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| **Clinical Policy Title:** | ramucirumab |
| **Policy Number:** | RxA.83 |
| **Drug(s) Applied:** | Cyramza® |
| **Original Policy Date:** | 02/07/2020 |
| **Last Review Date:** | 10/19/2023 |
| **Line of Business Policy Applies to:** | All lines of business (except Medicare) |

## Criteria

**I. Initial Approval Criteria**

**A. Esophageal, Esophagogastric Junction, and Gastric Cancer** (must meet all):

1. Diagnosis of advanced esophageal, EGJ or gastric cancer;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Prescribed as subsequent therapy in one of the following ways (a, b or c):
   a. As a single agent;
   b. In combination with paclitaxel*;
   c. In combination with irinotecan* with or without fluorouracil*;

   *Prior authorization may be required for paclitaxel, fluorouracil or irinotecan.
5. Disease is unresectable, locally advanced, recurrent, or metastatic;
6. Request meets one of the following (a or b):*
   a. Dose does not exceed 8 mg per kg every 2 weeks;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

   *Prescribed regimen must be FDA-approved or recommended by NCCN.

**Approval duration**
**Commercial:** 6 months
**Medicaid:** 6 months

**B. Non-Small Cell Lung Cancer** (must meet all)**:**

1. Diagnosis of metastatic, recurrent, or advanced NSCLC;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Request meets one of the following (a or b):
   a. Prescribed as subsequent therapy in combination with docetaxel*;
   b. Prescribed in combination with erlotinib*;

   *Prior authorization may be required for docetaxel or erlotinib
5. If prescribed in combination with erlotinib: Disease is positive for a sensitizing EGFR mutation (e.g., EGFR exon 19 deletions or exon 21 [L858R] substitution mutation);
6. Request meets one of the following (a, b or c):*
   a. In combination with docetaxel: Dose does not exceed 10 mg per kg on day 1 of a 21-day cycle;
   b. In combination with erlotinib: Dose does not exceed 10 mg per kg every 2 weeks;

c. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

*Prescribed regimen must be FDA-approved or recommended by NCCN.

**Approval Duration**
**Commercial:** 6 months
**Medicaid:** 6 months

**C. Colorectal Cancer** (must meet all):
1. Diagnosis of advanced or metastatic CRC;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Request is for one of the following (a or b):
   a. Primary treatment for unresectable metachronous metastases;
   b. For subsequent therapy;
5. Prescribed in combination with irinotecan* or FOLFIRI* (irinotecan, folinic acid, and 5-fluorouracil);
   *Prior authorization may be required for irinotecan or FOLFIRI
6. Request meets one of the following (a or b):*
   a. Dose does not exceed 8 mg per kg every 2 weeks;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

   *Prescribed regimen must be FDA-approved or recommended by NCCN.

**Approval duration**
**Commercial:** 6 months
**Medicaid:** 6 months

**D. Hepatocellular Carcinoma** (must meet all):
1. Diagnosis of progressive HCC;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. α-fetoprotein (AFP) ≥ 400 ng/mL;
5. Disease has progressed on or after therapy with Nexavar®*;
   *Prior authorization is required for Nexavar®
6. Request meets one of the following (a or b):*
   a. Dose does not exceed 8 mg per kg every 2 weeks;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

   *Prescribed regimen must be FDA-approved or recommended by NCCN.

**Approval duration**
**Commercial:** 6 months
**Medicaid:** 6 months

## II. Continued Therapy Approval

**A. All Indications in Section I** (must meet all)**:**
1. Member is currently receiving medication that has been authorized by RxAdvance or member has met initial approval criteria for the covered indications and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. If request is for a dose increase, request meets one of the following (a, b, c or d):*

a. Esophageal/EGJ/gastric cancer, CRC, HCC: new dose not exceed 8 mg per kg every 2 weeks;
b. NSCLC in combination with docetaxel: new dose does not exceed 10 mg per kg on day 1 of a 21-day cycle;
c. NSCLC in combination with erlotinib: new dose does not exceed 10 mg per kg every 2 weeks;
d. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

*Prescribed regimen must be FDA-approved or recommended by NCCN.

**Approval duration**
**Commercial:** 12 months
**Medicaid:** 12 months

**References**


1. National Comprehensive Cancer Network Guidelines. Esophageal and esophagogastric junction cancers (Version 4.2022). Available at: https://www.nccn.org/professionals/physician_gls/pdf/esophageal.pdf. Accessed October 03, 2022.
2. National Comprehensive Cancer Network Guidelines. Gastric cancer (Version 2.2022). Available at: https://www.nccn.org/professionals/physician_gls/pdf/gastric.pdf. Accessed October 03, 2022.
3. National Comprehensive Cancer Network Guidelines. Non-small cell lung cancer (Version 5.2022). Available at: https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf. Accessed October 03, 2022.
4. National Comprehensive Cancer Network Guidelines. Colon cancer (Version 1.2022). Available at: https://www.nccn.org/professionals/physician_gls/pdf/colon.pdf. Accessed October 03, 2022.
5. National Comprehensive Cancer Network Guidelines. Rectal cancer (Version 2.2022). Available at: https://www.nccn.org/professionals/physician_gls/pdf/rectal.pdf. Accessed October 03, 2022.
6. National Comprehensive Cancer Network. Hepatobiliary Cancers Version 2.2022. Available at: https://www.nccn.org/professionals/physician_gls/pdf/hepatobiliary.pdf. Accessed October 03, 2022.
7. Zhu AX, Kang YK, Yen CJ, et al. Ramucirumab after sorafenib in patients with advanced hepatocellular carcinoma and increased alpha-fetoprotein concentrations (REACH-2): a randomized, double-blind, placebo-controlled, phase 3 trial. Lancet Oncol 2019: 20:282-96. Available at: https://pubmed.ncbi.nlm.nih.gov/30665869/. Accessed October 03, 2022.


| Review/Revision History | Review/Revision Date | P&T Approval Date |
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| Policy was established | 01/2020 | 02/07/2020 |
| Policy was reviewed:<br>1. Clinical policy title was updated.<br>2. Medicaid & Commercial was added in both Initial and Continued therapy approval duration.<br>3. Initial approval criteria I.B was added with 4th ,5th & 6th b point, new criteria for new FDA indication of NSCLC in combination with erlotinib.<br>4. Continued therapy criteria II.A.1 was rephrased to “Member is currently receiving medication...” and 3c point was added.<br>5. References were reviewed and updated. | 02/02/2021 | 03/09/2021 |

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| Policy was reviewed:<br>1. Initial Approval Criteria, 1.A.4: Updated prescriber criteria from Prescribed as subsequent therapy either as a single agent or in combination with paclitaxel to Prescribed as subsequent therapy either as a single agent or in combination with paclitaxel or irinotecan with or without fluorouracil.<br>2. References were reviewed and updated. | 11/23/2021 | 1/17/2022 |
| Policy was reviewed:<br>1. Initial Approval Criteria, I.A.5: Updated to include new diagnostic criteria Disease is unresectable, locally advanced, recurrent, or metastatic.<br>2. Initial Approval Criteria, I.B.1: Updated indication from Diagnosis of metastatic NSCLC to Diagnosis of metastatic, recurrent, or advanced NSCLC.<br>3. Initial Approval Criteria, I.B.6.a: Updated indication from Dose does not exceed 10 mg per kg on day 1 of a 21-day cycle to In combination with docetaxel: Dose does not exceed 10 mg per kg on day 1 of a 21-day cycle.<br>4. Initial Approval Criteria, I.C.1: Updated indication from Diagnosis of metastatic CRC to Diagnosis of advanced or metastatic CRC.<br>5. Initial Approval Criteria, I.C.4: Updated to include new criteria pertaining to indication Colorectal Cancer, Request is for one of the following (a or b):<br>a. Primary treatment for unresectable metachronous metastases;<br>b. For subsequent therapy;<br>6. Initial Approval Criteria, I.D.1: Updated indication from Diagnosis of HCC to Diagnosis of progressive HCC.<br>7. Continued Therapy Approval Criteria, II.A.3.b: Updated dosing criteria from NSCLC: new dose does not exceed 10 mg per kg on day 1 of a 21-day cycle to NSCLC in combination with docetaxel: new dose does not exceed 10 mg per | 10/03/2022 | 01/17/2023 |

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| kg on day 1 of a 21-day cycle.<br>8. References were reviewed and updated. | | |
| Policy was reviewed. | 10/19/2023 | 10/19/2023 |