Rybrevant® (amivantamab-vmjw)
(Intravenous)

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I. Length of Authorization

- Initial: Prior authorization validity will be provided initially for 6 months.
- Renewal: Prior authorization validity may be renewed every 6 months thereafter.

II. Dosing Limits

Max Units (per dose and over time) [HCPCS Unit]:

- 875 billable units (1750 mg) every 7 days for 5 weeks, no dose on week 6, then 2100 billable units (4200 mg) every 42 days thereafter

III. Initial Approval Criteria [1]

Coverage is provided in the following conditions:

- Patient is at least 18 years of age; **AND**
- Patient has been instructed/counseled on limiting sun exposure and the use of protective clothing and/or broad-spectrum UVA/UVB sunscreen; **AND**

Non-Small Cell Lung Cancer (NSCLC) † ‡ [1-7]

- Patient has recurrent, advanced, or metastatic disease (excluding locoregional recurrence or symptomatic local disease without evidence of disseminated disease) or mediastinal lymph node recurrence with prior radiation therapy; **AND**
  - Used in combination with lazertinib; **AND**
    - Patient has epidermal growth factor receptor (EGFR) exon 19 deletion or exon 21 L858R mutation positive disease as detected by an FDA-approved or CLIA compliant test❖; **AND**
      - Used as first-line treatment; **OR**
      - Used as continuation of therapy following disease progression on amivantamab + lazertinib for asymptomatic disease, symptomatic brain lesions, or symptomatic systemic limited* progression; **OR**
  - Used in combination with carboplatin and pemetrexed in patients with nonsquamous histology; **AND**
    - Used as first-line therapy; **AND**
      - Patient has EGFR exon 20 insertion mutation positive disease as detected by an FDA-approved or CLIA compliant test❖; **OR**

        - Used as subsequent therapy; **AND**
            - Patient has EGFR exon 19 deletion or exon 21 L858R mutation positive disease as detected by an FDA-approved or CLIA compliant test❖; **AND**
                - Used following disease progression on or after treatment with an EFGR tyrosine kinase inhibitor (i.e., osimertinib); **OR**
    - Used as a single agent; **AND**
        - Used as subsequent therapy; **AND**
        - Patient has EGFR exon 20 insertion mutation positive disease as detected by an FDA-approved or CLIA compliant test❖

**Clinical trials have included up to 3 to 5 progressing sites.*

Central Nervous System (CNS) Cancers ‡ [2,8]

- Patient has brain metastases from EGFR exon 19 deletion or exon 21 L858R mutation positive NSCLC as confirmed by an FDA-approved or CLIA-compliant test❖; **AND**
- Used in combination with lazertinib OR in combination with carboplatin and pemetrexed; **AND**
    - Used as initial treatment in patients with small asymptomatic limited brain metastases for newly diagnosed or stable systemic disease or if reasonable systemic treatment options exist; **OR**
    - Used for recurrent limited brain metastases; **OR**
    - Used as primary treatment in patients with small asymptomatic extensive brain metastases; **OR**
    - Used for recurrent extensive brain metastases with stable systemic disease or reasonable systemic treatment options

❖ *If confirmed using an immunotherapy assay – http://www.fda.gov/companiondiagnostics*

† FDA Approved Indication(s); ‡ Compendia Recommended Indication(s); Φ Orphan Drug

IV. Renewal Criteria [1]

Coverage can be renewed based upon the following criteria:

- Patient continues to meet indication-specific relevant criteria identified in section III; **AND**
- Disease response with treatment as defined by stabilization of disease or decrease in size of tumor or tumor spread, unless otherwise specified in section III; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: severe infusion-related reactions, interstitial lung disease, pneumonitis, venous thromboembolic events (e.g., deep vein thrombosis, pulmonary embolism), dermatologic adverse reactions (e.g., dermatitis acneiform, pruritus, dry skin, toxic epidermal necrolysis [TEN]), ocular toxicity (e.g., keratitis, blepharitis, dry eye symptoms, conjunctival redness, blurred vision, visual impairment, ocular itching, eye pruritus, uveitis), etc.

V. Dosage/Administration [1,8]

<table>
<tr><th>Indication</th><th>Dose</th></tr>
<tr><td>NSCLC & CNS Cancers</td><td>
<u>In combination with carboplatin and pemetrexed:</u>
<table>
<tr><th>Body weight at baseline [a]</th><th>Recommended Dose</th><th>Dosing Schedule**</th></tr>
<tr><td rowspan="2">< 80 kg</td><td>1400 mg</td><td>Weekly (total of 4 doses) from Weeks 1 to 4
• Week 1: split infusion on Day 1 and Day 2
• Weeks 2 to 4: infusion on Day 1
• Weeks 5 and 6: no dose</td></tr>
<tr><td>1750 mg</td><td>Every 3 weeks starting at Week 7 onwards</td></tr>
<tr><td rowspan="2">≥ 80 kg</td><td>1750 mg</td><td>Weekly (total of 4 doses) from Weeks 1 to 4
• Week 1: split infusion on Day 1 and Day 2
• Weeks 2 to 4: infusion on Day 1
• Weeks 5 and 6: no dose</td></tr>
<tr><td>2100 mg</td><td>Every 3 weeks starting at Week 7 onwards</td></tr>
<tr><td colspan="3">****<u>NOTE</u>:** Continue treatment with Rybrevant until disease progression or unacceptable toxicity.</td></tr>
</table>
<u>Single agent (NSCLC ONLY) or in combination with lazertinib:</u>
<table>
<tr><th>Body weight at baseline [a]</th><th>Recommended Dose</th><th>Dosing Schedule**</th></tr>
<tr><td rowspan="2">< 80 kg</td><td rowspan="2">1050 mg</td><td>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</td></tr>
<tr><td>Every 2 weeks starting at Week 7 onwards</td></tr>
<tr><td rowspan="2">≥ 80 kg</td><td rowspan="2">1400 mg</td><td>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
Weeks 6: no dose</td></tr>
<tr><td>Every 2 weeks starting at Week 7 onwards</td></tr>
<tr><td colspan="3">****<u>NOTE</u>:** Continue treatment with Rybrevant until disease progression or unacceptable toxicity unless otherwise specified.</td></tr>
</table>
[a] Dose adjustments not required for subsequent body weight changes.
</td></tr>
</table>

VI. Billing Code/Availability Information

<u>HCPCS Code:</u>

- J9061 – Injection, amivantamab-vmjw, 2 mg; 1 billable unit = 2 mg

<u>NDC:</u>

- Rybrevant 350 mg/7 mL (50 mg/mL) solution as a single-dose vial: 57894-0501-xx

VII. References

1. Rybrevant [package insert]. Horsham, PA; Janssen Biotech, Inc.; February 2025. Accessed July 2025.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for amivantamab. National Comprehensive Cancer Network, 2025. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed July 2025.
3. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Non-Small Cell Lung Cancer, Version 7.2025. National Comprehensive Cancer Network, 2024. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed July 2025.
4. Cho BC, Lu S, Felip E, et al. Amivantamab plus lazertinib in previously untreated EGFR-mutated advanced NSCLC. N Engl J Med 2024;391:1486-1498.
5. Zhou C, Tang KJ, Cho BC, et al; PAPILLON Investigators. Amivantamab plus Chemotherapy in NSCLC with EGFR Exon 20 Insertions. N Engl J Med. 2023 Nov 30;389(22):2039-2051. doi: 10.1056/NEJMoa2306441. Epub 2023 Oct 21. PMID: 37870976.
6. Cho BC, Felip E, Hayashi H, et al. MARIPOSA: phase 3 study of first-line amivantamab + lazertinib versus osimertinib in EGFR-mutant non-small-cell lung cancer. Future Oncol. 2022 Feb;18(6):639-647. doi: 10.2217/fon-2021-0923. Epub 2021 Dec 16. PMID: 34911336.
7. Passaro A, Wang J, Wang Y, et al; MARIPOSA-2 Investigators. Amivantamab plus chemotherapy with and without lazertinib in EGFR-mutant advanced NSCLC after disease progression on osimertinib: primary results from the phase III MARIPOSA-2 study. Ann Oncol. 2024 Jan;35(1):77-90. doi: 10.1016/j.annonc.2023.10.117. Epub 2023 Oct 23. PMID: 37879444.
8. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Central Nervous System Cancers, Version 1.2025. National Comprehensive Cancer Network, 2025. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed July 2025.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C33	Malignant neoplasm of trachea
C34.00	Malignant neoplasm of unspecified main bronchus
C34.01	Malignant neoplasm of right main bronchus
C34.02	Malignant neoplasm of left main bronchus

ICD-10	ICD-10 Description
C34.10	Malignant neoplasm of upper lobe, unspecified bronchus or lung
C34.11	Malignant neoplasm of upper lobe, right bronchus or lung
C34.12	Malignant neoplasm of upper lobe, left bronchus or lung
C34.2	Malignant neoplasm of middle lobe, bronchus or lung
C34.30	Malignant neoplasm of lower lobe, unspecified bronchus or lung
C34.31	Malignant neoplasm of lower lobe, right bronchus or lung
C34.32	Malignant neoplasm of lower lobe, left bronchus or lung
C34.80	Malignant neoplasm of overlapping sites of unspecified bronchus and lung
C34.81	Malignant neoplasm of overlapping sites of right bronchus and lung
C34.82	Malignant neoplasm of overlapping sites of left bronchus and lung
C34.90	Malignant neoplasm of unspecified part of unspecified bronchus or lung
C34.91	Malignant neoplasm of unspecified part of right bronchus or lung
C34.92	Malignant neoplasm of unspecified part of left bronchus or lung
C79.31	Secondary malignant neoplasm of brain
Z85.118	Personal history of other malignant neoplasm of bronchus and lung

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

The preceding information is intended for non-Medicare coverage determinations. Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determinations (NCDs) and/or Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. Local Coverage Articles (LCAs) may also exist for claims payment purposes or to clarify benefit eligibility under Part B for drugs which may be self-administered. The following link may be used to search for NCD, LCD, or LCA documents: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications, including any preceding information, may be applied at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
J (10)	TN, GA, AL	Palmetto GBA
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC