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) 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 has had progression that occurs on or after fluoropyrimidine- or platinum-containing chemotherapy;

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 the disease has progressed on or after platinum-containing chemotherapy; **OR**
      2. Individual has presence of actionable molecular markers* and both of the following criteria are met:
         a. Disease has progressed on a U.S. Food & Drug Administration (FDA)-approved therapy for these mutations prior to receiving ramucirumab; **AND**
         b. Disease has progressed on or after platinum-containing chemotherapy;

OR

IV. Individual has a diagnosis of metastatic Non-small Cell Lung Cancer (NSCLC) and the following are met:

A. Individual has an EGFR exon 19 deletion or exon 21 (L858R) substitution mutation with test results confirmed; **AND**
B. Ramucirumab is used as first line therapy in combination with erlotinib ;

OR

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

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).

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. All other indications not listed above; including but not limited to:
   A. Breast cancer; **OR**
   B. Metastatic melanoma; **OR**
   C. Ovarian, fallopian tube or primary peritoneal cancer; **OR**
   D. Renal cell cancer.

***Note:** Actionable molecular markers include EGFR, ALK, ROS1, BRAF, NTRK, MET and RET mutations. The NCCN panel recommends testing prior to initiating therapy to help guide appropriate treatment. If there is insufficient tissue to allow testing for all of these markers, repeat biopsy and/or plasma testing should be done. If these are not feasible, treatment is guided by available results and, if unknown, these patients are treated as though they do not have driver oncogenes (NCCN 1, 2A).

Key References:

1. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.: 2023. 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.; 2023; 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™. © 2019 National Comprehensive Cancer Network, Inc. For additional information visit the NCCN website: http://www.nccn.org/index.asp.
    a. Esophageal and Esophagogastric Junction Cancers. V5.2022. Revised December 5, 2022.
    b. Gastric Cancer V2.2022. Revised December 5, 2022.
    c. Non-Small Cell Lung Cancer. V1.2023. Revised December 22, 2022.
    d. Colon Cancer. V2.2022. Revised October 27, 2022.
    e. Rectal Cancer V3.2022. Revised October 27, 202.
    f. Hepatobiliary Cancers. V4.2022. Revised December 9, 2022.
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.

Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.