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) [NDC Unit]:

- Cyramza 100 mg/10 mL: 4 vials per 14 days
- Cyramza 500 mg/50 mL: 2 vials per 14 days

B. Max Units (per dose and over time) [HCPCS Unit]:

Gastric, Gastroesophageal, HCC, and Colorectal Cancer:

- 180 billable units every 14 days

NSCLC:

- 240 billable units every 14 days

III. Initial Approval Criteria [1]

Coverage is provided in the following conditions:

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

Universal Criteria [1]

- Patient does not have uncontrolled severe hypertension; **AND**
- Patient must not have had a surgical procedure within the preceding 28 days or have a surgical wound that has not fully healed; **AND**

Gastric, Esophageal, and Gastro-esophageal Junction Adenocarcinoma † Φ [1,2,3,5,6,7]

- Used as second-line or subsequent therapy; **AND**
- Used as a single agent OR in combination with paclitaxel; **AND**
    - Patient has advanced or metastatic disease; **OR**

- Used as palliative therapy for locoregional disease in patients who are not surgical candidates or in patients who have recurrent disease

Non-Small Cell Lung Cancer † [1,3,8,12,13]

- Patient has recurrent, advanced, or metastatic disease; **AND**
  - Used as subsequent therapy following progression on a first-line cytotoxic regimen; **AND**
    - Used in combination with docetaxel; **AND**
    - Patient has not previously been treated with docetaxel or ramucirumab; **OR**
  - Used in combination with erlotinib for EGFR mutation-positive disease (excluding locoregional recurrence or symptomatic local disease with no evidence of disseminated disease, except for mediastinal lymph node recurrence with prior radiation therapy) ‡; **AND**
    - Used as first-line therapy; **OR**
    - Used for continuation of therapy following disease progression on combination erlotinib and ramucirumab therapy for asymptomatic disease, symptomatic brain lesions, or isolated systemic lesions

Colorectal Adenocarcinoma † [1,3,9,10,11]

- Used in combination with FOLFIRI (irinotecan, folinic acid/leucovorin, 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 FOLFIRI; **AND**
  - Used as first-line therapy for metastatic disease after adjuvant therapy with FOLFOX (fluorouracil, folinic acid/leucovorin, and oxaliplatin) or CapeOX (capecitabine and oxaliplatin) within the previous 12 months ‡; **OR**
  - Used as subsequent therapy for advanced or metastatic disease ‡; **AND**
    - Patient has not been previously treated with irinotecan-based therapy

Hepatocellular Carcinoma (HCC) † Φ [1,3,4]

- Used as single agent therapy; **AND**
- Used as subsequent therapy for progressive disease; **AND**
- Patient must have an alfa-fetoprotein (AFP) level of ≥ 400 ng/mL; **AND**
  - Patient was previously treated with sorafenib †; **OR**
  - Patient has unresectable disease and is not a transplant candidate; **OR**
  - Patient is inoperable by performance status or comorbidity, or has local disease or local disease with minimal extrahepatic disease only; **OR**
  - Patient has metastatic disease or extensive liver tumor burden

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

IV. Renewal Criteria[1,3,13]

Authorizations can be renewed based on the following criteria:

- Patient continues to meet universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. 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: hemorrhage, arterial thrombotic events, uncontrolled hypertension, infusion-related reactions, severe proteinuria (> 3g/24h)/nephrotic syndrome, gastrointestinal perforation, impaired wound healing, posterior reversible encephalopathy syndrome (PRES), thyroid dysfunction, worsening of pre-existing hepatic impairment, etc.; **AND**

Non-Small Cell Lung Cancer (additional renewal opportunity):

- Patient's disease has progressed on combination therapy with erlotinib and ramucirumab; **AND**
    - Used for continuation of therapy following disease progression on combination erlotinib and ramucirumab therapy for asymptomatic disease, symptomatic brain lesions, or isolated systemic lesions

V. Dosage/Administration[1,12]

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

VI. Billing Code/Availability Information

HCPCS code:

- 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; February 2020. Accessed April 2020.
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3. Referenced with permission from the NCCN Drugs and Biologics Compendium (NCCN Compendium®) for ramucirumab. National Comprehensive Cancer Network, 2020. 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 April 2020.
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10. Obermannová R, Van Cutsem E, Yoshino T, et al. Subgroup analysis in RAISE: a randomized, double-blind phase III study of irinotecan, folinic acid, and 5-fluorouracil

(FOLFIRI) plus ramucirumab or placebo in patients with metastatic colorectal carcinoma progression. Ann Oncol. 2016 Nov;27(11):2082-2090. Epub 2016 Aug 29.

11. Tabernero J, Yoshino T, Cohn AL, et al. Ramucirumab versus placebo in combination with second-line FOLFIRI in patients with metastatic colorectal carcinoma that progressed during or after first-line therapy with bevacizumab, oxaliplatin, and a fluoropyrimidine (RAISE): a randomised, double-blind, multicentre, phase 3 study. Lancet Oncol. 2015 May;16(5):499-508. doi: 10.1016/S1470-2045(15)70127-0. Epub 2015 Apr 12.
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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
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

ICD-10	ICD-10 Description
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
C22.8	Malignant neoplasm of liver, primary, unspecified as to type
C22.9	Malignant neoplasm of liver, not specified as primary or secondary
C33	Malignant neoplasm of trachea
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

ICD-10	ICD-10 Description
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), Local Coverage Determinations (LCDs), and Local Coverage Articles (LCAs) 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/LCA):

Jurisdiction(s): J & M	**NCD/LCD/LCA Document (s):** A56141
https://www.cms.gov/medicare-coverage-database/search/article-date-search.aspx?DocID=A56141&bc=gAAAAAAAAAAA	

Jurisdiction(s): 15	NCD/LCD/LCA Document (s): A57325
https://www.cms.gov/medicare-coverage-database/overview-and-quick-search.aspx?DocID=A57325&bc=gAAAAAAAAAAAAA	

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