

Evolent Clinical Guideline 3192 for Cyramza™ (ramucirumab)

Guideline Number: Evolent_CG_3192	<u>Applicable Codes</u>	
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Original Date: November 2014	Last Revised Date: October 2025	Implementation Date: October 2025

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STATEMENT

Purpose

To define and describe the accepted indications for Cyramza (ramucirumab) usage in the treatment of cancer, including FDA approved indications, and off-label indications.

Evolent is responsible for processing all medication requests from network ordering providers. Medications not authorized by Evolent may be deemed as not approvable and therefore not reimbursable.

The use of this drug must be supported by one of the following: FDA approved product labeling, CMS-approved compendia, National Comprehensive Cancer Network (NCCN), American Society of Clinical Oncology (ASCO) clinical guidelines, or peer-reviewed literature that meets the requirements of the CMS Medicare Benefit Policy Manual Chapter 15.

INDICATIONS

Continuation requests for a not-approvable medication shall be exempt from this Evolent policy provided

- The member has not experienced disease progression on the requested medication AND
- The requested medication was used within the last year without a lapse of more than 30 days of having an active authorization AND
- Additional medication(s) are not being added to the continuation request.

Colorectal Carcinoma

- NOTE: Cyramza (ramucirumab) +/- chemotherapy is not supported by Evolent Policy for the treatment of colorectal carcinoma. This policy position is based on a large meta-analysis of randomized clinical trials (referenced below) which showed increased serious (including fatal) treatment related toxicities with negligible benefits with the use of Cyramza (ramucirumab) in metastatic solid tumors, compared to Evolent recommended alternatives agents/regimens, including but not limited to regimens at Evolent Pathways.

Gastric, Gastroesophageal Junction, and Esophageal Cancers

- Cyramza (ramucirumab) may be used as monotherapy or in combination with Taxol (paclitaxel) as second line treatment of advanced or metastatic gastric, gastroesophageal junction, or esophageal adenocarcinoma.

Hepatocellular Carcinoma

- NOTE: Cyramza (ramucirumab) is not supported by Evolent Policy for the treatment of hepatocellular carcinoma. This policy position is based on a network meta-analysis (referenced below) demonstrating a lack of clinically meaningful improvement in overall survival (HR greater than 0.82) with Cyramza (ramucirumab) compared to Stivarga (regorafenib) or Cabometyx (cabozantinib) in the second line setting for

metastatic/recurrent hepatocellular cancer. Please refer to Evolent alternative agents/regimens recommended by Evolent, including but not limited to regimens available at [Evolent Pathways](#).

Non-Small Cell Lung Cancer (NSCLC)

- NOTE: Cyramza (ramucirumab) + Taxotere (docetaxel)/Tarseva (erlotinib) are not supported by Evolent Policy for the treatment of metastatic NSCLC. This policy position is based on a large meta-analysis of Randomized Clinical Trials (referenced below) which showed increased serious (including fatal) treatment related toxicities with negligible benefits with the use of Cyramza (ramucirumab) in metastatic solid tumors, compared to Evolent recommended alternatives agents/regimens, including but not limited to regimens at [Evolent Pathways](#).

CONTRAINDICATIONS/WARNINGS

- None

EXCLUSION CRITERIA

- Disease progression while taking Cyramza (ramucirumab).
- Dosing exceeds single dose limit of Cyramza (ramucirumab) 10 mg/kg.
- Investigational use of Cyramza (ramucirumab) with an off-label indication that is not sufficient in evidence or is not generally accepted by the medical community. Sufficient evidence that is not supported by CMS recognized compendia or acceptable peer reviewed literature is defined as any of the following:
 - Whether the clinical characteristics of the patient and the cancer are adequately represented in the published evidence.
 - Whether the administered chemotherapy/biologic therapy/immune therapy/targeted therapy/other oncologic therapy regimen is adequately represented in the published evidence.
 - Whether the reported study outcomes represent clinically meaningful outcomes experienced by patients. Generally, the definitions of Clinically Meaningful outcomes are those recommended by ASCO, e.g., Hazard Ratio of less than 0.80 and the recommended survival benefit for OS and PFS should be at least 3 months.
 - Whether the experimental design, considering the drugs and conditions under investigation, is appropriate to address the investigative question. (For example, in some clinical studies, it may be unnecessary or not feasible to use randomization, double blind trials, placebos, or crossover).
 - That non-randomized clinical trials with a significant number of subjects may be a basis for supportive clinical evidence for determining accepted uses of drugs.
 - That case reports are generally considered uncontrolled and anecdotal information and do not provide adequate supportive clinical evidence for determining accepted uses of drugs.

- That abstracts (including meeting abstracts) without the full article from the approved peer-reviewed journals lack supporting clinical evidence for determining accepted uses of drugs.

CODING AND STANDARDS

Codes

- J9308 - Injection, ramucirumab, 5 mg

Applicable Lines of Business

<input type="checkbox"/>	CHIP (Children's Health Insurance Program)
<input checked="" type="checkbox"/>	Commercial
<input checked="" type="checkbox"/>	Exchange/Marketplace
<input checked="" type="checkbox"/>	Medicaid
<input type="checkbox"/>	Medicare Advantage

POLICY HISTORY

Date	Summary
October 2025	<ul style="list-style-type: none">● Converted to new Evolent guideline template● This guideline replaces UM ONC_1261 Cyramza (ramucirumab)● Updated indication section● Updated references
October 2024	<ul style="list-style-type: none">● Updated NCH verbiage to Evolent

LEGAL AND COMPLIANCE

Guideline Approval

Committee

Reviewed / Approved by Evolent Specialty Services Clinical Guideline Review Committee

Disclaimer

Evolent Clinical Guidelines do not constitute medical advice. Treating health care professionals are solely responsible for diagnosis, treatment, and medical advice. Evolent uses Clinical Guidelines in accordance with its contractual obligations to provide utilization management. Coverage for services varies for individual members according to the terms of their health care coverage or government program. Individual members' health care coverage may not utilize some Evolent Clinical Guidelines. Evolent clinical guidelines contain guidance that requires prior authorization and service limitations. A list of procedure codes, services or drugs may not be all inclusive and does not imply that a service or drug is a covered or non-covered service or drug. Evolent reserves the right to review and update this Clinical Guideline in its sole discretion. Notice of any changes shall be provided as required by applicable provider agreements and laws or regulations. Members should contact their Plan customer service representative for specific coverage information.

REFERENCES

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7. Clinical Pharmacology Elsevier Gold Standard 2025.
8. Micromedex® Healthcare Series: Micromedex Drugdex Ann Arbor, Michigan 2025.
9. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium 2025.
10. AHFS Drug Information. American Society of Health-Systems Pharmacists or Wolters Kluwer Lexi-Drugs. Bethesda, MD 2025.
11. Ellis LM, et al. American Society of Clinical Oncology perspective: Raising the bar for clinical trials by defining clinically meaningful outcomes. *J Clin Oncol.* 2014 Apr 20;32(12):1277-80.
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<http://www.accessdata.fda.gov/scripts/drugshortages/default.cfm>.