


Prior Authorization Review Panel

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CHC-MCO Policy Submission

A separate copy of this form must accompany each policy submitted for review.
Policies submitted without this form will not be considered for review.

Plan: PA Health & Wellness	Submission Date: 02/01/202120
Policy Number: PA.CP.PHAR.119	Effective Date: 01/2018 Revision Date: 01/2021
Policy Name: Ramucirumab (Cyramza)	
<p>Type of Submission – <u>Check all that apply:</u></p> <p> <input type="checkbox"/> New Policy <input checked="" type="checkbox"/> Revised Policy* <input type="checkbox"/> Annual Review - No Revisions <input type="checkbox"/> Statewide PDL - <i>Select this box when submitting policies for Statewide PDL implementation and when submitting policies for drug classes included on the Statewide PDL.</i> </p>	
<p>*All revisions to the policy <u>must</u> be highlighted using track changes throughout the document.</p> <p>Please provide any changes or clarifying information for the policy below:</p> <p>1Q 2021 annual review: NSCLC - EGRF mutation requirement added if therapy in combination with erlotinib; references reviewed and updated.</p>	
Name of Authorized Individual (Please type or print): Auren Weinberg, MD	Signature of Authorized Individual: 

Clinical Policy: Ramucirumab (Cyramza)

Reference Number: PA.CP.PHAR.119

Effective Date: 01/2018

Last Review Date: 01/2021

[Coding Implications](#)
[Revision Log](#)

Description

Ramucirumab (Cyramza[®]) is an anti-vascular endothelial growth factor (VEGF) 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 (i.e., esophagogastric junction; EGJ) adenocarcinoma, with disease progression on or after prior fluoropyrimidine- or platinum-containing chemotherapy.
- In combination with erlotinib, for treatment of metastatic non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 (L858R) mutations.
- In combination with docetaxel, for treatment of metastatic non-small cell lung cancer (NSCLC) 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.
- As a single agent, for the treatment of hepatocellular carcinoma (HCC) in patients who have an alpha fetoprotein (AFP) of ≥ 400 ng/mL and have been treated with sorafenib.

Policy/Criteria

It is the policy of health plans affiliated with Pennsylvania Health and Wellness that Cyramza is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

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

1. Diagnosis of esophageal, EGJ, or gastric cancer and disease is one of the following (a or b):
 - a. Advanced, recurrent, or metastatic
 - b. Member is not a surgical candidate;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Prescribed as subsequent therapy in one of the following (a, b, or c)*:
 - a. As a single agent;
 - b. In combination with paclitaxel;
 - c. In combination with irinotecan with or without fluorouracil;

**Prior authorization may be required for paclitaxel, fluorouracil or irinotecan.*
5. Request meets one of the following (a or b):
 - a. Dose does not exceed 8 mg per 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, recurrent, or advanced NSCLC;
 2. Prescribed by or in consultation with an oncologist;
 3. Age \geq 18 years;
 4. Request meets one of the following (a or b):*
 - a. Prescribed as subsequent therapy in combination with docetaxel;
 - b. Prescribed in combination with erlotinib (Tarceva[®]);
- *Prior authorization may be required for docetaxel or erlotinib*
5. If prescribed in combination with erlotinib, disease is positive for a sensitizing EGFR mutation (e.g., EGFR exon 19 deletions or exon 21 [L858R] substitution mutation);
 6. Request meets one of the following (a or b):
 - a. In combination with docetaxel: dose does not exceed 10 mg/kg on day 1 of a 21-day cycle;
 - b. In combination with erlotinib: dose does not exceed 10 mg/kg on day 1 every 2 weeks;
 - c. 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

C. Colorectal Cancer (must meet all):

1. Diagnosis of advanced or metastatic CRC;
2. Prescribed by or in consultation with an oncologist;
3. Age \geq 18 years;
4. Prescribed in combination with irinotecan or FOLFIRI (irinotecan, folinic acid, and 5-fluorouracil);*

**Prior authorization may be required for irinotecan or FOLFIRI.*
5. Request meets one of the following (a or b):
 - a. Dose does not exceed 8 mg/kg every two 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

D. Hepatocellular Carcinoma (must meet all):

1. Diagnosis of progressive HCC;
2. Prescribed by or in consultation with an oncologist;
3. Age \geq 18 years;
4. α -fetoprotein (AFP) \geq 400 ng/mL;
5. Disease has progressed on or after therapy with Nexavar[®];

**Prior authorization is required for Nexavar*
6. Request meets one of the following (a or b):
 - a. Dose does not exceed 8 mg per 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*).

E. Other diagnoses/indications: Refer to PA.CP.PMN.53

II. Continued Approval

A. All Indications Listed in Section I (must meet all):

1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
2. Member is responding positively to therapy;
 1. If request is for a dose increase, request meets one of the following (a, b, c, or d):
 - a. Esophageal/EGJ/gastric cancer, CRC, HCC: new dose does not exceed 8 mg/kg every 2 weeks;
 - b. NSCLC in combination with docetaxel: new dose does not exceed 10 mg/kg on day 1 of a 21-day cycle;
 - c. NSCLC in combination with erlotinib: new dose does not exceed 10 mg/kg every 2 weeks;
 - d. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2):

1. Currently receiving medication via Pennsylvania Health and Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies.
Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to PA.CP.PMN.53

III. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

AFP: α -fetoprotein	HCC: Hepatocellular Carcinoma
CRC: colorectal carcinoma	FOLFIRI: fluorouracil, leucovorin, irinotecan
EGJ: esophagogastric junction	NSCLC: non-small cell lung cancer
EGFR: epidermal growth factor receptor	VEGF: vascular endothelial growth factor
FDA: Food and Drug Administration	

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
paclitaxel	Esophageal, EGF, or gastric cancer: Varies	Varies
docetaxel (Taxotere®)	NSCLC: Varies	Varies

Drug	Dosing Regimen	Dose Limit/ Maximum Dose
Erlotinib (Tarceva)	NSCLC: 150 mg PO QD	150 mg/day
irinotecan (Camptosar [®])	CRC: Varies	Varies
FOLFIRI (5-FU, leucovorin, irinotecan)	CRC: Varies	Varies
Nexavar (sorafenib)	HCC: 400 mg PO BID	800 mg/day

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.

Appendix C: Contraindications/Boxed Warnings

- None reported.

Appendix D: General Information

Hepatocellular carcinoma: A Cynamza REACH and REACH-2 pivotal trial pooled analysis of 542 patients with disease progression on or after Nexavar and a baseline AFP level of \geq 400 ng/mL showed that median overall survival was greater for patients who received Cynamza compared to patients who received placebo (8.1 vs 5.0 months, respectively; HR, 0.69; 95% CI, 0.57-0.84; P<0.001). For advanced HCC, Cynamza subsequent-line therapy post Nexavar therapy in cases where AFP is \geq 400 ng/mL is consistent with both FDA-approved labeling and NCCN guideline recommendations.

IV. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Gastric or EGJ adenocarcinoma, HCC	Gastric or EGJ adenocarcinoma, HCC 8 mg/kg every 2 weeks IV	8 mg/kg
NSCLC	10 mg/kg IV on day 1 of a 21-day cycle prior to docetaxel 10 mg/kg IV every 2 weeks with daily erlotinib	10 mg/kg
CRC	8 mg/kg every 2 weeks IV prior to FOLFIRI	8 mg/kg
Gastric or EGJ adenocarcinoma, HCC	Gastric or EGJ adenocarcinoma, HCC 8 mg/kg every 2 weeks IV	8 mg/kg

V. Product Availability

Single-dose vial: 100 mg/10 mL (10 mg/mL) solution, 500mg/50mL (10mg/mL) solution

VI. References

1. Cynamza Prescribing Information. Indianapolis, IN: Eli Lilly and Company; June 2020. Available at <http://uspl.lilly.com/cynamza/cynamza.html>. Accessed October 14, 2020.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at nccn.org. Accessed October 14, 2020
3. National Comprehensive Cancer Network Guidelines. Esophageal and Esophagogastric Junction Cancers Version 4.2020. Available at nccn.org. Accessed October 14, 2020.

4. National Comprehensive Cancer Network Guidelines. Gastric Cancer Version 3.2020. Available at nccn.org. Accessed October 14, 2020.
5. National Comprehensive Cancer Network Guidelines. Non-Small Cell Lung Cancer Version 8.2020. Available at nccn.org. Accessed October 14, 2020.
6. National Comprehensive Cancer Network Guidelines. Colon Cancer Version 4.2020. Available at nccn.org. Accessed October 14, 2020.
7. National Comprehensive Cancer Network Guidelines. Rectal Cancer Version 6.2020. Available at nccn.org. Accessed October 14, 2020.
8. National Comprehensive Cancer Network Guidelines. Hepatobiliary Cancers Version 5.2020. Available at nccn.org. Accessed October 14, 2020.
9. Zhu AX, Kang YK, Yen CJ, et al. Ramucirumab after sorafenib in patients with advanced hepatocellular carcinoma and increased alpha-fetoprotein concentrations (REACH-2): a randomized, double-blind, placebo-controlled, phase 3 trial. *Lancet Oncol* 2019; 20:282-96.

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
Age, dosing, specialist added. NCCN recommendations removed for lung and colon cancer. References reviewed and updated.	02/2018	
1Q 2019 annual review; NCCN and FDA-approved uses summarized for improved clarity - progression on specific therapies removed across indications; for CRC combination therapy with irinotecan is added; references reviewed and updated.	01/2019	
1Q 2020 annual review: Criteria added for new FDA indication as a single-agent therapy for the treatment of advanced HCC; removed BBW based on updated prescribing information; references reviewed and updated.	01/2020	
4Q 2020 annual review: added new indication NSCLC with EGFR mutations; added criteria for NSCLC for use in combo with Erlotinib; added criteria for advanced esophageal, EGJ or gastric cancer allowing combination with fluorouracil and irinotecan per NCCN; added disease characteristics criteria for all indications per NCCN; updated Appendix B; references reviewed and updated.	10/2020	
1Q 2021 annual review: NSCLC - EGRF mutation requirement added if therapy in combination with erlotinib; references reviewed and updated.	01/2021	