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

+

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

Dosing and Administration Guide

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 treatment of adult patients with locally advanced or metastatic NSCLC with EGFR exon 19 deletions or exon 21 L858R substitution mutations, whose disease has progressed on or after treatment with an EGFR tyrosine kinase inhibitor.
- 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.

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

Table of Contents

How RYBREVANT® Works

RYBREVANT® is a bispecific antibody that binds to the extracellular domains of EGFR and MET.[1]

In *in vitro* and *in vivo* studies, RYBREVANT® was able to disrupt EGFR and MET signaling functions in mutation models of exon 19 deletions, exon 21 L858R substitutions, and exon 20 insertions through blocking ligand binding or degradation of EGFR and MET.[1]

The presence of EGFR and MET on the surface of tumor cells also allows for targeting of these cells for destruction by immune effector cells, such as natural killer cells and macrophages, through antibody-dependent cellular cytotoxicity and trogocytosis mechanisms, respectively.[1]

RYBREVANT® is the first and only approved EGFR-MET bispecific antibody with immune cell–directing activity.[1,2]

LAZCLUZE™ is a third-generation TKI that is a suitable combination partner for RYBREVANT® because of high selectivity for mutant EGFR, low selectivity for wild-type EGFR, and because it is CNS–penetrant.[3,4]

CNS, central nervous system; EGFR, epidermal growth factor receptor; MET, mesenchymal-epithelial transition; TKI, tyrosine kinase inhibitors.

RYBREVANT® + LAZCLUZE™ is a chemotherapy-sparing combination that provides complementary extra and intracellular antitumor activity and CNS penetration.[1,3-5]

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

RYBREVANT® Preparation[1]

Dilute and prepare RYBREVANT® for intravenous infusion before administration.

- **Check that the RYBREVANT® solution is colorless to pale yellow**. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. Do not use if discoloration or visible particles are present
- **Determine the dose and number of vials of RYBREVANT® needed** based on patient's baseline weight. Each vial of RYBREVANT® contains 350 mg of amivantamab-vmjw
- **Withdraw and then discard a volume of** either 5% dextrose injection or 0.9% sodium chloride injection from the 250 mL infusion bag equal to the volume of RYBREVANT® to be added (ie, discard 7 mL diluent from the infusion bag for each RYBREVANT® vial)
    - **Only use infusion bags made of** PVC, PP, PE, or PP+PE
- **Withdraw 7 mL of RYBREVANT®** from each vial and add it to the infusion bag. The final volume in the infusion bag should be 250 mL
    - **Discard** any unused portion left in the vial
- **Gently invert the bag to mix the solution**. Do not shake
- **Diluted solutions should be administered within 10 hours** (including infusion time) at room temperature 59°F to 77°F (15°C to 25°C)

PE, polyethylene; PP, polypropylene; PP+PE, polyolefin blend; PVC, polyvinylchloride.

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

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

RYBREVANT® + LAZCLUZE™ Dosage and Administration[1]

The recommended dosage of RYBREVANT® in combination with LAZCLUZE™ is based on baseline body weight and administered as an intravenous infusion after dilution.

Administer via a peripheral line on Week 1 and Week 2 to reduce the risk of IRRs during initial treatment.

RYBREVANT® may be administered via a central line for subsequent weeks.

Refer to the full LAZCLUZE™ Prescribing Information for recommended LAZCLUZE™ dosing information.

Drug-to-drug interactions with LAZCLUZE™

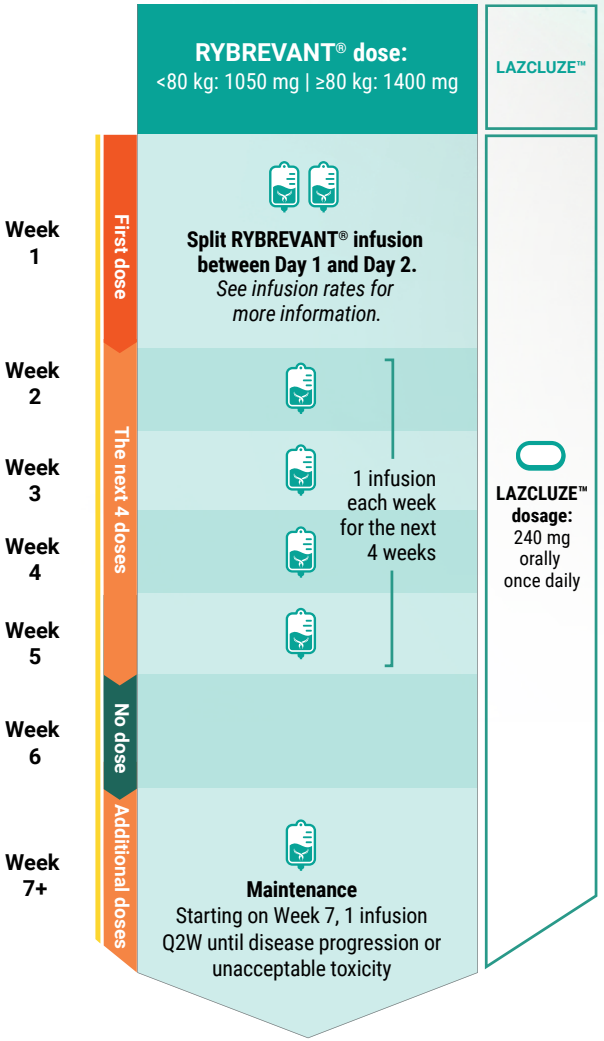
Avoid concomitant use of LAZCLUZE™ with strong and moderate CYP3A4 inducers. Consider an alternate concomitant medication with no potential to induce CYP3A4.[3]

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.[3]

Administer RYBREVANT® + LAZCLUZE™ until disease progression or unacceptable toxicity when used in combination.[1,3]

BCRP, breast cancer resistance protein; CYP3A4, cytochrome P450 3A4; IRRs, infusion-related reactions; Q2W, once every 2 weeks.

Recommended dosing schedule for RYBREVANT® + LAZCLUZE™[1,3]



RYBREVANT® + LAZCLUZE™ Administration

Administration for RYBREVANT®[1]

- Administer the diluted RYBREVANT® solution by intravenous infusion using an infusion set fitted with a flow regulator and with an in-line, sterile, non-pyrogenic, low protein-binding PES filter (pore size 0.2 micrometer)
- Administration sets must be made of PU, PBD, PVC, PP, or PE
- The administration set with filter **must** be primed with either 5% dextrose injection or 0.9% sodium chloride injection prior to the initiation of each RYBREVANT® infusion
- Do not infuse RYBREVANT® concomitantly in the same intravenous line with other agents

RYBREVANT® + LAZCLUZE™[1]

- Administer RYBREVANT® as a single agent infusion every 2 weeks intravenously until disease progression or unacceptable toxicity according to the infusion rates
- Administer RYBREVANT® via a peripheral line on Week 1 and Week 2 to reduce the risk of IRRs during initial treatment
- RYBREVANT® may be administered via a central line for subsequent weeks
- For the initial infusion, prepare RYBREVANT® as close to administration time as possible to allow for the possibility of extended infusion time in the event of an IRR

LAZCLUZE™ when given in combination with RYBREVANT®[3]

- Administer LAZCLUZE™ 240 mg orally, once daily
- Swallow LAZCLUZE™ tablets whole (with or without food). Do not crush, split, or chew. Continue treatment until disease progression or unacceptable toxicity
- If vomiting occurs any time after taking LAZCLUZE™, instruct the patient to take the next dose at its next regularly scheduled time
- If a patient misses a dose of LAZCLUZE™ within 12 hours, instruct the patient to take the missed dose. If more than 12 hours have passed since the dose was to be given, instruct the patient to take the next dose at its scheduled time

- **It is recommended to administer LAZCLUZE™ any time prior to RYBREVANT® when given on the same day**

PBD, polybutadiene; PES, polyethersulfone; PU, polyurethane.

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

Infusion rates for RYBREVANT® + LAZCLUZE™[1]

Body Weight Less Than 80 kg

Week	Dose (per 250 mL bag)	Initial infusion rate	Subsequent infusion rate*
Week 1 (split dose infusion)			
Week 1, Day 1	350 mg	50 mL/h	75 mL/h
Week 1, Day 2	700 mg	50 mL/h	75 mL/h
Week 2	1050 mg	85 mL/h	
Week 3	1050 mg	125 mL/h	
Week 4	1050 mg	125 mL/h	
Week 5	1050 mg	125 mL/h	
Week 6	No dose		
Week 7, and every 2 weeks thereafter	1050 mg	125 mL/h	

Body Weight Greater Than or Equal to 80 kg

Week	Dose (per 250 mL bag)	Initial infusion rate	Subsequent infusion rate*
Week 1 (split dose infusion)			
Week 1, Day 1	350 mg	50 mL/h	75 mL/h
Week 1, Day 2	1050 mg	35 mL/h	50 mL/h
Week 2	1400 mg	65 mL/h	
Week 3	1400 mg	85 mL/h	
Week 4	1400 mg	125 mL/h	
Week 5	1400 mg	125 mL/h	
Week 6	No dose		
Week 7, and every 2 weeks thereafter	1400 mg	125 mL/h	

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

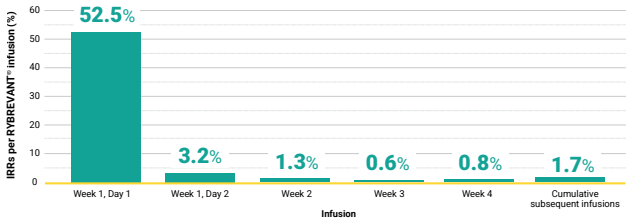
See Managing/Preventing ARs Across Indications section for more information.

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

RYBREVANT® + LAZCLUZE™ Administration (cont'd)

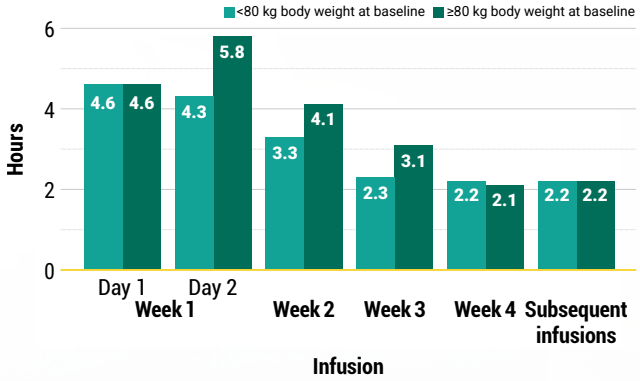
IRR Rates

In the MARIPOSA trial, most IRRs occurred during the first infusion (Week 1, Day 1) and rarely during subsequent infusions.[6]



In the MARIPOSA trial, infusion times decreased over time with RYBREVANT®[6]

Clinical trial median infusion times by hours*



Total infusion time is approximately 4 to 6 hours for Day 1 and 6 to 8 hours for Day 2. Subsequent infusion time is approximately 2 hours.[1]

*Data reflect results from 2-week dosing in the MARIPOSA study.

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

RYBREVANT®
(amivantamab-vmjw) +
Chemotherapy

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

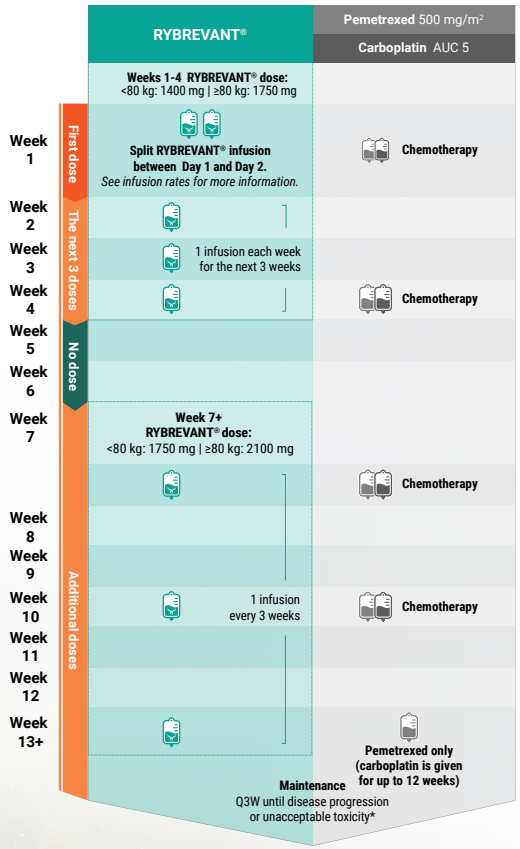
RYBREVANT® + Chemotherapy Recommended Dosage[1]

RYBREVANT® in combination with carboplatin and pemetrexed (chemotherapy)

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

Refer to the full Prescribing Information for pemetrexed and carboplatin for the respective dosing information.

Recommended Dosing Schedule for RYBREVANT® in combination with chemotherapy



*This refers only to RYBREVANT® and pemetrexed. Carboplatin should only be administered every 3 weeks for up to 12 weeks.
AUC, area under the curve; Q3W, once every 3 weeks.

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

RYBREVANT® + Chemotherapy Administration[1]

Administration for RYBREVANT®

- Administer the diluted RYBREVANT® solution by intravenous infusion using an infusion set fitted with a flow regulator and with an in-line, sterile, non-pyrogenic, low protein-binding PES filter (pore size 0.2 micrometer)
- Administration sets must be made of PU, PBD, PVC, PP, or PE
- The administration set with filter **must** be primed with either 5% dextrose injection or 0.9% sodium chloride injection prior to the initiation of each RYBREVANT® infusion
- Do not infuse RYBREVANT® concomitantly in the same intravenous line with other agents

RYBREVANT® in combination with carboplatin and pemetrexed[1]

- Administer RYBREVANT® in combination with carboplatin and pemetrexed infusions every 3 weeks intravenously until disease progression or unacceptable toxicity according to the infusion rates
- Administer RYBREVANT® via a peripheral line on Week 1 and Week 2 to reduce the risk of IRRs during initial treatment
- RYBREVANT® may be administered via a central line for subsequent weeks
- For the initial infusion, prepare RYBREVANT® as close to administration time as possible to allow for the possibility of extended infusion time in the event of an IRR
- Administer the pemetrexed infusion first, the carboplatin infusion second, and the RYBREVANT® infusion last

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

RYBREVANT® + Chemotherapy Administration (cont'd)[1]

Infusion rates for RYBREVANT® in combination with carboplatin and pemetrexed[1]

Body Weight Less Than 80 kg

Week	Dose (per 250 mL bag)	Initial infusion rate	Subsequent infusion rate*
Week 1 (split dose infusion)			
Week 1, Day 1	350 mg	50 mL/h	75 mL/h
Week 1, Day 2	1050 mg	33 mL/h	50 mL/h
Week 2	1400 mg	65 mL/h	
Week 3	1400 mg	85 mL/h	
Week 4	1400 mg	125 mL/h	
Weeks 5 and 6	No dose		
Week 7, and every 3 weeks thereafter	1750 mg	125 mL/h	

Body Weight Greater Than or Equal to 80 kg

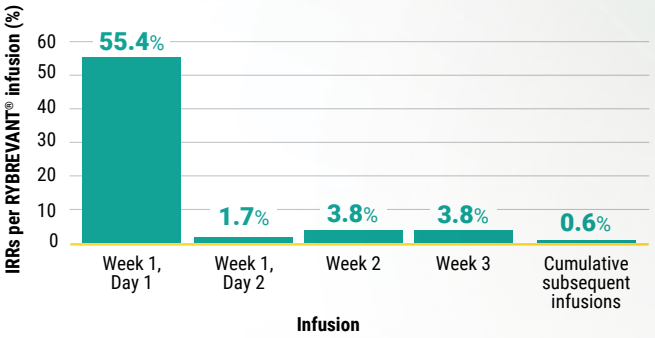
Week	Dose (per 250 mL bag)	Initial infusion rate	Subsequent infusion rate*
Week 1 (split dose infusion)			
Week 1, Day 1	350 mg	50 mL/h	75 mL/h
Week 1, Day 2	1400 mg	25 mL/h	50 mL/h
Week 2	1750 mg	65 mL/h	
Week 3	1750 mg	85 mL/h	
Week 4	1750 mg	125 mL/h	
Weeks 5 and 6	No dose		
Week 7, and every 3 weeks thereafter	2100 mg	125 mL/h	

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

See Managing/Preventing ARs Across Indications section for more information.

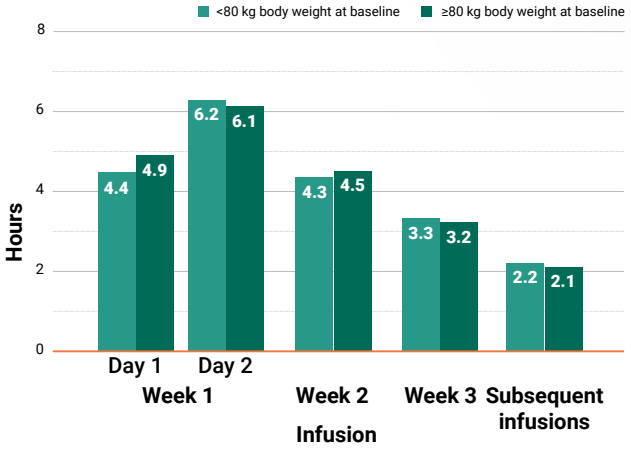
IRR Rates

In the MARIPOSA-2 trial, most IRRs occurred during the first infusion (Week 1, Day 1) and rarely during subsequent infusions[6]



In the MARIPOSA-2 trial, infusion times decreased over time with RYBREVANT®[6]

Clinical trial median infusion times by hours†



Total infusion time is approximately 4 to 6 hours for Day 1 and 6 to 8 hours for Day 2. Subsequent infusion time is approximately 2 hours.[1]

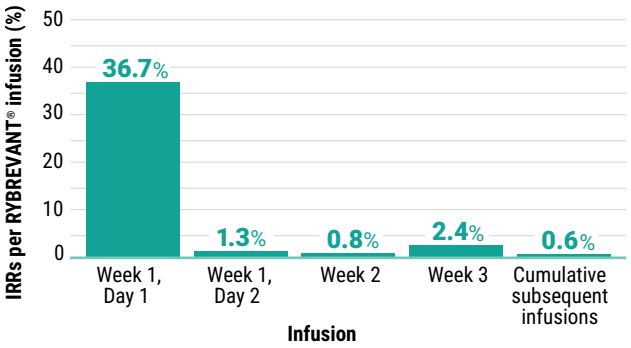
†Data reflect results from 3-week dosing in the MARIPOSA-2 study.

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

RYBREVANT® + Chemotherapy Administration (cont'd)

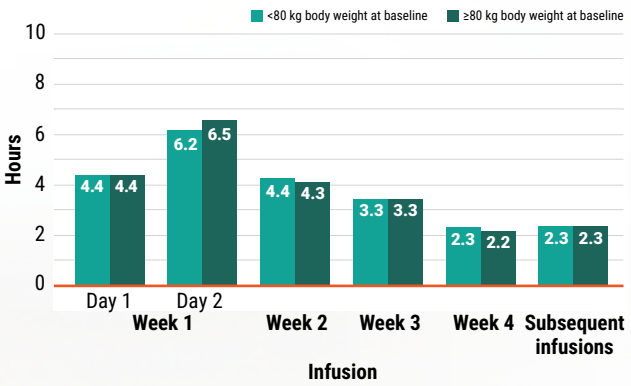
IRR Rates

In the PAPILLON trial, most IRRs occurred during the first infusion (Week 1, Day 1) and rarely during subsequent infusions.[6]



In the PAPILLON trial, infusion times decreased over time with RYBREVANT®[6]

Clinical trial median infusion times by hours*



Total infusion time is approximately 4 to 6 hours for Day 1 and 6 to 8 hours for Day 2. Day 2 chair time is longer because of increased dose from Day 1. Subsequent infusion time is approximately 2 hours.[1]

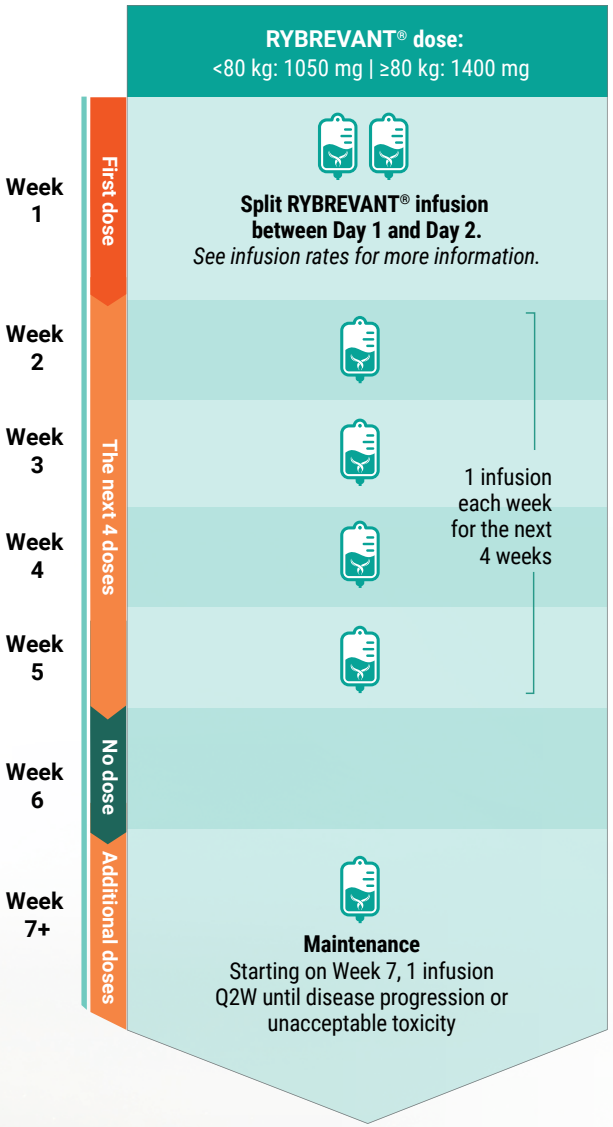
*Data reflect results from 3-week dosing in the PAPILLON study.

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

RYBREVANT® (amivantamab-vmjw) as a Single Agent

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

Recommended Dosing Schedule for RYBREVANT® as a Single Agent[1]



Administration for RYBREVANT® as a Single Agent[1]

- Administer the diluted RYBREVANT® solution by intravenous infusion using an infusion set fitted with a flow regulator and with an in-line, sterile, non-pyrogenic, low protein-binding PES filter (pore size 0.2 micrometer)
- Administration sets must be made of PU, PBD, PVC, PP, or PE
- The administration set with filter **must** be primed with either 5% dextrose injection or 0.9% sodium chloride injection prior to the initiation of each RYBREVANT® infusion
- Do not infuse RYBREVANT® concomitantly in the same intravenous line with other agents
- Administer RYBREVANT® as a single agent infusion every 2 weeks intravenously until disease progression or unacceptable toxicity according to the **infusion rates**
- Administer RYBREVANT® via a peripheral line on Week 1 and Week 2 to reduce the risk of IRRs during initial treatment
- RYBREVANT® may be administered via a central line for subsequent weeks
- For the initial infusion, prepare RYBREVANT® as close to administration time as possible to allow for the possibility of extended infusion time in the event of an IRR

Infusion rates for RYBREVANT® as a single agent[1]

Body Weight Less Than 80 kg			
Week	**Dose (per 250 mL bag)**	**Initial infusion rate**	**Subsequent infusion rate***
Week 1 (split dose infusion)			
Week 1, Day 1	350 mg	50 mL/h	75 mL/h
Week 1, Day 2	700 mg	50 mL/h	75 mL/h
Week 2	1050 mg	85 mL/h	
Week 3	1050 mg	125 mL/h	
Week 4	1050 mg	125 mL/h	
Week 5	1050 mg	125 mL/h	
Week 6	No dose		
Week 7, and every 2 weeks thereafter	1050 mg	125 mL/h	

Body Weight Greater Than or Equal to 80 kg			
Week	**Dose (per 250 mL bag)**	**Initial infusion rate**	**Subsequent infusion rate***
Week 1 (split dose infusion)			
Week 1, Day 1	350 mg	50 mL/h	75 mL/h
Week 1, Day 2	1050 mg	35 mL/h	50 mL/h
Week 2	1400 mg	65 mL/h	
Week 3	1400 mg	85 mL/h	
Week 4	1400 mg	125 mL/h	
Week 5	1400 mg	125 mL/h	
Week 6	No dose		
Week 7, and every 2 weeks thereafter	1400 mg	125 mL/h	

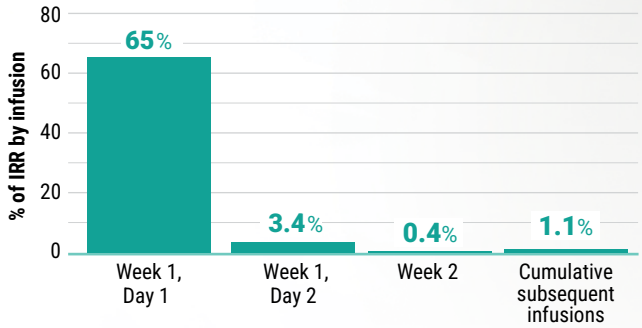
*In the absence of IRRs, increase the initial infusion rate to the subsequent infusion rate after 2 hours based on patient tolerance. Total infusion time is approximately 4 to 6 hours for Day 1 and 6 to 8 hours for Day 2. Subsequent infusion time is approximately 2 hours.

See Managing/Preventing ARs Across Indications section for more information.

Administration for RYBREVANT® as a single agent (cont'd)

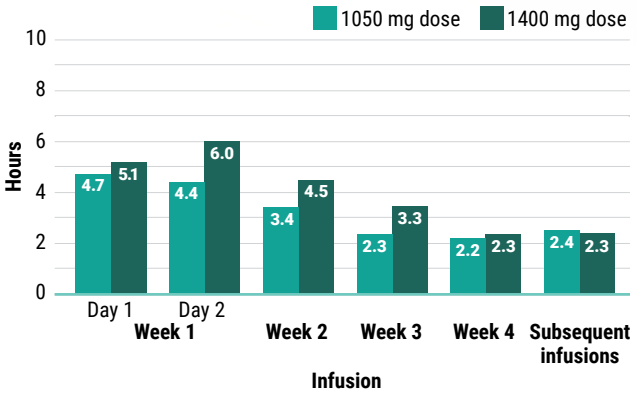
IRR rates[1]

In the CHRYSALIS trial, most IRRs occurred during the first infusion (Week 1, Day 1) and rarely during subsequent infusions.[6]



In the CHRYSALIS trial, infusion times decreased over time with RYBREVANT®[6]

Clinical trial median infusion times by hours*



Total infusion time is approximately 4 to 6 hours for Day 1 and 6 to 8 hours for Day 2. Day 2 chair time is longer because of increased dose from Day 1. Subsequent infusion time is approximately 2 hours.[1]

*Data reflect results from 2-week dosing in the CHRYSALIS study.

Initiating therapy[1]

Premedications for RYBREVANT®

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 1000 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)

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

Glucocorticoid administration is required for Week 1, Day 1 and 2 dose only and upon reinitiation 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

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.

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 ARs.

AR, adverse reaction; VTE, venous thromboembolism.

Infusion-Related Reactions[1]

RYBREVANT® can cause IRRs; 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® + LAZCLUZE™

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 IRR was 54%, and 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™.

RYBREVANT® + chemotherapy

Based on the pooled safety population, IRR occurred in 50% of patients treated with RYBREVANT® in combination with carboplatin and pemetrexed, including Grade 3 (3.2%) adverse reactions. The incidence of infusion modifications due to IRR was 46%, and 2.8% of patients permanently discontinued RYBREVANT® due to IRR.*

RYBREVANT® as a single agent

In CHRYSALIS, IRRs occurred in 66% of patients treated with RYBREVANT® as a single agent. 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 to 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 the 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 on page 12. 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.

*The pooled safety population described in Warnings and Precautions reflects exposure to RYBREVANT® in combination with carboplatin and pemetrexed in 281 patients in both the MARIPOSA-2 (n=130) and the PAPILLON (n=151) studies.

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

Monitoring & Management

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**
1050 mg	700 mg	300 mg	Discontinue RYBREVANT®
1400 mg	1050 mg	700 mg	
1750 mg	1400 mg	1050 mg	
2100 mg	1750 mg	1400 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™

Please refer to the LAZCLUZE™ Prescribing Information for dose modifications for specific adverse reactions.

Adverse Events Severity Scale[7]

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

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 adverse event

*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; AR, adverse reaction.

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

Monitoring & Management (cont'd)[1,3]

Recommended dosage modifications for ARs for RYBREVANT® + LAZCLUZE™

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

Adverse Reaction	Severity	Dose 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 LAZCLUZE™ and permanently discontinue RYBREVANT® • Administer anticoagulant treatment as clinically indicated • Once anticoagulant treatment has been initiated, treatment can continue with 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

ILD, interstitial lung disease; VTE, venous thromboembolism.

Monitoring & Management (cont'd)[1,3]

Adverse Reaction	Severity	Dosage Modifications
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
	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

Recommended dosage modifications for ARs for RYBREVANT® in combination with LAZCLUZE™

When administering RYBREVANT® in combination with LAZCLUZE™, if there is an AR requiring dose reduction after withholding treatment and resolution, then reduce the dose of RYBREVANT® first.

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 adverse reaction 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 adverse reaction 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 carboplatin and pemetrexed

When administering RYBREVANT® in combination with carboplatin and pemetrexed, modify the dosage of one or more drugs. Withhold or discontinue RYBREVANT® as shown in the table above. Refer to Prescribing Information for carboplatin and pemetrexed for additional dosage modification information.

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

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

Proactive Supportive Care Is Recommended

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

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

Skin Rash MASCC Guidelines[8]

- MASCC Guidelines recommend proactive measures (Weeks 1 to 6) and ongoing monitoring to reduce the risk of severe reactions:
  - Hydrocortisone 1% cream with moisturizer and sunscreen twice daily
  - Minocycline 100 mg daily OR doxycycline 100 mg twice daily

Paronychia MASCC Guidelines[8]

- Approaches to prevent superinfection:
  - Use of antimicrobial soaks
  - Avoid irritants

For RYBREVANT® only when combined with LAZCLUZE™, prophylaxis is recommended to prevent VTE

Consider prophylactic measures (eg, use of oral antibiotics) to reduce the risk of dermatologic adverse reactions[1]

MASCC, Multinational Association of Supportive Care in Cancer.

- Prophylactic treatment with an anticoagulation medicine is recommended for the first **4 months** of treatment with RYBREVANT® + LAZCLUZE™[1]
  - 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
  - Use of Vitamin K antagonist is not recommended

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) recommendations for cancer-associated VTE disease[9]

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

Learn more about Proactive Support Care measures at www.RYBREVANThcp.com.

*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.
†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.

NCCN, National Comprehensive Cancer Network.

How Is RYBREVANT® Supplied?[1]

RYBREVANT® injection is a sterile, preservative-free, colorless to pale yellow solution for intravenous infusion.

- Each single-dose vial contains 350 mg/7 mL (50 mg/mL) of RYBREVANT®
- Each vial is individually packed in a single carton (NDC 57894-501-01)

Storage and handling

Store vials in a refrigerator at 36°F to 46°F (2°C to 8°C) in the original carton to protect from light. Do not freeze.

Patient Counseling Information[1,3]

Advise the patient to read the FDA-approved patient labeling (Patient Information).

IRRs	Advise patients that RYBREVANT® can cause IRRs, the majority of which may occur with the first infusion. Advise patients to alert their healthcare provider immediately for any signs or symptoms of IRRs.
ILD/ pneumonitis	Advise patients of the risks of ILD/pneumonitis. Advise patients to immediately contact their healthcare provider for new or worsening respiratory symptoms.
VTE	When RYBREVANT® is used in combination with LAZCLUZE™, advise patients of the risks of VTEs, including DVT and pulmonary embolism. Advise patients that prophylactic anticoagulants are recommended to be used for the first 4 months of treatment. Advise patients to immediately contact their healthcare provider for signs and symptoms of VTE.
Dermatologic adverse reactions	Advise patients to apply alcohol-free (eg, isopropanol-free, ethanol-free) emollient cream to reduce the risk of skin reactions. Consider prophylactic measures (eg, use of oral antibiotics) to reduce the risk of dermatologic adverse reactions. Advise patients to limit direct sun exposure during and for 2 months after treatment, to use broad-spectrum UVA/UVB sunscreen, and to wear protective clothing during treatment with RYBREVANT®.
Ocular toxicity	Advise patients of the risk of ocular toxicity. Advise patients to contact their ophthalmologist if they develop eye symptoms and advise discontinuation of contact lenses until symptoms are evaluated.
Paronychia/ nail toxicity	Advise patients of the risk of paronychia. Advise patients to contact their healthcare provider for signs and symptoms of paronychia.
Embryo-fetal toxicity	Advise patients of reproductive potential of the potential risk to a fetus, to inform their healthcare provider of a known or suspected pregnancy and to use effective contraception: • During treatment with RYBREVANT® and for 3 months after the last dose • During treatment with LAZCLUZE™ and for 3 weeks after the last dose Advise male patients with partners of reproductive potential to use effective contraception during treatment with LAZCLUZE™ and for 3 weeks after the last dose.
Lactation	Advise women not to breastfeed: • During treatment with RYBREVANT® and for 3 months after the last dose • During treatment with LAZCLUZE™ and for 3 weeks after the last dose
Infertility	Advise males and females of reproductive potential of the potential risk for impaired fertility with LAZCLUZE™

DVT, deep vein thrombosis; UVA, ultraviolet A; UVB, ultraviolet B.

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

INDICATIONS AND IMPORTANT SAFETY 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 treatment of adult patients with locally advanced or metastatic NSCLC with EGFR exon 19 deletions or exon 21 L858R substitution mutations, whose disease has progressed on or after treatment with an EGFR tyrosine kinase inhibitor.
- 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

Based on the pooled safety population (n=281), IRR occurred in 50% of patients treated with RYBREVANT® in combination with carboplatin and pemetrexed, including Grade 3 (3.2%) adverse reactions. The incidence of infusion modifications due to IRR was 46%, and 2.8% of patients permanently discontinued RYBREVANT® due to IRR.

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.

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

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

INDICATIONS AND IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

RYBREVANT® with Carboplatin and Pemetrexed

Based on the pooled safety population, ILD/pneumonitis occurred in 2.1% treated with RYBREVANT® in combination with carboplatin and pemetrexed with 1.8% of patients experiencing Grade 3 ILD/pneumonitis. 2.1% discontinued RYBREVANT® due to ILD/pneumonitis.

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%) permanently 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 (VTE) 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).

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

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

Based on the pooled safety population, rash occurred in 82% of patients treated with RYBREVANT® in combination with carboplatin and pemetrexed, including Grade 3 (15%) adverse reactions. Rash leading to dose reductions occurred in 14% of patients, and 2.5% permanently discontinued RYBREVANT® and 3.1% 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.

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

INDICATIONS AND IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

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, reduce the dose, 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

Based on the pooled safety population, ocular toxicity occurred in 16% of patients treated with RYBREVANT® in combination with carboplatin and pemetrexed. All events were Grade 1 or 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, 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

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

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

INDICATIONS AND IMPORTANT SAFETY INFORMATION (cont'd)

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 130 patients in the MARIPOSA-2 clinical trial who received RYBREVANT® in combination with carboplatin and pemetrexed, the most common adverse reactions (≥20%) were rash (72%), infusion-related reactions (59%), fatigue (51%), nail toxicity (45%), nausea (45%), constipation (39%), edema (36%), stomatitis (35%), decreased appetite (31%), musculoskeletal pain (30%), vomiting (25%), and COVID-19 (21%). The most common Grade 3 to 4 laboratory abnormalities (≥2%) were decreased neutrophils (49%), decreased white blood cells (42%), decreased lymphocytes (28%), decreased platelets (17%), decreased hemoglobin (12%), decreased potassium (11%), decreased sodium (11%), increased alanine aminotransferase (3.9%), decreased albumin (3.8%), and increased gamma-glutamyl transferase (3.1%).

In MARIPOSA-2, serious adverse reactions occurred in 32% of patients who received RYBREVANT® in combination with carboplatin and pemetrexed. Serious adverse reactions in >2% of patients included dyspnea (3.1%), thrombocytopenia (3.1%), sepsis (2.3%), and pulmonary embolism (2.3%). Fatal adverse reactions occurred in 2.3% of patients who received RYBREVANT® in combination with carboplatin and pemetrexed; these included respiratory failure, sepsis, and ventricular fibrillation (0.8% each).

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%).

In PAPILLON, 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 read full Prescribing Information for RYBREVANT®.

Please read full Prescribing Information for LAZCLUZE™.

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

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

References: 1. RYBREVANT® [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc. **2.** RYBREVANT® (amivantamab-vmjw) plus LAZCLUZE™ (lazertinib) approved in the U.S. as a first-line chemotherapy-free treatment for patients with EGFR-mutated advanced lung cancer. Press release. Johnson & Johnson. August 20, 2024. Accessed August 20, 2024. https://www.prnewswire.com/news-releases/rybrevant-amivantamab-vmjw-plus-lazcluze-lazertinib-approved-in-the-us-as-a-firstline-chemotherapy-free-treatment-for-patients-with-egfr-mutated-advanced-lung-cancer-302226047.html **3.** LAZCLUZE™ [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc. **4.** Yun J, Hong MH, Kim SY, et al. YH25448, an irreversible EGFR-TKI with potent intracranial activity in EGFR mutant non–small cell lung cancer. *Clin Cancer Res*. 2019;25(8):2575-2587. **5.** Cho BC, Simi A, Sabari J, et al. Amivantamab, an epidermal growth factor receptor (EGFR) and mesenchymal-epithelial transition factor (MET) bispecific antibody, designed to enable multiple mechanisms of action and broad clinical applications. *Clin Lung Cancer.* 2023;24(2):89-97. **6.** Data on file. Janssen Biotech, Inc. **7.** US Department of Health and Human Services. National Cancer Institute. Common terminology criteria for adverse events (CTCAE). Version 5.0. Published November 27, 2017. Accessed June 7, 2024. https://ctep.cancer.gov/protocoldevelopment/electronic_applications/docs/CTCAE_v5_Quick_Reference_5x7.pdf **8.** Lacouture ME, Anadkat MJ, Bensadoun RJ, et al; MASCC Skin Toxicity Study Group. Clinical practice guidelines for the prevention and treatment of EGFR inhibitor-associated dermatologic toxicities. *Support Care Cancer.* 2011;19(8):1079-1095. **9.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Cancer-Associated Venous Thromboembolic Disease V2.2024. © National Comprehensive Cancer Network, Inc. 2024. All rights reserved. Accessed July 29, 2024. 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.

Infusion Checklist

Pre-infusion[1]

- ☐ Prior to initial infusion of RYBREVANT® (Week 1, Days 1 and 2), administer premedication as described in the table on page 12 to reduce the risk of IRRs
- ☐ Administer both antihistamine and antipyretic prior to all infusions
- ☐ Glucocorticoid administration is required for Week 1, Day 1 and 2 dose only and as necessary for subsequent infusions
- ☐ Do not infuse RYBREVANT® concomitantly in the same intravenous line with other agents
- ☐ Administer RYBREVANT® via a peripheral line on Week 1 and Week 2 to reduce the risk of IRRs during initial treatment. RYBREVANT® may be administered via a central line for subsequent weeks

During the infusion[1]

- ☐ 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
- ☐ Administer RYBREVANT® infusion intravenously according to the infusion rates in the charts within the section for the correct regimen

Reach out to an Oncology Clinical Educator (OCE)

OCEs are oncology nurses employed by Johnson & Johnson to provide product-specific and disease state education information to oncology patient-care team members, patient support groups, and advocacy organizations.

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