

UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Oncology (Injectable – Epidermal Growth Factor Receptor Exon 20 Mutation Agent) – Rybrevant Utilization Management Medical Policy

- Rybrevant® (amivantamab-vmjw intravenous infusion – Janssen)

REVIEW DATE: 04/02/2025

OVERVIEW

Rybrevant, a bispecific epidermal growth factor receptor (EGFR)-directed and mesenchymal epithelial transition (MET) receptor-directed antibody, is indicated for the treatment of locally advanced or metastatic **non-small cell lung cancer (NSCLC)**:¹

- In combination with Lazcluze™ (lazertinib tablets) for the first-line treatment of adults with *EGFR* exon 19 deletions, or exon 21 *L858R* substitution mutations, as detected by an FDA-approved test.
- In combination with carboplatin and pemetrexed, in adults 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 adults with *EGFR* exon 20 insertion mutations, as detected by an FDA-approved test.
- As a single agent, in adults with *EGFR* exon 20 insertion mutation, as detected by an FDA-approved test, whose disease has progressed on or after platinum-based chemotherapy.

Dosing

In combination with carboplatin and pemetrexed for the initial treatment, followed by in combination with pemetrexed:¹

- For patients < 80 kg, the recommended dose is 1,400 mg administered by intravenous (IV) infusion once weekly for the first four doses, then 1,750 mg IV once every 3 weeks until disease progression or unacceptable adverse events (AEs).
- For patients ≥ 80 kg, the recommended dose is 1,750 mg for the first four doses followed by 2,100 mg IV once every 3 weeks until disease progression or unacceptable AEs.

For first-line treatment in combination with Lazcluze or for previously treated NSCLC:

- For patients < 80 kg, the recommended dose is 1,050 mg and for patients ≥ 80 kg the recommended dose is 1,400 mg. Rybrevant is administered by IV infusion once weekly for 5 weeks, then once every 2 weeks until disease progression or unacceptable AEs.

The initial dose is split and given on Days 1 and 2 of Week 1. Dose modifications are recommended for adverse events.

Guidelines

The National Comprehensive Cancer Network (NCCN) non-small cell lung cancer guidelines (version 3.2025 – January 14, 2025) recommend Rybrevant for the first-line treatment, in combination with carboplatin and pemetrexed and subsequent treatment, as a single agent, of *EGFR* exon 20 insertion mutation positive recurrent, advanced, or metastatic NSCLC.^{2,3} Rybrevant, in combination with Lazcluze is recommended for the treatment of recurrent, advanced, or metastatic NSCLC with *EGFR* exon 19 deletion or exon 21 *L858R* mutations, as first-line or continuation of therapy following disease progression on Rybrevant and Lazcluze. In addition, Rybrevant is recommended for the subsequent treatment of recurrent, advanced, or metastatic NSCLC with *EGFR* exon 19 deletion or exon 21 *L858R*, in combination with carboplatin and pemetrexed, following disease progression on Tagrisso® (osimertinib tablets).

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of Rybrevant. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indication. Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with Rybrevant as well as the monitoring required for adverse events and long-term efficacy, approval requires Rybrevant to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Rybrevant is recommended in those who meet the following criteria:

FDA-Approved Indication

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1. **Non-Small Cell Lung Cancer.** Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):
- A) Patient is ≥ 18 years of age; AND
 - B) Patient has locally advanced or metastatic disease; AND
 - C) Patient has ONE of the following (i, ii, or iii):
 - i. Epidermal growth factor receptor (EGFR) exon 20 insertion mutations, as detected by an approved test; OR
 - ii. EGFR exon 19 deletions, as detected by an approved test; OR
 - iii. EGFR exon 21 L858R substitution mutations, as detected by an approved test; AND
 - D) The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve ONE of the following dosing regimens (A or B):

- A) In combination with carboplatin and pemetrexed for the initial treatment, followed by in combination with pemetrexed:
 - i. Weight < 80 kg: Approve up to 1,400 mg administered by intravenous infusion once weekly for the first four doses, then approve up to 1,750 mg administered intravenously no more frequently than once every 3 weeks; OR
Note: The initial dose is divided and given on two consecutive days in the first week.
 - ii. Weight ≥ 80 kg: Approve up to 1,750 mg administered by intravenous infusion once weekly for the first four doses, then approve up to 2,100 mg administered intravenously no more frequently than once every 3 weeks; OR
Note: The initial dose is divided and given on two consecutive days in the first week.
- B) First-line treatment in combination with Lazcluze (lazertinib tablets) or as subsequent treatment:
 - i. Weight < 80 kg: Approve up to 1,050 mg administered by intravenous infusion no more frequently than once weekly for the first 5 doses, then no more frequently than once every 2 weeks; OR
Note: The initial dose is divided and given on two consecutive days in the first week.
 - ii. Weight ≥ 80 kg: Approve up to 1,400 mg administered by intravenous infusion no more frequently than once weekly for the first 5 doses, then no more frequently than once every 2 weeks.

Note: The initial dose is divided and given on two consecutive days in the first week.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Rybrevant is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Rybrevant intravenous infusion [prescribing information]. Horsham, PA: Janssen; February 2025.
2. The NCCN Drugs & Biologics Compendium. © 2025 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed March 31, 2025. Search term; amivantamab.
3. The NCCN Non-Small Cell Lung Cancer Clinical Practice Guidelines in Oncology (version 3.2025 – January 14, 2025). © 2025 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed March 31, 2025.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	06/14/2023
Early Annual Revision	Non-Small Cell Lung Cancer: Added requirement that the patient has locally advanced or metastatic disease. Added option for approval that the medication is used as subsequent therapy and the patient has epidermal growth factor (EGFR) exon 19 deletion, EGFR exon 21 <i>L858R</i> mutation, or EGFR <i>S768I</i> , <i>L861Q</i> , and/or <i>G719X</i> mutation. Added first-line dosing regimens to Dosing section.	03/13/2024
Selected Revision	Non-Small Cell Lung Cancer: New option for approval for patients with epidermal growth factor receptor (EGFR) exon 20 insertion mutations, EGFR exon 19 deletions, or EGFR exon 21 <i>L858R</i> substitution mutations was added. Removed EGFR exon 19 deletion and EGFR exon 21 <i>L858R</i> mutation from option for approval for subsequent therapy. Added descriptor “in combination with carboplatin and pemetrexed” to First-line treatment in combination with carboplatin and pemetrexed. Revised “subsequent treatment” to First-line treatment in combination with Lazcluze or as subsequent therapy.	08/28/2024
Annual Revision	Non-Small Cell Lung Cancer: Medication is used as subsequent therapy and patient has EGFR <i>S768I</i> , <i>L861Q</i> , and/or <i>G719X</i> mutation was removed as an option for approval. In the dosing section, the descriptor first-line treatment was removed from in combination with carboplatin and pemetrexed.	02/26/2025
Early Annual Revision	The policy name was changed from “Oncology (Injectable) – Rybrevant UM Medical Policy” to “Oncology (Injectable – Epidermal Growth Factor Receptor Exon 20 Mutation Agent) – Rybrevant UM Medical Policy.” Non-Small Cell Lung Cancer: Added the following to the dosage regimen “for the initial treatment, followed by in combination with pemetrexed” to “in combination with carboplatin and pemetrexed for the initial treatment, followed by in combination with pemetrexed”.	04/02/2025