Drug Policy:

Cyramza™ (ramucirumab)

POLICY NUMBER UM ONC_1261	SUBJECT Cyramza™ (ramucirumab)		DEPT/PROGRAM UM Dept	PAGE 1 of 4
DATES COMMITTEE REVIEWED 11/12/14, 10/14/15, 06/22/16, 04/05/17, 04/11/18, 04/10/19, 12/11/19, 04/08/20, 07/08/20, 07/14/21, 11/15/21, 03/09/22, 05/11/22, 08/10/22, 09/14/22, 02/08/23, 03/08/23	APPROVAL DATE March 8, 2023	EFFECTIVE DATE March 31, 2023	COMMITTEE APPROVAL DATES 11/12/14, 10/14/15, 06/22/16, 04/05/17, 04/11/18, 04/10/19, 12/11/19, 04/08/20, 07/08/20, 07/14/21, 11/15/21, 03/09/22, 05/11/22, 08/10/22, 09/14/22, 02/08/23, 03/08/23	
PRIMARY BUSINESS OWNER: UM		COMMITTEE/BOARD APPROVAL Utilization Management Committee		
URAC STANDARDS HUM v8: UM 1-2; UM 2-1	NCQA STANDARDS UM 2		ADDITIONAL AREAS OF IMPACT	
CMS REQUIREMENTS	STATE/FEDERAL REQUIREMENTS		APPLICABLE LINES OF BUSINESS Commercial, Exchange, Medicaid	

I. PURPOSE

To define and describe the accepted indications for Cyramza (ramucirumab) usage in the treatment of cancer, including FDA approved indications, and off-label indications.

New Century Health (NCH) is responsible for processing all medication requests from network ordering providers. Medications not authorized by NCH may be deemed as not approvable and therefore not reimbursable.

The use of this drug must be supported by one of the following: FDA approved product labeling, CMS-approved compendia, National Comprehensive Cancer Network (NCCN), American Society of Clinical Oncology (ASCO) clinical guidelines, or peer-reviewed literature that meets the requirements of the CMS Medicare Benefit Policy Manual Chapter 15.

II. INDICATIONS FOR USE/INCLUSION CRITERIA

A. Continuation requests for a not-approvable medication shall be exempt from this NCH policy provided:

1. The requested medication was used within the last year, AND
2. The member has not experienced disease progression and/or no intolerance to the requested medication, AND
3. Additional medication(s) are not being added to the continuation request.

B. Gastric, Gastroesophageal Junction, and Esophageal Cancers/Colorectal Carcinoma

1. NOTE: Per NCH Policy, Cyramza (ramucirumab) +/- chemotherapy is Not Approvable for the treatment of Gastric, Esophageal, Gastroesophageal Junction Cancers, and colorectal carcinoma. This Policy Position is based on a large meta-analysis of Randomized Clinical Trials (referenced below) which showed increased serious (including fatal) treatment related toxicities with negligible benefits with the use of Cyramza (ramucirumab) in metastatic solid tumors, compared to NCH recommended alternatives agents/regimens, including but not limited to regimens at http://pathways.newcenturyhealth.com.

C. Hepatocellular Carcinoma

1. NOTE: Per NCH policy, Cyramza (ramucirumab) is a Not Approvable agent for the treatment of hepatocellular carcinoma. This Policy Position is based on a network meta-analysis (referenced below) demonstrating a lack of clinically meaningful improvement in overall survival (HR greater than 0.82) with Cyramza (ramucirumab) compared to Stivarga (regorafenib) or Cabometyx (cabozantinib) in the second line setting for metastatic/recurrent hepatocellular cancer. Please refer to NCH alternative agents/regimens recommended by NCH, including but not limited to regimens available at http://pathways.newcenturyhealth.com.

D. Non-Small Cell Lung Cancer (NSCLC)

1. NOTE: Per NCH Policy, Cyramza (ramucirumab) + Taxotere (docetaxel)/Tarceva (erlotinib) are Not Approvable for the treatment of metastatic NSCLC. This Policy Position is based on a large meta-analysis of Randomized Clinical Trials (referenced below) which showed increased serious (including fatal) treatment related toxicities with negligible benefits with the use of Cyramza (ramucirumab) in metastatic solid tumors, compared to NCH recommended alternatives agents/regimens, including but not limited to regimens at http://pathways.newcenturyhealth.com.

III. EXCLUSION CRITERIA

A. Disease progression while taking Cyramza (ramucirumab).

B. Dosing exceeds single dose limit of Cyramza (ramucirumab) 10 mg/kg.

C. Investigational use of Cyramza (ramucirumab) with an off-label indication that is not sufficient in evidence or is not generally accepted by the medical community. Sufficient evidence that is not supported by CMS recognized compendia or acceptable peer reviewed literature is defined as any of the following:

1. Whether the clinical characteristics of the patient and the cancer are adequately represented in the published evidence.
2. Whether the administered chemotherapy/biologic therapy/immune therapy/targeted therapy/other oncologic therapy regimen is adequately represented in the published evidence.
3. Whether the reported study outcomes represent clinically meaningful outcomes experienced by patients. Generally, the definitions of Clinically Meaningful outcomes are those recommended by ASCO, e.g., Hazard Ratio of less than 0.80 and the recommended survival benefit for OS and PFS should be at least 3 months.
4. Whether the experimental design, considering the drugs and conditions under investigation, is appropriate to address the investigative question. (For example, in some clinical studies, it may be unnecessary or not feasible to use randomization, double blind trials, placebos, or crossover).

5. That non-randomized clinical trials with a significant number of subjects may be a basis for supportive clinical evidence for determining accepted uses of drugs.
6. That case reports are generally considered uncontrolled and anecdotal information and do not provide adequate supportive clinical evidence for determining accepted uses of drugs.
7. That abstracts (including meeting abstracts) without the full article from the approved peer-reviewed journals lack supporting clinical evidence for determining accepted uses of drugs.

IV. MEDICATION MANAGEMENT

A. Please refer to the FDA label/package insert for details regarding these topics.

V. APPROVAL AUTHORITY

A. Review – Utilization Management Department

B. Final Approval – Utilization Management Committee

VI. ATTACHMENTS

A. None

VII. REFERENCES

A. Zhu AX, et al. REACH Clinical Trial . 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 Jul;16(7):859-70.

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C. Solimando AG, et al. Second-line treatments for Advanced Hepatocellular Carcinoma: A Systematic Review and Bayesian Network Meta-analysis. Clin Exp Med. 2022 Feb;22(1):65-74.

D. Chen J, Wang J, Xie F. Comparative efficacy and safety for second-line treatment with ramucirumab, regorafenib, and cabozantinib in patients with advanced hepatocellular carcinoma progressed on sorafenib treatment: A network meta-analysis. Medicine (Baltimore). 2021 Sep 24;100(38):e27013.

E. Effing SMA, et al. Assessing the risk-benefit profile of ramucirumab in patients with advanced solid tumors: A meta-analysis of randomized controlled trials. EClinicalMedicine. 2020 Jul 15;25:100458.

F. Cyramza prescribing information. Eli Lilly and Company, Indianapolis, IN 2020.

G. Clinical Pharmacology Elsevier Gold Standard 2023.

H. Micromedex® Healthcare Series: Micromedex Drugdex Ann Arbor, Michigan 2023

I. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium 2023.

J. AHFS Drug Information. American Society of Health-Systems Pharmacists or Wolters Kluwer Lexi-Drugs. Bethesda, MD 2023.

K. Ellis LM, et al. American Society of Clinical Oncology perspective: Raising the bar for clinical trials by defining clinically meaningful outcomes. J Clin Oncol. 2014 Apr 20;32(12):1277-80.

L. Medicare Benefit Policy Manual Chapter 15 Covered Medical and Other Health Services: https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/bp102c15.pdf.

M. NCQA UM 2023 Standards and Elements.