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Section:	Prescription Drugs	**Effective Date:**	January 1, 2025
Subsection:	Antineoplastic Agents	**Original Policy Date:**	June 11, 2021
Subject:	Rybrevant	**Page:**	1 of 5

Last Review Date: December 13, 2024

Rybrevant

Description

Rybrevant (amivantamab-vmjw)

Background
Rybrevant (amivantamab-vmjw) is a bispecific antibody that binds to the extracellular domains of epidermal growth factor receptor (EGFR) and MET. In studies, Rybrevant was able to disrupt EGFR and MET signaling functions through blocking ligand binding and, in exon 19 deletions, exon 21 L858R substitutions, and exon 20 insertion mutation models, degradation of EGFR and MET. The presence of EGFR and MET on the surface of tumor cells also allows for targeting of these cells for destruction by immune effector cells, such as natural killer cells and macrophages, through antibody-dependent cellular cytotoxicity and trogocytosis mechanisms, respectively (1).

Regulatory Status
FDA-approved indications: Rybrevant is a bispecific EGF receptor-directed and MET receptor-directed antibody indicated: (1)

- 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.
- in combination with carboplatin and pemetrexed for the 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, whose disease had progressed on or after treatment with an EGFR tyrosine kinase inhibitor.
- in combination with carboplatin and pemetrexed 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 20 insertion mutations, as detected by an FDA-approved test.
- as a single agent 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.

Rybrevant has warnings regarding the following: infusion-related reactions, interstitial lung disease/pneumonitis, venous thromboembolic (VTE) events with concomitant use with lazertinib, dermatologic adverse reactions, ocular toxicity, and embryo-fetal toxicity. When administering Rybrevant in combination with lazertinib, administer anticoagulant prophylaxis to prevent VTE events for the first four months of treatment (1).

Rybrevant can cause fetal harm when administered to a pregnant woman. Females of reproductive potential should be advised to use effective contraception during treatment and for 3 months after the final dose of Rybrevant (1).

Patients should be premedicated with antihistamines, antipyretics, and glucocorticoids as appropriate to reduce the risk of infusion-related reactions (1).

The safety and effectiveness of Rybrevant in pediatric patients less than 18 years of age have not been established (1).

Related policies

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Rybrevant may be considered **medically necessary** if the conditions indicated below are met.

Rybrevant may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 18 years of age or older

Diagnosis

Patient must have the following:

1. Locally advanced or metastatic non-small cell lung cancer (NSCLC) with **ONE** of the following:
    a. EGFR exon 19 deletions or exon 21 L858R substitution mutations, as detected by an FDA-approved test **AND ONE** of the following:
        i. Used in combination with Lazcluze (lazertinib) as first-line treatment
            1) Prescriber agrees to administer anticoagulant prophylaxis to prevent venous thromboembolic events (VTE) for at least the first four months of treatment
        ii. Used in combination with carboplatin and pemetrexed **AND** disease has progressed on or after treatment with an EGFR tyrosine kinase inhibitor
    b. EGFR exon 20 insertion mutations, as detected by an FDA-approved test **AND ONE** of the following:
        i. Used in combination with carboplatin and pemetrexed for first-line treatment
        ii. Used as a single agent **AND** disease has progressed on or after platinum-based chemotherapy

AND ALL of the following:

1. Patient will be premedicated with antihistamines, antipyretics, and glucocorticoids as appropriate
2. Female patients of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Rybrevant and for 3 months after the last dose

Prior – Approval *Renewal* Requirements

Age 18 years of age or older

Diagnosis

Patient must have the following:

1. Locally advanced or metastatic non-small cell lung cancer (NSCLC)

AND ALL of the following:

1. **NO** disease progression or unacceptable toxicity
2. Patient will be premedicated with antihistamines, antipyretics, and glucocorticoids as appropriate
3. Female patients of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Rybrevant and for 3 months after the last dose

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Duration 12 months

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary

Rybrevant (amivantamab-vmjw) is a bispecific antibody that binds to the extracellular domains of epidermal growth factor receptor (EGFR) and MET. It is indicated for the treatment of adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with certain epidermal growth factor receptor (EGFR) exon mutations. Rybrevant has warnings regarding the following: infusion-related reactions, interstitial lung disease/pneumonitis, venous thromboembolic (VTE) events with concomitant use with lazertinib, dermatologic adverse reactions, ocular toxicity, and embryo-fetal toxicity. The safety and effectiveness of Rybrevant in pediatric patients less than 18 years of age have not been established (1).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of Rybrevant while maintaining optimal therapeutic outcomes.

References

1. Rybrevant [package insert]. Horsham, PA: Janssen Biotech, Inc.; September 2024.
2. NCCN Drugs & Biologics Compendium® Amivantamab-vmjw 2024. National Comprehensive Cancer Network, Inc. Accessed on October 28, 2024.

Policy History

Date	Action
June 2021	Addition to PA
September 2021	Annual review and reference update
March 2022	Annual review and reference update
September 2023	Annual review and reference update
March 2024	Annual review and reference update
April 2024	Per PI update, added indication of NSCLC in combination with carboplatin and pemetrexed for first-line treatment. Also removed quantity limits
June 2024	Annual review and reference update
October 2024	Per PI update, added indication of NSCLC with EGFR exon 19 deletions or exon 21 L858R substitution mutations, in combination with lazertinib or in combination with carboplatin and pemetrexed
December 2024	Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on December 13, 2024 and is effective on January 1, 2025.