 mg/kg intravenously every 14 days until disease progression or unacceptable toxicity |

## Applicable Procedure Codes

| Code | Description |
|---|---|
| J9308 | Injection, ramucirumab, 5 mg |

## Applicable NDCs

| Code | Description |
|---|---|
| 00002-7669-01 | Cyramza 100mg/10mL, 1 vial, single-dose in 1 carton, 10 mL in 1 vial, single-dose |
| 00002-7678-01 | Cyramza 500mg/50mL. 1 vial, single-dose in 1 carton, 50 mL in 1 vial, single-dose |

## ICD-10 Diagnoses

| Code | Description |
|---|---|
| C15.3 | Malignant neoplasm of upper third of esophagus |
| C15.4 | Malignant neoplasm of middle third of esophagus |
| C15.5 | Malignant neoplasm of lower third of esophagus |
| C15.8 | Malignant neoplasm of overlapping sites of esophagus |
| C15.9 | Malignant neoplasm of esophagus, unspecified |
| C16.0 | Malignant neoplasm of cardia |
| C16.1 | Malignant neoplasm of fundus of stomach |
| C16.2 | Malignant neoplasm of body of stomach |
| C16.3 | Malignant neoplasm of pyloric antrum |
| C16.4 | Malignant neoplasm of pylorus |
| C16.5 | Malignant neoplasm of lesser curvature of stomach, unspecified |
| C16.6 | Malignant neoplasm of greater curvature of stomach, unspecified |
| C16.8 | Malignant neoplasm of overlapping sites of stomach |
| C16.9 | Malignant neoplasm of stomach, unspecified |
| C17.0 | Malignant neoplasm duodenum |
| C17.1 | Malignant neoplasm jejunum |
| C17.2 | Malignant neoplasm ileum |
| C17.8 | Malignant neoplasm of overlapping sites of small intestines |

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|---|---|
| C17.9 | Malignant neoplasm of small intestine, unspecified |
| C18.0 | Malignant neoplasm of cecum |
| C18.1 | Malignant neoplasm of appendix |
| C18.2 | Malignant neoplasm of ascending colon |
| C18.3 | Malignant neoplasm of hepatic flexure |
| C18.4 | Malignant neoplasm of transverse colon |
| C18.5 | Malignant neoplasm of splenic flexure |
| C18.6 | Malignant neoplasm of descending colon |
| C18.7 | Malignant neoplasm of sigmoid colon |
| C18.8 | Malignant neoplasm of overlapping sites of large intestines |
| C18.9 | Malignant neoplasm of colon, unspecified |
| C19 | Malignant neoplasm of rectosigmoid junction |
| C20 | Malignant neoplasm of rectum |
| C21.8 | Malignant neoplasm of overlapping sites of rectum, anus and anal canal |
| C33 | Malignant neoplasm of trachea |
| C34.00 | Malignant neoplasm of main bronchus |
| C34.01 | Malignant neoplasm of right main bronchus |
| C34.02 | Malignant neoplasm of left main bronchus |
| C34.10 | Malignant neoplasm of upper lobe, unspecified bronchus or lung |
| C34.11 | Malignant neoplasm of upper lobe, right bronchus or lung |
| C34.12 | Malignant neoplasm of upper lobe, left bronchus or lung |
| C34.2 | Malignant neoplasm of middle lobe, bronchus or lung |
| C34.30 | Malignant neoplasm of lower lobe, unspecified bronchus or lung |
| C34.31 | Malignant neoplasm of lower lobe, right bronchus or lung |
| C34.32 | Malignant neoplasm of lower lobe, left bronchus or lung |
| C34.80 | Malignant neoplasm of overlapping sites of unspecified bronchus and lung |
| C34.81 | Malignant neoplasm of overlapping sites of right bronchus and lung |
| C34.82 | Malignant neoplasm of overlapping sites of left bronchus and lung |
| C34.90 | Malignant neoplasm of unspecified part of unspecified bronchus or lung |
| C34.91 | Malignant neoplasm of unspecified part of right bronchus or lung |
| C34.92 | Malignant neoplasm of unspecified part of left bronchus or lung |
| C78.00 | Secondary malignant neoplasm of lung |
| C78.01 | Secondary malignant neoplasm of lung |
| C78.02 | Secondary malignant neoplasm of lung |
| C78.6 | Secondary malignant neoplasm of retroperitoneum and peritoneum |
| C78.7 | Secondary malignant neoplasm of liver and intrahepatic bile duct |
| D37.1 | Neoplasm of uncertain behavior of stomach |
| D37.8 | Neoplasm of uncertain behavior of other specified digestive organs |
| D37.9 | Neoplasm of uncertain behavior of digestive organ, unspecified |
| Z85.00 | Personal history of malignant neoplasm of unspecified digestive organ |
| Z85.01 | Personal history of malignant neoplasm of esophagus |
| Z85.028 | Personal history of other malignant neoplasm of stomach |
| Z85.038 | Personal history of malignant neoplasm of large intestine |
| Z85.118 | Personal history of other malignant neoplasm of bronchus and lung |

## Revision History

| Company(ies) | DATE | REVISION |
|---|---|---|
| EmblemHealth & ConnectiCare | 3/20/2024 | Annual Review: Removed PI link, added dosing chart, no criteria changes |
| EmblemHealth & ConnectiCare | 7/18/2023 | Annual Review:<br>Gastric, Esophageal and Gastro-esophageal Junction Cancers, initiation: Initial Criteria: Added" OR used in combination with irinotecan;"<br>Non-small cell lung cancer, initiation: Initial Criteria: Added " Patient meets of the following criteria (i or ii):<br>i. Cyramza will be used as first-line therapy; AND<br>a) Patient has epidermal growth factor receptor (EGFR) exon 19 deletion or L858R mutation<br>positive disease; AND<br>b) Cyramza will be used in combination with erlotinib; OR<br>ii. Cyramza will be used as subsequent therapy; AND<br>a) Cyramza will be used in combination with docetaxel intravenous infusion; AND<br>b) Patient has received targeted drug therapy if the patient's tumor is positive for a targetable<br>mutation<br>Note: Examples of targetable mutations include sensitizing epidermal growth factor receptor mutation, anaplastic lymphoma kinase fusions"<br>Removed " Patient's disease is metastatic; AND<br>In combination with erlotinib, for the first-line treatment of patients whose tumors have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 (L858R) substitution mutations; OR<br>Used as subsequent therapy following progression on or after platinum-based chemotherapy; AND<br>Cyramza must be used in combination with docetaxel; AND<br>Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving Cyramza"<br>Colorectal cancer, initiation: Initial Criteria Added " **OR** irinotecan"<br>Hepatocellular carcinoma: Initial Criteria Added "Patient has Child-Pugh Class A disease; AND" |
| EmblemHealth & ConnectiCare | 4/11/2022 | Transferred policy to new template |
| EmblemHealth & ConnectiCare | 06/17/2020 | Added Criteria for NSCLC indication: In combination with erlotinib, for the first-line treatment of patients whose tumors have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 (L858R) substitution mutations |
| EmblemHealth & ConnectiCare | 11/11/2019 | Added indication for Hepatocellular carcinoma; removed hepatocellular carcinoma from limitations/exclusions |

## References


1. Product Information: CYRAMZA® intravenous injection, ramucirumab intravenous injection. Eli LIlly and Company (per manufacturer), Indianapolis, IN, 2019.