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Summary of Investigation Results

Amivantamab (genetical recombination) Amivantamab (genetical recombination)/vorhyaluronidase alfa (genetical recombination) Lazertinib mesilate hydrate Apixaban

March 6, 2026

Non-proprietary name

- a. Amivantamab (genetical recombination)
- b. Amivantamab (genetical recombination)/vorhyaluronidase alfa (genetical recombination)
- c. Lazertinib mesilate hydrate
- d. Apixaban

Brand name (marketing authorization holder)

- a. Rybrevant Intravenous Infusion 350 mg (Janssen Pharmaceutical K.K.)
- b. Rybrofaz Combination Subcutaneous Injection (Janssen Pharmaceutical K.K.)
- c. Lazcluze Tablets 80 mg, 240 mg (Janssen Pharmaceutical K.K.)
- d. Eliquis tablets 2.5 mg, 5 mg (Bristol-Myers Squibb K.K.)

Japanese market launch

- a. November 2024
- b. Unreleased (as of the end of February 2026)
- c. May 2025
- d. February 2013

Indications

Pharmaceuticals and Medical Devices Agency

3-3-2 Kasumigaseki, Chiyoda-ku, Tokyo 100-0013 Japan
Contact: <https://www.pmda.go.jp/english/contact/0001.html>



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- a. b.
- *EGFR* exon 20 insertion mutation-positive unresectable advanced or recurrent non-small cell lung cancer
 - *EGFR* mutation-positive unresectable advanced or recurrent non-small cell lung cancer
- c. *EGFR* mutation-positive unresectable advanced or recurrent non-small cell lung cancer
- d. ▪ Prevention of ischemic stroke and systemic embolism in patients with nonvalvular atrial fibrillation
- Treatment and prevention of recurrence of venous thromboembolism (deep vein thrombosis and pulmonary thromboembolism)

Summary of revisions

- a. b.
1. The following statements should be added to the "7. PRECAUTIONS CONCERNING DOSAGE AND ADMINISTRATION" section: "Pay attention to the risk of bleeding by referring to the electronic package insert of apixaban when administering it to prevent venous thromboembolism associated with the concomitant use with lazertinib" and "Since apixaban cannot be administered in patients with renal failure (creatinine clearance [CLcr] < 15 mL/min), treatment options other than the concomitant use of amivantamab (genetical recombination) and lazertinib should be considered."
 2. A statement that "Since apixaban cannot be administered in patients with *EGFR* mutation-positive unresectable advanced or recurrent non-small cell lung cancer with renal failure (CLcr < 15 mL/min), the concomitant use with lazertinib should be avoided, and other treatment options should be considered" should be added to the "9.2 Patients with Renal Impairment" section in "9. PRECAUTIONS CONCERNING PATIENTS WITH SPECIFIC BACKGROUNDS."
- c.
1. The following statements should be added to the "7. PRECAUTIONS CONCERNING DOSAGE AND ADMINISTRATION" section: "Pay attention to the risk of bleeding by referring to the electronic package insert of apixaban when administering it to prevent venous thromboembolism associated with the concomitant use with amivantamab (genetical recombination)" and "Since apixaban cannot be administered in patients with



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renal failure (creatinine clearance [CLcr] < 15 mL/min), treatment options other than the concomitant use of amivantamab (genetical recombination) and lazertinib should be considered."

2. A statement that "Since apixaban cannot be administered in patients with renal failure (CLcr < 15 mL/min), other treatment options should be considered" should be added to the "9.2 Patients with Renal Impairment" section in "9. PRECAUTIONS CONCERNING PATIENTS WITH SPECIFIC BACKGROUNDS."

d.

1. "Patients with renal failure (creatinine clearance [CLcr] < 15 mL/min)" should be added to the "2. CONTRAINDICATIONS" section for apixaban administered for prevention of venous thromboembolism associated with the concomitant use of amivantamab (genetical recombination) and lazertinib.
2. The following statements should be added to the "9.2 Patients with Renal Impairment" section in "9. PRECAUTIONS CONCERNING PATIENTS WITH SPECIFIC BACKGROUNDS": "Do not administer this drug in patients with renal failure (CLcr < 15 mL/min) for prevention of venous thromboembolism associated with the concomitant use of amivantamab (genetical recombination) and lazertinib," and "the risk of bleeding may increase in patients with renal disorder (CLcr 15-50 mL/min)."

Investigation results and background of the revision

The MHLW/PMDA reviewed the necessity of providing a precautionary statement for patients with renal impairment in the concomitant use of amivantamab (genetical recombination), lazertinib mesilate hydrate, and apixaban. As a result of consultation with expert advisors, since apixaban cannot be administered in patients with renal failure (CLcr < 15 mL/min), the MHLW/PMDA concluded that revision of PRECAUTIONS was necessary. Regarding apixaban used for prevention of venous thromboembolism associated with the concomitant use of amivantamab (genetical recombination) and lazertinib, the MHLW/PMDA heard opinions from relevant academic societies regarding the impacts of contraindicating apixaban in patients with renal impairment on clinical settings and confirmed that the impact was limited.

The expert advisors present at the Expert Discussion regarding the current investigation were nominated based on their conflict of interest declarations concerning the relevant products, pursuant to the "Rules for Convening Expert Discussions, etc., by the Pharmaceuticals and Medical Devices Agency" (PMDA Administrative Rule No. 20-8, dated December 25, 2008).