Division: Pharmacy Policy	Subject: Prior Authorization Criteria
Original Development Date: Original Effective Date: Revision Date:	July 23, 2014 February 4, 2015, June 11, 2015, June 14, 2019

CYRAMZA® (ramucirumab)

LENGTH OF AUTHORIZATION: UP TO 3 MONTHS

CLINICAL NOTES:

Ramucirumab is a monoclonal antibody that binds to extracellular vascular endothelial growth factor (VEGF)-2 thereby preventing the binding of VEGF-A, VEGF-C and VEGF-D to the receptor. VEGF is known to promote cell proliferation and angiogenesis, therefore blocking the actions of VEGF on tumor cells may slow the progression of the tumor.

Ramucirumab is FDA approved for the treatment of advanced or metastatic gastric cancer or gastro-esophageal junction (GEJ) adenocarcinoma in patients who have experienced disease progression on therapy with a fluoropyrimidine or platinum-containing regimen.

Ramucirumab is also FDA approved for the treatment of metastatic non-small cell lung cancer (NSCLC), used in combination with docetaxel for patients who have experienced disease progression on or after platinum-based chemotherapy. NSCLC patients with epidermal growth factor receptor (EGFR) or anaplastic lymphoma kinase (ALK) genomic mutations should have experienced disease progression on FDA-approved therapies for these genetic mutations (examples include erlotinib, afatinib, crizotinib, ceritinib [list is not all-inclusive]).

Ramucirumab is also FDA approved for the treatment of metastatic colorectal cancer when given in combination with FOLFIRI (irinotecan, leucovorin, 5-fluorouracil) upon disease progression with prior therapy consisting of bevacizumab, oxaliplatin and a fluoropyrimidine.

Ramucirumab is also FDA approved for the treatment of hepatocellular carcinoma who have alpha fetoprotein (AFP of ≥ 400ng/mL and have been treated with sorafenib.

INITIAL REVIEW CRITERIA:

- Patient must be ≥18 years old AND
- Patient must have a confirmed diagnosis of advanced or metastatic gastric cancer or gastro-esophageal junction adenocarcinoma OR a diagnosis of metastatic non small cell lung cancer OR a diagnosis of metastatic colorectal cancer (mCRC) OR a diagnosis of alpha-fetoprotein-high liver cancer (hepatocellular carcinoma).
- Patients with a diagnosis of advanced or metastatic gastric cancer or gastro-esophageal junction adenocarcinoma must have had progressive disease or been intolerant to first line therapy. First line therapy must have been a fluoropyrimidine (e.g. 5-fluorouracil) or a platinum (e.g. cisplatin, carboplatin) based regimen.

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- Patients with a diagnosis of metastatic NSCLC must have had disease progression on or after platinum (e.g. cisplatin, carboplatin)-based therapy. Patients with EGFR or ALK genomic tumor mutations must have had progressive disease on appropriate targeted therapy (examples: erlotinib, crizotinib)
- Patients with metastatic colorectal cancer must have disease progression on or after treatment with bevacizumab, oxaliplatin and a fluoropyrimidine.
- Patients with a diagnosis of hepatocellular carcinoma must have an alpha fetoprotein of ≥ 400ng/mL AND have been treated with sorafenib.

CONTINUATION OF THERAPY

- Patient must have no evidence of disease progression while receiving ramucirumab
- Patient must not have intolerable toxicity such as severe bleeding, uncontrollable hypertension or proteinuria of greater than 3 grams/24 hours, or any other severe adverse event related to ramucirumab

DOSING & ADMINISTRATION:

- **For the treatment of gastric cancer or hepatocellular carcinoma**: The dose of ramucirumab is 8 mg/kg IV given over 60 minutes every two weeks
- **For the treatment of NSCLC**: The dose of ramucirumab is 10 mg/kg IV given over 60 minutes on day 1 of a 21-day cycle.
- **For the treatment of mCRC**: The dose of ramucirumab is 8 mg/kg IV given on day 1 over 60 minutes prior to FOLFIRI and repeated every 2 weeks

- Dosage Form: 100 mg/10 mL solution for injection, 500 mg/50 mL solution for injection