

5.21.176

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| Subsection: | Antineoplastic Agents | Original Policy Date: | June 11, 2021 |
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Last Review Date: March 6, 2026

Rybrevant

Description

Rybrevant (amivantamab-vmjw)

Rybrevant Faspro (amivantamab and hyaluronidase-lpuj)

Background

Rybrevant (amivantamab-vmjw) and Rybrevant Faspro (amivantamab and hyaluronidase lpuj) are bispecific antibodies that bind to the extracellular domains of epidermal growth factor receptor (EGFR) and MET. In studies, Rybrevant and Rybrevant Faspro were 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 trophocytosis mechanisms, respectively (1-2).

Regulatory Status

FDA-approved indications: Rybrevant is a bispecific EGF receptor-directed and MET receptor-directed antibody. Rybrevant Faspro is a combination of amivantamab, a bispecific EGF receptor-directed and MET receptor-directed antibody, and hyaluronidase, an endoglycosidase. Both are indicated: (1-2)

- 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

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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 been associated with infusion-related reactions (1).

Rybrevant and Rybrevant Faspro have warnings regarding the following: 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 (1-2).

Rybrevant and Rybrevant Faspro 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 or Rybrevant Faspro (1-2).

Patients should be premedicated with antihistamines, antipyretics, and glucocorticoids as appropriate to reduce the risk of infusion-related reactions (1-2).

The safety and effectiveness of Rybrevant and Rybrevant Faspro in pediatric patients less than 18 years of age have not been established (1-2).

Related policies

[Policy](#)

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

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

Rybrevant and Rybrevant Faspro 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

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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

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Rybrevant (amivantamab-vmjw) and Rybrevant Faspro are 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 and Rybrevant Faspro has warnings regarding the following: 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 and Rybrevant Faspro in pediatric patients less than 18 years of age have not been established (1-2).

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

References

1. Rybrevant [package insert]. Horsham, PA: Janssen Biotech, Inc.; February 2025.
2. Rybrevant Faspro [package insert]. Horsham, PA: Janssen Biotech, Inc.; December 2025.
3. NCCN Drugs & Biologics Compendium[®] Amivantamab-vmjw 2026. National Comprehensive Cancer Network, Inc. Accessed on February 3, 2026.

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 |
| March 2025 | Annual review and reference update |
| June 2025 | Annual review and reference update |
| February 2026 | Addition of Rybrevant Faspro to policy |
| March 2026 | Annual review and reference update |

Keywords

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This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 6, 2026 and is effective on April 1, 2026.