Clinical Policy: Ramucirumab (Cyramza)

Reference Number: CP.PHAR.119
Effective Date: 05/15
Last Review Date: 04/17

Coding Implications
Revision Log

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

Description
The intent of the criteria is to ensure that patients follow selection elements established by Centene® clinical policy for ramucirumab (Cyramza®).

Policy/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. Meets a or b:
   a. FDA approved use (all of the following):
      i. Diagnosis of esophagogastric junction (EGJ) or gastric cancer;
      ii. Disease is recurrent, metastatic, unresectable or member is a non-surgical candidate;
      iii. History of progression on or after fluoropyrimidine- or platinum-containing therapy;*
      iv. Will be used as a single agent or in combination with paclitaxel;
   b. Off-label NCCN recommended use (all of the following):
      i. Diagnosis of esophageal, EGJ or gastric cancer:
      ii. Disease is recurrent, metastatic, unresectable or member is a non-surgical candidate;
      iii. Will be used as palliative therapy as a single agent or in combination with paclitaxel.

Approval duration: 6 months

B. Non-Small Cell Lung Cancer (must meet all)**:**

1. Metastatic non-small cell lung cancer;
2. Subsequent therapy in combination with docetaxel for disease progression;
3. Dose does not exceed 10 mg/kg on day 1 of a 21-day cycle prior to docetaxel infusion.

Approval duration: 6 months

C. Colorectal Cancer (must meet all):

1. Diagnosis of colorectal cancer;
2. Meets a or b:
   a. FDA approved use (i, ii, and iii):

i. Metastatic disease;
ii. Previously treated with bevacizumab, oxaliplatin and fluoropyrimidine*;
iii. Will be used in combination with FOLFIRI*;

b. Off-label NCCN recommended use (i or ii):
i. Metastatic disease with previous FOLFOX* or CapeOX* therapy, in combination with irinotecan or FOLFIRI*;
ii. Unresectable or metastatic disease after first progression in combination with irinotecan or FOLRIRI*.

Approval duration: 6 months

D. Other diagnoses/indications: Refer to CP.PHAR.57 - Global Biopharm Policy.

II. Continued Approval

A. All Indications Listed in Section I. Initial Approval Criteria (must meet all)**:**
1. Currently receiving medication via Centene benefit or member has previously met all initial approval criteria;
2. Documentation of positive response to therapy (e.g.: no disease progression, not experiencing unacceptable toxicity).

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.PHAR.57 - Global Biopharm Policy.

**Examples of fluoropyrimidines: Capecitabine, floxuridine, fluorouracil (5-FU); examples of platinums: cisplatin, oxaliplatin, carboplatin; examples of fluoropyrimidine-based regimens: 5-FU/LV (fluorouracil, leucovorin); FOLFOX (5-FU, leucovorin, oxaliplatin); FOLFIRI (5-FU, leucovorin, irinotecan); FOLFOXIRI (5-FU, leucovorin, oxaliplatin, irinotecan); CapeOX (capecitabine, oxaliplatin).*

Background

Description/Mechanism of Action:

Ramucirumab is a recombinant human IgG1 monoclonal antibody that specifically binds to vascular endothelial growth factor receptor 2. Ramucirumab is a vascular endothelial growth factor receptor 2 antagonist that specifically binds VEGF Receptor 2 and blocks binding of VEGFR ligands, VEGF-A, VEGF-C, and VEGF-D. As a result, ramucirumab inhibits ligand-stimulated activation of VEGF Receptor 2, thereby inhibiting ligand-induced proliferation, and migration of human endothelial cells. Ramucirumab inhibited angiogenesis in an in vivo animal model.

Formulations:

Injection: 100 mg/10 mL (10 mg per mL) solution, single-dose vial 500 mg/50 mL (10 mg per mL) solution, single-dose vial

FDA Approved Indications:
Cyramza is a human vascular endothelial growth factor receptor 2 (VEGFR2) antagonist/intravenous formulation 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.

Appendices
Appendix A: Abbreviation Key
5-FU/LV: fluorouracil, leucovorin
5-FU: fluorouracil
ALK: anaplastic lymphoma kinase
CapeOX: capecitabine, oxaliplatin
EGFR: epidermal growth factor receptor
FOLFIRI: fluorouracil, leucovorin, irinotecan
FOLFOX: fluorouracil, leucovorin, oxaliplatin
FOLFOXIRI: fluorouracil, leucovorin, oxaliplatin, irinotecan
NSCLC: non-small cell lung cancer
VEGF: vascular endothelial growth factor
VEGFR: vascular endothelial growth factor receptor

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	Approval Date
Policy developed.	05/15	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.	04/16	05/16

Reviews, Revisions, and Approvals	Date	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.	03/17	04/17

References

1. Cyramza prescribing information. Indianapolis, IN: Eli Lilly and Company; February 2017. Available at http://uspl.lilly.com/cyramza/cyramza.html. Accessed March 29, 2017.
2. Ramucirumab. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at nccn.org. Accessed March 29, 2017.
3. Esophageal and esophagogastric junction cancers (Version 1.2017). In: National Comprehensive Cancer Network Guidelines. Available at nccn.org. Accessed March 29, 2017.
4. Gastric cancer (Version 1.2017). In: National Comprehensive Cancer Network Guidelines. Available at nccn.org. Accessed March 29, 2017.
5. Non-small cell lung cancer (Version 5.2017). In: National Comprehensive Cancer Network Guidelines. Available at nccn.org. Accessed March 23, 2017.
6. Colon cancer (Version 2.2017). In: National Comprehensive Cancer Network Guidelines. Available at nccn.org. Accessed March 23, 2017.
7. Rectal cancer (Version 3.2017). In: National Comprehensive Cancer Network Guidelines. Available at nccn.org. Accessed March 23, 2017.

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.

Note: For Medicare members, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Refer to the CMS website at http://www.cms.gov for additional information.