Draft Revised Policy: Do Not Implement

Ramucirumab (Cyramza®)

DESCRIPTION

Ramucirumab is a recombinant human IgG1 monoclonal antibody. As a vascular endothelial growth factor (VEGF) receptor 2 antagonist, ramucirumab binds specifically to VEGF receptor 2 or VEGFR2 This blocks the growth factor ligands VEGF-A, VEGF-C and VEGF-D from binding to the receptor which prevents ligand-stimulated activation of VEGFR2. This inhibits ligand-induced proliferation and migration of endothelial cells to inhibit angiogenesis and supplying increased blood flow to tumors. In this way ramucirumab prevents the growth of blood vessels necessary for tumor growth.

POLICY

- Ramucirumab for the treatment of the following is considered ***medically necessary*** if the medical appropriateness criteria are met. **(See Medical Appropriateness below.)**
  - Gastric, Esophageal, and ~~Esophagogastric junction cancer~~/Gastro-esophageal junction (GEJ) Adenocarcinoma
  - Non-small cell lung cancer (NSCLC) ~~(adenocarcinoma with mixed subtypes, squamous cell carcinoma, large cell carcinoma)~~
  - Colorectal Cancer ~~(adenocarcinoma)~~
  - ~~Esophageal Cancer (adenocarcinoma)~~
  - ~~Gastric cancer (adenocarcinoma)~~
  - Hepatocellular Carcinoma (HCC)
- Ramucirumab for the treatment of other conditions/diseases is considered ***investigational.***

MEDICAL APPROPRIATENESS

The proposal is to add text/statements in red and to delete text/statements with strikethrough:

INITIAL APPROVAL CRITERIA

- Patient is at least 18 years of age; **AND**

Universal Criteria

- Patient does not have uncontrolled severe hypertension; **AND**
- Patient must not have had a surgical procedure within the preceding 2 weeks ~~28 days~~ or have a surgical wound that has not fully healed; **AND**

Gastric, Esophageal, and Gastro-esophageal Junction (GEJ) **Adenocarcinoma**

- Used as subsequent therapy; **AND**
- Used as a single agent OR in combination with paclitaxel OR in combination with an irinotecan-based regimen; **AND**
  - Patient has unresectable locally advanced, recurrent, or metastatic disease; **OR**
  - Used as palliative therapy for locoregional disease in patients who are not surgical candidates

Non-Small Cell Lung Cancer (NSCLC)

- Patient has recurrent, advanced, or metastatic disease (excluding locoregional recurrence or symptomatic local disease without evidence of disseminated disease) or mediastinal lymph node recurrence with prior radiation therapy; **AND**

- Used as subsequent therapy for first progression after initial systemic therapy; ~~following progression on a first-line cytotoxic regimen~~; **AND**
  - Used in combination with docetaxel; **AND**
  - Patient has not previously been treated with docetaxel or ramucirumab; **OR**
- Used in combination with erlotinib for EGFR mutation-positive disease with exon 19 deletions or exon 21 (L858R) substitution mutations ~~(excluding locoregional recurrence or symptomatic local disease without evidence of disseminated disease, except for mediastinal lymph node recurrence with prior radiation therapy);~~ **AND**
  - Used as first-line therapy; **OR**
  - Used for continuation of therapy following disease progression on combination erlotinib and ramucirumab therapy for asymptomatic disease, symptomatic brain lesions, or symptomatic systemic limited metastases

Colorectal ~~Adenocarcinoma~~ Cancer (CRC)

- Used in combination with FOLFIRI (irinotecan, folinic acid/leucovorin, and 5-fluorouracil) for metastatic disease that progressed on or after therapy with bevacizumab, oxaliplatin, and a fluoropyrimidine; **OR**
- Used in combination with irinotecan or FOLFIRI; **AND**
  - Used as primary treatment ~~first-line therapy~~ for metastatic disease after adjuvant therapy with FOLFOX (fluorouracil, folinic acid/leucovorin, and oxaliplatin) or CapeOX (capecitabine and oxaliplatin) within the previous 12 months; **OR**
  - Used as subsequent therapy for advanced or metastatic disease; **AND**
    - Patient has not previously been treated with irinotecan-based therapy

Hepatocellular Carcinoma (HCC)

- Used as single agent therapy; **AND**
- Used as subsequent therapy for progressive disease; **AND**
- Patient has an alfa-fetoprotein (AFP) level of ≥ 400 ng/mL; **AND**
  - Patient was previously treated with sorafenib; **OR**
  - Patient has unresectable disease and is not a transplant candidate; **OR**
  - Patient has ~~local disease (i.e.,~~ liver confined disease~~)~~, inoperable by performance status, ~~or~~ comorbidity or with minimal or uncertain extrahepatic disease; **OR**
  - Patient has metastatic disease or extensive liver tumor burden

RENEWAL CRITERIA

- Patient continues to meet the universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in Initial Approval Criteria; **AND**
- Disease response with treatment as defined by stabilization of disease or decrease in size of tumor or tumor spread; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: hemorrhage, arterial thromboembolic events, uncontrolled hypertension, infusion-related reactions, severe proteinuria (> 3g/24h) /nephrotic syndrome, gastrointestinal perforations, impaired wound healing, posterior reversible encephalopathy syndrome (PRES), thyroid dysfunction, worsening of pre-existing hepatic impairment, etc.; **AND**

Non-Small Cell Lung Cancer (continuation of therapy in combination with erlotinib following disease progression):

- *Refer to Initial Approval Criteria*

DOSAGE/ADMINISTRATION

INDICATION	DOSE
Gastric, Esophageal/GEJ Adenocarcinoma, ~~gastroesophageal,~~ Hepatocellular Carcinoma and Colorectal Cancer	8 mg/kg intravenously every 14 days until disease progression or unacceptable toxicity
NSCLC	In combination with docetaxel: 10 mg/kg intravenously every 21 days until disease progression or unacceptable toxicity In combination with erlotinib: 10 mg/kg intravenously every 14 days until disease progression or unacceptable toxicity

LENGTH OF AUTHORIZATION

Coverage will be provided for 6 months and may be renewed.

DOSING LIMITS

Max Units (per dose and over time) [HCPCS Unit]:

Gastric, Esophageal, GEJ ~~Gastroesophageal,~~ HCC, and Colorectal Cancer:
- 180 billable units every 14 days

NSCLC:
- 240 billable units every 14 days

APPLICABLE TENNESSEE STATE MANDATE REQUIREMENTS

BlueCross BlueShield of Tennessee's Medical Policy complies with Tennessee Code Annotated Section 56-7-2352 regarding coverage of off-label indications of Food and Drug Administration (FDA) approved drugs when the off-label use is recognized in one of the statutorily recognized standard reference compendia or in the published peer-reviewed medical literature.

IMPORTANT REMINDER

We develop Medical Policies to provide guidance to Members and Providers. This Medical Policy relates only to the services or supplies described in it. The existence of a Medical Policy is not an authorization, certification, explanation of benefits or a contract for the service (or supply) that is referenced in the Medical Policy. For a determination of the benefits that a Member is entitled to receive under his or her health plan, the Member's health plan must be reviewed. If there is a conflict between the Medical Policy and a health plan, the express terms of the health plan will govern.

ADDITIONAL INFORMATION

For appropriate chemotherapy regimens, dosage information, contraindications, precautions, warnings, and monitoring information, please refer to one of the standard reference compendia (e.g., the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) published by the National Comprehensive Cancer Network®, Drugdex

Evaluations of Micromedex Solutions at Truven Health, or The American Hospital Formulary Service Drug Information).

SOURCES

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EFFECTIVE DATE

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