Medical Policy

Healthcare Services Department

Policy Name	Policy Number	Scope
Amivantamab-vmjw (Rybrevant®)	MP-RX-FP-79-23	☒ MMM MA ☒ MMM Multihealth

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®), 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).

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.

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- 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

Rybrevant is indicated by the FDA for the 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. This approval for this specific use has been granted under accelerated approval, primarily relying on overall response rate and duration of response as key indicators. The ongoing approval status for this use case may depend on further confirmation and a comprehensive explanation of the clinical benefits observed in the subsequent confirmatory trials.

Other Uses

See Background section above.

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, 10 mg [Rybrevant]

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ICD-10	Description
C34.00	Malignant neoplasm of unspecified main bronchus
C34.01	Malignant neoplasm of left main bronchus
C34.02	Malignant neoplasm of right main bronchus
C34.10-C34.92	Malignant neoplasm of main bronchus

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®)

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**
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.

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 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

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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.

Drug	Recommended Dose*	Recommended Treatment Regimen	Recommended Duration
Amivantamab-vmjw (Rybrevant®)	**Less than 80 kg**: 1,050 mg **≥ 80 kg**: 1,400 mg *Recommended dose is based on baseline weight and dose adjustments not required for subsequent body weight changes.	Weeks 1 to 4: Weekly (total of 4 doses) • Week 1: Split infusion on Day 1 and Day 2 • Weeks 2 to 4: Infusion on Day 1 Week 5 onwards: Every 2 weeks starting at Week 5	Until disease progression or unacceptable toxicity.
Exceptions			
None			

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Reference Information

1. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.: 2023. URL: http://www.clinicalpharmacology.com. Updated periodically.
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.

Policy History

Revision Type	Summary of Changes	P&T Approval Date	MPCC Approval Date
Policy Inception	Elevance Health's Medical Policy adoption.	N/A	11/30/2023
Select 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.	Click or tap to enter a date.	Click or tap to enter a date.

Revised: 11/17/2023