Billing and Coding Guide

INDICATIONS

- CYRAMZA as a single agent, or in combination with paclitaxel, is indicated for the treatment of patients with advanced or metastatic gastric or gastroesophageal junction (GEJ) adenocarcinoma with disease progression on or after prior fluoropyrimidine- or platinum-containing chemotherapy.

- CYRAMZA, in combination with erlotinib, is indicated for the first-line treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 (L858R) substitution mutations.

- CYRAMZA, in combination with docetaxel, is indicated for the treatment of patients with metastatic non-small cell lung cancer (NSCLC) with disease progression on or after platinum-based chemotherapy. Patients with epidermal growth factor receptor (EGFR) or anaplastic lymphoma kinase (ALK) genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving CYRAMZA.

- CYRAMZA, in combination with FOLFIRI (irinotecan, folinic acid, and fluorouracil), is indicated for the treatment of patients with metastatic colorectal cancer (mCRC) with disease progression on or after prior therapy with bevacizumab, oxaliplatin, and a fluoropyrimidine.

- CYRAMZA, as a single agent, is indicated for the treatment of patients with hepatocellular carcinoma (HCC) who have an alpha-fetoprotein (AFP) of ≥400 ng/mL and have been treated with sorafenib.

SELECT IMPORTANT SAFETY INFORMATION

Hemorrhage

- CYRAMZA increased the risk of hemorrhage and gastrointestinal hemorrhage, including Grade ≥3 hemorrhagic events. In 2137 patients with various cancers treated with CYRAMZA, the incidence of all Grade hemorrhage ranged from 13-55%. Grade 3-5 hemorrhage incidence ranged from 2-5%.

- Patients with gastric cancer receiving nonsteroidal anti-inflammatory drugs (NSAIDs) were excluded from enrollment in REGARD and RAINBOW; therefore, the risk of gastric hemorrhage in CYRAMZA-treated patients with gastric tumors receiving NSAIDs is unknown.

- Patients with NSCLC receiving therapeutic anticoagulation or with evidence of major airway invasion by cancer were excluded from REVEL. In addition, patients with NSCLC with a recent history of gross hemoptysis, those receiving chronic therapy with NSAIDs or other anti-platelet therapy other than once daily aspirin or with radiographic evidence of major airway or blood vessel invasion or intratumor cavitation were excluded from REVEL and RELAY; therefore the risk of pulmonary hemorrhage in these groups of patients is unknown.

- Permanently discontinue CYRAMZA in patients who experience severe (Grade 3 or 4) bleeding.

The following information is presented for informational purposes only and is not intended to provide reimbursement or legal advice. Laws, regulations, and policies concerning reimbursement are complex and are updated frequently. Individual coding decisions should be based upon diagnosis and treatment of individual patients. While we have made an effort to be current as of the issue date of this document, the information may not be as current or comprehensive when you view it. Providers are encouraged to contact third-party payers for specific information on their coverage, coding, and payment policies. Please consult with your legal counsel or reimbursement specialist for any reimbursement or billing questions. For more information please call the Lilly Oncology Support Center at 1-866-472-8663.

Please see Important Safety Information on pages 16-19 and full Prescribing Information for CYRAMZA.
The CYRAMZA Billing and Coding Guide is an all-indication reimbursement support resource.

Within this resource you will find:

- Dosing and administration information
- Diagnosis codes
- Healthcare Common Procedure Coding System (HCPCS) codes
- National Drug Codes (NDC)
- Sample claim forms for outpatient hospital facilities and physicians’ offices
- Lilly Oncology Support Center information for patients who may need additional assistance

SELECT IMPORTANT SAFETY INFORMATION

Gastrointestinal Perforations

- CYRAMZA can increase the risk of gastrointestinal perforation, a potentially fatal event. In 2137 patients with various cancers treated with CYRAMZA, the incidence of all Grade and Grade 3-5 gastrointestinal perforations ranged from <1-2%.
- Permanently discontinue CYRAMZA in patients who experience a gastrointestinal perforation.

Please see Important Safety Information on pages 16-19 and full Prescribing Information for CYRAMZA.
Advanced or Metastatic Gastric or Gastroesophageal Junction Cancer CYRAMZA Billing and Coding Information

Indication
CYRAMZA as a single agent, or in combination with paclitaxel, is indicated for the treatment of patients with advanced or metastatic gastric or gastroesophageal junction (GEJ) adenocarcinoma with disease progression on or after prior fluoropyrimidine- or platinum-containing chemotherapy.

CYRAMZA Dosing
• The recommended dose of CYRAMZA, either as a single agent or in combination with weekly paclitaxel, is 8 mg/kg every 2 weeks administered by intravenous (IV) infusion over 60 minutes
• If the first infusion is tolerated, all subsequent CYRAMZA infusions may be administered over 30 minutes
• Do not administer CYRAMZA as an IV push or bolus
• Continue CYRAMZA until disease progression or unacceptable toxicity
• When given in combination with paclitaxel, administer CYRAMZA prior to administration of paclitaxel
• Refer to the Prescribing Information for paclitaxel for dosage information

SELECT IMPORTANT SAFETY INFORMATION
Infusion-Related Reactions (IRR)
• IRR, including severe and life-threatening IRR, occurred in CYRAMZA clinical trials. Symptoms of IRR included rigors/tremors, back pain/spasms, chest pain and/or tightness, chills, flushing, dyspnea, wheezing, hypoxia, and paresthesia. In severe cases, symptoms included bronchospasm, supraventricular tachycardia, and hypotension. In 2137 patients with various cancers treated with CYRAMZA in which premedication was recommended or required, the incidence of all Grade IRR ranged from <1-9%. Grade 3-5 IRR incidence was <1%.
• Premedicate prior to each CYRAMZA infusion. Monitor patients during the infusion for signs and symptoms of IRR in a setting with available resuscitation equipment. Reduce the infusion rate by 50% for Grade 1-2 IRR. Permanently discontinue CYRAMZA for Grade 3-4 IRR.

All coding and documentation requirements for drugs should be confirmed with each payer.

Diagnosis Code for Gastric Cancer
Use this diagnosis code specifically for GEJ cancer.

<table>
<thead>
<tr>
<th>ICD-10 Code*</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>C16.0</td>
<td>Cardia, cardiac orifice, cardio-esophageal junction, gastroesophageal junction, esophagus, and stomach</td>
</tr>
</tbody>
</table>

Diagnosis Codes for Gastric Cancer

<table>
<thead>
<tr>
<th>ICD-10 Code*</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>C16.0</td>
<td>Cardia</td>
</tr>
<tr>
<td>C16.1</td>
<td>Fundus of stomach</td>
</tr>
<tr>
<td>C16.2</td>
<td>Body of stomach</td>
</tr>
<tr>
<td>C16.3</td>
<td>Pyloric antrum</td>
</tr>
<tr>
<td>C16.4</td>
<td>Pylorus</td>
</tr>
<tr>
<td>C16.5</td>
<td>Lesser curvature of stomach, unspecified</td>
</tr>
<tr>
<td>C16.6</td>
<td>Greater curvature of stomach, unspecified</td>
</tr>
<tr>
<td>C16.8</td>
<td>Overlapping sites of stomach</td>
</tr>
<tr>
<td>C16.9</td>
<td>Stomach, unspecified site</td>
</tr>
</tbody>
</table>

HCPCS Code

<table>
<thead>
<tr>
<th>CYRAMZA Specific Code</th>
<th>Description</th>
<th>Setting</th>
</tr>
</thead>
<tbody>
<tr>
<td>J9308</td>
<td>Injection, ramucirumab, 5 mg</td>
<td>Physician office and hospital outpatient</td>
</tr>
</tbody>
</table>

NDC
CYRAMZA is available in 100 mg/10 mL and 500 mg/50 mL (10 mg/mL) solution, single-dose vials.

<table>
<thead>
<tr>
<th>Vial Size</th>
<th>NDC*</th>
</tr>
</thead>
<tbody>
<tr>
<td>100 mg/10 mL</td>
<td>00002-7669-01</td>
</tr>
<tr>
<td>500 mg/50 mL</td>
<td>00002-7678-01</td>
</tr>
</tbody>
</table>

Drug Administration

<table>
<thead>
<tr>
<th>CPT Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>96413</td>
<td>Chemotherapy administration, intravenous infusion technique, up to 1 hour, single or initial substance/drug</td>
</tr>
</tbody>
</table>

*Please check to ensure that codes are used to the highest level of specificity. Providers should use current ICD-10-CM codes to report a patient’s diagnosis on claim submissions. This list of ICD-10-CM diagnosis codes may be reasonably related to a diagnosis within the product’s approved label. Other codes may be appropriate.

†FDA standard NDC has been “zero-filled” to ensure creation of an 11-digit code that meets HIPAA standards. The zero-fill location is indicated in bold.


CPT is a registered trademark of the American Medical Association.
Metastatic Non-Small Cell Lung Cancer

CYRAMZA Billing and Coding Information

Indication
- CYRAMZA, in combination with erlotinib, is indicated for the first-line treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumor has epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 (L858R) substitution mutations.
- CYRAMZA, in combination with docetaxel, is indicated for the treatment of patients with metastatic NSCLC with disease progression on or after platinum-based chemotherapy. Patients with EGFR or anaplastic lymphoma kinase (ALK) genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving CYRAMZA.

CYRAMZA First-line Dosing (In Combination With Erlotinib)
- The recommended dosage of CYRAMZA is 10 mg/kg every 2 weeks administered IV infusion over 60 minutes.
- In the event of a Grade 1 or 2 IRR, reduce infusion rate by 50%.
- Erlotinib 150 mg per day orally*
- For IV infusion only; do not administer as IV push or bolus

CYRAMZA Second-line Dosing (In Combination With Docetaxel)
- The recommended dosage of CYRAMZA is 10 mg/kg administered IV infusion over 60 minutes on Day 1 of a 21-day cycle prior to docetaxel infusion.
- For IV infusion only. Do not administer as IV push or bolus.
- Refer to the Prescribing Information for docetaxel for dosage information.

CYRAMZA General Dosing - Additional Information
- If the first infusion is tolerated, all subsequent CYRAMZA infusions may be administered over 30 minutes.
- Continue CYRAMZA until disease progression or unacceptable toxicity.

Click here to see Premedication and Dose Modifications for CYRAMZA on page 15.

CPT codes for EGFR mutation testing modalities that may be used*:

<table>
<thead>
<tr>
<th>Test Method</th>
<th>CPT Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Real-Time Polymerase Chain Reaction (PCR)</td>
<td>81235</td>
<td>EGFR (epidermal growth factor receptor) (eg, non-small cell lung cancer) gene analysis, common variants (eg, exon 19 LREA deletion, L858R, 790M, G719A, G719S, L810Q)</td>
</tr>
<tr>
<td>Next Generation Sequencing (NGS)</td>
<td>81155</td>
<td>Targeted genomic sequence analysis panel, solid organ neoplasm, DNA and RNA analysis, 5-50 genes</td>
</tr>
<tr>
<td></td>
<td>80020</td>
<td>Onccliniq DX Target Test; Targeted genomic sequence analysis panel, NSCLC, DNA and RNA analysis of 23 genes</td>
</tr>
<tr>
<td></td>
<td>80037</td>
<td>FoundationOne CxDs / Targeted genomic sequence analysis, solid organ neoplasm, DNA analysis of 324 genes</td>
</tr>
<tr>
<td>Acromatomic Pathology</td>
<td>88356</td>
<td>In situ hybridization (ISH); FISH; per specimen; initial single probe stain procedure</td>
</tr>
<tr>
<td></td>
<td>88376</td>
<td>Morphometric analysis, each multiplex probe stain procedure; automated</td>
</tr>
<tr>
<td></td>
<td>88377</td>
<td>Morphometric analysis, each multiplex probe stain procedure; manual</td>
</tr>
<tr>
<td></td>
<td>88378</td>
<td>Immunohistochemistry or immunocytochemistry; per specimen; initial single antibody stain procedure</td>
</tr>
</tbody>
</table>

Notes: Per AMA CPT Code Book 2019, applicable CPT codes for EGFR as denoted by the Molecular Pathology Gene Table include 81235, 81445, and 81455. CPT is a registered trademark of the American Medical Association.

*Refer to the Prescribing Information for erlotinib for dosing information.

Please note that this is not an all-inclusive list of available diagnostic tests and testing methods to identify EGFR-gene alterations. The laboratory is responsible for selecting the appropriate billing code for the test that is performed.

PLA (Proprietary Laboratory Assay) code. PLA codes are alpha-numeric; CPT codes with a corresponding descriptor, for labs or manufacturers to specifically identify proprietary tests. Tests with PLA codes may not be described using otherwise-applicable CPT codes.

Sources: AMA CPT Code Book; LabCorp Website; Quest Diagnostics Website; Neogenomics Website.

All coding and documentation requirements for drugs should be confirmed with each payer.

Diagnosis Codes for NSCLC

<table>
<thead>
<tr>
<th>ICD-10 Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>C33</td>
<td>Trachea</td>
</tr>
<tr>
<td>C34.00</td>
<td>Unspecified main bronchus</td>
</tr>
<tr>
<td>C34.01</td>
<td>Right main bronchus</td>
</tr>
<tr>
<td>C34.02</td>
<td>Left main bronchus</td>
</tr>
<tr>
<td>C34.10</td>
<td>Upper lobe, unspecified bronchus or lung</td>
</tr>
<tr>
<td>C34.11</td>
<td>Upper lobe, right bronchus or lung</td>
</tr>
<tr>
<td>C34.12</td>
<td>Upper lobe, left bronchus or lung</td>
</tr>
<tr>
<td>C34.13</td>
<td>Middle lobe, bronchus or lung</td>
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<tr>
<td>C34.30</td>
<td>Lower lobe, unspecified bronchus or lung</td>
</tr>
<tr>
<td>C34.31</td>
<td>Lower lobe, right bronchus or lung</td>
</tr>
<tr>
<td>C34.32</td>
<td>Lower lobe, left bronchus or lung</td>
</tr>
<tr>
<td>C34.40</td>
<td>Overlapping sites of unspecified bronchus and lung</td>
</tr>
<tr>
<td>C34.41</td>
<td>Overlapping sites of right bronchus and lung</td>
</tr>
<tr>
<td>C34.42</td>
<td>Overlapping sites of left bronchus and lung</td>
</tr>
<tr>
<td>C34.90</td>
<td>Unspecified part of unspecified bronchus or lung</td>
</tr>
<tr>
<td>C34.91</td>
<td>Unspecified part of right bronchus or lung</td>
</tr>
<tr>
<td>C34.92</td>
<td>Unspecified part of left bronchus or lung</td>
</tr>
</tbody>
</table>

Diagnosis Codes for NSCLC

<table>
<thead>
<tr>
<th>ICD-10 Code</th>
<th>Description</th>
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</thead>
<tbody>
<tr>
<td>C33</td>
<td>Trachea</td>
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<tr>
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</tr>
<tr>
<td>C34.01</td>
<td>Right main bronchus</td>
</tr>
<tr>
<td>C34.02</td>
<td>Left main bronchus</td>
</tr>
<tr>
<td>C34.10</td>
<td>Upper lobe, unspecified bronchus or lung</td>
</tr>
<tr>
<td>C34.11</td>
<td>Upper lobe, right bronchus or lung</td>
</tr>
<tr>
<td>C34.12</td>
<td>Upper lobe, left bronchus or lung</td>
</tr>
<tr>
<td>C34.13</td>
<td>Middle lobe, bronchus or lung</td>
</tr>
<tr>
<td>C34.30</td>
<td>Lower lobe, unspecified bronchus or lung</td>
</tr>
<tr>
<td>C34.31</td>
<td>Lower lobe, right bronchus or lung</td>
</tr>
<tr>
<td>C34.32</td>
<td>Lower lobe, left bronchus or lung</td>
</tr>
<tr>
<td>C34.40</td>
<td>Overlapping sites of unspecified bronchus and lung</td>
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<tr>
<td>C34.41</td>
<td>Overlapping sites of right bronchus and lung</td>
</tr>
<tr>
<td>C34.42</td>
<td>Overlapping sites of left bronchus and lung</td>
</tr>
<tr>
<td>C34.90</td>
<td>Unspecified part of unspecified bronchus or lung</td>
</tr>
<tr>
<td>C34.91</td>
<td>Unspecified part of right bronchus or lung</td>
</tr>
<tr>
<td>C34.92</td>
<td>Unspecified part of left bronchus or lung</td>
</tr>
</tbody>
</table>

HCPCS Code

<table>
<thead>
<tr>
<th>CYRAMZA Specific Code</th>
<th>Description</th>
<th>Setting</th>
</tr>
</thead>
<tbody>
<tr>
<td>JS308</td>
<td>Injection, ramucirumab, 5 mg</td>
<td>Physician office and hospital outpatient</td>
</tr>
</tbody>
</table>

NDC

<table>
<thead>
<tr>
<th>NDC</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>100 mg/10 mL</td>
<td>00002-7649-01</td>
</tr>
<tr>
<td>500 mg/50 mL</td>
<td>00002-7678-01</td>
</tr>
</tbody>
</table>

Drug Administration

CPT Code

<table>
<thead>
<tr>
<th>CPT Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>96413</td>
<td>Chemotherapy administration, intravenous infusion technique; up to 1 hour, single or initial substance/drug</td>
</tr>
</tbody>
</table>

Please check to ensure that codes are used to the highest level of specificity. Providers should use current ICD-10-MHS codes to report a patient’s diagnosis on claim submissions. This list of ICD-10-MHS diagnosis codes may be reasonably related to a diagnosis within the product’s approved label. Other codes may be appropriate.

FDA standard NDC has been “zero-filled” to ensure creation of an 11-digit code that meets HIPAA standards. The zero-fill location is indicated in bold.


SELECT IMPORTANT SAFETY INFORMATION

Infusion-Related Reactions (IRR)
- IRR, including severe and life-threatening IRR, occurred in CYRAMZA clinical trials. Symptoms of IRR included rashes/tremors, back pain/spasms, chest pain and/or tightening, chills, flushing, dyspnea, wheezing, hypoxia, and paresthesia. In severe cases, symptoms included bronchospasm, supraventricular tachycardia, and hypotension. In 2137 patients with various cancers treated with CYRAMZA in which premedication was recommended or required, the incidence of all Grade IRR ranged from <1-9%. Grade 3-5 IRR incidence was <1%.
- Premedicate prior to each CYRAMZA infusion. Monitor patients during the infusion for signs and symptoms of IRR in a setting with available resuscitation equipment.
- Reduce the infusion rate by 50% for Grade 3-4 IRR. Permanently discontinue CYRAMZA for Grade 3-4 IRR.

Please see Important Safety Information on pages 16-19 and full Prescribing Information for CYRAMZA.
Metastatic Colorectal Cancer
CYRAMZA Billing and Coding Information

Indication
CYRAMZA in combination with FOLFIRI (irinotecan, folinic acid, and fluorouracil), is indicated for the treatment of patients with metastatic colorectal cancer (mCRC) with disease progression on or after prior therapy with bevacizumab, oxaliplatin, and a fluoropyrimidine.

CYRAMZA Dosing
• The recommended dosage of CYRAMZA is 8 mg/kg every 2 weeks administered by IV infusion over 60 minutes prior to FOLFIRI administration
• If the first infusion is tolerated, all subsequent CYRAMZA infusions may be administered over 30 minutes
• Do not administer as an IV push or bolus
• Continue CYRAMZA until disease progression or unacceptable toxicity
• Refer to the Prescribing Information for fluorouracil, leucovorin, and irinotecan for dosing information

Click here to see Premedication and Dose Modifications for CYRAMZA on page 15.

Diagnosis Codes for CRC

<table>
<thead>
<tr>
<th>ICD-10 Code*</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>C18.0</td>
<td>Cecum</td>
</tr>
<tr>
<td>C18.1</td>
<td>Appendix</td>
</tr>
<tr>
<td>C18.2</td>
<td>Ascending colon</td>
</tr>
<tr>
<td>C18.3</td>
<td>Hepatic flexure</td>
</tr>
<tr>
<td>C18.4</td>
<td>Transverse colon</td>
</tr>
<tr>
<td>C18.5</td>
<td>Splenic flexure</td>
</tr>
<tr>
<td>C18.6</td>
<td>Descending colon</td>
</tr>
<tr>
<td>C18.7</td>
<td>Sigmoid colon</td>
</tr>
<tr>
<td>C18.8</td>
<td>Overlapping sites of colon</td>
</tr>
<tr>
<td>C18.9</td>
<td>Colon, unspecified</td>
</tr>
<tr>
<td>C19</td>
<td>Rectosigmoid junction</td>
</tr>
<tr>
<td>C20</td>
<td>Rectum</td>
</tr>
<tr>
<td>C21.8</td>
<td>Overlapping sites of rectum, anus, and anal canal</td>
</tr>
</tbody>
</table>

*Please check to ensure that codes are used to the highest level of specificity. Providers should use current ICD-10-CM codes to report a patient’s diagnosis on claim submissions. This list of ICD-10-CM diagnosis codes may be reasonably related to a diagnosis within the product’s approved label. Other codes may be appropriate.

 AFP-High (≥400 ng/mL) Hepatocellular Carcinoma
CYRAMZA Billing and Coding Information

Indication
CYRAMZA, as a single agent, is indicated for the treatment of patients with hepatocellular carcinoma (HCC) who have an alpha-fetoprotein (AFP) of ≥400 ng/mL and have been treated with sorafenib.

CYRAMZA Dosing
• Do not administer as IV push or bolus
• The recommended dosage of CYRAMZA is 8 mg/kg every 2 weeks administered by IV infusion over 60 minutes. If the first infusion is tolerated, all subsequent CYRAMZA infusions may be administered over 30 minutes
• Continue CYRAMZA until disease progression or unacceptable toxicity

Click here to see Premedication and Dose Modifications for CYRAMZA on page 15.

Diagnosis Codes for HCC

<table>
<thead>
<tr>
<th>ICD-10 Code†</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>C22.0</td>
<td>Liver cell carcinoma*</td>
</tr>
<tr>
<td>C22.8</td>
<td>Malignant neoplasm of liver, primary, unspecified as to type</td>
</tr>
</tbody>
</table>

*Please check to ensure that codes are used to the highest level of specificity. Providers should use current ICD-10-CM codes to report a patient’s diagnosis on claim submissions. This list of ICD-10-CM diagnosis codes may be reasonably related to a diagnosis within the product’s approved label. Other codes may be appropriate.

†Applicable to hepatocellular carcinoma and hepatoma.

Diagnosis Codes for HCC

<table>
<thead>
<tr>
<th>HCPCS Code for CRC and HCC</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>J9308</td>
<td>Injection, ramucirumab, 5 mg</td>
</tr>
</tbody>
</table>

Physician office and hospital outpatient

NDC for CRC and HCC

CYRAMZA is available in 100 mg/10 mL and 500 mg/50 mL (10 mg/mL) solution, single-dose vials.

<table>
<thead>
<tr>
<th>Concentration</th>
<th>NDC Code</th>
<th>NDC Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>100 mg/10 mL</td>
<td>0002-7669-01</td>
<td>0002-7678-01</td>
</tr>
<tr>
<td>500 mg/50 mL</td>
<td>0002-7669-01</td>
<td>0002-7678-01</td>
</tr>
</tbody>
</table>

Please see Important Safety Information on pages 16-19 and full Prescribing Information for CYRAMZA.

Infusion-Related Reactions (IRR)
• IRR, including severe and life-threatening IRR, occurred in CYRAMZA clinical trials. Symptoms of IRR included rigors/tremors, back pain/spasms, chest pain and/or tightness, chills, flushing, dyspnea, wheezing, hypoxia, and pain. In severe cases, symptoms included bronchospasm, supraventricular tachycardia, and hypotension. In 2137 patients with various cancers treated with CYRAMZA in which premedication was recommended or required, the incidence of all Grade IRR ranged from <1-9%. Grade 3-5 IRR incidence was <1%.
• Premedicate prior to each CYRAMZA infusion. Monitor patients during the infusion for signs and symptoms of IRR in a setting with available resuscitation equipment. Reduce the infusion rate by 50% for Grade 1-2 IRR. Permanently discontinue CYRAMZA for Grade 3-4 IRR.

Please see Important Safety Information on pages 16-19 and full Prescribing Information for CYRAMZA.
**Sample Claim Form CMS-1450 (UB-04) (Hospital Outpatient)**

**FL 42 & 43: Revenue Codes and Description**
Enter the revenue codes that correspond to HCPCS or CPT codes outlined in FL 44. Payers may vary on revenue code requirements for each procedure/service performed.

**FL 44: Product and Procedure Coding**
Enter the HCPCS drug code and CPT code for the administration of CYRAMZA.

- **HCPCS:** J9308: Injection, ramucirumab, 5 mg
- **CPT:** 96413: Chemotherapy administration, intravenous infusion technique; up to 1 hour, single or initial substance/drug

**FL 46: Service Units**
One (1) billable unit=5 mg. Total units reported will depend on total dosage given. Please confirm specific billing requirements, including wastage, with each individual payer.

**FL 56: Diagnosis Codes**
Enter the appropriate ICD diagnosis code(s) that correspond(s) to the type and location of the disease with which the patient has been diagnosed.

**FL 80: Remarks**
To support the review and payment of the claim, include additional information as required by respective payers. This may include NDC, total dosage, and date CYRAMZA was administered.

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All coding and documentation requirements for drugs should be confirmed with each payer.
Sample Claim Form CMS-1500 (Physician Office)

BOX 19: Additional Claim Information
Box 19 of the CMS-1500 claim form (or its electronic equivalent) is frequently utilized to obtain information regarding the use of drugs. The information will vary, but may include some or all of these items:

- Drug name
- NDC
- Date of treatment
- Amount of drug wasted

Please refer to the payer’s most current instructions regarding the use of this field.

BOX 21: Diagnosis or Nature of Illness or Injury
Enter the appropriate diagnosis code in lines A-L to identify the patient’s diagnosis/condition and the applicable ICD indicator to identify which ICD code version is being reported. Use the highest level of specificity.

BOX 24A: Date(s) of Service
When required by payers to provide the NDC, enter the code.

BOX 24D: Procedures, Services, or Supplies
Enter the HCPCS or CPT code and modifier(s) from the appropriate code set.

HCPCS:
J9308: Injection, ramucirumab, 5 mg

CPT:
96413: Chemotherapy administration, intravenous infusion technique; up to 1 hour, single or initial substance/drug

BOX 24E: Diagnosis Pointer
Enter the diagnosis code reference letter, as shown in Box 21, to relate the date of service and the procedures performed to the primary diagnosis. Enter only one reference letter per line item.

BOX 24G: Days or Units
One (1) billable unit=5 mg. Total units reported will depend on total dosage given. Please confirm specific billing requirements, including wastage, with each individual payer.

All coding and documentation requirements for drugs should be confirmed with each payer.
Lilly Oncology Support Center: Support and Reimbursement

Find resources and programs to help support your eligible patients during treatment

The Lilly Oncology Support Center is committed to helping qualified patients when they’re prescribed a Lilly Oncology product. We focus on financial and coverage issues, offering resources and individualized support for eligible patients, whether they’re uninsured, underinsured, or insured. Services include help with benefit verification, prior authorization, paying for medicine, and specialty-pharmacy coordination.

The Lilly Oncology Support Center also can provide support beyond financial assistance for certain products, and it helps patients connect with non-Lilly resources, such as therapeutic-support groups for specific types of cancer.

Savings Card Program
• Supports eligible, commercially insured patients with Savings Cards and coinsurance costs for prescribed Lilly Oncology products* for an FDA-approved use
• No income eligibility requirement
• Provides an annual maximum patient benefit of $25,000

*The offer is invalid for patients whose prescription claims are eligible to be reimbursed, in whole or in part, by any governmental program.

For more information, visit LillyOncologySupportCenter.com.

Offer good until 12/31/2021 for up to 12 months. Patients must use card by 12/31/2020. Patient must have coverage for the Lilly Oncology product. For more information about Lilly Oncology Support Center, call 1-866-472-8663, or visit LillyOncologySupportCenter.com.

Preceded by law and subject to change or discontinue without notice. Card activation is required. Subject to additional terms and conditions, which can be found at https://www.lillyoncologysupport.com/cyramza-financial-support.

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Offer good until 12/31/2021 for up to 12 months. Patients must use card by 12/31/2020. Patient must have coverage for the Lilly Oncology infused product through their commercial drug insurance to pay as little as $25 per dose. Offer subject to a monthly cap of wholesales acquisition cost plus usual and customary fees and a separate annual cap of $25,000. Patient is responsible for any applicable taxes, fees, or amounts exceeding monthly or annual caps. This offer is invalid for patients without commercial drug insurance or whose prescription claims for the Lilly Oncology product are eligible to be reimbursed, in whole or in part, by any governmental program, including, without limitation, Medicaid, Medicare, Medicare Part D, Medicaid, DoD, VA, TRICARE®, CHAMPUS, or any state patient or pharmaceutical assistance program. Offer void where prohibited by law and subject to change or discontinue without notice. Card activation is required. Subject to additional terms and conditions, which can be found at https://www.lillyoncologysupport.com/cyramza-financial-support.

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Important Safety Information for CYRAMZA® (ramucirumab)

Warnings and Precautions

Hemorrhage
- CYRAMZA increased the risk of hemorrhage and gastrointestinal hemorrhage, including Grade ≥3 hemorrhagic events. In 2137 patients with various cancers treated with CYRAMZA, the incidence of all Grade hemorrhage ranged from 11-26%. Grade 3-5 hemorrhage incidence ranged from 6-15%. In 223 patients with NSCLC receiving CYRAMZA in combination with erlotinib in the RELAY study, the incidence of new or worsening hemorrhage was higher (45%), as was the incidence of Grade 3-5 hemorrhage (24%). Of the patients experiencing new or worsening hemorrhage in RELAY N=100 CYRAMZA and erlotinib, N=27 placebo and erlotinib), 13% of those treated with CYRAMZA and erlotinib required initiation of 3 or more antihypertensive medications compared to 4% of patients treated with placebo and erlotinib.
- Control hypertension prior to initiating treatment with CYRAMZA. Monitor blood pressure every two weeks or more frequently as indicated during treatment. Withhold CYRAMZA for severe hypertension until medically controlled. Permanently discontinue CYRAMZA for medically significant hypertension that cannot be controlled with antihypertensive therapy or in patients with hypertensive crisis or hypertensive encephalopathy.

Infusion-Related Reactions (IRR)
- IRR, including severe and life threatening IRR, occurred in CYRAMZA clinical trials. Symptoms of IRR included rigors/tremors, back pain/spasms, chest pain and/or tightness, chills, flushing, dyspnea, wheezing, hypotension, and paresthesia. In severe cases, symptoms included bronchospasm, supraventricular tachycardia, and hypotension. In 2137 patients with various cancers treated with CYRAMZA in which premedication was recommended or required, the incidence of all Grade IRR ranged from <1-9%. Grade 3-5 IRR incidence was <1%.
- Premedicate prior to each CYRAMZA infusion. Monitor patients during the infusion for signs and symptoms of IRR in a setting with available resuscitation equipment. Reduce the infusion rate by 50% for Grade 1-2 IRR. Permanently discontinue CYRAMZA for Grade 3-4 IRR.

Gastrointestinal Perforations
- CYRAMZA can increase the risk of gastrointestinal perforation, a potentially fatal event. In 2137 patients with various cancers treated with CYRAMZA, the incidence of all Grade and Grade 3-5 gastrointestinal perforations ranged from <1-2%.
- Permanently discontinue CYRAMZA in patients who experience severe Grade 3 or 4 bleeding.

Worsening of Pre-existing Hepatic Impairment
- In 2137 patients with various cancers treated with CYRAMZA, the incidence of all Grade proteinuria ranged from 3-34%. Grade 3 proteinuria (including 4 patients with nephrotic syndrome) incidence ranged from <1-3%.

Posterior Reversible Encephalopathy Syndrome (PRES)
- PRES (also known as Reversible Posterior Leukoencephalopathy Syndrome [RPLS]) has been reported in <0.1% of 2137 patients with various cancers treated with CYRAMZA. Symptoms of PRES include seizure, headache, nausea/vomiting, blindness, or altered consciousness, with or without associated hypertension.
- Permanently discontinue CYRAMZA in patients who develop PRES. Symptoms may resolve or improve within days, although some patients with PRES can experience ongoing neurologic sequelae or death.

Proteinuria Including Nephrotic Syndrome
- In 2137 patients with various cancers treated with CYRAMZA, the incidence of Grade 1-2 proteinuria ranged from 3-34%. Grade 3 proteinuria (including 4 patients with nephrotic syndrome) incidence ranged from <1-3%.
- Monitor for proteinuria. Withhold CYRAMZA for urine protein levels that are 2 or more grams over 24 hours. Reinitiate CYRAMZA at a reduced dose once the urine protein level returns to less than 2 grams over 24 hours. Permanently discontinue CYRAMZA for urine protein levels greater than 3 grams over 24 hours or in the setting of nephrotic syndrome.

Thyroid Dysfunction
- In 2137 patients with various cancers treated with CYRAMZA, the incidence of Grade 1-2 hypothyroidism ranged from <1-3%; there were no reports of Grade 3-5 hypothyroidism. Monitor thyroid function during treatment with CYRAMZA.

Embryo-Fetal Toxicity
- CYRAMZA can cause fetal harm when administered to pregnant women. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with CYRAMZA and for 3 months after the last dose.

Lactation
- Because of the potential risk for serious adverse reactions in breastfed children from ramucirumab, advise women not to breastfeed during treatment with CYRAMZA and for 2 months after the last dose.

Adverse Reactions

REGARD:
- The most common adverse reactions (All Grades) observed in single agent CYRAMZA-treated gastric cancer patients at a rate of 25% and 22% higher than placebo were hypertension (16% vs 8%), diarrhea (14% vs 9%), headache (9% vs 3%), and hypotension (6% vs 2%).
- The most common serious adverse reactions with CYRAMZA were anemia (3.8%) and intestinal obstruction (2.1%). Red blood cell transfusions were given to 11% of CYRAMZA-treated patients vs 8.7% of patients who received placebo.
- Clinically relevant adverse reactions reported in >1% and ≤5% of CYRAMZA-treated patients in REGARD were: neutropenia (4.7%), epistaxis (4.7%), rash (4.2%), intestinal obstruction (2.1%) and arterial thromboembolic events (1.7%).
- Across clinical trials of CYRAMZA administered as a single agent, clinically relevant adverse reactions including Grade ≥3 reported in CYRAMZA-treated patients included proteinuria, gastrointestinal perforation, and IRR. In REGARD, according to laboratory assessment, 8% of CYRAMZA-treated patients developed proteinuria vs 3% of placebo-treated patients. Two patients discontinued CYRAMZA due to proteinuria. The rate of gastrointestinal perforation in REGARD was 0.8% and the rate of IRR was 0.4%.

Please see Important Safety Information continued on pages 18-19 and full Prescribing Information for CYRAMZA.
Important Safety Information for CYRAMZA® (ramucirumab), Continued

RAINY:
- The most common adverse reactions (all Grades) observed in patients treated with CYRAMZA with paclitaxel at a rate of ≥5% and <10% were: hyperbilirubinemia (6%), nausea (4%), vomiting (4%), neutropenia (3%), diarrhea (2%), and lymphopenia (2%).
- The most common adverse reactions (all Grades) observed in patients receiving CYRAMZA with docetaxel were: neutropenia (2.4%), febrile neutropenia (1.6%), diarrhea (1.5%), and proteinuria (1%).
- Treatment discontinuation due to adverse reactions occurred in 18% of CYRAMZA-treated patients, with proteinuria (8.6%) and gastrointestinal hemorrhage events (10% vs 6%).
- The most common serious adverse reactions with CYRAMZA with docetaxel were: deep vein thrombosis (1%), pulmonary embolism (1%), and pneumothorax (1.8%). Red blood cell transfusions were given to 3.2% of CYRAMZA-treated patients versus 0% of placebo with docetaxel.
- Clinically relevant adverse reactions reported in ≥5% of patients receiving CYRAMZA with docetaxel were: s Kiss (3.1%), including 5 fatal events, and gastrointestinal perforations (1.2%), including 1 fatal event.

REVEL:
- The most common adverse reactions (all Grades) observed in patients with squamous histology were: neutropenia (55% vs 46%), fatigue (25% vs 11%), stomatitis/mucosal inflammation (37% vs 19%), epistaxis (19% vs 7%), febrile neutropenia (16% vs 10%), peripheral edema (16% vs 9%), thrombocytopenia (13% vs 5%), lacrimation increased (13% vs 5%), and hypertension (11% vs 5%).
- The most common serious adverse reactions with CYRAMZA with docetaxel were: febrile neutropenia (14%), hypertension (9%), and pneumonia (8%). The use of granulocyte colony-stimulating factors was 42% in CYRAMZA with docetaxel-treated patients versus 37% in patients who received placebo with docetaxel.
- Treatment discontinuation due to adverse reactions occurred more frequently in CYRAMZA with docetaxel-treated patients (9%) than in placebo with docetaxel-treated patients (5%). The most common adverse reactions leading to treatment discontinuation of CYRAMZA were: neutropenia (2.4%); 19% of patients who received CYRAMZA with paclitaxel received granulocyte colony-stimulating factors.
- For patients with non-squamous histology, the overall incidence of pulmonary hemorrhage was 7% and the incidence of Grade ≥2 pulmonary hemorrhage was 1% for CYRAMZA with docetaxel compared to 6% overall incidence and 1% for Grade ≥3 pulmonary hemorrhage for placebo with docetaxel. For patients with squamous histology, the overall incidence of pulmonary hemorrhage was 10% and the incidence of Grade ≥3 pulmonary hemorrhage was 2% for CYRAMZA with docetaxel compared to 12% overall incidence and 2% for Grade ≥3 pulmonary hemorrhage for placebo with docetaxel.
- Clinically relevant adverse reactions reported in ≥1% and <5% of CYRAMZA with docetaxel-treated patients in REVEL were: hypernatremia (4.8%) and proteinuria (3.3%).

RELAY:
- The most common adverse reactions (all Grades) observed in patients treated with CYRAMZA with docetaxel at a rate of ≥5% and <10% were: hyperbilirubinemia (61%), nausea (49%), vomiting (46%), diarrhea (45%), and lymphopenia (15%).
- For patients with non-squamous histology, the overall incidence of pulmonary hemorrhage was 7% and the incidence of Grade ≥2 pulmonary hemorrhage was 1% for CYRAMZA with docetaxel compared to 6% overall incidence and 1% for Grade ≥3 pulmonary hemorrhage for placebo with docetaxel. For patients with squamous histology, the overall incidence of pulmonary hemorrhage was 10% and the incidence of Grade ≥3 pulmonary hemorrhage was 2% for CYRAMZA with docetaxel compared to 12% overall incidence and 2% for Grade ≥3 pulmonary hemorrhage for placebo with docetaxel.
- Clinically relevant adverse reactions reported in ≥1% and <5% of CYRAMZA with docetaxel-treated patients in RELAY were: hypernatremia (4.8%) and proteinuria (3.3%).

RAISE:
- The most common adverse reactions (all Grades) observed in patients treated with CYRAMZA with FOLFIRI at a rate of ≥5% and <10% were: neutropenia (55% vs 46%), fatigue (25% vs 11%), stomatitis/mucosal inflammation (37% vs 19%), epistaxis (19% vs 7%), febrile neutropenia (16% vs 10%), peripheral edema (16% vs 9%), thrombocytopenia (13% vs 5%), lacrimation increased (13% vs 5%), and hypertension (11% vs 5%).
- The most common serious adverse reactions with CYRAMZA with docetaxel were: febrile neutropenia (14%), hypertension (9%), and pneumonia (8%). The use of granulocyte colony-stimulating factors was 42% in CYRAMZA with docetaxel-treated patients versus 37% in patients who received placebo with docetaxel.
- Treatment discontinuation due to adverse reactions occurred more frequently in CYRAMZA with docetaxel-treated patients (9%) than in placebo with docetaxel-treated patients (5%). The most common adverse reactions leading to treatment discontinuation of CYRAMZA were: neutropenia (2.4%); 19% of patients who received CYRAMZA with paclitaxel received granulocyte colony-stimulating factors.
- For patients with non-squamous histology, the overall incidence of pulmonary hemorrhage was 7% and the incidence of Grade ≥2 pulmonary hemorrhage was 1% for CYRAMZA with docetaxel compared to 6% overall incidence and 1% for Grade ≥3 pulmonary hemorrhage for placebo with docetaxel. For patients with squamous histology, the overall incidence of pulmonary hemorrhage was 10% and the incidence of Grade ≥3 pulmonary hemorrhage was 2% for CYRAMZA with docetaxel compared to 12% overall incidence and 2% for Grade ≥3 pulmonary hemorrhage for placebo with docetaxel.
- Clinically relevant adverse reactions reported in ≥1% and <5% of CYRAMZA with docetaxel-treated patients in RELAY were: hypernatremia (4.8%) and proteinuria (3.3%).

REACH-2:
- The most common adverse reactions (all Grades) observed in single agent CYRAMZA-treated HCC patients at a rate of ≥5% and <10% were: hyperbilirubinemia (61%), nausea (49%), vomiting (46%), diarrhea (45%), and lymphopenia (15%).
- For patients with non-squamous histology, the overall incidence of pulmonary hemorrhage was 7% and the incidence of Grade ≥2 pulmonary hemorrhage was 1% for CYRAMZA with docetaxel compared to 6% overall incidence and 1% for Grade ≥3 pulmonary hemorrhage for placebo with docetaxel. For patients with squamous histology, the overall incidence of pulmonary hemorrhage was 10% and the incidence of Grade ≥3 pulmonary hemorrhage was 2% for CYRAMZA with docetaxel compared to 12% overall incidence and 2% for Grade ≥3 pulmonary hemorrhage for placebo with docetaxel.
- Clinically relevant adverse reactions reported in ≥1% and <5% of CYRAMZA with docetaxel-treated patients in RELAY were: hypernatremia (4.8%) and proteinuria (3.3%).

Please see full Prescribing Information for CYRAMZA.

Reference
**ADVANCED OR METASTATIC GASTRIC OR GEJ ADENOCARCINOMA**

**INDICATION**
CYRAMZA as a single agent, or in combination with paclitaxel, is indicated for the treatment of patients with advanced or metastatic gastric or gastroesophageal junction (GEJ) adenocarcinoma with disease progression on or after prior fluoropyrimidine- or platinum-containing chemotherapy.

**METASTATIC NSCLC**

**INDICATION**
CYRAMZA, in combination with erlotinib, is indicated for the first-line treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 (L858R) substitution mutations.

**INDICATION**
CYRAMZA, in combination with docetaxel, is indicated for the treatment of patients with metastatic non-small cell lung cancer (NSCLC) with disease progression on or after platinum-based chemotherapy. Patients with epidermal growth factor receptor (EGFR) or anaplastic lymphoma kinase (ALK) genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving CYRAMZA.

**mCRC**

**INDICATION**
CYRAMZA, in combination with FOLFIRI (irinotecan, folinic acid, and fluorouracil), is indicated for the treatment of patients with metastatic colorectal cancer (mCRC) with disease progression on or after prior therapy with bevacizumab, oxaliplatin, and a fluoropyrimidine.

**AFP-HIGH (≥400 ng/mL) HCC**

**INDICATION**
CYRAMZA, as a single agent, is indicated for the treatment of patients with hepatocellular carcinoma (HCC) who have an alpha-fetoprotein (AFP) of ≥400 ng/mL and have been treated with sorafenib.

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**Hemorrhage**

- CYRAMZA increased the risk of hemorrhage and gastrointestinal hemorrhage, including Grade ≥3 hemorrhagic events. In 2137 patients with various cancers treated with CYRAMZA, the incidence of all Grade hemorrhage ranged from 13-55%. Grade 3-5 hemorrhage incidence ranged from 2-5%.

- Patients with gastric cancer receiving nonsteroidal anti-inflammatory drugs (NSAIDs) were excluded from enrollment in REGARD and RAINBOW; therefore, the risk of gastric hemorrhage in CYRAMZA-treated patients with gastric tumors receiving NSAIDs is unknown.

- Patients with NSCLC receiving therapeutic anticoagulation or with evidence of major airway invasion by cancer were excluded from REVEL. In addition, patients with NSCLC with a recent history of gross hemoptysis, those receiving chronic therapy with NSAIDs or other anti-platelet therapy other than once daily aspirin or with radiographic evidence of major airway or blood vessel invasion or intratumor cavitation were excluded from REVEL and RELAY; therefore the risk of pulmonary hemorrhage in these groups of patients is unknown.

- Permanently discontinue CYRAMZA in patients who experience severe [Grade 3 or 4] bleeding.

**Please see Important Safety Information on pages 16-19 and full Prescribing Information for CYRAMZA.**

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