Cyramza® (ramucirumab)
(Intravenous)

-E-

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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/Esophageal/Esophagogastric Junction Cancers, 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 of age; **AND**

Universal Criteria [1]

- Patient does not have uncontrolled severe hypertension; **AND**
- Patient must not have had a surgical procedure within the preceding 2 weeks or have a surgical wound that has not fully healed; **AND**

Colorectal Cancer (CRC) † [1,3,9-11,17,18,25e,28e-30e]

- Will not be used in combination with an anti-EGFR agent (e.g., panitumumab or cetuximab); **AND**

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- Used in combination with irinotecan or FOLFIRI (irinotecan, folinic acid/leucovorin, and 5-fluorouracil); **AND**
- Used as subsequent therapy for progression of advanced or metastatic disease after prior therapy with bevacizumab, oxaliplatin and a fluoropyrimidine; **AND**

• Use of ramucirumab will be restricted to patients with a contraindication, intolerance, or inadequate response to bevacizumab

Gastric, Esophageal, and Esophagogastric Junction Cancers † Φ [1-3,5-7,14,17,2e,5e]

- Patient has adenocarcinoma histology; **AND**
- Used as subsequent therapy after fluoropyrimidine- or platinum-containing chemotherapy; **AND**
- Used as a single agent OR in combination with paclitaxel; **AND**
- Used for one of the following:
  - Patient has unresectable locally advanced, recurrent, or metastatic disease
  - Patient is not a surgical candidate; **AND**

<u>Ramucirumab as a single agent ONLY:</u> • Patient must demonstrate an inadequate response, unless there is a contraindication or intolerance, to a generically available agent/regimen (e.g., docetaxel, paclitaxel, irinotecan, etc. [*see NCCN Esophageal and Esophagogastric Junction Cancers guidelines and Gastric Cancer guidelines for additional alternative agents/regimens*])

Hepatocellular Carcinoma (HCC) † Φ [1,3,4,16,31e-34e]

- Used as a single agent; **AND**
- Used as subsequent therapy for progressive disease; **AND**
- Patient has an alfa-fetoprotein (AFP) level of ≥ 400 ng/mL; **AND**
- Patient has Child-Pugh Class A hepatic impairment (i.e., excludes class B and C impairments); **AND**
- Patient was previously treated with sorafenib or lenvatinib; **AND**
  - Patient has unresectable disease and is not a transplant candidate ‡; **OR**
  - Patient has liver-confined disease that is inoperable by performance status, comorbidity, or with minimal or uncertain extrahepatic disease ‡; **OR**
  - Patient has metastatic disease or extensive liver tumor burden ‡

Non-Small Cell Lung Cancer (NSCLC) † ‡ [1,3,8,12,13,12e,13e,15e,35e,41e]

- Patient has recurrent, advanced, or metastatic disease (excluding locoregional recurrence or symptomatic local disease without evidence of disseminated disease) or mediastinal lymph node recurrence with prior radiation therapy; **AND**
  - Used in combination with docetaxel; **AND**

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- Used as subsequent therapy for first progression after initial platinum-based systemic therapy; **AND**
- Patient has not previously been treated with docetaxel or ramucirumab; **AND**

Patients with no previous immunotherapy ONLY:
▪ Use of ramucirumab will be restricted to patients with a contraindication or intolerance to pembrolizumab, nivolumab, or atezolizumab; **OR**

- Used in combination with erlotinib for EGFR mutation-positive disease with exon 19 deletions or exon 21 (L858R) substitution mutations; **AND**
  - Used as first-line therapy; **AND**

▪ Use of ramucirumab in combination with erlotinib as first-line therapy will be restricted to patients with a contraindication or intolerance to osimertinib or dacomitinib; **OR**

  - Used for continuation of therapy following disease progression on combination erlotinib and ramucirumab therapy for asymptomatic disease, symptomatic brain lesions, or symptomatic systemic limited metastases; **AND**
    - Patient has T790M negative disease

Preferred therapies and recommendations are determined by review of clinical evidence. NCCN category of recommendation is taken into account as a component of this review. Regimens deemed equally efficacious (i.e., those having the same NCCN categorization) are considered to be therapeutically equivalent.

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

IV. Renewal Criteria [1,3,13]

Coverage may be renewed based upon the following criteria:

- Patient continues to meet the 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 thromboembolic events, uncontrolled hypertension, infusion-related reactions, severe proteinuria (> 3g/24h)/nephrotic syndrome, gastrointestinal perforations, impaired wound healing, posterior reversible encephalopathy syndrome (PRES), thyroid dysfunction, worsening of pre-existing hepatic impairment, etc.

Non-Small Cell Lung Cancer (continuation of therapy in combination with erlotinib following disease progression):

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- *Refer to Section III for criteria*

V. Dosage/Administration [1,13-15,17]

Indication	Dose
Gastric/Esophageal/ Esophagogastric Junction Cancers, Hepatocellular Carcinoma, and Colorectal Cancer	8 mg/kg intravenously every 14 days until disease progression or unacceptable toxicity
Non-Small Cell Lung Cancer	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 until disease progression or unacceptable toxicity

VI. Billing Code/Availability Information

HCPCS Code:

- J9308 – Injection, ramucirumab, 5 mg; 1 billable unit = 5 mg

NDC(s):

- 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 (STANDARD)

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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
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
C18.0	Malignant neoplasm of cecum
C18.2	Malignant neoplasm of ascending colon

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ICD-10	ICD-10 Description
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
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

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ICD-10	ICD-10 Description
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
Z85.118	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: https://www.cms.gov/medicare-coverage-database/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): 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

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