Cyramza (ramucirumab)

Override(s)	Approval Duration
Prior Authorization	1 year

Medications
Cyramza (ramucirumab)

APPROVAL CRITERIA

Requests for Cyramza (ramucirumab) may be approved if the following criteria are met:

I. Individual has a diagnosis of Hepatocellular Carcinoma and the following are met:
   A. Individual has inoperable or metastatic disease (NCCN 1); **AND**
   B. Individual has had disease progression on or after prior treatment with Sorafenib; **AND**
   C. Ramucirumab is used as a single agent; **AND**
   D. Individual has a baseline serum α–fetoprotein (AFP) concentrations of ≥ 400 ng/mL at initiation of therapy;

OR

II. Individual has a diagnosis of Esophageal, Gastric, or Gastro-esophageal Junction Adenocarcinoma and the following criteria are met:
   A. Individual has advanced (non-resectable), recurrent, or metastatic disease; **AND**
   B. Ramucirumab is used as a single-agent or in combination with paclitaxel, or in combination with irinotecan; **AND**
   C. Individual is using as second-line or subsequent therapy;

OR

III. Individual has a diagnosis of metastatic Non-small Cell Lung Cancer (NSCLC) and the following are met (Label, NCCN 2A):
   A. Ramucirumab is used in combination with docetaxel; **AND**
   B. Individual meets either of the following:
      1. Individual does not have presence of actionable molecular markers* **AND**;
      2. Individual is using as subsequent therapy;
         OR
      3. Individual has presence of actionable molecular markers*; **AND**
         i. Disease has progressed on a U.S. Food & Drug Administration (FDA)-approved therapy for these mutations prior to receiving ramucirumab;

OR

IV. Individual has a diagnosis of recurrent, advanced, or metastatic Non-small Cell Lung Cancer (NSCLC) and the following are met:
   A. Individual has test results showing EGFR exon 19 deletion or exon 21 (L858R) substitution mutation; **AND**

B. Ramucirumab is used as first line or continuation therapy in combination with erlotinib;

OR

V. Individual has a diagnosis of Colorectal Cancer and the following are met:
   A. Individual has had disease progression on or after prior bevacizumab- (or bevacizumab biosimilar), oxaliplatin-, and fluoropyrimidine- containing chemotherapy (Label); **AND**
   B. Ramucirumab is used in combination with FOLFIRI (irinotecan, folinic acid, and 5-fluorouracil);

   OR
   C. Individual has proficient mismatch/repair/microsatellite-stable (pMMR/MSS), deficient mismatch repair/microsatellite instability-high [dMMR/MSI-H], or POLE/POLD1 mutation (NCCN 2A); **AND**
   D. Individual is using in combination with irinotecan or FOLFIRI (irinotecan, folinic acid, and 5-fluorouracil);

OR

VI. Individual has a diagnosis of Urothelial Cancer originating from the bladder, urethra, ureter, or renal pelvis and the following are met (Petrylak 2017):
   A. Individual is 18 years of age or older; **AND**
   B. Ramucirumab is used in combination with docetaxel; **AND**
   C. Individual has a current Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1; **AND**
   D. Individual has locally advanced, unresectable, or metastatic disease that has progressed after platinum-containing chemotherapy (cisplatin or carboplatin); **AND**
   E. Individual has received treatment with no more than one immune checkpoint inhibitor (such as, atezolizumab, avelumab, durvalumab, nivolumab or pembrolizumab); **AND**
   F. Individual has received treatment with no more than one prior systemic chemotherapy regimen in the relapsed or metastatic setting; **AND**
   G. Individual has received no prior systemic taxane therapy in any setting (that is, neoadjuvant, adjuvant, or metastatic);

OR

VII. Individual has a diagnosis of pleural mesothelioma, pericardial mesothelioma, or tunica vaginalis testis mesothelioma and the following is met:
   A. Individual is using as subsequent therapy; **AND**
   B. Individual is using Cyramza in combination with gemcitabine;

OR

VIII. Individual has a diagnosis of thymic carcinoma; **AND**
   A. Individual is using for pre- or postoperative treatment in combination with carboplatin and paclitaxel; **OR**
   B. Individual is using as first-line therapy for recurrent, advanced, or metastatic disease in combination with carboplatin and paclitaxel.

Requests for Cyramza (ramucirumab) may **not** be approved for the following:

I. Ramucirumab is used for colorectal cancer in combination with the same irinotecan-based regimen that was previously used in combination with bevacizumab (or bevacizumab biosimilar); **OR**

II. The following diagnoses:
   A. Breast cancer; **OR**
   B. Metastatic melanoma; **OR**
   C. Ovarian, fallopian tube or primary peritoneal cancer; **OR**
   D. Renal cell cancer; **OR**

III. When the above criteria have not been met and for all other indications.

Key References:

1. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.: 2025. URL: http://www.clinicalpharmacology.com. Updated periodically.
2. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm. Updated periodically.
3. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
4. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2025; Updated periodically.
5. Nakagawa K, Garon EB, Seto T, et al. Ramucirumab plus erlotinib in patients with untreated, EGFR-mutated, advanced non-small-cell lung cancer (RELAY): a randomized, double-blind, placebo-controlled, phase 3 trial. Lancet Oncol 2019; 20:1655-1669.
6. NCCN Clinical Practice Guidelines in Oncology™. © 2025 National Comprehensive Cancer Network, Inc. For additional information visit the NCCN website: http://www.nccn.org/index.asp.
   a. Esophageal and Esophagogastric Junction Cancers. V5.2024. Revised December 20, 2024.
   b. Gastric Cancer V5.2024. Revised December 20, 2024.
   c. Non-Small Cell Lung Cancer. V1.2025. Revised December 20, 2024.
   d. Mesothelioma: Pleural. V1.2025. Revised November 21, 2024.
   e. Colon Cancer. V5.2024. Revised August 22, 2024.
   f. Rectal Cancer V4.2024. Revised August 22, 2024.
   g. Hepatocellular Carcinoma V3.2024. Revised September 24, 2024.
   h. Thymomas and Thymic Carcinomas: V1.2025. Revised October 30, 2024.
7. Petrylak DP, de Wit R, Chi KN, et al. Ramucirumab plus docetaxel versus placebo plus docetaxel in patients with locally advanced or metastatic urothelial carcinoma after platinum-based therapy (RANGE): a randomised, double-blind, phase 3 trial. Lancet. 2017; 390(10109):2266-2277.
8. Tabernero J, Yoshino T, Cohn AL, et al. Ramucirumab versus placebo in combination with second-line FOLFIRI in patients with metastatic colorectal carcinoma that progressed during or after first-line therapy with bevacizumab, oxaliplatin, and a fluoropyrimidine (RAISE): a randomised, double-blind, multicentre, phase 3 study. Lancet Oncol. 2015; 16(5):499-508. Correction: 2015; 16(6):e262.
9. Zhu AX, Park JO, Ryoo BY, et al. Ramucirumab versus placebo as second-line treatment in patients with advanced hepatocellular carcinoma following first-line therapy with sorafenib (REACH): a randomised, double-blind, multicentre, phase 3 trial. Lancet Oncol. 2015; 16(7):859-870.
10. Zhu AX, Kang YK, Yen CJ, et al. Ramucirumab after sorafenib in patients with advanced hepatocellular carcinoma and increased α-fetoprotein concentrations (REACH-2): a randomised, double-blind, placebo-controlled, phase 3 trial. Lancet Oncol. 2019; 20(2):282-296.