RYBREVANT® (amivantamab-vmjw)
Injection for IV Use | 350 mg/7 mL (50 mg/mL)

+

LAZCLUZE™ (lazertinib)
Tablets | 240 mg/80 mg

For first-line treatment of adult patients with locally advanced or metastatic EGFR+ *mNSCLC*[1]

Dosage and Administration

INDICATION

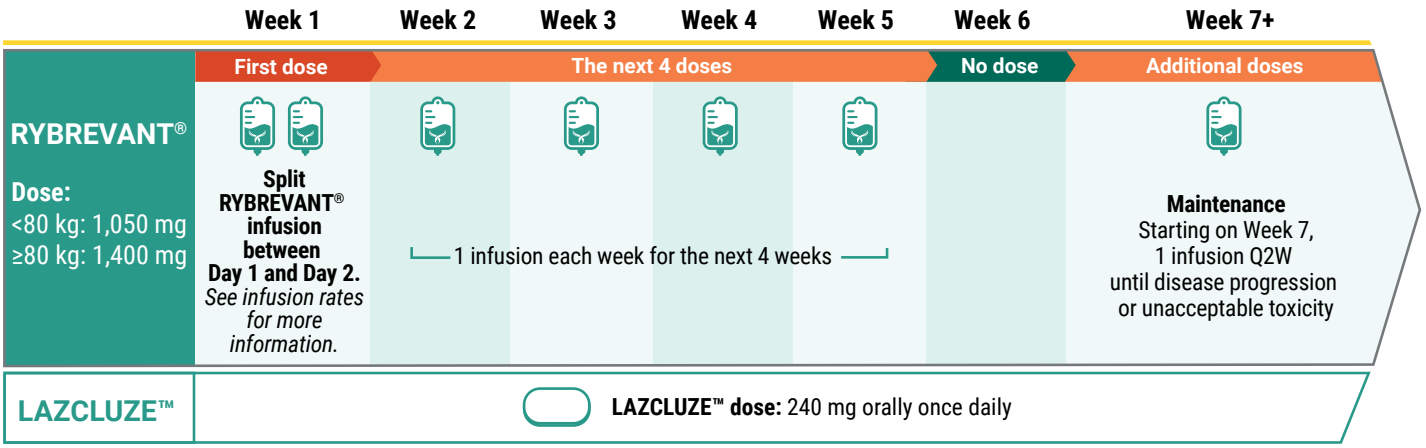
RYBREVANT® (amivantamab-vmjw) is indicated in combination with LAZCLUZE™ (lazertinib) for the first-line treatment of adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with *EGFR* exon 19 deletions or exon 21 L858R substitution mutations, as detected by an FDA-approved test.

RYBREVANT® recommended dosing[1]

The recommended dose of RYBREVANT® is based on baseline body weight and is administered as an intravenous infusion after dilution.

For additional guidance on dosage and administration or preparation of RYBREVANT®, please see the full Prescribing Information.

Recommended dosage schedule for RYBREVANT® + LAZCLUZE™[1,2]



When given in combination with LAZCLUZE™, administer LAZCLUZE™ any time before RYBREVANT® when given on the same day.
Refer to the full LAZCLUZE™ Prescribing Information for additional guidance regarding LAZCLUZE™ treatment.

EGFR, epidermal growth factor receptor; mNSCLC, metastatic non–small cell lung cancer; Q2W, once every 2 weeks.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Infusion-Related Reactions

RYBREVANT® can cause infusion-related reactions (IRR); signs and symptoms of IRR include dyspnea, flushing, fever, chills, nausea, chest discomfort, hypotension, and vomiting. The median time to IRR onset is approximately 1 hour.

Please see full Important Safety Information throughout. Please read full Prescribing Information for RYBREVANT® and full Prescribing Information for LAZCLUZE™.

Dosage and Administration

Administration for RYBREVANT®[1]

As an intravenous solution

- Administer the diluted solution by intravenous infusion using an infusion set fitted with a flow regulator and with an in-line, sterile, non-pyrogenic, low protein-binding polyethersulfone (PES) filter (pore size 0.2 micrometer)
- Administration sets must be made of either PU, PBD, PVC, PP, or PE
- The administration set with filter must be primed with either 5% dextrose injection or 0.9% sodium chloride injection prior to the initiation of each RYBREVANT® infusion

Do not infuse RYBREVANT® concomitantly in the same intravenous line with other agents.

In combination with LAZCLUZE™

- Administer RYBREVANT® infusion every 2 weeks intravenously until disease progression or unacceptable toxicity according to the infusion rates (see page 3)
- Administer RYBREVANT® via a peripheral line on Week 1 and Week 2, given the high incidence of IRRs during initial treatment
- RYBREVANT® may be administered via central line for subsequent weeks
- For the initial infusion, prepare RYBREVANT® as close to administration time as possible to allow for the possibility of extended infusion time in the event of an IRR
- When given in combination with LAZCLUZE™, administer RYBREVANT® any time after LAZCLUZE™ when given on the same day
- Swallow LAZCLUZE™ tablets whole (with or without food). Do not crush, split, or chew. Continue treatment until disease progression or unacceptable toxicity
- If a patient misses a dose of LAZCLUZE™ within 12 hours, instruct the patient to take the missed dose. If more than 12 hours have passed since the dose was to be given, instruct the patient to take the next dose at its scheduled time
- If vomiting occurs any time after taking LAZCLUZE™, instruct the patient to take the next dose at its next regularly scheduled time

For additional dosage and administration, please see the full Prescribing Information.

Drug-to-drug interactions with LAZCLUZE™

Avoid concomitant use of LAZCLUZE™ with strong and moderate CYP3A4 inducers. Consider an alternate concomitant medication with no potential to induce CYP3A4.

Monitor for adverse reactions associated with a CYP3A4 or BCRP substrate where minimal concentration changes may lead to serious adverse reactions, as recommended in the approved product labeling for the CYP3A4 or BCRP substrate.

Please see full LAZCLUZE™ Prescribing Information for information regarding dosage and administration and drug interactions.

BCRP, breast cancer resistance protein; CYP3A4, cytochrome P450 3A4; IRR, infusion-related reaction; PBD, polybutadiene; PE, polyethylene; PP, polypropylene; PU, polyurethane; PVC, polyvinyl chloride.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Infusion-Related Reactions (cont'd)

RYBREVANT® with LAZCLUZE™

RYBREVANT® in combination with LAZCLUZE™ can cause infusion-related reactions. In MARIPOSA (n=421), IRRs occurred in 63% of patients treated with RYBREVANT® in combination with LAZCLUZE™, including Grade 3 in 5% and Grade 4 in 1% of patients.

Please see full Important Safety Information throughout.
Please read full Prescribing Information for RYBREVANT®
and full Prescribing Information for LAZCLUZE™.

RYBREVANT® (amivantamab-vmjw) Injection for IV Use | 350 mg/7 mL (50 mg/mL) + LAZCLUZE™ (lazertinib) Tablets | 240 mg/80 mg

Dosage and Administration

Infusion rates for RYBREVANT® + LAZCLUZE™[1]

Body Weight Less Than 80 kg			
Week	**Dose (per 250 mL bag)**	**Initial infusion rate**	**Subsequent infusion rate***
Week 1 (split dose infusion)			
Week 1, Day 1	350 mg	50 mL/hr	75 mL/hr
Week 1, Day 2	700 mg	50 mL/hr	75 mL/hr
Week 2	1,050 mg	85 mL/hr	
Week 3	1,050 mg	125 mL/hr	
Week 4	1,050 mg	125 mL/hr	
Week 5	1,050 mg	125 mL/hr	
Week 6	No dose		
Week 7, and every 2 weeks thereafter	1,050 mg	125 mL/hr	

Body Weight Greater Than or Equal to 80 kg			
Week	**Dose (per 250 mL bag)**	**Initial infusion rate**	**Subsequent infusion rate***
Week 1 (split dose infusion)			
Week 1, Day 1	350 mg	50 mL/hr	75 mL/hr
Week 1, Day 2	1,050 mg	35 mL/hr	50 mL/hr
Week 2	1,400 mg	65 mL/hr	
Week 3	1,400 mg	85 mL/hr	
Week 4	1,400 mg	125 mL/hr	
Week 5	1,400 mg	125 mL/hr	
Week 6	No dose		
Week 7, and every 2 weeks thereafter	1,400 mg	125 mL/hr	

*In the absence of IRRs, increase the initial infusion rate to the subsequent infusion rate after 2 hours based on patient tolerance. Total infusion time approximately 4 to 6 hours for Day 1 and 6 to 8 hours for Day 2. Subsequent infusion time is approximately 2 hours.
IRR, infusion-related reaction.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

The incidence of infusion modifications due to IRR was 54% of patients, and IRRs leading to dose reduction of RYBREVANT® occurred in 0.7% of patients. Infusion-related reactions leading to permanent discontinuation of RYBREVANT® occurred in 4.5% of patients receiving RYBREVANT® in combination with LAZCLUZE™.

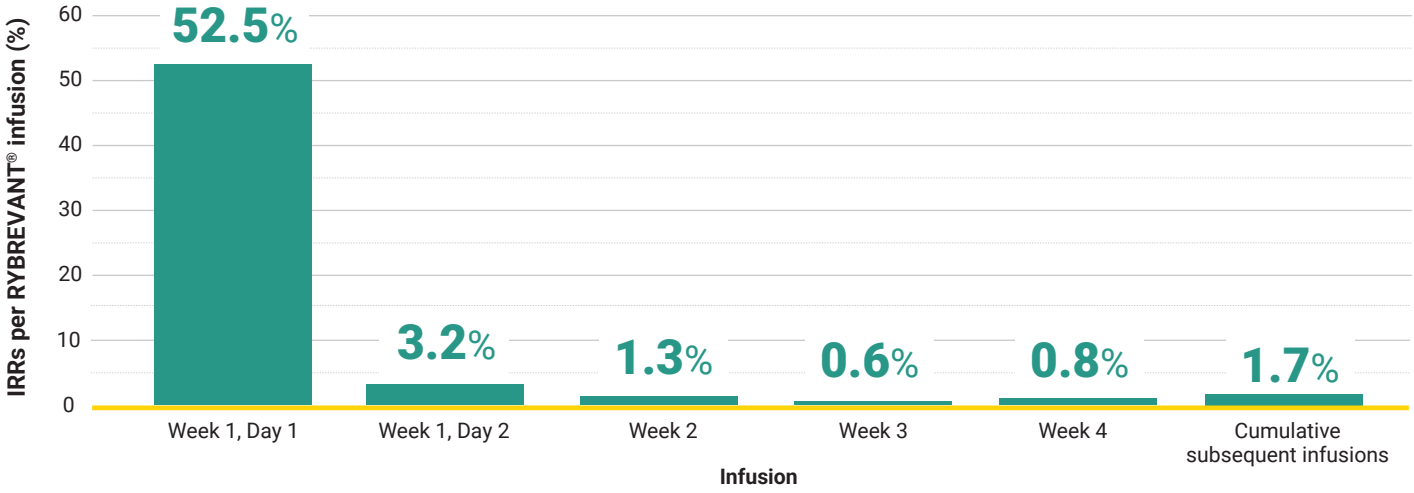
Premedicate with antihistamines, antipyretics, and glucocorticoids and infuse RYBREVANT® as recommended. Administer RYBREVANT® via a peripheral line on Week 1 and Week 2 to reduce the risk of infusion-related reactions. Monitor patients for signs and symptoms of infusion reactions during RYBREVANT® infusion in a setting where cardiopulmonary resuscitation medication and equipment are available. Interrupt infusion if IRR is suspected. Reduce the infusion rate or permanently discontinue RYBREVANT® based on severity.

Please see full Important Safety Information throughout.
Please read full Prescribing Information for RYBREVANT® and full Prescribing Information for LAZCLUZE™.

Dosage and Administration

IRR rates with RYBREVANT® + LAZCLUZE™[3]

In the MARIPOSA trial, most IRRs occurred during the first infusion (Week 1, Day 1) and rarely during subsequent infusions



- 92.3% of IRRs were Grades 1 to 2[3]
- Median time to onset of first IRR was 1 hour (range, 0.05 to 52.5 hours)[3]
- Monitor patients for any signs and symptoms of IRRs during RYBREVANT® infusion in a setting where cardiopulmonary resuscitation medication and equipment are available. Interrupt infusion if IRR is suspected. Reduce the infusion rate or permanently discontinue RYBREVANT® based on severity[1]
- Signs and symptoms of IRR include dyspnea, flushing, fever, chills, nausea, chest discomfort, hypotension, and vomiting[1]

IRR, infusion-related reaction.

Please refer to section 2 of the RYBREVANT® Prescribing Information for complete dosing and administration information.

For more detailed information regarding treatment with RYBREVANT® + LAZCLUZE™, connect with an Oncology Clinical Educator (OCE) by visiting Find Your OCE.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Interstitial Lung Disease/Pneumonitis

RYBREVANT® can cause severe and fatal interstitial lung disease (ILD)/pneumonitis.

RYBREVANT® with LAZCLUZE™
In MARIPOSA, ILD/pneumonitis occurred in 3.1% of patients treated with RYBREVANT® in combination with LAZCLUZE™, including Grade 3 in 1.0% and Grade 4 in 0.2% of patients. There was one fatal case (0.2%) of ILD/pneumonitis and 2.9% of patients permanently discontinued RYBREVANT® and LAZCLUZE™ due to ILD/pneumonitis.

Please see full Important Safety Information throughout.
Please read full Prescribing Information for RYBREVANT® and full Prescribing Information for LAZCLUZE™.

RYBREVANT® (amivantamab-vmjw) Injection for IV Use | 350 mg/7 mL (50 mg/mL) + LAZCLUZE™ (lazertinib) Tablets | 240 mg/80 mg

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Monitor patients for new or worsening symptoms indicative of ILD/pneumonitis (e.g., dyspnea, cough, fever). For patients receiving RYBREVANT® in combination with LAZCLUZE™, immediately withhold both drugs in patients with suspected ILD/pneumonitis and permanently discontinue if ILD/pneumonitis is confirmed. For patients receiving RYBREVANT® as a single agent or in combination with carboplatin and pemetrexed, immediately withhold RYBREVANT® in patients with suspected ILD/pneumonitis and permanently discontinue if ILD/pneumonitis is confirmed.

Venous Thromboembolic (VTE) Events with Concomitant Use of RYBREVANT® and LAZCLUZE™

RYBREVANT® in combination with LAZCLUZE™ can cause serious and fatal venous thromboembolic (VTEs) events, including deep vein thrombosis and pulmonary embolism. The majority of these events occurred during the first four months of therapy.

In MARIPOSA, VTEs occurred in 36% of patients receiving RYBREVANT® in combination with LAZCLUZE™, including Grade 3 in 10% and Grade 4 in 0.5% of patients. On-study VTEs occurred in 1.2% of patients (n=5) while receiving anticoagulation therapy. There were two fatal cases of VTE (0.5%), 9% of patients had VTE leading to dose interruptions of RYBREVANT®, and 7% of patients had VTE leading to dose interruptions of LAZCLUZE™; 1% of patients had VTE leading to dose reductions of RYBREVANT®, and 0.5% of patients had VTE leading to dose reductions of LAZCLUZE™; 3.1% of patients had VTE leading to permanent discontinuation of RYBREVANT®, and 1.9% of patients had VTE leading to permanent discontinuation of LAZCLUZE™. The median time to onset of VTEs was 84 days (range: 6 to 777).

Administer prophylactic anticoagulation for the first four months of treatment. The use of Vitamin K antagonists is not recommended. Monitor for signs and symptoms of VTE events and treat as medically appropriate.

Withhold RYBREVANT® and LAZCLUZE™ based on severity. Once anticoagulant treatment has been initiated, resume RYBREVANT® and LAZCLUZE™ at the same dose level at the discretion of the healthcare provider. In the event of VTE recurrence despite therapeutic anticoagulation, permanently discontinue RYBREVANT® and continue treatment with LAZCLUZE™ at the same dose level at the discretion of the healthcare provider.

Dermatologic Adverse Reactions

RYBREVANT® can cause severe rash including toxic epidermal necrolysis (TEN), dermatitis acneiform, pruritus, and dry skin.

RYBREVANT® with LAZCLUZE™
In MARIPOSA, rash occurred in 86% of patients treated with RYBREVANT® in combination with LAZCLUZE™, including Grade 3 in 26% of patients. The median time to onset of rash was 14 days (range: 1 to 556 days). Rash leading to dose interruptions occurred in 37% of patients for RYBREVANT® and 30% for LAZCLUZE™, rash leading to dose reductions occurred in 23% of patients for RYBREVANT® and 19% for LAZCLUZE™, and rash leading to permanent discontinuation occurred in 5% of patients for RYBREVANT® and 1.7% for LAZCLUZE™.

Instruct patients to limit sun exposure during and for 2 months after treatment with RYBREVANT® or LAZCLUZE™ in combination with RYBREVANT®. Advise patients to wear protective clothing and use broad-spectrum UVA/UVB sunscreen. Alcohol-free (e.g., isopropanol-free, ethanol-free) emollient cream is recommended for dry skin.

When initiating RYBREVANT® treatment with or without LAZCLUZE™, administer alcohol-free emollient cream to reduce the risk of dermatologic adverse reactions. Consider prophylactic measures (e.g. use of oral antibiotics) to reduce the risk of dermatologic reactions. If skin reactions develop, start topical corticosteroids and topical and/or oral antibiotics. For Grade 3 reactions, add oral steroids and consider dermatologic consultation. Promptly refer patients presenting with severe rash, atypical appearance or distribution, or lack of improvement within 2 weeks to a dermatologist. For patients receiving RYBREVANT® in combination with LAZCLUZE™, withhold, dose reduce or permanently discontinue both drugs based on severity. For patients receiving RYBREVANT® as a single agent or in combination with carboplatin and pemetrexed, withhold, dose reduce or permanently discontinue RYBREVANT® based on severity.

Please see full Important Safety Information throughout.
Please read full Prescribing Information for RYBREVANT® and full Prescribing Information for LAZCLUZE™.

Dosage and Administration

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Ocular Toxicity

RYBREVANT® can cause ocular toxicity including keratitis, blepharitis, dry eye symptoms, conjunctival redness, blurred vision, visual impairment, ocular itching, eye pruritus, and uveitis.

RYBREVANT® with LAZCLUZE™

In MARIPOSA, ocular toxicity occurred in 16% of patients treated with RYBREVANT® in combination with LAZCLUZE™, including Grade 3 or 4 ocular toxicity in 0.7% of patients. Withhold, reduce the dose, or permanently discontinue RYBREVANT® and continue LAZCLUZE™ based on severity.

Promptly refer patients with new or worsening eye symptoms to an ophthalmologist. Withhold, dose reduce or permanently discontinue RYBREVANT® based on severity.

Embryo-Fetal Toxicity

Based on its mechanism of action and findings from animal models, RYBREVANT® and LAZCLUZE™ can cause fetal harm when administered to a pregnant woman. Advise females of reproductive potential of the potential risk to the fetus.

Advise female patients of reproductive potential to use effective contraception during treatment and for 3 months after the last dose of RYBREVANT®.

Advise females of reproductive potential to use effective contraception during treatment with LAZCLUZE™ and for 3 weeks after the last dose. Advise male patients with female partners of reproductive potential to use effective contraception during treatment with LAZCLUZE™ and for 3 weeks after the last dose.

Adverse Reactions

RYBREVANT® with LAZCLUZE™

For the 421 patients in the MARIPOSA clinical trial who received RYBREVANT® in combination with LAZCLUZE™, the most common adverse reactions (≥20%) were rash (86%), nail toxicity (71%), infusion-related reactions (RYBREVANT®, 63%), musculoskeletal pain (47%), stomatitis (43%), edema (43%), VTE (36%), paresthesia (35%), fatigue (32%), diarrhea (31%), constipation (29%), COVID-19 (26%), hemorrhage (25%), dry skin (25%), decreased appetite (24%), pruritus (24%), nausea (21%), and ocular toxicity (16%). The most common Grade 3 or 4 laboratory abnormalities (≥2%) were decreased albumin (8%), decreased sodium (7%), increased ALT (7%), decreased potassium (5%), decreased hemoglobin (3.8%), increased AST (3.8%), increased GGT (2.6%), and increased magnesium (2.6%).

Serious adverse reactions occurred in 49% of patients who received RYBREVANT® in combination with LAZCLUZE™. Serious adverse reactions occurring in ≥2% of patients included VTE (11%), pneumonia (4%), ILD/pneumonitis and rash (2.9% each), COVID-19 (2.4%), and pleural effusion and infusion-related reaction (RYBREVANT®) (2.1% each). Fatal adverse reactions occurred in 7% of patients who received RYBREVANT® in combination with LAZCLUZE™ due to death not otherwise specified (1.2%); sepsis and respiratory failure (1% each); pneumonia, myocardial infarction, and sudden death (0.7% each); cerebral infarction, pulmonary embolism (PE), and COVID-19 infection (0.5% each); and ILD/pneumonitis, acute respiratory distress syndrome (ARDS), and cardiopulmonary arrest (0.2% each).

LAZCLUZE™ Drug Interactions

Avoid concomitant use of LAZCLUZE™ with strong and moderate CYP3A4 inducers. Consider an alternate concomitant medication with no potential to induce CYP3A4.

Monitor for adverse reactions associated with a CYP3A4 or BCRP substrate where minimal concentration changes may lead to serious adverse reactions, as recommended in the approved product labeling for the CYP3A4 or BCRP substrate.

Please read full Prescribing Information for RYBREVANT®.

Please read full Prescribing Information for LAZCLUZE™.

cp-464671v1

References: 1. RYBREVANT® [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc. **2.** LAZCLUZE™ [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc. **3.** Data on file. Janssen Biotech, Inc.

Johnson&Johnson

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