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

+

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

PROACTIVE THERAPY MANAGEMENT

START

When initiating treatment with RYBREVANT® + LAZCLUZE™, proactive therapy management is recommended and may help reduce the risk and severity of select ARs

IRRs premedications: Due to the risk of IRRs, administer premedications prior to initial infusion of RYBREVANT® (Week 1, Days 1 and 2). Glucocorticoid administration is required for Week 1, Days 1 and 2 dose only and upon re-initiation after prolonged dose interruptions, then as necessary for subsequent infusions. Administer both antihistamine and antipyretic prior to all infusions. Interrupt infusion if IRR is suspected. Reduce the infusion rate or permanently discontinue RYBREVANT® based on severity.[1]

VTE prophylaxis: When initiating treatment with RYBREVANT® in combination with LAZCLUZE™, administer anticoagulant prophylaxis to prevent VTE events for the first 4 months of treatment. The use of Vitamin K antagonists is not recommended. If there are no signs or symptoms of VTE during the first 4 months of treatment, consider discontinuation of anticoagulant prophylaxis at the discretion of the healthcare provider.[1]

Dermatologic ARs prophylaxis: When initiating treatment with RYBREVANT® in combination with LAZCLUZE™, administer alcohol-free (eg, isopropanol-free, ethanol-free) emollient cream and encourage patients to limit sun exposure during and for 2 months after treatment, to wear protective clothing and use broad-spectrum UVA/UVB sunscreen to reduce the risk of dermatologic ARs. Consider prophylactic measures (eg, use of oral antibiotics) to reduce the risk of dermatologic ARs.[1]

Refer to the **Prescribing Information** for LAZCLUZE™ for information about concomitant medications.

AR, adverse reaction; IRR, infusion-related reaction; mNSCLC, metastatic non–small cell lung cancer; VTE, venous thromboembolism; UVA, ultraviolet A; UVB, ultraviolet B.

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 epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 L858R substitution mutations, as detected by an FDA-approved test.

SELECT IMPORTANT SAFETY INFORMATION

Warnings and precautions for RYBREVANT® and LAZCLUZE™ include infusion-related reactions, interstitial lung disease/pneumonitis, venous thromboembolic events, dermatologic adverse reactions, ocular toxicity, and embryo-fetal toxicity.

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

Relevant ARs with RYBREVANT® + LAZCLUZE™ in MARIPOSA

In MARIPOSA (n=421), IRRs occurred in 63% of patients treated with RYBREVANT® + LAZCLUZE™, including Grade 3 in 5% and Grade 4 in 1% of patients. VTEs occurred in 36% of patients receiving RYBREVANT® + LAZCLUZE™, including Grade 3 in 10% and Grade 4 in 0.5% of patients. Rash occurred in 86% of patients treated with RYBREVANT® + LAZCLUZE™, including Grade 3 in 26% of patients. Nail toxicity occurred in 71% of patients receiving RYBREVANT® + LAZCLUZE™, including Grade 3 or 4 in 11% of patients.[1]

Additional proactive therapy management was evaluated in the SKIPPirr and COCOON trials

SKIPPirr:

A Phase 2 study evaluating prophylactic strategies to reduce the incidence of IRRs with RYBREVANT®[2]

SKIPPirr was a Phase 2 prospective study that assessed prophylactic strategies to reduce incidence and/or severity of first-dose IRRs with RYBREVANT®, with the dexamethasone 8 mg cohort reaching the expansion stage.* The primary endpoint was the incidence of IRR events on Week 1, Day 1.[2,3]

Limitations

- SKIPPirr was not a comparative study[2]
- The dexamethasone 8 mg oral cohort sample size was n=40[2]

COCOON:

An ongoing Phase 2 study evaluating prophylactic skin regimen to reduce the incidence of dermatologic ARs with RYBREVANT® + LAZCLUZE™[4]

COCOON is a Phase 2, open-label, randomized study evaluating the effect of enhanced versus standard dermatologic management strategies in patients treated with RYBREVANT® + LAZCLUZE™ in 1L. The primary endpoint is incidence of Grade ≥2 dermatologic ARs of interest in the first 12 weeks after treatment initiation.[4]

COCOON is also the first trial of RYBREVANT® + LAZCLUZE™ that required 4 months of prophylactic anticoagulation, with a secondary endpoint of VTE incidence and severity.[4,5]

*A Simon's two-stage design with an expansion stage was used. Stage 1 n=6. Stage 2 n=16. Expansion stage n=40. See full presentation for more details.
1L, first-line.

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Timing of prophylactic protocols used in SKIPPirr and COCOON[1,2,4,6,7]

These prophylactic protocols are not part of dosing and administration of RYBREVANT® + LAZCLUZE™.

Begin RYBREVANT® + LAZCLUZE™

SKIPPirr IRR prophylaxis*	COCOON VTE prophylaxis
Days -2 and -1: Oral dexamethasone 8 mg twice daily **1 hour before first infusion:** Dexamethasone 8 mg	**Months 0-4** Oral anticoagulation (eg, DOACs or LMWHs)†

COCOON dermatologic prophylaxis

Weeks 1-12: Doxycycline or minocycline 100 mg twice daily	**Weeks 13+:** Topical clindamycin lotion 1% on the scalp before bedtime
Daily: Chlorhexidine 4% on the fingernails and toenails once daily	
Daily: Ceramide-based moisturizer on the body and face at least once daily	
Daily: Wear protective clothing and broad-spectrum sunscreen (SPF ≥30)	

*Includes standard premedication (antihistamines, antipyretics, and glucocorticoids).
†NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) recommendations for cancer-associated VTE disease: anticoagulant options for VTE prophylaxis for ambulatory patients with cancer include DOACs and LMWHs.[7‡§¶]
‡Recommendations derived from clinical trials of ambulatory patients with cancer with high thrombosis risk (>18 years, Khorana VTE Risk Score of ≥2, initiating new course of chemotherapy) and are not included in product labeling. Prophylaxis duration should be 6 months or longer if risk persists.[7]
§Always refer to the NCCN Guidelines® for the comprehensive and most up-to-date recommendations on cancer-associated VTE when considering prophylaxis.
¶When using RYBREVANT® in combination with LAZCLUZE™, please refer to the Prescribing Information for VTE prophylaxis recommendation.
DOAC, direct oral anticoagulant; LMWH, low molecular weight heparin; NCCN, National Comprehensive Cancer Network.

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Indications and Important Safety Information

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 epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 L858R substitution mutations, as detected by an FDA-approved test.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Infusion-Related Reactions

RYBREVANT® can cause infusion-related reactions (IRR) including anaphylaxis; 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.

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. If an anaphylactic reaction occurs, permanently discontinue RYBREVANT®.

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.

Indications and Important Safety Information (cont'd)

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.

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Indications and Important Safety Information (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, reduce the dose, 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).

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Indications and Important Safety Information (cont'd)

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™.

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7. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Cancer-Associated Venous Thromboembolic Disease V.1.2025. © National Comprehensive Cancer Network, Inc. 2025. All rights reserved. Accessed March 7, 2025. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

Help your patients get the most out of their treatment from the start. Learn more about proactive therapy management strategies by visiting **www.RYBREVANThcp.com/proactive-therapy-management**

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