Clinical Policy: Amivantamab-vmjw (Rybrevant)

Reference Number: LA.PHAR.544
Effective Date: 09.29.23
Last Review Date: 06.23.25
Line of Business: Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

****Please note: This policy is for medical benefit****

Description

Amivantamab-vmjw (Rybrevant®) is a bispecific epidermal growth factor (EGF) receptor-directed and MET receptor-directed antibody.

FDA Approved Indication(s)

Rybrevant is indicated in adult patients:

- In combination with lazertinib for the first-line treatment of locally advanced or metastatic non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 L858R substitution mutations, as detected by an FDA-approved test
- In combination with carboplatin and pemetrexed for locally advanced or metastatic NSCLC with EGFR exon 19 deletions or exon 21 L858R substitution mutations, whose disease has progressed on or after treatment with an EGFR tyrosine kinase inhibitor
- In combination with carboplatin and pemetrexed for the first-line treatment of locally advanced or metastatic NSCLC with EGFR exon 20 insertion mutations, as detected by an FDA-approved test
- As a single agent for the treatment of locally advanced or metastatic NSCLC with EGFR exon 20 insertion mutations, as detected by an FDA-approved test, whose disease has progressed on or after platinum-based chemotherapy

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of Louisiana Healthcare Connections® that Rybrevant is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

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

1. Diagnosis of recurrent, advanced, or metastatic NSCLC;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. One of the following (a, b, or c):
   a. Disease is positive for EGFR exon 20 insertion mutations, and Rybrevant is prescribed for one of the following uses (i or ii):

i. As first line therapy in combination with carboplatin and pemetrexed;
ii. As a single agent for disease that has progressed on or after platinum-based therapy;

b. Rybrevant is prescribed as subsequent therapy after progression on an EGFR tyrosine kinase inhibitor (e.g., erlotinib, Gilotrif®, Tagrisso®) AND all of the following (i, ii, and iii):
i. Disease is positive for sensitizing EGFR mutation (e.g., exon 18 [G719X], exon 19 deletion, exon 20 [S768I], exon 21 [L858R, L861Q]);
ii. Prescribed in combination with carboplatin and pemetrexed;
iii. For disease that is positive for EGFR mutation in exon 18 (G719X), exon 20 (S768I), or exon 21 (L861Q): Presence of symptomatic systemic disease with multiple lesions;

c. Rybrevant is prescribed in combination with Lazcluze™ for disease that is positive for EGFR exon 19 deletion(s) or exon 21 L858R substitution mutation(s) AND one of the following (i or ii):
i. Prescribed as first-line therapy;
ii. Prescribed for continuation of therapy following disease progression on the combination of Rybrevant and Lazcluze for asymptomatic disease, symptomatic brain lesions, or symptomatic systemic limited progression;

5. Request meets one of the following (a, b, or c):*
a. For Rybrevant prescribed as a single agent or in combination with Lazcluze: Dose does not exceed the appropriate weight-based dose (i or ii) per week for 5 weeks, then every 2 weeks thereafter (*see section V for dosing regimen*):
i. Body weight < 80 kg (both 1 and 2):
1) 1,050 mg;
2) 3 vials;
ii. Body weight ≥ 80 kg (both 1 and 2):
1) 1,400 mg;
2) 4 vials;

b. For Rybrevant prescribed in combination with carboplatin and pemetrexed: Dose does not exceed the appropriate weight-based dose (1 or 2) per week for 4 weeks (i), then every 3 weeks thereafter (ii) (*see section V for dosing regimen*):
i. For the first four weeks (1 or 2):
1) Body weight < 80 kg (both a and b):
a) 1,400 mg;
b) 4 vials;
2) Body weight ≥ 80 kg (both a and b):
a) 1,750 mg;
b) 5 vials;
ii. For every three weeks thereafter (1 or 2):
1) Body weight < 80 kg (both a and b):
a) 1,750 mg;
b) 5 vials;
2) Body weight ≥ 80 kg (both a and b):

a) 2,100 mg;
b) 6 vials;

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: 6 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to LA.PMN.255
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy LA.PMN.53.

II. Continued Therapy

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

1. Currently receiving medication via Louisiana Healthcare Connections benefit, or documentation supports that member is currently receiving Rybrevant for NSCLC 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, or c):*
   a. For Rybrevant prescribed as a single agent or in combination with Lazcluze: New dose does not exceed the appropriate weight-based dose (i or ii) every 2 weeks (*see section V for dosing regimen)*:
      i. Body weight < 80 kg (both 1 and 2):
         1) 1,050 mg;
         2) 3 vials;
      ii. Body weight ≥ 80 kg (both 1 and 2):
         1) 1,400 mg;
         2) 4 vials;
   b. For Rybrevant prescribed in combination with carboplatin and pemetrexed: New dose does not exceed the appropriate weight-based dose (i or ii) every 3 weeks (*see section V for dosing regimen)*:
      i. Body weight < 80 kg (both 1 and 2):
         1) 1,750 mg;
         2) 5 vials;
      ii. Body weight ≥ 80 kg (both 1 and 2):
         1) 2,100 mg;
         2) 6 vials;
   c. 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: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to LA.PMN.255
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy LA.PMN.53.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy – LA.PMN.53.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

FDA: Food and Drug Administration
MET: mesenchymal-epithelial transition
NSCLC: non-small cell lung cancer
EGFR: epidermal growth factor receptor

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
platinum-based chemotherapy (e.g., cisplatin, carboplatin)	Varies	Varies
Examples of EGFR tyrosine kinase inhibitors: erlotinib (Tarceva®), gefitinib (Iressa®), Gilotrif® (afatinib), Tagrisso® (osimertinib), Vizimpro® (dacomitinib)	Varies	Varies

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

None reported

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
NSCLC	Rybrevant in combination with carboplatin and pemetrexed:	See regimen

Indication	Dosing Regimen	Maximum Dose
	Weight-based dose IV weekly for 4 weeks, with the initial dose as a split infusion in Week 1 on Day 1 and Day 2, then every 3 weeks thereafter: Week 1, day 1: • Body weight < 80 kg: 350 mg (1 vial) • Body weight ≥ 80 kg: 350 mg (1 vial) Week 1, day 2: • Body weight < 80 kg: 1,050 mg (3 vials) • Body weight ≥ 80 kg: 1,400 mg (3 vials) Week 2 to 4: • Body weight < 80 kg: 1,400 mg (4 vials) • Body weight ≥ 80 kg: 1,750 mg (5 vials) Week 7 and thereafter: • Body weight < 80 kg: 1,750 mg (5 vials) • Body weight ≥ 80 kg: 2,100 mg (6 vials) <u>Rybrevant in combination with lazertinib or Rybrevant as a single agent:</u> Weight-based dose IV weekly for 5 weeks, with the initial dose as a split infusion in Week 1 on Day 1 and Day 2, then every 2 weeks thereafter: Week 1, day 1: • Body weight < 80 kg: 350 mg (1 vial) • Body weight ≥ 80 kg: 350 mg (1 vial) Week 1, day 2: • Body weight < 80 kg: 700 mg (2 vials) • Body weight ≥ 80 kg: 1,050 mg (3 vials) Week 2 and thereafter: • Body weight < 80 kg: 1,050 mg (3 vials) • Body weight ≥ 80 kg: 1,400 mg (4 vials)	

VI. Product Availability

Solution for injection in a single-dose vial: 350 mg/7 mL (50 mg/mL)

VII. References

1. Rybrevant Prescribing Information. Horsham, PA: Janssen Biotech, Inc.; September 2024. Available at: https://www.Rybrevant.com/. Accessed October 9, 2024.
2. Cho BC, Lu S, Felip E, et al. Amivantamab plus lazertinib in previously untreated *EGFR*-mutated advanced NSCLC. N Engl J Med. Published online June 26, 2024.

3. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed October 9, 2024.
4. National Comprehensive Cancer Network. Non-Small Cell Lung Cancer. Version 10.2024. Available at: http://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf. Accessed October 9, 2024.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J9061	Injection, amivantamab-vmjw, 2 mg

Reviews, Revisions, and Approvals	Date	LDH Approval Date
Policy created	05.01.23	08.28.23
Annual review: added criteria for new indication of first-line treatment of adults with NSCLC; added monotherapy criterion for NSCLC with EGFR exon 20 insertion mutations whose disease has progressed on or after platinum-based chemotherapy per Prescribing Information and NCCN; removed "locally" as qualifying advanced NSCLC per NCCN; for Rybrevant prescribed as a single agent corrected initial dosing to be weekly for 5 weeks instead of 4 weeks.	04.28.24	07.10.24
Added criteria for new indication for NSCLC in combination with Lazcluze; for Rybrevant prescribed as subsequent therapy after Tagrisso, exon 19 insertion mutation was removed, and the sensitizing EGFR mutations were revised according to NCCN exon characterization.	10.10.24	01.27.25
Added criteria for new indication in combination with carboplatin and pemetrexed for NSCLC with EGFR exon 19 deletions or exon 21 L858R substitution mutations after progression on EGFR tyrosine kinase inhibitor; to align with the new labeled indication, revised requirement for progression on "Tagrisso" to be progression on "an EGFR tyrosine kinase inhibitor" and specified that requirement for presence of symptomatic systemic disease with multiple lesions only applies to the off-label EGFR mutations; per NCCN Compendium, added option of combination Rybrevant + Lazcluze as continuation of therapy.	06.23.25	

Important Reminder

CLINICAL POLICY
Amivantamab-vmjw

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. LHCC makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable LHCC administrative policies and procedures.

This clinical policy is effective as of the date determined by LHCC. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. LHCC retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom LHCC has no control or right of control. Providers are not agents or employees of LHCC.