Medical Policy

Utilization Management and Clinical Medical Policy

Policy Name:	Policy Number:	Scope:	Origination Date:	Effective Date:
Amivantamab-vmjw (Rybrevant®)	MP-RX-FP-79-23	☒ MMM MA ☒ MMM MultiHealth	11/30/2023	2/22/2026
			Last Review Date: 2/22/2026	Frequently Revision: 11/10/2026

Service Category

☐ Anesthesia
☐ Surgery
☐ Radiology Procedures
☐ Pathology and Laboratory Procedures
☐ Medicine Services and Procedures
☐ Evaluation and Management Services
☐ DME/Prosthetics or Supplies
☒ Part B DRUG

Service Description

This document addresses the use of *Amivantamab-vmjw (Rybrevant®) and Amivantamab and hyaluronidase-lpuj (RYBREVANT FASPRO™)* a bispecific EGF receptor-directed and MET receptor-directed antibody approved by the Food and Drug Administration (FDA) for the treatment of certain patients with locally advanced or metastatic non-small cell lung cancer (NSCLC).

Background Information

Rybrevant is a bispecific epidermal growth factor (EGF) receptor- directed and mesenchymal-epithelial transition (MET) receptor-directed antibody used to treat non-small cell lung cancer (NSCLC). Binding to extracellular domains of EGF and MET receptors on the surface of tumor cells disrupts normal signaling and targets them for destruction by the immune system.

Rybrevant is indicated for the treatment of adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with EGFR exon 20 insertion mutations whose disease has progressed on or after platinum-based chemotherapy. It is under accelerated approval for this indication; and continued approval may be contingent upon verification of clinical benefit in confirmatory trials.

Rybrevant differs from other FDA approved oral EGFR tyrosine kinase inhibitors (TKIs) such as osimertinib, erlotinib or gefitinib as they target different EGFR sensitizing mutations: exon 19 deletions or exon 21 (L858R) substitution mutations. EGFR exon 20 mutations, present in about 2 to 3% of NSCLCs, are a heterogeneous group of mutations that may or may not be responsive to targeted therapy. Individuals in the efficacy population from the clinical trial for Rybrevant were genetically evaluated using the FDA approved companion diagnostic test, Guardant360. The phase 1 clinical trial evaluated for FDA approval included 81 patients with NSCLC previously treated with platinum-based chemotherapy. The overall response rate was 40% with a median duration of response of 11.1 months. Rybrevant is currently being studied in phase 3 trials in combination with a novel oral third generation tyrosine kinase inhibitor, and in combination with platinum-based chemotherapy. Currently, it is approved for use as a single agent. The National Comprehensive Cancer Network® (NCCN) guidelines recommend the use of Rybrevant in recurrent, advanced or metastatic NSCLC with EGFR exon 20 insertion mutations as subsequent therapy (if not used previously).

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Definitions and Measures:

- Line of Therapy:
  - First-line therapy: The first or primary treatment for the diagnosis, which may include surgery, chemotherapy, radiation therapy or a combination of these therapies.
  - Second-line therapy: Treatment given when initial treatment (first-line therapy) is not effective or there is disease progression.
  - Third-line therapy: Treatment given when both initial (first-line therapy) and subsequent treatment (second-line therapy) are not effective or there is disease progression.
- Metastasis: The spread of cancer from one part of the body to another; a metastatic tumor contains cells that are like those in the original (primary) tumor and have spread.
- Monoclonal antibody: A protein developed in the laboratory that can locate and bind to specific substances in the body and on the surface of cancer cells.
- Progressive Disease (PD): Cancer that is growing, spreading, or getting worse. Refractory Disease: Illness or disease that does not respond to treatment.
- Relapse or recurrence: After a period of improvement, during which time a disease (for example, cancer) could not be detected, the return of signs and symptoms of illness or disease. For cancer, it may come back to the same place as the original (primary) tumor or to another place in the body.

Approved Indications

A. Treatment of adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) exon 20 insertion mutations, as detected by an FDA-approved test, whose disease has progressed on or after platinum-based chemotherapy.
B. In combination with lazertinib for the first-line treatment of adult patients with 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.
C. In combination with carboplatin and pemetrexed for the treatment of adult patients with 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.
D. In combination with carboplatin and pemetrexed for the first-line treatment of adult patients with locally advanced or metastatic NSCLC with EGFR exon 20 insertion mutations, as detected by an FDA-approved test.

Other Uses

i. See Background section above.

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Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

HCPCS	Description
J9061	Injection, amivantamab-vmjw, 2 mg [Rybrevant]

ICD-10	Description
C33	Malignant neoplasm of trachea
C34.00 – C34.92	Malignant neoplasm of bronchus and lung
C79.31	Secondary malignant neoplasm of brain

Medical Necessity Guidelines

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Amivantamab-vmjw (Rybrevant®) and Amivantamab and hyaluronidase-lpuj (RYBREVANT FASPRO™)

A. Criteria For Initial Approval (*Provider must submit documentation [such as office chart notes, lab results, pathology reports, imaging studies, and any other pertinent clinical information] supporting the patient's diagnosis for the drug and confirming that the patient has met **all** approval criteria.)*

i. Individual has a diagnosis of recurrent, advanced or metastatic Non-small Cell Lung Cancer (NSCLC) (Label, NCCN 2A); **AND**

ii. Lung cancer has epidermal growth factor receptor (EGFR) exon 20 insertion mutations; **AND**

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iii. Individual has disease progression on or after platinum-based chemotherapy; **AND**
iv. Individual has not progressed on prior therapy with Rybrevant (amivantamab-vmjw); **AND**
v. Individual is using Rybrevant (amivantamab-vmjw) as a single agent.

OR

vi. Individual has a diagnosis of locally advanced or metastatic Non-small Cell Lung Cancer (NSCLC) (Label, NCCN 1); **AND**
vii. Lung cancer has epidermal growth factor receptor (EGFR) exon 20 insertion mutations; **AND**
viii. Individual is using Rybrevant (amivantamab-vmjw) as first-line therapy in combination with carboplatin and pemetrexed;

OR

ix. Individual has a diagnosis of recurrent, advanced, or metastatic Non-small Cell Lung Cancer (NSCLC) (NCCN 1); **AND**
x. Lung cancer has epidermal growth factor receptor (EGFR) exon 19 deletion or exon 21 L858R mutations; **AND**
xi. Individual is using Rybrevant (amivantamab-vmjw) as subsequent therapy in combination with carboplatin and pemetrexed; **AND**
xii. Individual has had disease progression on osimertinib;

OR

xiii. Individual has a diagnosis of locally advanced or metastatic Non-small Cell Lung Cancer (NSCLC) (Label); **AND**
xiv. Lung cancer has epidermal growth factor receptor (EGFR) exon 19 deletion or exon 21 L858R substitution mutations; **AND**
xv. Individual is using Rybrevant (amivantamab-vmjw) as first-line therapy in combination with Lazertinib; **OR**
xvi. Individual is using as continuation of therapy following disease progression on Rybrevant (amivantamab-vmjw) and lazertinib;

OR

xvii. Individual has a diagnosis of Central Nervous System Cancer (NCCN 2A); **AND**
xviii. Individual has a primary diagnosis of Non-small Cell Lung Cancer (NSCLC), and disease has metastasized to the brain; **AND**
xix. Cancer has epidermal growth factor receptor (EGFR) exon 19 deletion or exon 21 L858R substitution mutation; **AND**
xx. Individual is using Rybrevant (amivantamab-vmjw) in combination with Lazertinib; **OR**
xxi. Individual is using Rybrevant (amivantamab-vmjw) in combination with carboplatin and pemetrexed.

B. Criteria For Continuation of Therapy

i. MMM considers continuation of Amivantamab-vmjw (Rybrevant®) therapy medically necessary in members requesting reauthorization for an indication listed in Section A above (Criteria for Initial Approval) when there is no evidence of unacceptable toxicity or disease

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progression while on the current regimen. The following information should be submitted for reauthorization:

A. A current oncology note documenting the patient's response to treatment showing no progression of disease.

B. Current imaging studies and other objective measures, as appropriate, showing no progression of disease when compared with previous results.

C. Authorization Duration

i. Initial Approval Duration: Up to 6 months
ii. Reauthorization Approval Duration: Up to 6 months

D. Conditions Not Covered

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive):

i. Requests for Rybrevant (amivantamab-vmjw) may not be approved if the above criteria are not met and for all indications not included above.

Limits or Restrictions

A. Quantity Limitations

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. The chart below includes dosing recommendations as per the FDA-approved prescribing information.

RYBREVANT® (amivantamab-vmjw) injection, for intravenous use

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Body Weight at Baseline*	Recommended Dose	Recommended Dosing Schedule**
***RYBREVANT®* in combination with Carboplatin and Pemetrexed**		
Less than 80 kg	1,400 mg	Weekly (total of 4 doses) from weeks 1 to 4 - Week 1: split infusion on day 1 and 2 - Weeks 2 to 4: infusion on day 1 - Weeks 5 and 6: no dose
	1,750 mg	Every 3 weeks starting at Week 7 onwards
Greater than or equal to 80 kg	1,750 mg	Weekly (total of 4 doses) from weeks 1 to 4 - Week 1: split infusion on day 1 and 2 - Weeks 2 to 4: infusion on day 1 - Weeks 5 and 6: no dose
	2,100 mg	Every 3 weeks starting at week 7 onwards
***RYBREVANT®* in Combination with Lazertinib or RYBREVANT as a Single Agent**		
Less than 80 kg	1,050 mg	Weekly (total of 5 doses) from weeks 1 to 5 - Week 1: split infusion on day 1 and day 2 - Weeks 2 to 5: infusion on day 1 - Week 6: no dose
		Every 2 weeks starting at week 7 onwards
Greater than or equal to 80 kg	1,400 mg	Weekly (total of 5 doses) from weeks 1 to 5 - Week 1: split infusion on day 1 and day 2 - Weeks 2 to 5: infusion on day 1 - Week 6: no dose
		Every 3 weeks starting at week 7 onwards
Exceptions		
*Dose adjustment is not required for subsequent body weight changes. ** Recommended duration: Until disease progression or unacceptable toxicity.		

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RYBREVANT FASPRO™ (amivantamab and hyaluronidase-lpuj) injection, for subcutaneous use

Body Weight at Baseline*	Recommended Dose	Recommended Dosing Schedule**
RYBREVANT FASPRO™ **in combination with Carboplatin and Pemetrexed**		
Less than 80 kg	1,600 mg amivantamab and 20,000 units hyaluronidase	- First dose at Week 1 Day 1
	1,400 mg amivantamab and 30,000 units hyaluronidase	Weekly (total of 2 doses) from Weeks 2 to 3 • Weeks 2 to 3 – Injection on Day 1
		Every 3 weeks starting at Week 4 onwards
Greater than or equal to 80 kg	2,240 mg amivantamab and 28,000 units hyaluronidase	- First dose at Week 1 Day 1
	3,360 mg amivantamab and 42,000 units hyaluronidase	Weekly (total of 2 doses) from Weeks 2 to 3 • Weeks 2 to 3 – Injection on Day 1
		Every 3 weeks starting at Week 4 onwards
RYBREVANT FASPRO™ **in Combination with Lazertinib or RYBREVANT as a Single Agent**		
Less than 80 kg	1,600 mg amivantamab and 20,000 units hyaluronidase	- weekly (total of 4 doses) from Weeks 1 to 4 - • Weeks 1 to 4 – Injection on Day 1
		Every 2 weeks starting at Week 5 onwards
Greater than or equal to 80 kg	2,240 mg amivantamab and 28,000 units hyaluronidase	- Weekly (total of 4 doses) from Weeks 1 to 4 • Weeks 1 to 4 – Injection on Day 1
		Every 2 weeks starting at Week 5 onwards
Exceptions		
*Dose adjustment is not required for subsequent body weight changes. ** Recommended duration: Until disease progression or unacceptable toxicity.		

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Reference Information

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2. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm. Updated periodically.
3. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
4. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2023; Updated periodically.
5. NCCN Clinical Practice Guidelines in Oncology™. © 2023 National Comprehensive Cancer Network, Inc. For additional information visit the NCCN website: http://www.nccn.org/index.asp. Accessed on April 14, 2023.
    a. Non-Small Cell Lung Cancer. V3.2023. Revised April 13, 2023

Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.

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Policy History

Revision Type	Summary of Changes	P&T Approval Date	UM/CMPC Approval Date
Focus Review	Addition of new formulation RYBREVANT FASPRO™ (amivantamab and hyaluronidase-lpuj) injection, for subcutaneous use in clinical criteria and dosage regimen in quantity limits.	2/5/2026	2/22/2026
Annual Review	Add use in NSCLC with brain metastases per NCCN. Coding Reviewed: Added ICD-10-CM C79.31. Remove select exon 21 mutations from subsequent therapy indication per NCCN and label; update references. Coding Reviewed: Updated description for HCPCS J9061.	10/31/2025	11/10/2025
Annual Review	Add new indication as first line therapy in combination with Lazertinib. Add use as subsequent therapy after progression on osimertinib for non-small cell lung cancer with exon 19 deletion or certain exon 21 mutations; add recurrent disease to first-line use; update references. Add new FDA approved indication for first-line therapy of NSCLC. Coding Reviewed: Add ICD-10-CM C33 and revised naming of C34.00-C34.92 to Malignant neoplasm of bronchus and lung.	3/14/2025	4/2/2025
Focus Review	Update statement for criteria for initial approval: Provider must submit documentation [such as office chart notes, lab results, pathology reports, imaging studies, and any other pertinent clinical information] supporting the patient's diagnosis for the drug and confirming that the patient has met all approval criteria.	3/25/2024	5/9/2024
Policy Inception	Elevance Health's Medical Policy adoption.	N/A	11/30/2023