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

Reference Number: PA.CP.PHAR.544
Effective Date: 08/2022
Last Review Date: 04/2026

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 PA Health & Wellness® 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, d or e):
   a. Disease is positive for EGFR exon 20 insertion mutations, and 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 deletion or exon 21 mutation [L858R];
   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;
e. Other category 1, 2A, or 2B NCCN-recommended uses not listed;

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*).

Approval duration: 12 months

B. Other diagnoses/indications

1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

II. Continued Therapy

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

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies;
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*).

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies.
   Approval duration: Duration of request or 12 months (whichever is less); or
2. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

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 – PA.CP.PMN.53

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

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

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 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:	See regimen

Drug Name	Dosing Regimen	Maximum Dose
	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) <u>For NSCLC in combination with lazertinib or as a single agent:</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 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 (1 vial) • Body weight ≥ 80 kg: 3,360 mg amivantamab and 42,000 units hyaluronidase (1 vial)	See regimen

Drug Name	Dosing Regimen	Maximum Dose
	Week 4 and thereafter: • Body weight < 80 kg: 2,400 mg amivantamab and 30,000 units hyaluronidase (1 vial) • Body weight ≥ 80 kg: 3,360 mg amivantamab and 42,000 units hyaluronidase (1 vial) <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: • 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) <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 4 weeks thereafter: Weeks 1 to 4, 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) Week 5 and thereafter: • Body weight < 80 kg: 3,520 mg amivantamab and 44,000 units hyaluronidase (1 vial) • Body weight ≥ 80 kg: 4,640 mg amivantamab and 58,000 units hyaluronidase (2 vials)	

VI. Product Availability

Drug Name	Availability
Amivantamab-vmjw (Rybrevant)	Solution for injection in a single-dose vial: 350 mg/7 mL (50 mg/mL)

Drug Name	Availability
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) • 2,400 mg amivantamab and 30,000 units hyaluronidase/15 mL (160 mg and 2,000 units/mL) • 3,520 mg amivantamab and 44,000 units hyaluronidase/22 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.; February 2026. Available at: /https://www.jnjlabels.com/package-insert/product-monograph/prescribing-information/RYBREVANT+Faspro-pi.pdf. Accessed March 9, 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 March 9, 2026.
5. National Comprehensive Cancer Network. Non-Small Cell Lung Cancer. Version 4.2026. Available at: http://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf. Accessed March 9, 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
Policy created	07/2022
3Q 2023 annual review: no significant changes; references reviewed and updated.	07/2023
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.	04/2024

Reviews, Revisions, and Approvals	Date
3Q 2024 annual review: RT4: added criteria for new indication for NSCLC in new 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.; reviewed and updated.	07/2024
RT4: 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.	02/2025
3Q 2025 annual review: for initial criteria, removed "for disease that is positive for EGFR mutation in exon 18 (G719X), 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.	07/2025
RT4: added new formulation of Rybrevant Faspro; 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 to 12 months; added two new Rybrevant Faspro dosage strengths of 2,400 mg amivantamab and 30,000 units hyaluronidase/15 mL and 3,520 mg amivantamab and 44,000 units hyaluronidase/22 mL.	04/2026