CYRAMZA®
ramucirumab injection
10 mg/mL solution
A Lilly Medicine

Billing and Coding Guide

INDICATIONS

- **CYRAMZA as a single agent, or in combination with paclitaxel, is indicated for the treatment of adults 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 adults with metastatic non-small cell lung cancer NSCLC whose tumors have EGFR exon 19 deletions or exon 21 (L858R) substitution mutations.**
- **CYRAMZA, in combination with docetaxel, is indicated for the treatment of adults with metastatic non-small cell lung cancer (NSCLC) with disease progression on or after platinum-based chemotherapy. Adults 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 adults 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 adults 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 Support Services™ for Oncology at 1-800-LillyRx (1-800-545-5979).

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

Lilly
A MEDICINE COMPANY

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
- ☑ Drug administration Current Procedural Terminology (CPT) codes
- ☑ National Drug Codes (NDC)
- ☑ Sample claim forms for outpatient hospital facilities and physicians' offices
- ☑ Lilly Support Services™ for Oncology 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.

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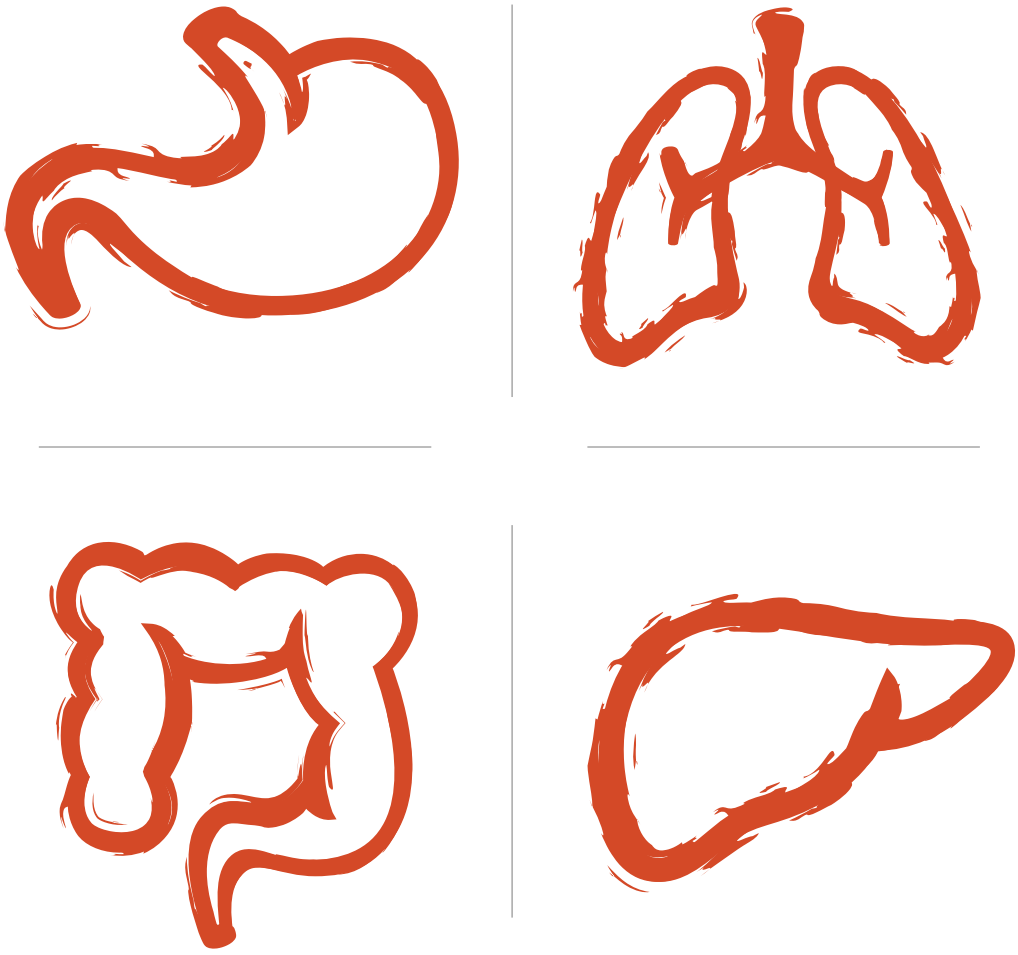

Please see Important Safety Information on pages 16-19 and full Prescribing Information for CYRAMZA.

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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

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

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.

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

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

Diagnosis Code for Gastroesophageal Junction Cancer

Use this diagnosis code specifically for GEJ cancer.

ICD-10 Code*	Description
C16.0	Cardia, cardiac orifice, cardio-esophageal junction, gastroesophageal junction, esophagus, and stomach

Diagnosis Codes for Gastric Cancer

ICD-10 Code*	Description
	Malignant neoplasm of:
C16.0	Cardia
C16.1	Fundus of stomach
C16.2	Body of stomach
C16.3	Pyloric antrum
C16.4	Pylorus
C16.5	Lesser curvature of stomach, unspecified
C16.6	Greater curvature of stomach, unspecified
C16.8	Overlapping sites of stomach
C16.9	Stomach, unspecified site

HCPCS Code

CYRAMZA Specific Code	Description	Setting
J9308	Injection, ramucirumab, 5 mg	Physician office and hospital outpatient

NDC

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

Vial Size	NDC†
100 mg/10 mL	**0**0002-7669-01
500 mg/50 mL	**0**0002-7678-01

Drug Administration CPT® Code

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

*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=Current Procedural Terminology; HCPCS=Healthcare Common Procedure Coding System; HIPAA=Health Insurance Portability and Accountability Act; ICD=International Classification of Diseases; NDC=National Drug Code.

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 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 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 by 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 by 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†

Test Method	CPT Code	Description
Real-Time Polymerase Chain Reaction (PCR)	81235	EGFR (epidermal growth factor receptor) (eg, non-small cell lung cancer) gene analysis, common variants (eg, exon 19 LREA deletion, L858R, T790M, G719A, G719S, L861Q)
Next Generation Sequencing (NGS)	81445	Targeted genomic sequence analysis panel, solid organ neoplasm, DNA and RNA analysis, 5-50 genes
	81455	Targeted genomic sequence analysis panel, solid organ or hematolymphoid neoplasm, DNA and RNA analysis, > 50 genes
	0022U‡	Oncomine DX Target Test; Targeted genomic sequence analysis panel, NSCLC, DNA and RNA analysis of 23 genes
	0037U‡	FoundationOne CDx; Targeted genomic sequence analysis, solid organ neoplasm, DNA analysis of 324 genes
	0048U‡	MSK-IMPACT; Oncology (solid organ neoplasia), DNA, targeted sequencing of protein-coding exons of 468 genes
Anatomic Pathology	88365	In situ hybridization (eg, FISH), per specimen; initial single probe stain procedure
	88374	Morphometric analysis, each multiplex probe stain procedure; automated
	88377	Morphometric analysis, each multiplex probe stain procedure; manual
	88342	Immunohistochemistry or immunocytochemistry, per specimen; initial single antibody stain

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.

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

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

Diagnosis Codes for NSCLC

ICD-10 Code[§]	Description
	Malignant neoplasm of:
C33	Trachea
C34.00 C34.01 C34.02	Unspecified main bronchus Right main bronchus Left main bronchus
C34.10 C34.11 C34.12	Upper lobe, unspecified bronchus or lung Upper lobe, right bronchus or lung Upper lobe, left bronchus or lung
C34.2	Middle lobe, bronchus or lung
C34.30 C34.31 C34.32	Lower lobe, unspecified bronchus or lung Lower lobe, right bronchus or lung Lower lobe, left bronchus or lung
C34.80 C34.81 C34.82	Overlapping sites of unspecified bronchus and lung Overlapping sites of right bronchus and lung Overlapping sites of left bronchus and lung
C34.90 C34.91 C34.92	Unspecified part of unspecified bronchus or lung Unspecified part of right bronchus or lung Unspecified part of left bronchus or lung

HCPCS Code

CYRAMZA Specific Code	Description	Setting
J9308	Injection, ramucirumab, 5 mg	Physician office and hospital outpatient

NDC

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

Vial Size	NDC[¶]
100 mg/10 mL	**0**0002-7669-01
500 mg/50 mL	**0**0002-7678-01

Drug Administration CPT Code

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

[§]Please check to ensure that codes are used to the highest level of specificity. Providers should use current ICD-10-MMS codes to report a patient's diagnosis on claim submissions. This list of ICD-10-MMS 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=Current Procedural Terminology; HCPCS=Healthcare Common Procedure Coding System; HIPAA=Health Insurance Portability and Accountability Act; ICD=International Classification of Diseases; NDC=National Drug Code.

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.

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

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A Lilly Medicine

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.

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

Diagnosis Codes for CRC

ICD-10 Code*	Description
	Malignant neoplasm of:
C18.0	Cecum
C18.1	Appendix
C18.2	Ascending colon
C18.3	Hepatic flexure
C18.4	Transverse colon
C18.5	Splenic flexure
C18.6	Descending colon
C18.7	Sigmoid colon
C18.8	Overlapping sites of colon
C18.9	Colon, unspecified
C19	Rectosigmoid junction
C20	Rectum
C21.8	Overlapping sites of rectum, anus, and anal canal

*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.

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

Diagnosis Codes for HCC

ICD-10 Code†	Description
C22.0	Liver cell carcinoma‡
C22.8	Malignant neoplasm of liver, primary, unspecified as to type

HCPCS Codes for CRC and HCC

CYRAMZA Specific Code	Description	Setting
J9308	Injection, ramucirumab, 5 mg	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.

Vial Size	NDC§
100 mg/10 mL	**0**0002-7669-01
500 mg/50 mL	**0**0002-7678-01

Drug Administration CPT Code for CRC and HCC

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

†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.

§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=Current Procedural Terminology; HCPCS=Healthcare Common Procedure Coding System; HIPAA=Health Insurance Portability and Accountability Act; ICD=International Classification of Diseases; NDC=National Drug Code.

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.

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

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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.

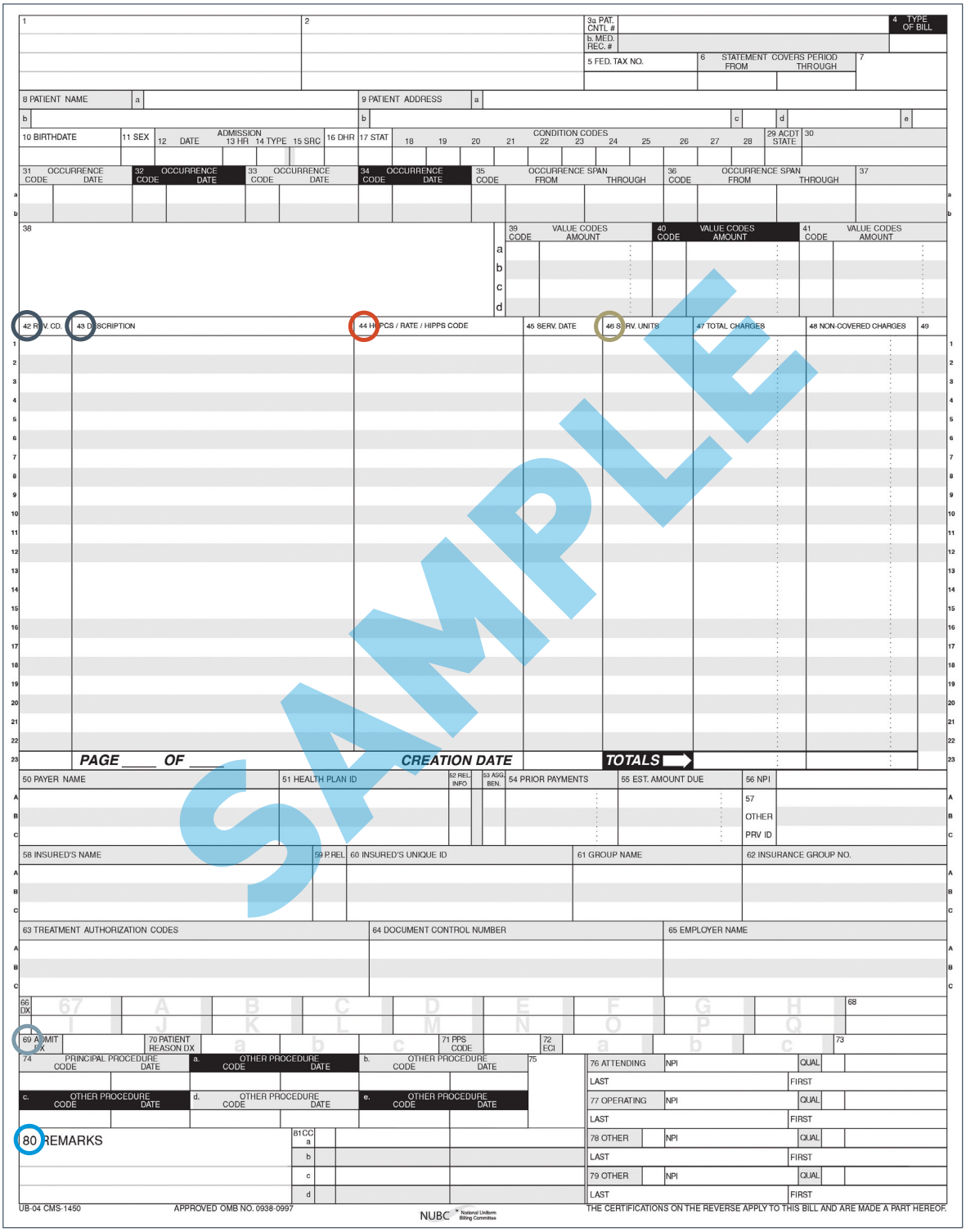
FL 66: Diagnosis Codes

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.

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



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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
- Total dose administered
- Route of administration
- 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

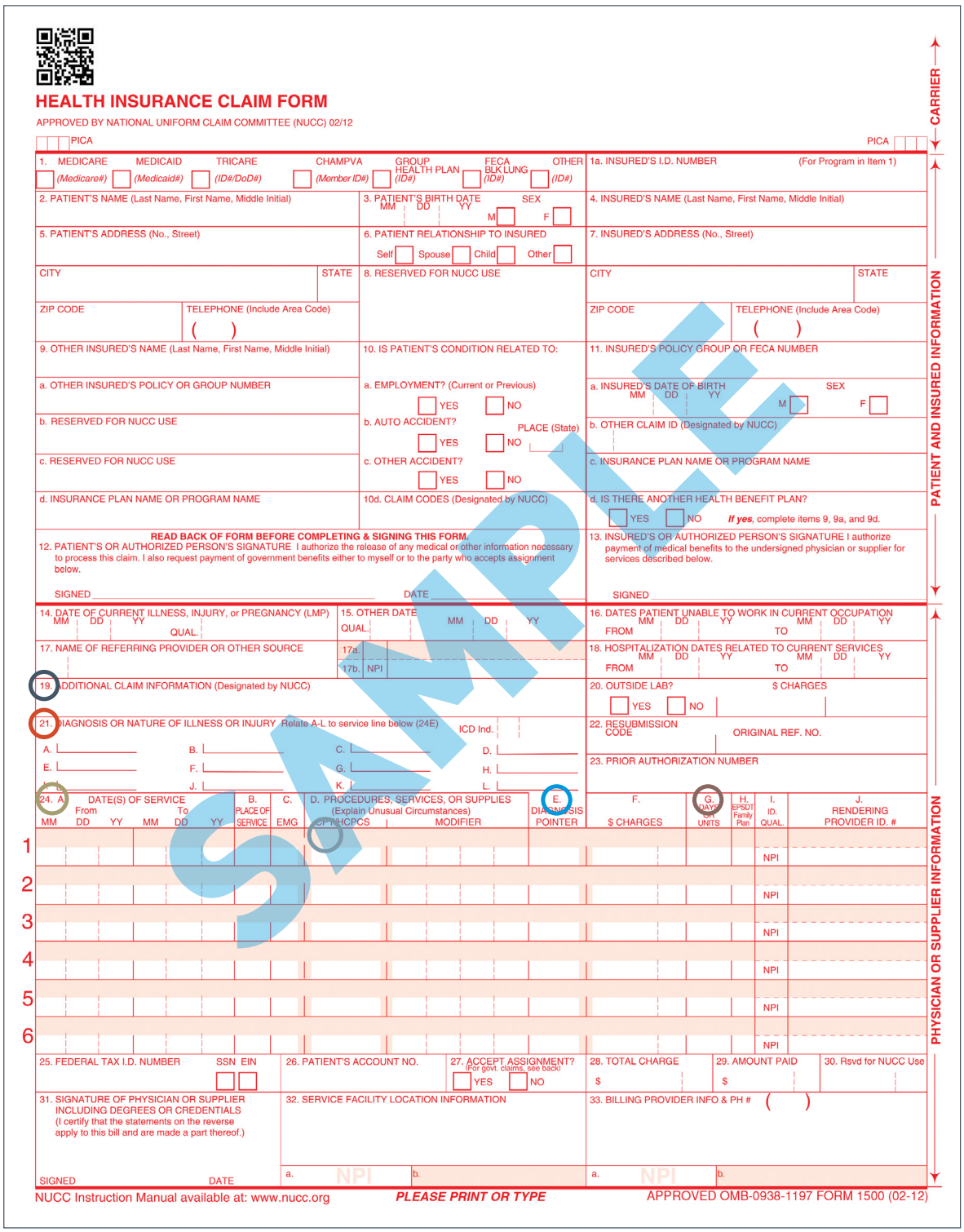
BOX 24E: Diagnosis Pointer

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.



HEALTH INSURANCE CLAIM FORM

APPROVED BY NATIONAL UNIFORM CLAIM COMMITTEE (NUCC) 02/12

PICA

1. MEDICARE (Medicare#) MEDICAID (Medicaid#) TRICARE (ID#/DoD#) CHAMPVA (Member ID#) GROUP HEALTH PLAN (ID#) FECA BLK LUNG (ID#) OTHER (ID#)

1a. INSURED'S I.D. NUMBER (For Program in Item 1)

2. PATIENT'S NAME (Last Name, First Name, Middle Initial)

3. PATIENT'S BIRTH DATE MM DD YY SEX M F

4. INSURED'S NAME (Last Name, First Name, Middle Initial)

5. PATIENT'S ADDRESS (No., Street)

6. PATIENT RELATIONSHIP TO INSURED Self Spouse Child Other

7. INSURED'S ADDRESS (No., Street)

CITY STATE

8. RESERVED FOR NUCC USE

CITY STATE

ZIP CODE TELEPHONE (Include Area Code) ( )

ZIP CODE TELEPHONE (Include Area Code) ( )

9. OTHER INSURED'S NAME (Last Name, First Name, Middle Initial)

10. IS PATIENT'S CONDITION RELATED TO:

11. INSURED'S POLICY GROUP OR FECA NUMBER

a. OTHER INSURED'S POLICY OR GROUP NUMBER

a. EMPLOYMENT? (Current or Previous) YES NO

a. INSURED'S DATE OF BIRTH MM DD YY SEX M F

b. RESERVED FOR NUCC USE

b. AUTO ACCIDENT? PLACE (State) YES NO

b. OTHER CLAIM ID (Designated by NUCC)

c. RESERVED FOR NUCC USE

c. OTHER ACCIDENT? YES NO

c. INSURANCE PLAN NAME OR PROGRAM NAME

d. INSURANCE PLAN NAME OR PROGRAM NAME

10d. CLAIM CODES (Designated by NUCC)

d. IS THERE ANOTHER HEALTH BENEFIT PLAN? YES NO *If yes*, complete items 9, 9a, and 9d.

READ BACK OF FORM BEFORE COMPLETING & SIGNING THIS FORM.

12. PATIENT'S OR AUTHORIZED PERSON'S SIGNATURE I authorize the release of any medical or other information necessary to process this claim. I also request payment of government benefits either to myself or to the party who accepts assignment below.

SIGNED DATE

13. INSURED'S OR AUTHORIZED PERSON'S SIGNATURE I authorize payment of medical benefits to the undersigned physician or supplier for services described below.

SIGNED

14. DATE OF CURRENT ILLNESS, INJURY, or PREGNANCY (LMP) MM DD YY QUAL.

15. OTHER DATE QUAL. MM DD YY

16. DATES PATIENT UNABLE TO WORK IN CURRENT OCCUPATION MM DD YY FROM MM DD YY TO

17. NAME OF REFERRING PROVIDER OR OTHER SOURCE

17a.

17b. NPI

18. HOSPITALIZATION DATES RELATED TO CURRENT SERVICES MM DD YY FROM MM DD YY TO

19. ADDITIONAL CLAIM INFORMATION (Designated by NUCC)

20. OUTSIDE LAB? YES NO $ CHARGES

21. DIAGNOSIS OR NATURE OF ILLNESS OR INJURY Relate A-L to service line below (24E) ICD Ind.

A. B. C. D.

E. F. G. H.

I. J. K. L.

22. RESUBMISSION CODE ORIGINAL REF. NO.

23. PRIOR AUTHORIZATION NUMBER

24. A DATE(S) OF SERVICE From MM DD YY	To MM DD YY	B. PLACE OF SERVICE	C. EMG	D. PROCEDURES, SERVICES, OR SUPPLIES (Explain Unusual Circumstances) CPT/HCPCS	MODIFIER	E. DIAGNOSIS POINTER	F. $ CHARGES	G. DAYS OR UNITS	H. EPSDT Family Plan	I. ID. QUAL.	J. RENDERING PROVIDER ID. #
1										NPI	
2										NPI	
3										NPI	
4										NPI	
5										NPI	
6										NPI	

25. FEDERAL TAX I.D. NUMBER SSN EIN

26. PATIENT'S ACCOUNT NO.

27. ACCEPT ASSIGNMENT? (For govt. claims, see back) YES NO

28. TOTAL CHARGE $

29. AMOUNT PAID $

30. Rsvd for NUCC Use

31. SIGNATURE OF PHYSICIAN OR SUPPLIER INCLUDING DEGREES OR CREDENTIALS (I certify that the statements on the reverse apply to this bill and are made a part thereof.)

SIGNED DATE

32. SERVICE FACILITY LOCATION INFORMATION

a. NPI b.

33. BILLING PROVIDER INFO & PH # ( )

a. NPI b.

NUCC Instruction Manual available at: www.nucc.org

PLEASE PRINT OR TYPE

APPROVED OMB-0938-1197 FORM 1500 (02-12)

CARRIER

PATIENT AND INSURED INFORMATION

PHYSICIAN OR SUPPLIER INFORMATION

SAMPLE

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

CYRAMZA®
ramucirumab injection
10 mg/mL solution
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Lilly Support Services™ for Oncology: Support and Reimbursement

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

The Lilly Support Services™ for Oncology 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 Support Services™ for Oncology 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

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

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Insurance Support

- Eligibility information
- Benefits investigation
- Prior authorization assistance
- Appeals information
- Specialty pharmacy coordination

Resources

- Billing and Coding information
- Payment methodologies and allowables
- Payer policy information
- Pricing information

†Governmental beneficiaries excluded. Eligibility required, terms and conditions apply. Savings subject to monthly and annual limits. Card eligibility and terms and conditions may be terminated, rescinded, revoked, or amended by Lilly at any time without notice and for any reason. **PROGRAM IS NOT INSURANCE. Review full terms and conditions at https://oncologysupport.lilly.com/cyramza-financial-support#terms-and-conditions.**

For more information about Lilly Support Services™ for Oncology, call 1-800-545-5979, Monday–Friday, 8 AM–10 PM ET, or visit OncologySupport.Lilly.com.

Premedication and Dose Modification Information for All CYRAMZA Indications

Premedication for CYRAMZA

- Prior to each CYRAMZA infusion, premedicate all patients with an IV histamine-1 receptor antagonist (eg, diphenhydramine hydrochloride)
- For patients who have experienced a grade 1 or 2 IRR, premedicate with a histamine-1 receptor antagonist, dexamethasone (or equivalent), and acetaminophen prior to each CYRAMZA infusion

Dose Modifications for CYRAMZA

Dosage Modifications for CYRAMZA

Adverse Reaction	Severity†	Dosage Modification
Hemorrhage	Grade 3 or 4	• **Permanently discontinue CYRAMZA**
Gastrointestinal Perforation	All Grades	• **Permanently discontinue CYRAMZA**
Wound Healing Complications	All Grades	• **Withhold CYRAMZA** for 28 days prior to elective surgery. Resume CYRAMZA no sooner than 2 weeks after surgery and until adequate wound healing • The safety of resumption of CYRAMZA after resolution of wound healing complications has not been established
Arterial Thromboembolic Events	All Grades	• **Permanently discontinue CYRAMZA**
Hypertension	Severe hypertension	• **Withhold CYRAMZA** until controlled with medical management
	Severe hypertension that cannot be controlled with antihypertensive therapy	• **Permanently discontinue CYRAMZA**
Infusion-Related Reaction (IRR)	Grade 1 or 2 IRR	• **Reduce the infusion rate of CYRAMZA by 50%**
	Grade 3 or 4 IRR	• **Permanently discontinue CYRAMZA**
Posterior Reversible Encephalopathy Syndrome (PRES)	All Grades	• **Permanently discontinue CYRAMZA**
Proteinuria	First occurrence of increased urine protein levels greater than or equal to 2 g per 24 hours	• **Withhold CYRAMZA** until urine protein level is less than 2 g per 24 hours • **Resume CYRAMZA at a reduced dose:** — Reduce 10 mg/kg dose to 8 mg/kg — Reduce 8 mg/kg dose to 6 mg/kg
	Reoccurrence of urine protein level greater than 2 g per 24 hours following initial dose reduction	• **Withhold CYRAMZA** until urine protein level is less than 2 g per 24 hours • **Resume CYRAMZA** at a reduced dose: — Reduce 8 mg/kg dose to 6 mg/kg — Reduce 6 mg/kg dose to 5 mg/kg
	Urine protein level greater than 3 g per 24 hours or in the setting of nephrotic syndrome	• **Permanently discontinue CYRAMZA**

†National Cancer Institute Common Toxicity Criteria for Adverse Events (NCI CTCAE) version 4.0 used to identify adverse reactions.
IV=intravenous.

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.

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

CYRAMZA®
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Important Safety Information for CYRAMZA® (ramucirumab)

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 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.

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.

Impaired Wound Healing - CYRAMZA has the potential to adversely affect wound healing. CYRAMZA has not been studied in patients with serious or non-healing wounds.

- Withhold CYRAMZA for 28 days prior to elective surgery. Do not administer CYRAMZA for at least 2 weeks following a major surgical procedure and until adequate wound healing. The safety of resumption of CYRAMZA after resolution of wound healing complications has not been established.

Arterial Thromboembolic Events (ATEs) - Serious, sometimes fatal, ATEs, including myocardial infarction, cardiac arrest, cerebrovascular accident, and cerebral ischemia, occurred across clinical trials. In 2137 patients with various cancers treated with CYRAMZA, the incidence of all Grade ATE was 1-3%. Grade 3-5 ATE incidence was <1-2%.

- Permanently discontinue CYRAMZA in patients who experience an ATE.

Hypertension - An increased incidence of severe hypertension occurred in patients receiving CYRAMZA. Across five clinical studies, excluding RELAY, in 1916 patients with various cancers treated with CYRAMZA, the incidence of all Grade hypertension ranged from 11-26%. Grade 3-5 hypertension incidence ranged from 6-15%. In 221 patients with NSCLC receiving CYRAMZA in combination with erlotinib in the RELAY study, the incidence of new or worsening hypertension was higher (45%), as was the incidence of Grade 3-5 hypertension (24%). Of the patients experiencing new or worsening hypertension 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), 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.

Please see Important Safety Information continued on pages 17-19 and full Prescribing Information for CYRAMZA.

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Important Safety Information for CYRAMZA® (ramucirumab), Continued

Worsening of Pre-existing Hepatic Impairment - Clinical deterioration, manifested by new onset or worsening encephalopathy, ascites, or hepatorenal syndrome, was reported in patients with Child-Pugh B or C cirrhosis who received single agent CYRAMZA. Use CYRAMZA in patients with Child-Pugh B or C cirrhosis only if the potential benefits of treatment are judged to outweigh the risks of clinical deterioration.

- Based on safety data from REACH-2, in patients with Child-Pugh A liver cirrhosis, the pooled incidence of hepatic encephalopathy and hepatorenal syndrome was higher for patients who received CYRAMZA (6%) compared to patients who received placebo (0%).

Posterior Reversible Encephalopathy Syndrome (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 all Grade 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 ≥5% and ≥2% higher than placebo were hypertension (16% vs 8%), diarrhea (14% vs 9%), headache (9% vs 3%), and hyponatremia (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.

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Important Safety Information for CYRAMZA® (ramucirumab), Continued

RAINBOW:

- The most common adverse reactions (all Grades) observed in patients treated with CYRAMZA with paclitaxel at a rate of ≥5% and ≥2% higher than placebo with paclitaxel were fatigue/asthenia (57% vs 44%), neutropenia (54% vs 31%), diarrhea (32% vs 23%), epistaxis (31% vs 7%), hypertension (25% vs 6%), peripheral edema (25% vs 14%), stomatitis (20% vs 7%), proteinuria (17% vs 6%), thrombocytopenia (13% vs 6%), hypoalbuminemia (11% vs 5%), and gastrointestinal hemorrhage events (10% vs 6%).
- The most common serious adverse reactions with CYRAMZA with paclitaxel were neutropenia (3.7%) and febrile neutropenia (2.4%); 19% of patients who received CYRAMZA with paclitaxel received granulocyte colony-stimulating factors.
- Adverse reactions resulting in discontinuation of any component of the CYRAMZA with paclitaxel combination in ≥2% of patients in RAINBOW were neutropenia (4%) and thrombocytopenia (3%).
- Clinically relevant adverse reactions reported in ≥1% and <5% of patients receiving CYRAMZA with paclitaxel were sepsis (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 treated with CYRAMZA with docetaxel at a rate of ≥5% and ≥2% higher than placebo with docetaxel were neutropenia (55% vs 46%), fatigue/asthenia (55% vs 50%), 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%), pneumonia (6%), and neutropenia (5%). 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 IRR (0.5%) and epistaxis (0.3%).
- For patients with non-squamous histology, the overall incidence of pulmonary hemorrhage was 7% and the incidence of Grade ≥3 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 hyponatremia (4.8%) and proteinuria (3.3%).

RELAY:

- The most common adverse reactions (all Grades) observed in patients treated with CYRAMZA with erlotinib at a rate of ≥5% and ≥2% higher than placebo with erlotinib were infections (81% vs 76%), diarrhea (70% vs 71%), hypertension (45% vs 12%), stomatitis (42% vs 36%), alopecia (34% vs 20%), epistaxis (34% vs 12%), proteinuria (34% vs 8%), peripheral edema (23% vs 4%), headache (15% vs 7%), gastrointestinal hemorrhage (10% vs 3%), gingival bleeding (9% vs 1%), and pulmonary hemorrhage (7% vs 2%).
- The most common serious adverse reactions with CYRAMZA with erlotinib were pneumonia (3.2%), cellulitis (1.8%), and pneumothorax (1.8%). Red blood cell transfusions were given to 3.2% of CYRAMZA-treated patients versus 0 patients who received placebo.
- Treatment discontinuation of all study drugs due to adverse reactions occurred in 13% of CYRAMZA with erlotinib-treated patients, with increased alanine aminotransferase (1.4%) and paronychia (1.4%) being the most common. The most common adverse reactions leading to treatment discontinuation of CYRAMZA were proteinuria (8.6%) and hyperbilirubinemia (6%).

Please see Important Safety Information continued on page 19 and full Prescribing Information for CYRAMZA.

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Important Safety Information for CYRAMZA® (ramucirumab), Continued

- Of the 221 patients who received CYRAMZA with erlotinib, 119 (54%) were 65 and over, while 29 (13%) were 75 and over. Adverse reactions occurring at a 10% or higher incidence in patients receiving CYRAMZA with erlotinib and with a 10% or greater difference between patients aged 65 or older compared to patients aged less than 65 years were: diarrhea (75% versus 65%), hypertension (50% versus 40%), increased ALT (49% versus 35%), increased AST (49% versus 33%), stomatitis (46% versus 36%), decreased appetite (32% versus 19%), dysgeusia (23% versus 12%), and weight loss (19% versus 6%).

RAISE:

- The most common adverse reactions (all Grades) observed in patients treated with CYRAMZA with FOLFIRI at a rate of ≥5% and ≥2% higher than placebo with FOLFIRI were diarrhea (60% vs 51%), neutropenia (59% vs 46%), decreased appetite (37% vs 27%), epistaxis (33% vs 15%), stomatitis (31% vs 21%), thrombocytopenia (28% vs 14%), hypertension (26% vs 9%), peripheral edema (20% vs 9%), proteinuria (17% vs 5%), palmar-plantar erythrodysesthesia syndrome (13% vs 5%), gastrointestinal hemorrhage events (12% vs 7%), and hypoalbuminemia (6% vs 2%). Twenty percent of patients treated with CYRAMZA with FOLFIRI received granulocyte colony- stimulating factors.
- The most common serious adverse reactions with CYRAMZA with FOLFIRI were diarrhea (3.6%), intestinal obstruction (3.0%), and febrile neutropenia (2.8%).
- Treatment discontinuation of any study drug due to adverse reactions occurred more frequently in CYRAMZA with FOLFIRI-treated patients (29%) than in placebo with FOLFIRI-treated patients (13%). The most common adverse reactions leading to discontinuation of any component of CYRAMZA with FOLFIRI as compared to placebo with FOLFIRI were neutropenia (12.5% vs 5.3%) and thrombocytopenia (4.2% vs 0.8%). The most common adverse reactions leading to treatment discontinuation of CYRAMZA were proteinuria (1.5%), and gastrointestinal perforation (1.7%).
- Clinically relevant adverse reaction reported in ≥1% and <5% of patients receiving CYRAMZA with FOLFIRI was gastrointestinal perforation (1.7%), including 4 fatal events.
- Thyroid-stimulating hormone (TSH) levels were evaluated in 224 patients (115 CYRAMZA with FOLFIRI-treated patients and 109 placebo with FOLFIRI-treated patients) with normal baseline TSH levels. Increased TSH levels were observed in 53 (46%) patients treated with CYRAMZA with FOLFIRI compared with 4 (4%) patients treated with placebo with FOLFIRI.

REACH-2:

- The most common adverse reactions (all Grades) observed in single agent CYRAMZA-treated HCC patients at a rate of ≥10% and ≥2% higher than placebo were fatigue (36% vs 20%), peripheral edema (25% vs 14%), hypertension (25% vs 13%), abdominal pain (25% vs 16%), decreased appetite (23% vs 20%), proteinuria (20% vs 4%), nausea (19% vs 12%), ascites (18% vs 7%), headache (14% vs 5%), epistaxis (14% vs 3%), insomnia (11% vs 6%), pyrexia (10% vs 3%), vomiting (10% vs 7%), and back pain (10% vs 7%).
- The most common serious adverse reactions with CYRAMZA were ascites (3%) and pneumonia (3%).
- Treatment discontinuations due to adverse reactions occurred in 18% of CYRAMZA-treated patients, with proteinuria being the most frequent (2%).
- Clinically relevant adverse reactions reported in ≥1% and <10% of CYRAMZA-treated patients in REACH-2 were IRR (9%), hepatic encephalopathy (5%) including 1 fatal event, and hepatorenal syndrome (2%) including 1 fatal event.

RB-P HCP ISI 14SEP2022

Please see full Prescribing Information for CYRAMZA.

Reference

CYRAMZA (ramucirumab) [package insert]. Indianapolis, IN: Eli Lilly and Company; 2020.

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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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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.

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

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