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: 11/01/2020**
Policy Number: PA.CP.PHAR.119	**Effective Date: 01/2018** **Revision Date: 10/2020**
Policy Name: Ramucirumab (Cyramza)	

Type of Submission – Check all that apply:

- ☐ **New Policy**
- ✓ **Revised Policy***
- ☐ **Annual Review - No Revisions**
- ☐ **Statewide PDL** - *Select this box when submitting policies for Statewide PDL implementation and when submitting policies for drug classes included on the Statewide PDL.*

***All revisions to the policy must be highlighted using track changes throughout the document.**

Please provide any changes or clarifying information for the policy below:

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.

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: 01/18
Last Review Date: 10/2020

Coding Implications
Revision Log

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 (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 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 advanced esophageal, EGJ, or gastric cancer;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Prescribed as subsequent therapy as one of the following (a, b, or c)*:
   a. As a single agent;
   b. In combination with paclitaxel;
   c. In combination with fluorouracil and irinotecan;
   **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/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).
   **Prescribed regimen must be FDA-approved or recommended by NCCN*

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 ≥ 18 years;
4. Prescribed in combination with one of the following (a or b)*:
   a. Docetaxel, as subsequent therapy;
   b. Erlotinib;
   **Prior authorization may be required for docetaxel or erlotinib.*
5. Request meets one of the following (a or b):*
   a. Dose does not exceed 10 mg/kg on day 1 of a 21-day cycle or 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).*
   **Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 6 months

C. Colorectal Cancer (must meet all):
1. Diagnosis of metastatic CRC;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Prescribed as subsequent therapy in combination with irinotecan or FOLFIRI (irinotecan, folinic acid, and 5-fluorouracil)*;
   **Prior authorization may be required for irinotecan or FOLFIRI*
5. Disease is advanced or metastatic;
6. 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 ≥ 18 years;
4. α-fetoprotein (AFP) ≥ 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).*
   **Prescribed regimen must be FDA-approved or recommended by NCCN*

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;
3. If request is for a dose increase, request meets one of the following (a, b, or c):
   a. Esophageal/EGJ/gastric cancer, CRC, HCC: new dose not exceed 8 mg/kg every 2 weeks;
   b. NSCLC: new dose does not exceed 10 mg/kg on day 1 of a 21-day cycle or every 2 weeks;
   c. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use *(prescriber must submit supporting evidence).*

**Prescribed regimen must be FDA-approved or recommended by NCCN*

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

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
Irinotecan (Camptosar®)	CRC: Varies	Varies
FOLFIRI (5-FU, leucovorin, irinotecan)	CRC: Varies	Varies
Nexavar® (sorafenib)	HCC: 400 mg PO BID	800 mg / day
Erlotinib (Tarceva®)	NSCLC: 150 mg PO once daily in combination with ramucirumab (10 mg/kg	150 mg / day

Drug	Dosing Regimen	Dose Limit/ Maximum Dose
	IV over 60 minutes every 2 weeks) until disease progression or unacceptable toxicity	

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: Serum levels of alpha-fetoprotein (AFP) are typically higher for advanced HCC compared to early HCC, but overall, levels do not correlate well with clinical features of HCC, such as tumor size or vascular invasion. Not all tumors secrete AFP. The biomarker at concentrations higher than 400 ng/mL is associated with poor prognosis. After treatment with sorafenib, half the patients express alpha-fetoprotein concentrations greater than 400 ng/mL. In the pivotal trial (REACH-2), both Cyramza and placebo groups had baseline alpha-fetoprotein labs greater than 400 ng/mL. While there is debate regarding sensitivity and specificity of this biomarker, the criteria for AFP ≥ 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	8 mg/kg every 2 weeks in combination with paclitaxel administered as an intravenous infusion over 60 minutes.	8 mg/kg
NSCLC	10 mg/kg administered as an intravenous infusion every 2 weeks with erlotinib daily OR 10 mg/kg on day 1 of a 21-day cycle prior to docetaxel infusion over 60 minutes.	10 mg/kg
CRC	8 mg/kg every 2 weeks administered by intravenous infusion over 60 minutes prior to FOLFIRI administration.	8 mg/kg
HCC	8 mg/kg every 2 weeks administered as an intravenous infusion over 60 minutes.	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. Cyramza Prescribing Information. Indianapolis, IN: Eli Lilly and Company; June 2020. Available at http://uspl.lilly.com/cyramza/cyramza.html. Accessed August 4, 2020.

2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at nccn.org. Accessed August 4, 2020
3. Esophageal and esophagogastric junction cancers (Version 3.2020). National Comprehensive Cancer Network Guidelines. Available at nccn.org. Accessed August 4, 2020.
4. Gastric cancer (Version 2.2020). National Comprehensive Cancer Network Guidelines. Available at nccn.org. Accessed August 4, 2020.
5. Non-small cell lung cancer (Version 6.2020). National Comprehensive Cancer Network Guidelines. Available at nccn.org. Accessed August 4, 2020.
6. Colon cancer (Version 4.2020). National Comprehensive Cancer Network Guidelines. Available at nccn.org. Accessed August 4, 2020.
7. Rectal cancer (Version 6.2020). National Comprehensive Cancer Network Guidelines. Available at nccn.org. Accessed August 4, 2020.
8. Hepatobiliary Cancer (Version 5.2020). National Comprehensive Cancer Network Guidelines. Available at nccn.org. Accessed August 4, 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.	02/18	
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.	01/19	
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	