

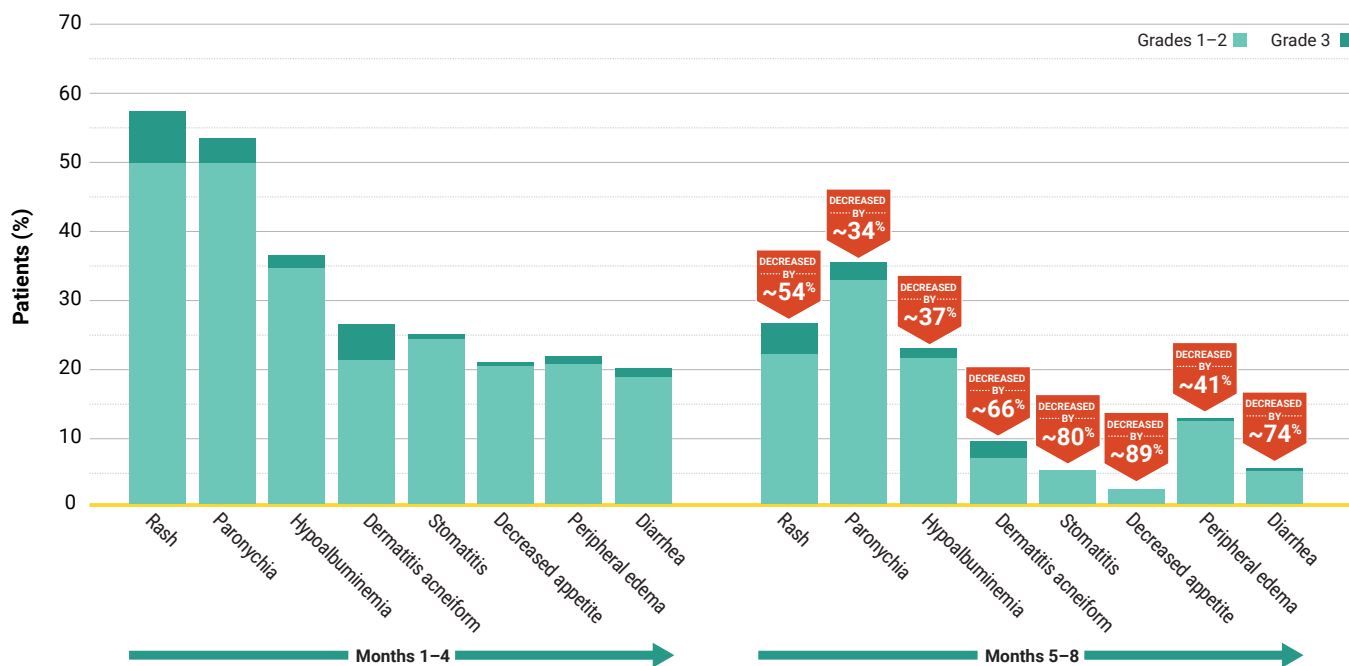


**For first-line treatment of adult patients with locally advanced or metastatic EGFR+ NSCLC<sup>1</sup>**  
**Adverse Reaction (AR) Monitoring and Management**

**INDICATION**

RYBREVANT<sup>®</sup> (amivantamab-vmjw) is indicated in combination with LAZCLUZE<sup>™</sup> (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.

**Key ARs occurred most frequently during the first 4 months and declined over the next 4 months<sup>2\*†</sup>**



The most common ARs ( $\geq 20\%$ ) were rash, nail toxicity, IRR, musculoskeletal pain, stomatitis, edema, VTE, paresthesia, fatigue, diarrhea, constipation, COVID-19, hemorrhage, dry skin, decreased appetite, pruritus, nausea, and ocular toxicity.<sup>1</sup>

Some of these most common ARs are not present in the figure above.

\*These analyses are not in the Prescribing Information for RYBREVANT<sup>®</sup> and LAZCLUZE<sup>™</sup>. These are post hoc exploratory analyses.

<sup>†</sup>Patients with PFS events or censored in the first 4 months were excluded from this analysis.

EGFR, epidermal growth factor receptor; IRR, infusion-related reaction; VTE, venous thromboembolism.

**IMPORTANT SAFETY INFORMATION**

**WARNINGS AND PRECAUTIONS**

**Infusion-Related Reactions**

RYBREVANT<sup>®</sup> 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 Important Safety Information throughout. Please read full Prescribing Information for RYBREVANT<sup>®</sup> and full Prescribing Information for LAZCLUZE<sup>™</sup>.**

# AR Monitoring and Management

## Dosage modifications for ARs

### Recommended RYBREVANT® dose reductions for ARs<sup>1</sup>

Dose reductions for ARs			
Dose at which the AR occurred	1st Dose Reduction	2nd Dose Reduction	3rd Dose Reduction
1,050 mg	700 mg	350 mg	Discontinue RYBREVANT®
1,400 mg	1,050 mg	700 mg	

### Recommended LAZCLUZE™ dose reductions for ARs<sup>3</sup>

Dose reductions for ARs			
Dose at which the AR occurred	1st Dose Reduction	2nd Dose Reduction	3rd Dose Reduction
240 mg once daily (one 240-mg tablet)	160 mg once daily (two 80 mg tablets)	80 mg once daily (one 80 mg tablet)	Discontinue LAZCLUZE™

## 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. 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 Important Safety Information throughout.

Please read full Prescribing Information for RYBREVANT®

2 and full Prescribing Information for LAZCLUZE™.



# AR Monitoring and Management

## Recommended dosage modifications for ARs for RYBREVANT® + LAZCLUZE™<sup>1</sup>

Adverse Reaction	Severity	Dosage Modifications
VTE events (applies to RYBREVANT® + LAZCLUZE™ combination only)	Grades 2 or 3	<b>RYBREVANT® + LAZCLUZE™</b> <ul style="list-style-type: none"><li>Withhold RYBREVANT® and LAZCLUZE™</li><li>Administer anticoagulant treatment as clinically indicated</li><li>Once anticoagulant treatment has been initiated, resume RYBREVANT® and LAZCLUZE™ at the same dose level, at the discretion of the healthcare provider</li></ul>
	Grade 4 or recurrent Grade 2 or 3 despite therapeutic level anticoagulation	<b>RYBREVANT® + LAZCLUZE™</b> <ul style="list-style-type: none"><li>Withhold LAZCLUZE™ and permanently discontinue RYBREVANT®</li><li>Administer anticoagulant treatment as clinically indicated</li><li>Once anticoagulant treatment has been initiated, treatment can continue with LAZCLUZE™ at the same dose level at the discretion of the healthcare provider</li></ul>

### 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.

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.

##### 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.

Please see Important Safety Information throughout.

Please read full Prescribing Information for RYBREVANT®

3 and full Prescribing Information for LAZCLUZE™.



# AR Monitoring and Management

## Recommended dosage modifications for ARs for RYBREVANT® + LAZCLUZE™ (cont'd)<sup>1,3</sup>

Adverse Reaction	Severity	Dosage Modifications
IRR	Grades 1 to 2	<b>RYBREVANT®</b> <ul style="list-style-type: none"> <li>Interrupt RYBREVANT® infusion if IRR is suspected and monitor patient until reaction symptoms resolve</li> <li>Resume the infusion at 50% of the infusion rate at which the reaction occurred</li> <li>If there are no additional symptoms after 30 minutes, the infusion rate may be escalated</li> <li>Include corticosteroid with premedications for subsequent dose</li> </ul>
	Grade 3	<b>RYBREVANT®</b> <ul style="list-style-type: none"> <li>Interrupt RYBREVANT® infusion and administer supportive care medications. Continuously monitor patient until reaction symptoms resolve</li> <li>Resume the infusion at 50% of the infusion rate at which the reaction occurred</li> <li>If there are no additional symptoms after 30 minutes, the infusion rate may be escalated</li> <li>Include corticosteroid with premedications for subsequent dose. For recurrent Grade 3, permanently discontinue RYBREVANT®</li> </ul>
	Grade 4	<b>RYBREVANT®</b> <ul style="list-style-type: none"> <li>Permanently discontinue RYBREVANT®</li> </ul>
Adverse Reaction	Severity	Dosage Modifications
ILD/pneumonitis	Any Grade	<b>RYBREVANT®</b> <ul style="list-style-type: none"> <li>Withhold RYBREVANT® if ILD/pneumonitis is suspected</li> <li>Permanently discontinue RYBREVANT® if ILD/pneumonitis is confirmed</li> </ul>
		<b>LAZCLUZE™</b> <ul style="list-style-type: none"> <li>Withhold LAZCLUZE™ if ILD/pneumonitis is suspected</li> <li>Permanently discontinue LAZCLUZE™ if ILD/pneumonitis is confirmed</li> </ul>

ILD, interstitial lung disease; IRR, infusion-related reaction.

### IMPORTANT SAFETY INFORMATION (cont'd)

#### WARNINGS AND PRECAUTIONS (cont'd)

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).

Please see Important Safety Information throughout.

Please read full Prescribing Information for RYBREVANT®

4 and full Prescribing Information for LAZCLUZE™.



# AR Monitoring and Management

## Recommended dosage modifications for ARs for RYBREVANT® + LAZCLUZE™ (cont'd)<sup>1,3</sup>

Adverse Reaction	Severity	Dosage Modifications
Dermatologic ARs (including dermatitis acneiform, pruritus, dry skin)	<b>Grade 1</b>	<p><b>RYBREVANT®</b></p> <ul style="list-style-type: none"> <li>Initiate supportive care management</li> <li>Reassess after 2 weeks; if rash does not improve, consider dose reduction</li> </ul> <p><b>LAZCLUZE™</b></p> <ul style="list-style-type: none"> <li>Initiate supportive care management</li> </ul>
	<b>Grade 2</b>	<p><b>RYBREVANT®</b></p> <ul style="list-style-type: none"> <li>Initiate supportive care management</li> <li>Reassess after 2 weeks; if rash does not improve, consider dose reduction</li> </ul> <p><b>LAZCLUZE™</b></p> <ul style="list-style-type: none"> <li>Initiate supportive care management</li> <li>If there is no improvement after 2 weeks, reduce RYBREVANT® dose and continue LAZCLUZE™ at the same dose</li> <li>Reassess every 2 weeks; if no improvement, reduce LAZCLUZE™ dose until ≤Grade 1, then may resume previous dose of LAZCLUZE™ at the discretion of the healthcare provider</li> </ul>
	<b>Grade 3</b>	<p><b>RYBREVANT®</b></p> <ul style="list-style-type: none"> <li>Withhold RYBREVANT® and initiate supportive care management</li> <li>Upon recovery to ≤Grade 2, resume RYBREVANT® at reduced dose</li> <li>If no improvement within 2 weeks, permanently discontinue treatment</li> </ul> <p><b>LAZCLUZE™</b></p> <ul style="list-style-type: none"> <li>Withhold LAZCLUZE™ and RYBREVANT®</li> <li>Initiate supportive care management</li> <li>Upon recovery to ≤Grade 2, resume LAZCLUZE™ at the same dose or consider dose reduction; resume RYBREVANT® at a reduced dose</li> <li>If there is no improvement within 2 weeks, permanently discontinue both LAZCLUZE™ and RYBREVANT®</li> </ul>
	<b>Grade 4</b> (including severe bullous, blistering, or exfoliating skin conditions, including TEN for RYBREVANT®)	<p><b>RYBREVANT®</b></p> <ul style="list-style-type: none"> <li>Permanently discontinue RYBREVANT®</li> </ul> <p><b>LAZCLUZE™</b></p> <ul style="list-style-type: none"> <li>Initiate supportive care management and withhold LAZCLUZE™ until recovery ≤Grade 2 or baseline</li> <li>Upon recovery to ≤Grade 2, resume LAZCLUZE™ at a reduced dose at the discretion of the healthcare provider</li> </ul>

TEN, toxic epidermal necrolysis.

### IMPORTANT SAFETY INFORMATION (cont'd)

#### WARNINGS AND PRECAUTIONS (cont'd)

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.

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



# AR Monitoring and Management

## Recommended dosage modifications for ARs for RYBREVANT® + LAZCLUZE™ (cont'd)<sup>1,3</sup>

Adverse Reaction	Severity	Dosage Modifications
Other adverse reactions	Grade 3	<b>RYBREVANT®</b> <ul style="list-style-type: none"><li>Withhold RYBREVANT® until recovery to ≤Grade 1 or baseline</li><li>Resume at the same dose if recovery occurs within 1 week</li><li>Resume at reduced dose if recovery occurs after 1 week but within 4 weeks</li><li>Permanently discontinue if recovery does not occur within 4 weeks</li></ul> <b>LAZCLUZE™</b> <ul style="list-style-type: none"><li>Withhold LAZCLUZE™ and RYBREVANT® until the adverse reaction resolves to ≤Grade 1 or baseline</li><li>Resume both drugs at a reduced dose or LAZCLUZE™ alone</li><li>Consider permanently discontinuing both LAZCLUZE™ and RYBREVANT® if recovery does not occur within 4 weeks</li></ul>
	Grade 4	<b>RYBREVANT®</b> <ul style="list-style-type: none"><li>Withhold RYBREVANT® until recovery to ≤Grade 1 or baseline</li><li>Resume at reduced dose if recovery occurs within 4 weeks</li><li>Permanently discontinue if recovery does not occur within 4 weeks</li><li>Permanently discontinue for recurrent Grade 4 reactions</li></ul> <b>LAZCLUZE™</b> <ul style="list-style-type: none"><li>Withhold LAZCLUZE™ and RYBREVANT® until the adverse reaction resolves to ≤Grade 1 or baseline</li><li>Resume both drugs at a reduced dose or LAZCLUZE™ alone</li><li>Consider permanently discontinuing both LAZCLUZE™ and RYBREVANT® if recovery does not occur within 4 weeks</li></ul>

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)

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.

#### 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.

Please see Important Safety Information throughout.

Please read full [Prescribing Information](#) for RYBREVANT® and full [Prescribing Information](#) for LAZCLUZE™.





# AR Monitoring and Management

## IMPORTANT SAFETY INFORMATION (cont'd)

### WARNINGS AND PRECAUTIONS (cont'd)

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 ( $\geq 20\%$ ) 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 ( $\geq 2\%$ ) 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  $\geq 2\%$  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. Data on file. Janssen Biotech, Inc. 3. LAZCLUZE™ [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc.

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