CARECONTINUUM™

UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Oncology (Injectable) – Cyramza Utilization Management Medical Policy
- Cyramza® (ramucirumab intravenous infusion – Eli Lilly)

REVIEW DATE: 06/03/2026

OVERVIEW

Cyramza, a human vascular endothelial growth factor receptor 2 (VEGFR2) antagonist, is indicated for the following uses:[1]

- **Colorectal cancer**, metastatic, in combination with FOLFIRI (irinotecan, leucovorin, and 5-fluorouracil [5-FU]) for patients with disease progression on or after prior therapy with bevacizumab, oxaliplatin, and a fluoropyrimidine.
- **Gastric** or **gastroesophageal junction adenocarcinoma**, as a single agent or in combination with paclitaxel for patients with advanced or metastatic disease with disease progression on or after prior fluoropyrimidine- or platinum-containing chemotherapy.
- **Hepatocellular carcinoma**, as a single agent in patients who have an alpha fetoprotein of ≥ 400 ng/mL and have been treated with sorafenib (Nexavar®, generic).
- **Non-small cell lung cancer** (NSCLC), metastatic, in combination with docetaxel for 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.
- **NSCLC**, metastatic, in combination with erlotinib for the first-line treatment of NSCLC with *EGFR* exon 19 deletions or exon 21 (L858R) mutations.

Dosing

The recommended dose of Cyramza is 8 mg/kg administered by intravenous (IV) infusion once every 2 weeks for gastric cancer, colorectal cancer, and hepatocellular cancinoma.[1] The recommended dose for NSCLC is 10 mg/kg administered by IV infusion no more frequently than once every 2 weeks. Cyramza is continued until disease progression or unacceptable adverse events. The dose of Cyramza is reduced, withheld, or discontinued to manage adverse events.

Guidelines

The use of Cyramza is recommended across multiple National Comprehensive Cancer Network (NCCN) guidelines and the NCCN Compendium.[4] Recommendations with a category of evidence of 2B or higher support the approval criteria outlined below.

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of Cyramza. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indications. Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with Cyramza as well as the monitoring required for adverse events and long-term efficacy, approval requires Cyramza to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Cyramza is recommended in those who meet one of the following criteria:

FDA-Approved Indications

1. **Colon or Rectal Cancer**. Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** Patient meets ONE of the following (i, ii, or iii):
     - **i.** Patient meets BOTH of the following (a and b):
       - **a)** Patient has unresectable metachronous metastases; AND
       - **b)** Patient has been previously treated with FOLFOX or CapeOX; OR
         Note: FOLFOX includes 5-fluorouracil (5-FU), leucovorin, and oxaliplatin and CapeOX includes capecitabine and oxaliplatin.
     - **ii.** The medication is used as adjuvant therapy; OR
     - **iii.** Patient meets ALL of the following (a, b, and c):
       - **a)** Patient has advanced or metastatic disease; AND
       - **b)** The medication is used as subsequent therapy; AND
       - **c)** Patient has been previously treated with oxaliplatin-based therapy; AND
   - **C)** The medication will be used in combination with ONE of the following (i or ii):
     - **i.** Irinotecan; OR
     - **ii.** FOLFIRI; AND
       Note: FOLFIRI includes irinotecan, folinic acid (leucovorin), and 5-fluorouracil (5-FU); AND
   - **D)** The medication is prescribed by or in consultation with an oncologist.

   Dosing. Approve up to 8 mg/kg as an intravenous infusion administered no more frequently than once every 2 weeks.

2. **Gastric, Esophagogastric Junction, or Esophageal Cancer**. Approve for 1 year if the patient meets ALL of the following (A, B, and C):
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** The medication is used as subsequent therapy; AND
   - **C)** The medication is prescribed by or in consultation with an oncologist.

   Dosing. Approve up to 8 mg/kg as an intravenous infusion administered no more frequently than once every 2 weeks.

3. **Hepatocellular Carcinoma.** Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** The medication will be used as subsequent therapy; AND
   - **C)** Patient has an alpha fetoprotein level of ≥ 400 ng/mL; AND
   - **D)** The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve up to 8 mg/kg as an intravenous infusion administered no more frequently than once every 14 days.

4. **Non-Small Cell Lung Cancer.** Approve for 1 year if the patient meets ALL of the following (A, B, and C):
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** Patient meets ONE of the following (i or ii):
     - **i.** Patient meets BOTH of the following (a and b):
       - **a)** Patient has epidermal growth factor receptor (*EGFR*) exon 19 deletion or exon 21 L858R mutation-positive disease; AND
       - **b)** The medication will be used in combination with erlotinib; OR
     - **ii.** Patient meets BOTH of the following (a and b):
       - **a)** The medication will be used as subsequent therapy; AND
       - **b)** The medication will be used in combination with docetaxel; AND
   - **C)** The medication is prescribed by or in consultation with an oncologist.

   Dosing. Approve up to 10 mg/kg as an intravenous infusion no more frequently than once every 3 weeks.

Other Uses with Supportive Evidence

5. **Mesothelioma**. Approve for 1 year if the patient meets ALL of the following (A, B, C, D, and E):
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** Patient has ONE of the following (i, ii, or iii):
     - **i.** Pleural mesothelioma; OR
     - **ii.** Pericardial mesothelioma; OR
     - **iii.** Tunica vaginalis testis mesothelioma; AND
   - **C)** The medication is used as subsequent therapy; AND
   - **D)** The medication is used in combination with gemcitabine; AND
   - **E)** The medication is prescribed by or in consultation with an oncologist.

   Dosing. Approve up to 10 mg/kg as an intravenous infusion no more frequently than once every 3 weeks.

6. **Thymic Carcinoma.** Approve for 1 year if the patient meets ALL of the following (A, B, and C):
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** The medication will be used with carboplatin and paclitaxel; AND
   - **C)** The medication is prescribed by or in consultation with an oncologist.

   Dosing. Approve up to 10 mg/kg as an intravenous infusion no more frequently than once every 3 weeks.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Cyramza is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Cyramza® intravenous infusion [prescribing information]. Indianapolis, IN: Eli Lilly; August 2025.
2. The NCCN Colon Cancer Clinical Practice Guidelines in Oncology (version 2.2026 – April 7, 2026). © 2026 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on May 18, 2026.
3. The NCCN Rectal Cancer Clinical Practice Guidelines in Oncology (version 2.2026 – April 7, 2026). © 2026 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on May 18, 2026.
4. The NCCN Drugs & Biologics Compendium. © 2026 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on May 13, 2026 Search term: ramucirumab.
5. The NCCN Gastric Cancer Clinical Practice Guidelines in Oncology (version 2.2026 – January 21, 2026). © 2026 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on May 18, 2026.
6. The NCCN Esophageal and Esophagogastric Junction Cancers Clinical Practice Guidelines in Oncology (version 2.2026 – January 21, 2026). © 2026 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on May 18, 2026.
7. The NCCN Non-Small Cell Lung Cancer Clinical Practice Guidelines in Oncology (version 5.2026 – March 13, 2026). © 2026 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on May 18, 2026.
8. The NCCN Hepatocellular Carcinoma Clinical Practice Guidelines in Oncology (version 1.2026 – March 10, 2026). © 2026 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on May 18, 2026.
9. The NCCN Mesothelioma: Pleural Clinical Practice Guidelines in Oncology (version 2.2026 – October 3, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on May 18, 2026.
10. Pinto C, Zucali PA, Pagano M, et al. Gemcitabine with or without ramucirumab as second-line treatment for malignant pleural mesothelioma (RAMES): a randomized, double-blind, placebo-controlled, phase 2 trial. *Lancet Oncol*. 2021;22:1438-1447.
11. The NCCN Thymomas and Thymic Carcinomas Clinical Practice Guidelines in Oncology (version 2.2026 – April 10, 2026). © 2026 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on May 18, 2026.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	**Hepatocellular Carcinoma:** Removed requirements that the patient has been treated with Nexavar (sorafenib tablet) and patient has Child-Pugh Class A disease. Added requirement that Cyramza will be used as subsequent therapy.	06/12/2024
Annual Revision	**Thymic Carcinomas:** Added new condition of approval and criteria. **Colon, Rectal, or Appendiceal Cancer:** Removed the requirement that the "patient has received oxaliplatin and fluoropyrimidine.. Added options for approval for patient with unresectable metachronous metastases, if proficient mismatch repair/microsatellite-stable (pMMR/MSS) or deficient mismatch repair/microsatellite instability-high (dMMR/MSI-H) or polymerase epsilon/delta (POLE/POLD1) mutation positive with ultra-hypermutated phenotype, and if the patient has been previously treated with FOLFOX or CapeOX or the medication is used as adjuvant therapy. For advanced or metastatic disease; added a requirement that disease is (pMMR/MSS) or ineligible for or progressed on checkpoint inhibitor therapy for (dMMR/MSI-H) or polymerase epsilon/delta (POLE/POLD1) mutation positive with ultra-hypermutated phenotype, if the patient has not previously been treated with irinotecan, and the medication is used for subsequent therapy. **Gastric, Esophagogastric Junction, or Esophageal Cancer:** Removed the requirement that the"patient has received chemotherapy with 5-Fluorouracil (5-FU), capecitabine, cisplatin, carboplatin, or oxaliplatin. Added a requirement that "the medication is used as subsequent therapy.. **Non-Small Cell Lung Cancer:** Removed the requirement that "Cyramza will be used as first-line or continuation therapy" and that the "patient has received targeted drug therapy if the patient's tumor is positive for a targetable mutation".	06/11/2025
Annual Revision	**Colon or Rectal Cancer:** The indication was changed to as noted. Previously it was "Colon, Rectal, or Appendiceal Cancer". Removed requirement of proficient mismatch repair/microsatellite stable (pMMR/MSS) or deficient mismatch repair/microsatellite instability high (dMMR/MSI-H) or polymerase epsilon/delta (POLE/POLD1) mutation positive with ultra hypermutated phenotype. The requirement that the patient has not been treated with irinotecan was removed. Added requirement that the patient has been previously treated with oxaliplatin-based therapy. **Gastric, Esophagogastric Junction, or Esophageal Cancer:** Removed options that the medication is used as a single agent or in combination with paclitaxel or in combination with irinotecan. **Hepatocellular Carcinoma:** Removed requirement that the medication will be used as a single agent. **Thymic Carcinoma:** Removed option that the medication will be used as maintenance therapy.	06/03/2026