RXADVANCE
2 Park Central Drive
Southborough, MA 01772

Clinical Policy Title: **Ramucirumab (Cyramza)**
Policy Number: **RxA.83**
Drug(s) Applied: **Ramucirumab (Cyramza®)**
Last Review Date: **04/2020**
Line of Business: Commercial, **Medicaid, HIM-Medical Benefit**

Background

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

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

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

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

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 either as a single agent or in combination with paclitaxel;
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 NSCLC;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Prescribed as subsequent therapy in combination with docetaxel;
5. Request meets one of the following (a or b):
   a. Dose does not exceed 10 mg per kg on day 1 of a 21-day cycle;
   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

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);
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

D. Hepatocellular Carcinoma (must meet all):

1. Diagnosis of 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)*.

Approval duration: 6 months

II. Continued Therapy

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

1. Currently receiving medication that has been authorized by RxAdvance, or documentation supports that member is currently receiving Cyramza for a covered indication and has received this medication for at least 30 days;
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 per kg every 2 weeks;
   b. NSCLC: new dose does not exceed 10 mg per kg on day 1 of a 21-day cycle;
   c. 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

III. Appendices

Appendix A: Abbreviation/Acronym Key

AFP: α-fetoprotein
CRC: colorectal carcinoma
EGJ: esophagogastric junction
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

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.

References

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2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at nccn.org. Accessed July 7, 2019.
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4. Gastric cancer (Version 2.2018). National Comprehensive Cancer Network Guidelines. Available at nccn.org. Accessed July 7, 2019.
5. Non-small cell lung cancer (Version 6.2018). National Comprehensive Cancer Network Guidelines. Available at nccn.org. Accessed July 7, 2019.
6. Colon cancer (Version 3.2018). National Comprehensive Cancer Network Guidelines. Available at nccn.org. Accessed July 7, 2019.
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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.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy was established	01/2020	02/07/2020
Update line of business	04/2020	05/21/2020