Clinical Policy: Ramucirumab (Cyramza)

Reference Number: CP. PHAR.119
Effective Date: 05.01.15
Last Review Date: 02.18
Line of Business: Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Ramucirumab (Cyramza®) is an anti-vascular endothelial growth factor antibody.

FDA Approved Indication(s)

Cyramza is indicated:

- As a single agent or in combination with paclitaxel, for treatment of advanced gastric or gastro-esophageal junction adenocarcinoma, with disease progression on or after prior fluoropyrimidine- or platinum-containing chemotherapy.
- In combination with docetaxel, for treatment of metastatic non-small cell lung cancer with disease progression on or after platinum-based chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving Cyramza.
- In combination with FOLFIRI (irinotecan, folinic acid, and 5-fluorouracil), for the treatment of metastatic colorectal cancer with disease progression on or after prior therapy with bevacizumab, oxaliplatin, and a fluoropyrimidine

Policy/Criteria

Provider must submit documentation (which may include office chart notes and lab results) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Cyramza is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Esophageal/Esophagogastric Junction/Gastric Cancer (must meet all):

1. Diagnosis of esophagogastric junction or gastric cancer;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Meets (a or b):
   a. FDA approved use: Progression on or after fluoropyrimidine- or platinum-containing therapy;
   b. NCCN recommended use: Prescribed for palliative therapy;
5. Will be used as a single agent or in combination with paclitaxel;
6. Request meets one of the following (a or b):
   a. Dose does not exceed 8 mg/kg every 2 weeks;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

Approval duration: 6 months

B. Non-Small Cell Lung Cancer (must meet all)**:**
1. Diagnosis of metastatic non-small cell lung cancer;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Progression on or after platinum-based chemotherapy;
5. Prescribed in combination with docetaxel;
6. Dose does not exceed 10 mg/kg on day 1 of a 21-day cycle.

Approval duration: 6 months

C. Colorectal Cancer (must meet all):
1. Diagnosis of metastatic colorectal cancer;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Disease progression on or after bevacizumab, oxaliplatin and fluoropyrimidine;
5. Prescribed in combination with FOLFIRI (irinotecan, folinic acid, and 5-fluorouracil);
6. Dose does not exceed 8 mg/kg every 2 weeks.

Approval duration: 6 months

D. Other diagnoses/indications
1. Refer to CP.PMN.53 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**
1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Cyramza for esophageal/gastric cancer, non-small cell lung cancer, or colorectal cancer and has received this medication for at least 30 days;
2. Member is responding positively to therapy (e.g., no disease progression or unacceptable toxicity);
3. If request is for a dose increase, request meets one of the following (a, b or c):
   a. Esophageal/gastric cancer: New dose not exceed 8 mg/kg every 2 weeks;
   b. Non-small cell lung cancer: New dose does not exceed 10 mg/kg on day 1 of a 21-day cycle;
   c. Colorectal cancer: New dose does not exceed 8 mg/kg every 2 weeks.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to CP.PMN.53 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy – CP.PMN.53 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

5-FU/LV: fluorouracil, leucovorin
ALK: anaplastic lymphoma kinase
CapeOX: capecitabine, oxaliplatin
FOLFIRI: fluorouracil, leucovorin, irinotecan
FOLFOX: fluorouracil, leucovorin, oxaliplatin
FOLFOXIRI: fluorouracil, leucovorin, oxaliplatin, irinotecan

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

Drug	Dosing Regimen	Dose Limit/ Maximum Dose
Fluoropyrimidine- or platinum-based therapy		
Examples of fluoropyrimidines: Xeloda® (capecitabine), floxuridine, fluorouracil (5-FU)	Varies upon protocol and patient tolerance	
Examples of platinums: cisplatin, oxaliplatin, carboplatin		
Examples of fluoropyrimidine- and platinum-based regimens: 5-FU/LV (fluorouracil, leucovorin) FOLFOX (5-FU, leucovorin, oxaliplatin) FOLFIRI (5-FU, leucovorin, irinotecan) FOLFOXIRI (5-FU, leucovorin, oxaliplatin, irinotecan) CapeOX (Xeloda® [capecitabine], oxaliplatin)		
Bevacizumab		
Avastin® (bevacizumab)	Varies upon protocol and patient tolerance	
Docetaxel and Paclitaxel		
Docetaxel (Taxotere®)	Varies upon protocol and patient tolerance	
Paclitaxel		

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Gastric cancer	8 mg/kg every 2 weeks administered as an intravenous infusion over 60 minutes.	8 mg/kg

Indication	Dosing Regimen	Maximum Dose
Non-small cell lung cancer	10 mg/kg administered by intravenous infusion over 60 minutes on day 1 of a 21-day cycle prior to docetaxel infusion.	10 mg/kg
Colorectal cancer	8 mg/kg every 2 weeks administered by intravenous infusion over 60 minutes prior to FOLFIRI administration.	8 mg/kg

VI. Product Availability

Injection: 200 mg/10 mL (20 mg/mL) solution in single-dose vial

VII. References

1. Cyramza Prescribing Information. Indianapolis, IN: Eli Lilly and Company; March 2017. Available at http://uspl.lilly.com/cyramza/cyramza.html. Accessed November 2017.
2. Ramucirumab. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at nccn.org. Accessed November 2017.
3. Esophageal and esophagogastric junction cancers (Version 1.2017). In: National Comprehensive Cancer Network Guidelines. Available at nccn.org. Accessed November 2017.
4. Gastric cancer (Version 5.2017). In: National Comprehensive Cancer Network Guidelines. Available at nccn.org. Accessed November 2017.
5. Non-small cell lung cancer (Version 9.2017). In: National Comprehensive Cancer Network Guidelines. Available at nccn.org. Accessed November 2017.
6. Colon cancer (Version 2.2017). In: National Comprehensive Cancer Network Guidelines. Available at nccn.org. Accessed November 2017.
7. Rectal cancer (Version 3.2017). In: National Comprehensive Cancer Network Guidelines. Available at nccn.org. Accessed November 2017.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J9308	Injection, ramucirumab, 5mg

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy developed.	05.01.15	05.15
Policy converted to new template. Gastric cancer: removed requirement of failing a fluoropyrimidine- or platinum-containing chemotherapy; edited to allow approval if disease progress on/after prior chemotherapy per NCCN.	04.01.16	05.16

Reviews, Revisions, and Approvals	Date	P&T Approval Date
NSCLC: removed requirement of failure of platinum-based chemotherapy, simplified language to include appropriate treatment regarding ALK and EGFR aberration status. Colorectal cancer: changed requirement for the use of bevacizumab, oxaliplatin, and a fluoropyrimidine to a prior regimen containing bevacizumab per NCCN. Changed requirement of concurrent use with FOLFIRI to irinotecan containing regimen instead per NCCN; changed initial approval duration to 3 months; added impaired wound healing to reasons to discontinue per PI boxed warning.		
Esophageal cancer added to section A. Lung cancer notations of specific required prior therapy are removed. Colorectal cancer indications updated around FDA and NCCN uses. Safety criteria removed as there are no contraindications or black box warnings precluding treatment. Changed initial approval duration to 6 months. Changed continued approval to 12 months.	03.01.17	04.17
1Q18 annual review: - Age, dosing, specialist added. - NCCN recommendations removed for lung and colon cancer. - References reviewed and updated.	12.01.17	02.18

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and

limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.