

## 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 single-dose vial: 4 vials per 14 days
- Cyramza 500 mg/50 mL single-dose vial: 2 vials per 14 days

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

| Indication   | Billable Units (BU) | Per unit time (days) |
|--|---------------------|----------------------|
| Gastric/Esophageal/Esophagogastric Junction Cancers, Colorectal Cancer & HCC | 180 BU              | 14 days              |
| NSCLC  | 240 BU              | 14 days              |
| MPM  | 240 BU              | 21 days              |

### III. Initial Approval Criteria <sup>1</sup>

Coverage is provided in the following conditions:

- Patient is at least 18 years of age; **AND**

#### Universal Criteria <sup>1</sup>

- 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**

- Used in combination with irinotecan or FOLFIRI (irinotecan, folinic acid/leucovorin, and fluorouracil); **AND**
- Used as subsequent therapy for progression of advanced or metastatic disease after prior therapy with bevacizumab, oxaliplatin, and a fluoropyrimidine; **AND**
- Patient has not previously been treated with irinotecan-based therapy; **AND**

• Use of ramucirumab will be restricted to patients with a contraindication or intolerance to bevacizumab (or a commercially available bevacizumab biosimilar product)

### Gastric, Esophageal, and Esophagogastric Junction Cancers † Φ 1-3,5-7,14,15,17,2e,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**

#### Ramucirumab used as a single agent ONLY:

- 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  $\geq 400$  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**
  - 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,51e

- 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**
  - 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:**

- 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 progression; **AND**
    - Patient has T790M negative disease

**Malignant Pleural Mesothelioma (MPM) †<sup>3,19,20</sup>**

- Used in combination with gemcitabine as second-line therapy for locally advanced or metastatic disease; **AND**
- Patient has progressed during or following previous therapy with pemetrexed in combination with a platinum

**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); ◊ Orphan Drug

**IV. Renewal Criteria** <sup>1,3,13</sup>

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):**

- Refer to Section III for criteria

**V. Dosage/Administration** <sup>1,13-15,17,18,20</sup>

| Indication   | Dose   |
|--|--|
| Gastric/Esophageal/<br>Esophagogastric Junction Cancers,<br>Hepatocellular Carcinoma, and<br>Colorectal Cancer | Administer 8 mg/kg intravenously every 14 days until disease progression or unacceptable toxicity  |
| Non-Small Cell Lung Cancer   | <u>In combination with docetaxel:</u><br>Administer 10 mg/kg intravenously every 21 days until disease progression or unacceptable toxicity<br><u>In combination with erlotinib:</u><br>Administer 10 mg/kg intravenously every 14 days until disease progression or unacceptable toxicity |
| Malignant Pleural Mesothelioma   | <u>In combination with gemcitabine:</u><br>Administer 10 mg/kg intravenously every 21 days until tumor 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                           |

| 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          |
| C45.0  | Mesothelioma of pleura   |
| 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           |

| ICD-10  | ICD-10 Description  |
|---------|---|
| 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             |
| Z85.118 | 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                           |