Clinical Policy: Amivantamab-vmjw (Rybrevant), Amivantamab/Hyaluronidase-lpuj (Rybrevant Faspro)

Reference Number: CP.PHAR.544
Effective Date: 09.01.21
Last Review Date: 08.25
Line of Business: Commercial, HIM, Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Amivantamab-vmjw (Rybrevant®) is a bispecific epidermal growth factor (EGF) receptor-directed and MET receptor-directed antibody. Amivantamab/hyaluronidase-lpuj (Rybrevant Faspro™) is a combination of amivantamab and hyaluronidase, an endoglycosidase.

FDA Approved Indication(s)

Rybrevant and Rybrevant Faspro are indicated in adult patients:

- In combination with lazertinib for the first-line treatment of 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 locally advanced or metastatic NSCLC 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 locally advanced or metastatic NSCLC with EGFR exon 20 insertion mutations, as detected by an FDA-approved test
- As a single agent for the treatment of locally advanced or metastatic NSCLC with EGFR exon 20 insertion mutations, as detected by an FDA-approved test, whose disease has progressed on or after platinum-based chemotherapy

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Rybrevant and Rybrevant Faspro are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Non-Small Cell Lung Cancer (must meet all)**:**

1. Diagnosis of recurrent, advanced, or metastatic NSCLC;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. One of the following (a, b, c, or d):
   a. Disease is positive for EGFR exon 20 insertion mutations, and Rybrevant/Rybrevant Faspro is prescribed for one of the following uses (i or ii):
      i. As first line therapy in combination with carboplatin and pemetrexed;

ii. As a single agent for disease that has progressed on or after platinum-based therapy;

b. Rybrevant/Rybrevant Faspro is prescribed as subsequent therapy after progression on an EGFR tyrosine kinase inhibitor (e.g., erlotinib, Gilotrif®, Lazcluze™, Tagrisso®) AND both of the following (i and ii):
   i. Disease is positive for EGFR exon 19 deletions or exon 21 L858R substitution mutations;
   ii. Prescribed in combination with carboplatin and pemetrexed;

c. Rybrevant/Rybrevant Faspro is prescribed in combination with Lazcluze for disease that is positive for EGFR exon 19 deletion(s) or exon 21 L858R substitution mutation(s) AND one of the following (i, ii, or iii):
   i. Prescribed as first-line therapy;
   ii. Prescribed for continuation of therapy following disease progression on the combination of Rybrevant/Rybrevant Faspro and Lazcluze for asymptomatic disease, symptomatic brain lesions, or symptomatic systemic limited progression;
   iii. Prescribed as subsequent therapy following disease progression after administration of one of the following (1 or 2):
      1) Tagrisso for symptomatic systemic disease with multiple lesions;
      2) Tagrisso/(carboplatin or cisplatin)/pemetrexed;

d. Member has brain metastases, and both of the following (i and ii):
   i. Disease is positive for EGFR exon 19 deletion(s) or exon 21 L858R substitution mutation(s);
   ii. Rybrevant/Rybrevant Faspro is prescribed in combination with one of the following (1 or 2):
      1) Carboplatin and pemetrexed;
      2) Lazcluze;

5. Request meets one of the following (a or b):*
   a. Dose does not exceed the maximum indicated regimen in section V;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid/HIM - 12 months
Commercial - 6 months or to the member's renewal date, whichever is longer

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business:

CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Non-Small Cell Lung Cancer (must meet all)**:**

1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Rybrevant/Rybrevant Faspro for NSCLC and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. If request is for a dose increase, request meets one of the following (a or b):*
   a. Dose does not exceed the maximum indicated regimen in section V;
   b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid/HIM - 12 months
Commercial - 6 months or to the member's renewal date, whichever is longer

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

FDA: Food and Drug Administration
MET: mesenchymal-epithelial transition
NSCLC: non-small cell lung cancer
EGFR: epidermal growth factor receptor

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
platinum-based chemotherapy (e.g., cisplatin, carboplatin)	Varies	Varies
Examples of EGFR tyrosine kinase inhibitors: erlotinib (Tarceva®), gefitinib (Iressa®), Gilotrif® (afatinib), Tagrisso® (osimertinib), Vizimpro® (dacomitinib)	Varies	Varies

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): patients with known hypersensitivity to hyaluronidase or to any of its excipients (*Rybrevant Faspro only*)
- Boxed warning(s): none reported

V. Dosage and Administration

Drug Name	Dosing Regimen	Maximum Dose
Amivantamab-vmjw (Rybrevant)	<u>For NSCLC in combination with carboplatin and pemetrexed:</u> Weight-based dose IV weekly for 4 weeks, with the initial dose as a split infusion in Week 1 on Day 1 and Day 2, then every 3 weeks thereafter: Week 1, day 1: • Body weight < 80 kg: 350 mg (1 vial) • Body weight ≥ 80 kg: 350 mg (1 vial) Week 1, day 2: • Body weight < 80 kg: 1,050 mg (3 vials) • Body weight ≥ 80 kg: 1,400 mg (3 vials) Week 2 to 4: • Body weight < 80 kg: 1,400 mg (4 vials) • Body weight ≥ 80 kg: 1,750 mg (5 vials) Week 7 and thereafter: • Body weight < 80 kg: 1,750 mg (5 vials) • Body weight ≥ 80 kg: 2,100 mg (6 vials)	See regimen

Drug Name	Dosing Regimen	Maximum Dose
	<u>For NSCLC in combination with lazertinib or as a single agent:</u> Weight-based dose IV weekly for 5 weeks, with the initial dose as a split infusion in Week 1 on Day 1 and Day 2, then every 2 weeks thereafter: Week 1, day 1: • Body weight < 80 kg: 350 mg (1 vial) • Body weight ≥ 80 kg: 350 mg (1 vial) Week 1, day 2: • Body weight < 80 kg: 700 mg (2 vials) • Body weight ≥ 80 kg: 1,050 mg (3 vials) Week 2 and thereafter: • Body weight < 80 kg: 1,050 mg (3 vials) • Body weight ≥ 80 kg: 1,400 mg (4 vials)	
Amivantamab/ hyaluronidase-lpuj (Rybrevant Faspro)	<u>For NSCLC in combination with carboplatin and pemetrexed:</u> Weight-based dose SC administered weekly for 3 weeks on Day 1 of each week, then every 3 weeks thereafter: Week 1, day 1: • Body weight < 80 kg: 1,600 mg amivantamab and 20,000 units hyaluronidase (1 vial) • Body weight ≥ 80 kg: 2,240 mg amivantamab and 28,000 units hyaluronidase (1 vial) Weeks 2 to 3, day 1: • Body weight < 80 kg: 2,400 mg amivantamab and 30,000 units hyaluronidase (2 vials) • Body weight ≥ 80 kg: 3,360 mg amivantamab and 42,000 units hyaluronidase (2 vials) Week 4 and thereafter: • Body weight < 80 kg: 2,400 mg amivantamab and 30,000 units hyaluronidase (2 vials) • Body weight ≥ 80 kg: 3,360 mg amivantamab and 42,000 units hyaluronidase (2 vials) <u>For NSCLC in combination with lazertinib or as a single agent:</u> Weight-based dose SC administered weekly for 4 weeks on Day 1 of each week, then every 2 weeks thereafter: Weeks 1 to 4, day 1:	See regimen

Drug Name	Dosing Regimen	Maximum Dose
	• Body weight < 80 kg: 1,600 mg amivantamab and 20,000 units hyaluronidase (1 vial) • Body weight ≥ 80 kg: 2,240 mg amivantamab and 28,000 units hyaluronidase (1 vial) Week 5 and thereafter: • Body weight < 80 kg: 1,600 mg amivantamab and 20,000 units hyaluronidase (1 vial) • Body weight ≥ 80 kg: 2,240 mg amivantamab and 28,000 units hyaluronidase (1 vial)	

VI. Product Availability

Drug Name	Availability
Amivantamab-vmjw (Rybrevant)	Solution for injection in a single-dose vial: 350 mg/7 mL (50 mg/mL)
Amivantamab/ hyaluronidase-lpuj (Rybrevant Faspro)	Solution for injection in single-dose vials: • 1,600 mg amivantamab and 20,000 units hyaluronidase/10 mL (160 mg and 2,000 units/mL) • 2,240 mg amivantamab and 28,000 units hyaluronidase/14 mL (160 mg and 2,000 units/mL)

VII. References

1. Rybrevant Prescribing Information. Horsham, PA: Janssen Biotech, Inc.; February 2025. Available at: https://www.Rybrevant.com/. Accessed April 10, 2025.
2. Rybrevant Faspro Prescribing Information. Horsham, PA: Janssen Biotech, Inc.; December 2025. Available at: /https://www.jnjlabels.com/package-insert/product-monograph/prescribing-information/RYBREVANT+Faspro-pi.pdf. Accessed January 7, 2026.
3. Cho BC, Lu S, Felip E, et al. Amivantamab plus lazertinib in previously untreated *EGFR*-mutated advanced NSCLC. N Engl J Med. Published online June 26, 2024.
4. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed January 7, 2026.
5. National Comprehensive Cancer Network. Non-Small Cell Lung Cancer. Version 3.2026. Available at: http://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf. Accessed January 7, 2026.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J9061	Injection, amivantamab-vmjw, 2 mg
C9399	Unclassified drugs or biologicals
J9999	Not otherwise classified, antineoplastic drugs

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	06.15.21	08.21
3Q 2022 annual review: no significant changes; updated HCPCS code; per NCCN compendium added additional option for recurrent NSCLC; references reviewed and updated.	05.03.22	08.22
Template changes applied to other diagnoses/indications.	10.06.22	
3Q 2023 annual review: no significant changes; references reviewed and updated.	05.08.23	08.23
RT4: added criteria for new indication of first-line treatment of adults with NSCLC; added monotherapy criterion for NSCLC with EGFR exon 20 insertion mutations whose disease has progressed on or after platinum-based chemotherapy per Prescribing Information and NCCN; removed "locally" as qualifying advanced NSCLC per NCCN; for Rybrevant prescribed as a single agent corrected initial dosing to be weekly for 5 weeks instead of 4 weeks.	03.25.24	
3Q 2024 annual review: for initial criteria, updated EGFR exon point mutation examples per NCCN; revised approval duration for Commercial line of business to 6 months or to the member's renewal date, whichever is longer; references reviewed and updated.	05.13.24	08.24
RT4: added criteria for new indication for NSCLC in combination with Lazcluze; for Rebervant prescribed as subsequent therapy after Tagrisso, exon 19 insertion mutation was removed and the sensitizing EGFR mutations were revised according to NCCN exon characterization.	08.29.24	
RT4: added criteria for new indication in combination with carboplatin and pemetrexed for NSCLC with EGFR exon 19 deletions or exon 21 L858R substitution mutations after progression on EGFR tyrosine kinase inhibitor; to align with the new labeled indication, revised requirement for progression on "Tagrisso" to be progression on "an EGFR tyrosine kinase inhibitor" and specified that requirement for presence of symptomatic systemic disease with multiple lesions only applies to the off-label EGFR mutations; per NCCN Compendium, added option of combination Rybrevant + Lazcluze as continuation of therapy.	10.09.24	
3Q 2025 annual review: for initial criteria, removed "for disease that is positive for EGFR mutation in exon 18 (G719X), exon 20 (S768I), or exon 21 (L861Q): Presence of symptomatic systemic disease with multiple lesions" as not supported in NCCN compendium and guideline update; references reviewed and updated.	04.10.25	08.25

Reviews, Revisions, and Approvals	Date	P&T Approval Date
RT4: added new formulation of Rybrevant Faspro; removed the EGFR mutations G719X, S768I, and L861Q from criteria per NCCN; added additional options for combination with Lazcluze as subsequent therapy and for brain metastases per NCCN; replaced Rybrevant-specific maximum dose criteria with a reference to the indicated regimen in section V; revised initial approval duration for Medicaid/HIM lines of business to 12 months.	01.07.26	

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.