Cyramza™ (ramucirumab)
(Intravenous)

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I. Length of Authorization

Coverage will be provided for 6 months and may be renewed.

II. Dosing Limits

A. Quantity Limit (max daily dose) [Pharmacy Benefit]:

- Cyramza 100 mg/10 mL: 4 vials per 14 days
- Cyramza 500 mg/50 mL: 1 vial per 14 days

B. Max Units (per dose and over time) [Medical Benefit]:

Gastric, gastroesophageal, HCC, and colorectal cancer:

- 180 billable units every 14 days

NSCLC:

- 240 billable units every 21 days

III. Initial Approval Criteria

Coverage is provided in the following conditions:

- Patient is at least 18 years old; **AND**

Gastric, Esophageal and Gastro-esophageal Junction Adenocarcinoma †

- Patient has unresectable advanced, recurrent or metastatic disease; **AND**
- Used as a single agent OR in combination with paclitaxel; **AND**
- Must be used as subsequent therapy

Non-Small Cell Lung Cancer †

- Patient's disease is recurrent, advanced or metastatic; **AND**
- Used as subsequent therapy following progression on a first-line cytotoxic regimen; **AND**
- Must be used in combination with docetaxel; **AND**

- Patient has not previously been treated with docetaxel or ramucirumab

Colorectal Adenocarcinoma †

- Used in combination with FOLFIRI (irinotecan, folinic acid, and 5-fluorouracil) for metastatic disease that progressed on or after therapy with bevacizumab, oxaliplatin and a fluoropyrimidine†; **OR**
- Used in combination with irinotecan or irinotecan-based regimen (e.g., FOLFIRI); **AND**
    - Used as first-line therapy for metastatic disease after adjuvant therapy with FOLFOX (fluorouracil, folinic acid, and oxaliplatin) or CapeOX (capecitabine and oxaliplatin) within previous 12 months ‡; **OR**
    - Used as subsequent therapy after first progression for unresectable advanced or metastatic disease ‡; **AND**
        - Patient has not been previously treated with irinotecan-based therapy

Hepatocellular Carcinoma (HCC) ‡

- Used as single agent therapy for adenocarcinoma; **AND**
- Used as subsequent therapy for progressive disease; **AND**
- Patient must have an alfa-fetoprotein (AFP) level of ≥ 400 ng/mL; **AND**
    - Patient has unresectable disease and is not a transplant candidate; **OR**
    - Patient is not a surgical candidate based on performance status or comorbidity; **OR**
    - Patient has local disease with or without minimal extrahepatic disease, metastatic disease, or extensive liver tumor burden

† FDA Approved Indication(s); ‡ Compendia recommended indication(s)

IV. Renewal Criteria

Authorizations can be renewed based on the following criteria:

- Patient continues to meet criteria identified in section III; **AND**
- Disease response with treatment as defined by stabilization of disease or decrease in size of tumor or tumor spread; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include the following: hemorrhage, arterial thrombotic events, uncontrolled hypertension, infusion-related reactions, severe proteinuria (> 3g/24h)/nephrotic syndrome, gastrointestinal perforation, wound healing complications, reversible posterior leukoencephalopathy syndrome (RPLS), thyroid dysfunction, etc.

V. Dosage/Administration

Indication	Dose
Gastric, gastroesophageal, hepatocellular carcinoma and colorectal cancer	8 mg/kg intravenously every 14 days until disease progression or unacceptable toxicity
NSCLC	10 mg/kg intravenously every 21 days until disease progression or unacceptable toxicity

VI. Billing Code/Availability Information

Jcode:

J9308 - Injection, ramucirumab, 5 mg: 1 billable unit = 5 mg

NDC:

- Cyramza 100 mg/10 mL solution, single dose vial: 00002-7669-xx
- Cyramza 500 mg/50 mL solution, single dose vial: 00002-7678-xx

VII. References

1. Cyramza [package insert]. Indianapolis, IN; Eli Lilly and Company; November 2018. Accessed January 2019.
2. Fuchs CS, Tomasek J, Yong CJ, et al. Ramucirumab monotherapy for previously treated advanced gastric or gastro-esophageal junction adenocarcinoma (REGARD): an international, randomised, multicentre, placebo-controlled, phase 3 trial. Lancet. 2014 Jan 4; 383(9911):31-9. doi: 10.1016/S0140-6736(13)61719-5. Epub 2013 Oct 3.
3. Referenced with permission from the NCCN Drugs and Biologics Compendium (NCCN Compendium®) for ramucirumab. National Comprehensive Cancer Network, 2019. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed January 2019.
4. Zhu AX, Kang YK, Yen CJ, et al. REACH-2: A randomized, double-blind, placebo-controlled phase 3 study of ramucirumab versus placebo as second-line treatment in patients with advanced hepatocellular carcinoma (HCC) and elevated baseline alpha-fetoprotein (AFP) following first-line sorafenib. J Clin Oncol 2018;36:4003

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C15.3	Malignant neoplasm of upper third of esophagus
C15.4	Malignant neoplasm of middle third of esophagus

ICD-10	ICD-10 Description
C15.5	Malignant neoplasm of lower third of esophagus
C15.8	Malignant neoplasm of overlapping sites of esophagus
C15.9	Malignant neoplasm of esophagus, unspecified
C16.0	Malignant neoplasm of cardia
C16.1	Malignant neoplasm of fundus of stomach
C16.2	Malignant neoplasm of body of stomach
C16.3	Malignant neoplasm of pyloric antrum
C16.4	Malignant neoplasm of pylorus
C16.5	Malignant neoplasm of lesser curvature of stomach, unspecified
C16.6	Malignant neoplasm of greater curvature of stomach, unspecified
C16.8	Malignant neoplasm of overlapping sites of stomach
C16.9	Malignant neoplasm of stomach, unspecified
C17.0	Malignant neoplasm duodenum
C17.1	Malignant neoplasm jejunum
C17.2	Malignant neoplasm ileum
C17.8	Malignant neoplasm of overlapping sites of small intestines
C17.9	Malignant neoplasm of small intestine, unspecified
C18.0	Malignant neoplasm of cecum
C18.1	Malignant neoplasm of appendix
C18.2	Malignant neoplasm of ascending colon
C18.3	Malignant neoplasm of hepatic flexure
C18.4	Malignant neoplasm of transverse colon
C18.5	Malignant neoplasm of splenic flexure
C18.6	Malignant neoplasm of descending colon
C18.7	Malignant neoplasm of sigmoid colon
C18.8	Malignant neoplasm of overlapping sites of large intestines
C18.9	Malignant neoplasm of colon, unspecified
C19	Malignant neoplasm of rectosigmoid junction
C20	Malignant neoplasm of rectum
C21.8	Malignant neoplasm of overlapping sites of rectum, anus and anal canal
C22.0	Liver cell carcinoma
C22.9	Malignant neoplasm of liver, not specified as primary or secondary
C33	Malignant neoplasm of trachea

ICD-10	ICD-10 Description
C34.00	Malignant neoplasm of main bronchus
C34.01	Malignant neoplasm of right main bronchus
C34.02	Malignant neoplasm of left main bronchus
C34.10	Malignant neoplasm of upper lobe, unspecified bronchus or lung
C34.11	Malignant neoplasm of upper lobe, right bronchus or lung
C34.12	Malignant neoplasm of upper lobe, left bronchus or lung
C34.2	Malignant neoplasm of middle lobe, bronchus or lung
C34.30	Malignant neoplasm of lower lobe, unspecified bronchus or lung
C34.31	Malignant neoplasm of lower lobe, right bronchus or lung
C34.32	Malignant neoplasm of lower lobe, left bronchus or lung
C34.80	Malignant neoplasm of overlapping sites of unspecified bronchus and lung
C34.81	Malignant neoplasm of overlapping sites of right bronchus and lung
C34.82	Malignant neoplasm of overlapping sites of left bronchus and lung
C34.90	Malignant neoplasm of unspecified part of unspecified bronchus or lung
C34.91	Malignant neoplasm of unspecified part of right bronchus or lung
C34.92	Malignant neoplasm of unspecified part of left bronchus or lung
C78.00	Secondary malignant neoplasm of lung
C78.01	Secondary malignant neoplasm of lung
C78.02	Secondary malignant neoplasm of lung
C78.6	Secondary malignant neoplasm of retroperitoneum and peritoneum
C78.7	Secondary malignant neoplasm of liver and intrahepatic bile duct
D37.1	Neoplasm of uncertain behavior of stomach
D37.8	Neoplasm of uncertain behavior of other specified digestive organs
D37.9	Neoplasm of uncertain behavior of digestive organ, unspecified
Z85.00	Personal history of malignant neoplasm of unspecified digestive organ
Z85.01	Personal history of malignant neoplasm of esophagus
Z85.028	Personal history of other malignant neoplasm of stomach
Z85.038	Personal history of malignant neoplasm of large intestine
Z85.068	Personal history of other malignant neoplasm of small intestine
Z85.118	Personal history of other malignant neoplasm of bronchus and lung

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage

Determination (NCD) and Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. They can be found at: http://www.cms.gov/medicare-coverage-database/search/advanced-search.aspx. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC