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

+

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

Proactive Supportive Care Guide for Adverse Reactions

For all RYBREVANT®-based regimens

INDICATIONS

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.
- in combination with carboplatin and pemetrexed for the first-line treatment of adult patients with 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 adult patients with 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.

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™.

What to expect

Consider RYBREVANT®-based regimens for mNSCLC across multiple indications

EGFR+ mNSCLC with exon 19 deletions or exon 21 L858R substitution mutations[1]	*EGFR*+ mNSCLC with exon 20 insertion mutations[1]
First line (in combination with LAZCLUZE™)	First line (in combination with carboplatin and pemetrexed)
	Second line, after platinum-based chemotherapy (as single agent)

This guide aims to review the proactive and reactive measures that may help you and your patients prepare for, identify, and manage adverse reactions (ARs) that may occur when treating with a RYBREVANT®-based regimen.

EGFR, epidermal growth factor receptor; mNSCLC, metastatic non–small cell lung cancer.

IMPORTANT SAFETY INFORMATION (cont'd)

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.

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™.

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

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1L, first-line; CTCAE, Common Terminology Criteria for Adverse Events; exon20ins, exon 20 insertion mutations; MASCC, Multinational Association of Supportive Care in Cancer; VTE, venous thromboembolism.

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

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

1L *EGFR*+ mNSCLC MARIPOSA

RYBREVANT® (amivantamab-vmjw) + LAZCLUZE™ (lazertinib)

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

Warnings and precautions

RYBREVANT® + LAZCLUZE™: First-line treatment of locally advanced or metastatic NSCLC with *EGFR* exon 19 deletions or exon 21 L858R substitution mutations[1]

Infusion-Related Reactions[1]

RYBREVANT® can cause IRRs; signs and symptoms of IRRs include dyspnea, flushing, fever, chills, nausea, chest discomfort, hypotension, and vomiting. The median time to IRR onset is approximately 1 hour. RYBREVANT® in combination with LAZCLUZE™ can cause IRRs.

In MARIPOSA, 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 IRRs was 54%. IRRs leading to dose reduction of RYBREVANT® occurred in 0.7% of patients. IRRs 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 IRRs.

Monitor patients for any 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.

Interstitial Lung Disease/Pneumonitis[1]

RYBREVANT® can cause severe and fatal ILD/pneumonitis. In MARIPOSA, ILD/pneumonitis occurred in 3.1% of patients treated with RYBREVANT® in combination with LAZCLUZE™, including Grade 3 in 1% and Grade 4 in 0.2% of patients. There was one fatal case 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 (eg, dyspnea, cough, fever). Immediately withhold RYBREVANT® in patients with suspected ILD/pneumonitis and permanently discontinue if ILD/pneumonitis is confirmed.

Venous Thromboembolic Events With Concomitant Use With LAZCLUZE™[1]

RYBREVANT® in combination with LAZCLUZE™ can cause serious and fatal VTE events, including deep vein thrombosis and pulmonary embolism. The majority of these events occurred during the first 4 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 2 fatal cases of VTE (0.5%), 9% of patients had VTE leading to dose interruptions of RYBREVANT®, 1% of patients had VTE leading to dose reductions of RYBREVANT®, and 3.1% of patients had VTE leading to permanent discontinuation of RYBREVANT®. The median time to onset of VTEs was 84 days (range, 6 to 777).

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®. Treatment can continue with LAZCLUZE™ at the same dose level at the discretion of the healthcare provider. Refer to the LAZCLUZE™ prescribing information for recommended LAZCLUZE™ dosage modification.

Dermatologic Adverse Reactions[1]

RYBREVANT® can cause severe rash including toxic epidermal necrolysis (TEN), dermatitis, acneiform, pruritus, and dry skin. 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 of RYBREVANT® occurred in 37% of patients, rash leading to dose reductions of RYBREVANT® occurred in 23% of patients, and rash leading to permanent discontinuation of RYBREVANT® occurred in 5% of patients.

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

When initiating treatment with RYBREVANT®, administer alcohol-free (eg, isopropanol-free, ethanol-free) emollient cream to reduce the risk of dermatologic ARs. Consider prophylactic measures (eg, use of oral antibiotics) to reduce the risk of dermatologic ARs. 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. Withhold, dose reduce, or permanently discontinue RYBREVANT® based on severity.

Ocular Toxicity[1]

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

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, dose reduce, 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[1]

Based on its mechanism of action and findings from animal models, RYBREVANT® can cause fetal harm when administered to a pregnant woman. Administration of other EGFR inhibitor molecules to pregnant animals has resulted in an increased incidence of impairment of embryo-fetal development, embryo lethality, and abortion. Advise patients of reproductive potential of the potential risk to the fetus. Advise patients of reproductive potential to use effective contraception during treatment and for 3 months after the last dose of RYBREVANT®.

ILD, interstitial lung disease; IRR, infusion-related reaction; NSCLC, non–small cell lung cancer; UVA, ultraviolet A; UVB, ultraviolet B.

What to expect

Adverse reactions

Majority of ARs were Grades 1 and 2[1]

ARs (≥10%) in patients in MARIPOSA[1]

Adverse Reactions	RYBREVANT® + LAZCLUZE™ (N=421)		Osimertinib (N=428)	
	All Grades (%)	Grades 3–4 (%)	All Grades (%)	Grades 3–4 (%)
Skin and subcutaneous tissue disorder				
Rash*	86	26	48	1.2
Nail toxicity*	71	11	34	0.7
Dry skin*	25	1	18	0.2
Pruritus	24	0.5	17	0.2
Injury, poisoning, and procedural complications				
Infusion-related reaction†	63	6	0	0
Musculoskeletal and connective tissue disorders				
Musculoskeletal pain*	47	2.1	39	1.9
Gastrointestinal disorders				
Stomatitis*	43	2.4	27	0.5
Diarrhea*	31	2.6	45	0.9
Constipation	29	0	13	0
Nausea	21	1.2	14	0.2
Vomiting	12	0.5	5	0
Abdominal pain*	11	0	10	0
Hemorrhoids	10	0.2	2.1	0.2
General disorders and administration site conditions				
Edema*	43	2.6	8	0
Fatigue*	32	3.8	20	1.9
Pyrexia	12	0	9	0
Vascular disorders				
Venous thromboembolism*	36	11	8	2.8
Hemorrhage*	25	1	13	1.2
Nervous system disorders				
Paresthesia*	35	1.7	10	0.2
Dizziness*	14	0	10	0
Headache*	13	0.2	13	0
Infections and infestations				
COVID-19	26	1.7	24	1.4
Conjunctivitis	11	0.2	1.6	0
Metabolism and nutrition disorders				
Decreased appetite	24	1	18	1.4
Respiratory, thoracic, and mediastinal disorders				
Cough*	19	0	23	0
Dyspnea*	14	1.7	17	3.5
Eye disorders				
Ocular toxicity*	16	0.7	7	0
Psychiatric disorders				
Insomnia	10	0	11	0

*Grouped terms.
†Applicable for RYBREVANT® only.

Learn more about proactive supportive care and how to manage ARs for your patients.

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

What to expect

Laboratory abnormalities

Select laboratory abnormalities (≥ 20%) that worsened from baseline in MARIPOSA[1]*

Laboratory Abnormality	RYBREVANT® + LAZCLUZE™ (N=421)		Osimertinib (N=428)	
	All Grades (%)	Grades 3–4 (%)	All Grades (%)	Grades 3–4 (%)
Chemistry				
Decreased albumin	89	8	22	0.2
Increased ALT	65	7	29	2.6
Increased AST	52	3.8	36	1.9
Increased alkaline phosphatase	45	0.5	15	0.5
Decreased calcium (corrected)	41	1.4	27	0.7
Increased GGT	39	2.6	24	1.9
Decreased sodium	38	7	35	5
Decreased potassium	30	5	15	1.2
Increased creatinine	26	0.7	35	0.7
Decreased magnesium	25	0.7	10	0.2
Increased magnesium	12	2.6	20	4.8
Hematology				
Decreased platelet count	52	0.7	57	1.4
Decreased hemoglobin	47	3.8	56	1.9
Decreased white blood cell	38	1	66	0.7
Decreased neutrophils	15	1.4	33	1.4

*The denominator used to calculate the rate is the number of patients with a baseline value and at least one post-treatment value for the specific lab test.

- **The most common Grade 3 or 4 laboratory abnormalities (≥2%)** were decreased albumin, decreased sodium, increased ALT, decreased potassium, decreased hemoglobin, increased AST, increased GGT, and increased magnesium[1]

Safety profile of MARIPOSA clinical study

- **Serious ARs** occurred in 49% of patients with RYBREVANT® + LAZCLUZE™ and 33% with osimertinib[1,2]
- **Serious ARs in ≥2% of patients** included VTE (11%), pneumonia (4%), rash (2.9%), ILD/pneumonitis (2.9%), COVID-19 (2.4%), pleural effusion (2.1%), and IRR (2.1%)[1]
- **Fatal ARs** occurred in 7% of patients who received RYBREVANT® + LAZCLUZE™ and 7% with osimertinib[1,2]
- **The most common ARs** (≥20%) were rash, nail toxicity, IRRs, musculoskeletal pain, stomatitis, edema, VTE, paresthesia, fatigue, diarrhea, constipation, COVID-19, hemorrhage, dry skin, decreased appetite, pruritus, nausea, and ocular toxicity[1]
- **Clinically relevant ARs** in <10% of patients who received RYBREVANT® + LAZCLUZE™ included ILD/pneumonitis (3.1%)[1]

ALT, alanine aminotransferase; AST, aspartate transferase; GGT, gamma-glutamyl transferase.

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

What to expect

Discontinuation rates/dose modifications

RYBREVANT® + LAZCLUZE™: First-line treatment of locally advanced or metastatic NSCLC with *EGFR* exon 19 deletions or exon 21 L858R substitution mutations[1]

Discontinuation rates:

- Median duration of treatment was 18.5 months for RYBREVANT® + LAZCLUZE™ and 18 months for osimertinib[2]
- Permanent discontinuation of RYBREVANT® due to an AR occurred in 34% of patients[1]
  - ARs leading to RYBREVANT® discontinuation in ≥1% of patients included rash, IRRs, nail toxicity, VTE, ILD/pneumonitis, pneumonia, edema, hypoalbuminemia, fatigue, paresthesia, and dyspnea
- Permanent discontinuation of LAZCLUZE™ due to an AR occurred in 21% of patients[3]
  - ARs that resulted in permanent discontinuation of LAZCLUZE™ in ≥1% of patients included ILD/pneumonitis, pneumonia, VTE, rash, respiratory failure, and sudden death

Dose interruption:

- Dose interruptions of RYBREVANT® due to an AR occurred in 88% of patients. ARs requiring dose interruptions in ≥5% of patients were IRRs, rash, nail toxicity, COVID-19, VTE, increased ALT, edema, and hypoalbuminemia[1]
- Dose interruptions of LAZCLUZE™ due to an AR occurred in 72% of patients. ARs requiring dose interruptions in ≥5% of patients were rash, nail toxicity, COVID-19, VTE, increased ALT, increased AST[3]

Dose reductions:

- Dose reductions of RYBREVANT® due to an AR occurred in 46% of patients. ARs requiring dose reductions in ≥5% of patients were rash and nail toxicity[1]
- Dose reductions of LAZCLUZE™ due to an AR occurred in 42% of patients. ARs requiring dose reductions in ≥5% of patients were rash and nail toxicity[3]

The rate of discontinuation of all agents due to treatment-related ARs was 10% for RYBREVANT® + LAZCLUZE™[2]

1L *EGFR*+ exon20ins mNSCLC PAPILLON

RYBREVANT® (amivantamab-vmjw) + chemotherapy*

Note: For second-line patients in the CHRYSALIS study, see the full Prescribing Information.

*Chemotherapy is carboplatin and pemetrexed.

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

Warnings and precautions

RYBREVANT® + chemotherapy: First-line treatment of locally advanced or metastatic NSCLC with *EGFR* exon 20 insertion mutations[1]

Infusion-Related Reactions[1]

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

In PAPILLON, IRRs occurred in 42% of patients treated with RYBREVANT® in combination with carboplatin and pemetrexed, including Grade 3 (1.3%) ARs. The incidence of infusion modifications due to IRRs was 40%, and 0.7% of patients permanently discontinued RYBREVANT®.

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 IRRs.

Monitor patients for any 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.

Interstitial Lung Disease/Pneumonitis[1]

RYBREVANT® can cause severe and fatal ILD/pneumonitis.

In PAPILLON, Grade 3 ILD/pneumonitis occurred in 2.6% of patients treated with RYBREVANT® in combination with carboplatin and pemetrexed; all patients required permanent discontinuation.

Monitor patients for new or worsening symptoms indicative of ILD/pneumonitis (eg, dyspnea, cough, fever). Immediately withhold RYBREVANT® in patients with suspected ILD/pneumonitis and permanently discontinue if ILD/pneumonitis is confirmed.

Dermatologic Adverse Reactions[1]

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

In PAPILLON, rash occurred in 89% of patients treated with RYBREVANT® in combination with carboplatin and pemetrexed, including Grade 3 (19%) ARs. Rash leading to dose reductions occurred in 19% of patients, and 2% permanently discontinued RYBREVANT® and 1.3% discontinued pemetrexed.

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

When initiating treatment with RYBREVANT®, administer alcohol-free (eg, isopropanol-free, ethanol-free) emollient cream to reduce the risk of dermatologic adverse reactions. Consider prophylactic measures (eg, use of oral antibiotics) to reduce the risk of dermatologic ARs. 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. Withhold, dose reduce, or permanently discontinue RYBREVANT® based on severity.

Ocular Toxicity[1]

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

In PAPILLON, ocular toxicity including blepharitis, dry eye, conjunctival redness, blurred vision, and eye pruritus occurred in 9%. All events were Grade 1 to 2.

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

Embryo-Fetal Toxicity[1]

Based on its mechanism of action and findings from animal models, RYBREVANT® can cause fetal harm when administered to a pregnant woman. Administration of other EGFR inhibitor molecules to pregnant animals has resulted in an increased incidence of impairment of embryo-fetal development, embryo lethality, and abortion. Advise patients of reproductive potential of the potential risk to the fetus. Advise patients of reproductive potential to use effective contraception during treatment and for 3 months after the last dose of RYBREVANT®.

What to expect

Adverse reactions

Majority of ARs were Grades 1 and 2[1]

ARs (≥10%) observed in PAPILLON clinical study[1]

Adverse Reactions*	RYBREVANT® + Chemotherapy (n=151)		Chemotherapy (n=155)	
	All Grades (%)	Grades 3–4 (%)	All Grades (%)	Grades 3–4 (%)
Skin and subcutaneous tissue disorder				
Rash†	90	19	19	0
Nail toxicity†	62	7	3	0
Dry skin†	17	0	6	0
Gastrointestinal disorders				
Stomatitis†	43	4	11	0
Constipation	40	0	30	0.7
Nausea	36	0.7	42	0
Vomiting	21	3.3	19	0.7
Diarrhea	21	3	13	1.3
Hemorrhoids	12	1	1.3	0
Abdominal pain†	11	0.7	8	0
General disorders and administration site conditions				
Infusion-related reactions	42	1.3	1.3	0
Fatigue†	42	6	45	3.9
Edema†	40	1.3	19	0
Pyrexia†	17	0	6	0
Metabolism and nutrition disorders				
Decreased appetite	36	2.6	28	1.3
Infections and infestations				
COVID-19	24	2	14	0.6
Pneumonia†	13	5	6	1.9
Vascular disorders				
Hemorrhage†	18	0.7	11	1.9
Respiratory, thoracic, and mediastinal disorders				
Cough†	17	0	16	0
Dyspnea†	11	1.3	16	3.2
Investigations				
Weight decreased	14	0.7	8	0
Nervous system disorders				
Dizziness†	11	0	12	0
Psychiatric disorders				
Insomnia	11	0	13	0

*ARs were graded using CTCAE version 5.0.
†Grouped term.

- **Serious ARs** occurred in 37% of patients who received RYBREVANT® + chemotherapy and 31% of patients who received chemotherapy alone. Serious ARs in ≥2% of patients included rash, pneumonia, ILD, pulmonary embolism, vomiting, and COVID-19[1,4]
- **Fatal ARs** occurred in 4.6% of patients who received RYBREVANT® + chemotherapy and 3% of patients who received chemotherapy alone[1,4]
- **The most common ARs** (≥20%) were rash, nail toxicity, stomatitis, IRR, fatigue, edema, constipation, decreased appetite, nausea, COVID-19, diarrhea, and vomiting[1]
- **Clinically relevant ARs** in <10% of patients who received RYBREVANT® + chemotherapy included pulmonary embolism, deep vein thrombosis, skin ulcer, conjunctivitis, and ILD/pneumonitis[1]

What to expect

Lab abnormalities

Summary of laboratory abnormalities (≥20%) in PAPILLON[1]

Laboratory Abnormality*	RYBREVANT® + Chemotherapy† (N=151)		Chemotherapy‡ (N=155)	
	All Grades (%)	Grades 3–4 (%)	All Grades (%)	Grades 3–4 (%)
Hematology				
Decreased white blood cell	89	17	76	10
Decreased hemoglobin	79	11	85	13
Decreased neutrophils	76	36	61	23
Decreased platelets	70	10	54	12
Decreased lymphocytes	61	11	49	13
Chemistry				
Decreased albumin	87	7	34	1
Increased aspartate aminotransferase	60	1	61	1
Increased alanine aminotransferase	57	4	54	1
Increased sodium	55	7	39	4
Increased alanine phosphatase	51	1	28	0
Decreased potassium	44	11	17	1
Decreased magnesium	39	2	30	1
Increased gamma-glutamyl transferase	38	4	43	4
Decreased calcium (corrected)	27	1	18	1

*ARs were graded using CTCAE version 5.0.
†The denominator used to calculate the rate varied from 113 to 150 based on the number of patients with a baseline value and at least one post-treatment value.
‡The denominator used to calculate the rate varied from 119 to 154 based on the number of patients with a baseline value and at least one post-treatment value.

- **Grade 3 to 4 laboratory abnormalities (≥2%)** were decreased albumin, increased alanine aminotransferase, increased gamma-glutamyl transferase, decreased sodium, decreased potassium, decreased magnesium, and decreases in white blood cells, hemoglobin, neutrophils, platelets, and lymphocytes[1]

Learn more about proactive supportive care and how to manage ARs for your patients.

What to expect

Discontinuation rates/dose modifications

RYBREVANT® + chemotherapy: First-line treatment of locally advanced or metastatic NSCLC with *EGFR* exon 20 insertion mutations[1]

Discontinuation rates[1]:

- Permanent discontinuation of RYBREVANT® due to ARs occurred in 11% of patients
- ARs resulting in permanent discontinuation of RYBREVANT® in ≥1% of patients were rash and ILD

Dose interruptions[1]:

- Dose interruption due to ARs occurred in 64% of patients. ARs requiring dose interruption in ≥5% of patients included rash and nail toxicity
- IRRs requiring infusion interruptions occurred in 38% of patients

Dose reductions[1]

- Dose reductions due to ARs occurred in 36% of patients
- ARs requiring dose reductions in ≥5% of patients included rash and nail toxicity

PROACTIVE SUPPORTIVE CARE

Proactive approach

Proactive supportive care is recommended

EGFR is a critical oncogenic driver for many patients with mNSCLC[5,6]

Treatments targeting EGFR such as RYBREVANT® or LAZCLUZE™ commonly cause on-target ARs[5]

EGFR inhibitor-related ARs can affect patients' quality of life[5]

A proactive supportive-care approach is needed to help give patients the best chance of tolerating and staying on EGFR-targeting treatment[6]

Proactive supportive care was not mandatory across RYBREVANT® studies. Some recommendations are based on the clinical trial experience while others are from guidelines.

Dermatologic care

Proactive supportive care may reduce the risk and severity of dermatologic ARs

Use of prophylactic antibiotics (with or without topical skin therapies) has demonstrated[7]*:

64% REDUCTION

in the risk of developing Grades 2 to 4 skin rash eruptions

46% REDUCTION

in the risk of all grades skin rash

39% REDUCTION

in the risk of paronychia

*Based on a systematic review and meta-analysis of 13 studies including 1,073 patients.

Implement proactive supportive care with your patients to support them throughout their treatment journey.

Skin rash MASCC guidelines

Multinational Association of Supportive Care in Cancer (MASCC)

MASCC guidelines recommend proactive measures (Weeks 1 to 6) and ongoing monitoring to reduce the risk of severe reactions.[8]

Hydrocortisone 1% cream with moisturizer and sunscreen twice daily

Minocycline 100 mg daily OR doxycycline 100 mg twice daily

IMPORTANT SAFETY INFORMATION (*cont'd*)

RYBREVANT® with Carboplatin and Pemetrexed
In PAPILLON (n=151), infusion-related reactions occurred in 42% of patients treated with RYBREVANT® in combination with carboplatin and pemetrexed, including Grade 3 (1.3%) adverse reactions. The incidence of infusion modifications due to IRR was 40%, and 0.7% of patients permanently discontinued RYBREVANT®.

RYBREVANT® as a Single Agent
In CHRYSALIS (n=302), IRR occurred in 66% of patients treated with RYBREVANT®. Among patients receiving treatment on Week 1 Day 1, 65% experienced an IRR, while the incidence of IRR was 3.4% with the Day 2 infusion, 0.4% with the Week 2 infusion, and cumulatively 1.1% with subsequent infusions. Of the reported IRRs, 97% were Grade 1-2, 2.2% were Grade 3, and 0.4% were Grade 4. The median time to onset was 1 hour (range 0.1 to 18 hours) after start of infusion. The incidence of infusion modifications due to IRR was 62% and 1.3% of patients permanently discontinued RYBREVANT® due to IRR.

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

Skin rash lifestyle tips

Proactive lifestyle approach to help reduce the risk of dermatologic ARs[1]

Use alcohol-free (eg, isopropanol-free, ethanol-free) emollient cream

Limit sun exposure during and for 2 months after treatment

Wear protective clothing and use broad-spectrum UVA/UVB sunscreen

Consider prophylactic measures (eg, use of oral antibiotics) to reduce the risk of dermatologic adverse reactions

Based on RYBREVANT® Prescribing Information.

IMPORTANT SAFETY INFORMATION (*cont'd*)

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.

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

Paronychia

Proactive lifestyle approach to help reduce the risk of paronychia

Paronychia, an inflammation of the nail folds of the fingernails and toenails, can lead to infection, and the consequent swelling and tenderness often affect patients' activities of daily living.[8]

Lifestyle modifications[8]

Management approaches are aimed at:

- Minimizing/avoiding trauma and decreasing inflammation in the periungual area
- Preventing superinfection
- Eliminating excessive granulation tissue

MASCC guidelines recommendations[8]

Approaches to prevent superinfection:

- Use of antimicrobial soaks
- Avoid irritants

IMPORTANT SAFETY INFORMATION (*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.

RYBREVANT® with Carboplatin and Pemetrexed

In PAPILLON, Grade 3 ILD/pneumonitis occurred in 2.6% of patients treated with RYBREVANT® in combination with carboplatin and pemetrexed, all patients required permanent discontinuation.

RYBREVANT® as a Single Agent

In CHRYSALIS, ILD/pneumonitis occurred in 3.3% of patients treated with RYBREVANT®, with 0.7% of patients experiencing Grade 3 ILD/pneumonitis. Three patients (1%) discontinued RYBREVANT® due to ILD/pneumonitis.

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

VTE

For RYBREVANT® only when combined with LAZCLUZE™

Prophylaxis is recommended to prevent VTE

Drug-related prophylaxis[1]

Prophylactic treatment with an anticoagulation medication is recommended for the first **4 months** of treatment of RYBREVANT® + LAZCLUZE™.

- 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
- The use of Vitamin K antagonists is not recommended

~97% patients in the RYBREVANT® + LAZCLUZE™ arm did not receive prophylactic anticoagulation for the first 4 months.[9]

VTE, which includes DVT and PE, is a key cause of morbidity among patients with lung cancer.[10]

People living with cancer are at **9 times the risk** of developing a VTE compared with the general population[11]

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) recommendations for cancer-associated VTE disease[12]

Anticoagulant options for VTE prophylaxis for ambulatory patients with cancer include direct oral anticoagulants (DOACs) and low molecular weight heparins (LMWHs).*†‡

*Recommendations derived from clinical trials of high thrombosis risk ambulatory cancer patients (>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.

†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.

DVT, deep vein thrombosis; NCCN, National Comprehensive Cancer Network; PE, pulmonary embolism.

IMPORTANT SAFETY INFORMATION (*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.

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

Initiating Therapy

Premedications for RYBREVANT®[1]

Prior to the initial infusion of RYBREVANT® (Week 1, Day 1 and 2), administer premedication to reduce the risk of IRRs.

Medication	Dose	Route of Administration	Dosing Window Prior to RYBREVANT® Administration	Frequency
Antihistamine	Diphenhydramine (25 to 50 mg) or equivalent	Intravenous	15 to 30 minutes	All doses
		Oral	30 to 60 minutes	
Antipyretic	Acetaminophen (650 to 1,000 mg)	Intravenous	15 to 30 minutes	All doses
		Oral	30 to 60 minutes	
Glucocorticoid	Dexamethasone (20 mg) or equivalent	Intravenous	45 to 60 minutes	Week 1, Day 1
Glucocorticoid	Dexamethasone (10 mg) or equivalent	Intravenous	45 to 60 minutes	Week 1, Day 2 (optional for subsequent doses)

Glucocorticoid administration is required for Week 1, Day 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.

Concomitant Medications[1]

When initiating treatment with RYBREVANT® in combination with LAZCLUZE™, administer anticoagulant prophylaxis to prevent VTE events for the first 4 months of treatment.

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

Consider prophylactic measures (eg, use of oral antibiotics) to reduce the risk of dermatologic adverse reactions.

Dose reductions

Recommended RYBREVANT® Dose Reductions for ARs[1]

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	
1,750 mg	1,400 mg	1,050 mg	
2,100 mg	1,750 mg	1,400 mg	

Recommended LAZCLUZE™ Dose Reductions for ARs[3]

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™

Adverse event CTCAE grades

Based on the Common Terminology Criteria for Adverse Events (CTCAE) grades v5.0[13]*

Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated	Moderate; minimal, local, or noninvasive intervention indicated; limiting age-appropriate instrumental ADL†	Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care ADL‡	Life-threatening consequences; urgent intervention indicated	Death related to AE

*CTCAE definition may differ from the Prescribing Information.
†Instrumental ADL refer to preparing meals, shopping for groceries or clothes, using the telephone, managing money, etc.
‡Self-care ADL refer to bathing, dressing and undressing, feeding self, using the toilet, taking medications, and not bedridden.

ADL, activities of daily living; AE, adverse event.

Dosage modifications & management

Recommended dosage modifications for ARs for RYBREVANT® and LAZCLUZE™[1,3]

For RYBREVANT® + LAZCLUZE™, refer to **both** the RYBREVANT® and LAZCLUZE™ recommendations. For RYBREVANT® + chemotherapy or RYBREVANT® as a single agent, refer only to the RYBREVANT® recommendations.

Adverse Reaction[1]	Severity	Dosage Modifications
VTE Events (applies to RYBREVANT® + LAZCLUZE™ combination only)	**Grades 2 or 3**	**RYBREVANT® + LAZCLUZE™** • Withhold RYBREVANT® and LAZCLUZE™ • Administer anticoagulant treatment as clinically indicated • Once anticoagulant treatment has been initiated, resume RYBREVANT® and LAZCLUZE™ at the same dose level, at the discretion of the healthcare provider
	Grade 4 or recurrent Grade 2 or 3 despite therapeutic level anticoagulation	**RYBREVANT® + LAZCLUZE™** • Withhold RYBREVANT® and LAZCLUZE™ • Administer anticoagulant treatment as clinically indicated • Once anticoagulant treatment has been initiated, resume RYBREVANT® and LAZCLUZE™ at the same dose level, at the discretion of the healthcare provider
IRR	**Grades 1 to 2**	**RYBREVANT®** • Interrupt RYBREVANT® infusion if IRR is suspected and monitor patient until reaction symptoms resolve • Resume the infusion at 50% of the infusion rate at which the reaction occurred • If there are no additional symptoms after 30 minutes, the infusion rate may be escalated • Include corticosteroid with premedications for subsequent dose
	Grade 3	**RYBREVANT®** • Interrupt RYBREVANT® infusion and administer supportive care medications. Continuously monitor patient until reaction symptoms resolve • Resume the infusion at 50% of the infusion rate at which the reaction occurred • If there are no additional symptoms after 30 minutes, the infusion rate may be escalated • Include corticosteroid with premedications for subsequent dose. For recurrent Grade 3, permanently discontinue RYBREVANT®
	Grade 4	**RYBREVANT®** • Permanently discontinue RYBREVANT®
ILD/pneumonitis	**Any Grade**	**RYBREVANT®** • Withhold RYBREVANT® if ILD/pneumonitis is suspected • Permanently discontinue RYBREVANT® if ILD/pneumonitis is confirmed **LAZCLUZE™** • Withhold LAZCLUZE™ if ILD/pneumonitis is suspected • Permanently discontinue LAZCLUZE™ if ILD/pneumonitis is confirmed
Dermatologic ARs (including dermatitis acneiform, pruritus, dry skin)	**Grade 1**	**RYBREVANT®** • Initiate supportive care management • Reassess after 2 weeks; if rash does not improve, consider dose reduction **LAZCLUZE™** • Initiate supportive care management
	Grade 2	**RYBREVANT®** • Initiate supportive care management • Reassess after 2 weeks; if rash does not improve, consider dose reduction **LAZCLUZE™** • Initiate supportive care management • If there is no improvement after 2 weeks, reduce RYBREVANT® dose and continue LAZCLUZE™ at the same dose • 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

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

Dosage modifications & management (cont'd)

Recommended dosage modifications for ARs for RYBREVANT® and LAZCLUZE™[1,3]

For RYBREVANT® + LAZCLUZE™, refer to **both** the RYBREVANT® and LAZCLUZE™ recommendations. For RYBREVANT® + chemotherapy or RYBREVANT® as a single agent, refer only to the RYBREVANT® recommendations.

Adverse Reaction	Severity	Dosage Modifications
Dermatologic ARs (including dermatitis acneiform, pruritus, dry skin)	**Grade 3**	**RYBREVANT®** • Withhold RYBREVANT® and initiate supportive care management • Upon recovery to ≤Grade 2, resume RYBREVANT® at reduced dose • If no improvement within 2 weeks, permanently discontinue treatment **LAZCLUZE™** • Withhold LAZCLUZE™ and RYBREVANT® • Initiate supportive care management • Upon recovery to ≤Grade 2, resume LAZCLUZE™ at the same dose or consider dose reduction, resume RYBREVANT® at a reduced dose • If there is no improvement within 2 weeks, permanently discontinue both LAZCLUZE™ and RYBREVANT®
	Grade 4 (including severe bullous, blistering, or exfoliating skin conditions, including TEN for RYBREVANT®)	**RYBREVANT®** • Permanently discontinue RYBREVANT® **LAZCLUZE™** • Initiate supportive care management and withhold LAZCLUZE™ until recovery ≤Grade 2 or baseline • Upon recovery to ≤Grade 2, resume LAZCLUZE™ at a reduced dose at the discretion of the healthcare provider

TEN, toxic epidermal necrolysis.

Adverse Reaction	Severity	Dosage Modifications
Other Adverse Reactions	**Grade 3**	**RYBREVANT®** • Withhold RYBREVANT® until recovery to ≤Grade 1 or baseline • Resume at the same dose if recovery occurs within 1 week • Resume at reduced dose if recovery occurs after 1 week but within 4 weeks • Permanently discontinue if recovery does not occur within 4 weeks **LAZCLUZE™** • Withhold LAZCLUZE™ and RYBREVANT® until the AR resolves to ≤Grade 1 or baseline • Resume both drugs at a reduced dose or LAZCLUZE™ alone • Consider permanently discontinuing both LAZCLUZE™ and RYBREVANT® if recovery does not occur within 4 weeks
	Grade 4	**RYBREVANT®** • Withhold RYBREVANT® until recovery to ≤Grade 1 or baseline • Resume at reduced dose if recovery occurs within 4 weeks • Permanently discontinue if recovery does not occur within 4 weeks • Permanently discontinue for recurrent Grade 4 reactions **LAZCLUZE™** • Withhold LAZCLUZE™ and RYBREVANT® until the AR resolves to ≤Grade 1 or baseline • Resume both drugs at a reduced dose or LAZCLUZE™ alone • Consider permanently discontinuing both LAZCLUZE™ and RYBREVANT® if recovery does not occur within 4 weeks

Recommended Dosage Modifications for ARs for RYBREVANT® in Combination With LAZCLUZE™[1]
When administering RYBREVANT® in combination with LAZCLUZE™, if there is an AR requiring dose reduction after withholding treatment and resolution, reduce the dose of RYBREVANT® first.

Recommended Dosage Modifications for ARs for RYBREVANT® in Combination With Carboplatin and Pemetrexed[1]
When administering RYBREVANT® in combination with carboplatin and pemetrexed, modify the dosage of one or more drugs. Withhold or discontinue RYBREVANT® based on the table above. Refer to Prescribing Information for carboplatin and pemetrexed for additional dosage modification information.

INDICATIONS

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.
- in combination with carboplatin and pemetrexed for the first-line treatment of adult patients with 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 adult patients with 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.

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.

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™.

RYBREVANT® with Carboplatin and Pemetrexed
In PAPILLON (n=151), infusion-related reactions occurred in 42% of patients treated with RYBREVANT® in combination with carboplatin and pemetrexed, including Grade 3 (1.3%) adverse reactions. The incidence of infusion modifications due to IRR was 40%, and 0.7% of patients permanently discontinued RYBREVANT®.

RYBREVANT® as a Single Agent
In CHRYSALIS (n=302), IRR occurred in 66% of patients treated with RYBREVANT®. Among patients receiving treatment on Week 1 Day 1, 65% experienced an IRR, while the incidence of IRR was 3.4% with the Day 2 infusion, 0.4% with the Week 2 infusion, and cumulatively 1.1% with subsequent infusions. Of the reported IRRs, 97% were Grade 1-2, 2.2% were Grade 3, and 0.4% were Grade 4. The median time to onset was 1 hour (range 0.1 to 18 hours) after start of infusion. The incidence of infusion modifications due to IRR was 62% and 1.3% of patients permanently discontinued RYBREVANT® due to IRR.

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.

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.

RYBREVANT® with Carboplatin and Pemetrexed
In PAPILLON, Grade 3 ILD/pneumonitis occurred in 2.6% of patients treated with RYBREVANT® in combination with carboplatin and pemetrexed, all patients required permanent discontinuation.

RYBREVANT® as a Single Agent
In CHRYSALIS, ILD/pneumonitis occurred in 3.3% of patients treated with RYBREVANT®, with 0.7% of patients experiencing Grade 3 ILD/pneumonitis. Three patients (1%) discontinued RYBREVANT® 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. 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).

IMPORTANT SAFETY INFORMATION *(cont'd)*

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™.

RYBREVANT® with Carboplatin and Pemetrexed
In PAPILLON, rash occurred in 89% of patients treated with RYBREVANT® in combination with carboplatin and pemetrexed, including Grade 3 (19%) adverse reactions. Rash leading to dose reductions occurred in 19% of patients, and 2% permanently discontinued RYBREVANT® and 1.3% discontinued pemetrexed.

RYBREVANT® as a Single Agent
In CHRYSALIS, rash occurred in 74% of patients treated with RYBREVANT® as a single agent, including Grade 3 rash in 3.3% of patients. The median time to onset of rash was 14 days (range: 1 to 276 days). Rash leading to dose reduction occurred in 5% of patients, and RYBREVANT® was permanently discontinued due to rash in 0.7% of patients.

Toxic epidermal necrolysis occurred in one patient (0.3%) treated with RYBREVANT® as a single agent.

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.

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.

RYBREVANT® with Carboplatin and Pemetrexed
In PAPILLON, ocular toxicity including blepharitis, dry eye, conjunctival redness, blurred vision, and eye pruritus occurred in 9%. All events were Grade 1-2.

RYBREVANT® as a Single Agent
In CHRYSALIS, keratitis occurred in 0.7% and uveitis occurred in 0.3% of patients treated with RYBREVANT®. All events were Grade 1-2.

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.

IMPORTANT SAFETY INFORMATION *(cont'd)*

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).

RYBREVANT® with Carboplatin and Pemetrexed

For the 151 patients in the PAPILLON clinical trial who received RYBREVANT® in combination with carboplatin and pemetrexed, the most common adverse reactions (≥20%) were rash (90%), nail toxicity (62%), stomatitis (43%), infusion-related reaction (42%), fatigue (42%), edema (40%), constipation (40%), decreased appetite (36%), nausea (36%), COVID-19 (24%), diarrhea (21%), and vomiting (21%). The most common Grade 3 to 4 laboratory abnormalities (≥2%) were decreased albumin (7%), increased alanine aminotransferase (4%), increased gamma-glutamyl transferase (4%), decreased sodium (7%), decreased potassium (11%), decreased magnesium (2%), and decreases in white blood cells (17%), hemoglobin (11%), neutrophils (36%), platelets (10%), and lymphocytes (11%).

Serious adverse reactions occurred in 37% of patients who received RYBREVANT® in combination with carboplatin and pemetrexed. Serious adverse reactions in ≥2% of patients included rash, pneumonia, ILD, pulmonary embolism, vomiting, and COVID-19. Fatal adverse reactions occurred in 7 patients (4,6%) due to pneumonia, cerebrovascular accident, cardio-respiratory arrest, COVID-19, sepsis, and death not otherwise specified.

RYBREVANT® as a Single Agent

For the 129 patients in the CHRYSALIS clinical trial who received RYBREVANT® as a single agent, the most common adverse reactions (≥20%) were rash (84%), IRR (64%), paronychia (50%), musculoskeletal pain (47%), dyspnea (37%), nausea (36%), fatigue (33%), edema (27%), stomatitis (26%), cough (25%), constipation (23%), and vomiting (22%). The most common Grade 3 to 4 laboratory abnormalities (≥2%) were decreased lymphocytes (8%), decreased albumin (8%), decreased phosphate (8%), decreased potassium (6%), increased alkaline phosphatase (4.8%), increased glucose (4%), increased gamma-glutamyl transferase (4%), and decreased sodium (4%).

Serious adverse reactions occurred in 30% of patients who received RYBREVANT®. Serious adverse reactions in ≥2% of patients included pulmonary embolism, pneumonitis/ILD, dyspnea, musculoskeletal pain, pneumonia, and muscular weakness. Fatal adverse reactions occurred in 2 patients (1.5%) due to pneumonia and 1 patient (0.8%) due to sudden death.

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

cp-213274v5

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

Help your patients get the most out of their treatment from the start

Prepare for, identify, and proactively manage RYBREVANT® adverse reactions

For additional support, reach out to an Oncology Clinical Educator (OCE). OCEs are oncology nurses who are employed by Johnson & Johnson and can educate Patient Care Teams (PCTs) on product-specific and disease state information to share with their team and patients.

Reach out to Oncology Clinical Educators by visiting www.RYBREVANThcp.com.

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