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

+

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

Administration and Management Guide

Your guide to starting and keeping your patients on treatment with RYBREVANT®-based regimens.

INDICATIONS

RYBREVANT *FASPRO*™ (amivantamab and hyaluronidase-lpuj) and RYBREVANT® (amivantamab-vmjw) are indicated:

- in combination with LAZCLUZE® (lazertinib) for the first-line treatment of adult patients with locally advanced or metastatic NSCLC with 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.

SELECT IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

RYBREVANT *FASPRO*™ is contraindicated in patients with known hypersensitivity to hyaluronidase or to any of its excipients.

WARNINGS AND PRECAUTIONS for RYBREVANT® and RYBREVANT *FASPRO*™ include: IRRs (RYBREVANT®), Hypersensitivity & ARRs (RYBREVANT *FASPRO*™), ILD/Pneumonitis, VTE, Dermatologic Adverse Reactions, Ocular Toxicity and Embryo-Fetal Toxicity.

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

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Reach out to an Oncology Clinical Educator (OCE) at www.RYBREVANThcp.com/contact-a-representative. 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

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

Overview

Premedications[1]

Administer antihistamine, antipyretic, and glucocorticoids*:

15 to 60 minutes prior to each infusion according to the recommended premedications.

*Glucocorticoid administration is required for week 1, days -2, -1, 1, and 2 doses only and upon reinitiation after prolonged dose interruptions, then as necessary for subsequent infusions.

Learn more >

Decreasing infusion times[2†]

In the MARIPOSA trial, infusion times decreased over time.†

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

View data >

Proactive medications[1]

To help reduce the risk of select ARs

- **Dermatologic AR prophylaxis:**
  - Oral/topical antibiotics and ceramide-based moisturizer
  - Advise patients to limit direct sun exposure‡
- **VTE concomitant medications (when combined with LAZCLUZE®):** Anticoagulant prophylaxis for the first 4 months of treatment

‡During and for 2 months after treatment.

See details >

Appropriate patients currently receiving RYBREVANT® may switch to RYBREVANT *FASPRO*™ (amivantamab and hyaluronidase-lpuj)[3]

AR, adverse reaction; VTE, venous thromboembolism.

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

Preparation & storage[1]

STEP 1

During preparation and prior to administration, **check the vial labels** to ensure that the drug being prepared and administered is RYBREVANT® and not subcutaneous RYBREVANT *FASPRO*™ (amivantamab and hyaluronidase-lpuj)[3]

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

STEP 2

Determine the dose required of RYBREVANT® based on patient's baseline weight
- Each vial of RYBREVANT® contains 350 mg of amivantamab-vmjw

STEP 3

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

STEP 4

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

STEP 5

Gently invert the bag to mix the solution. Do not shake

STEP 6

Diluted solutions should be administered within 10 hours (including infusion time) at room temperature

IV, intravenous; PE, polyethylene; PP, polypropylene; PVC, polyvinyl chloride.

Dilute and prepare RYBREVANT® for IV infusion before administration

RYBREVANT® 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)
- 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

Premedications for RYBREVANT®[1]

IRR management

Medication	Dose	Administration	Frequency
Glucocorticoid	Dexamethasone (8 mg) or equivalent	**Oral** 48 hours, 24 hours, and 60 minutes prior	Week 1, day -2 (twice daily), day -1 (twice daily), day 1 (one dose)
Glucocorticoid	Dexamethasone (20 mg) or equivalent	**IV** 45–60 minutes prior	Week 1, day 1 (one dose)
Glucocorticoid	Dexamethasone (10 mg) or equivalent	**IV** 45–60 minutes prior	Week 1, day 2 (one dose)
Antihistamine	Diphenhydramine (25–50 mg) or equivalent	**IV** 15–30 minutes prior OR **Oral** 30–60 minutes prior	All doses
Antipyretic	Acetaminophen (650–1,000 mg)	**IV** 15–30 minutes prior OR **Oral** 30–60 minutes prior	All doses
Glucocorticoid (optional)	Dexamethasone (10 mg) or equivalent	**IV** 45–60 minutes prior	Optional for subsequent doses

Interrupt infusion if IRR is suspected. Reduce the infusion rate or permanently discontinue RYBREVANT® based on severity. If an anaphylactic reaction occurs, permanently discontinue RYBREVANT®.

IRR, infusion-related reaction.

Prophylactic and concomitant medications[1]

Dermatologic AR prophylaxis

Prophylactic measures (eg, use of oral/topical antibiotics) are recommended to reduce the risk of dermatologic ARs. When initiating treatment with RYBREVANT®, ceramide-based moisturizer is recommended.

VTE concomitant medications

When initiating treatment with RYBREVANT® in combination with LAZCLUZE®, implement anticoagulant prophylaxis to reduce the risk of 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 **Prescribing Information** for LAZCLUZE® for information about concomitant medications.

See the next page for additional information on prophylaxis

Proactive strategies that may help patients start and stay on RYBREVANT® + LAZCLUZE®

IRR premedications[1]

Glucocorticoid (week 1, days -2 and -1, and day 1 an hour before first infusion*)

Antihistamine and antipyretic prior to each infusion

Month	1	2	3	4	5	6	7

At-home treatment protocol

VTE prophylaxis[1,4,5]

Months 1–4: Anticoagulation (eg, DOACs or LMWHs)†

COCOON dermatologic prophylaxis[1,4]

Months 1–3: Doxycycline or minocycline 100 mg twice daily

Months 4–12: Topical clindamycin 1% lotion on the scalp before bedtime

Daily: Ceramide-based moisturizer on the body and face at least once daily

Daily: Wear protective clothing and broad-spectrum sunscreen (SPF ≥30)

Daily: Chlorhexidine 4% wash on fingernails and toenails for paronychia

Learn more about the importance of proactive therapy management to help optimize outcomes

Month = month of treatment with RYBREVANT® and LAZCLUZE®.

*Optional for subsequent doses.[1]
†NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) recommendations for cancer-associated VTE disease: anticoagulant options for VTE prophylaxis for ambulatory patients with cancer include DOACs and LMWHs.[5‡]
‡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.[5]

1L, first-line; DOAC, direct oral anticoagulant; LMWH, low molecular-weight heparin; NCCN, National Comprehensive Cancer Network.

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

Administering RYBREVANT® infusions with 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

When given in combination with LAZCLUZE®, administer RYBREVANT® any time after LAZCLUZE® when given on the same day

Administer premedications before each RYBREVANT® dose as recommended to reduce the risk of IRRs.

- Administer the diluted solution by IV 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 IV line with other agents

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

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

Administering LAZCLUZE® when used in combination with RYBREVANT®[6]

Administer LAZCLUZE® 240 mg orally once daily

- ✓ Swallow LAZCLUZE® tablets whole (with or without food). Do not crush, split, or chew
- ✓ If a patient misses a dose of LAZCLUZE® within 12 hours, instruct the patient to take the missed dose. If more than 12 hours have passed since the dose was to be given, instruct the patient to take the next dose at its scheduled time
- ✓ If vomiting occurs any time after taking LAZCLUZE®, instruct the patient to take the next dose at its next regularly scheduled time

Drug interactions with LAZCLUZE®

- ✗ Avoid concomitant use of LAZCLUZE® with strong and moderate CYP3A4 inducers. Consider an alternate concomitant medication with no potential to induce CYP3A4
- ✓ Monitor for adverse reactions associated with a CYP3A4 or BCRP substrate where minimal concentration changes may lead to serious adverse reactions, as recommended in the approved product labeling for the CYP3A4 or BCRP substrate

BCRP, breast cancer resistance protein; CYP3A4, cytochrome P450 3A4.

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

Recommended dosing schedule for RYBREVANT® + LAZCLUZE® (Q2W)[1,6]

RYBREVANT®

The recommended dosage is based on baseline body weight and can be administered as an intravenous infusion after dilution.[1]

With LAZCLUZE®

Administer RYBREVANT® any time after LAZCLUZE® when given on the same day.[1]

Appropriate patients may switch from RYBREVANT® Q2W dosing to RYBREVANT *FASPRO*™ (amivantamab and hyaluronidase-lpuj) Q2W dosing at their next scheduled dose on or after week 5.[3]

*Dose adjustments not required for subsequent body weight changes.[1]
Q2W, every 2 weeks.

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

Infusion rates for RYBREVANT® + LAZCLUZE® by body weight[1]

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

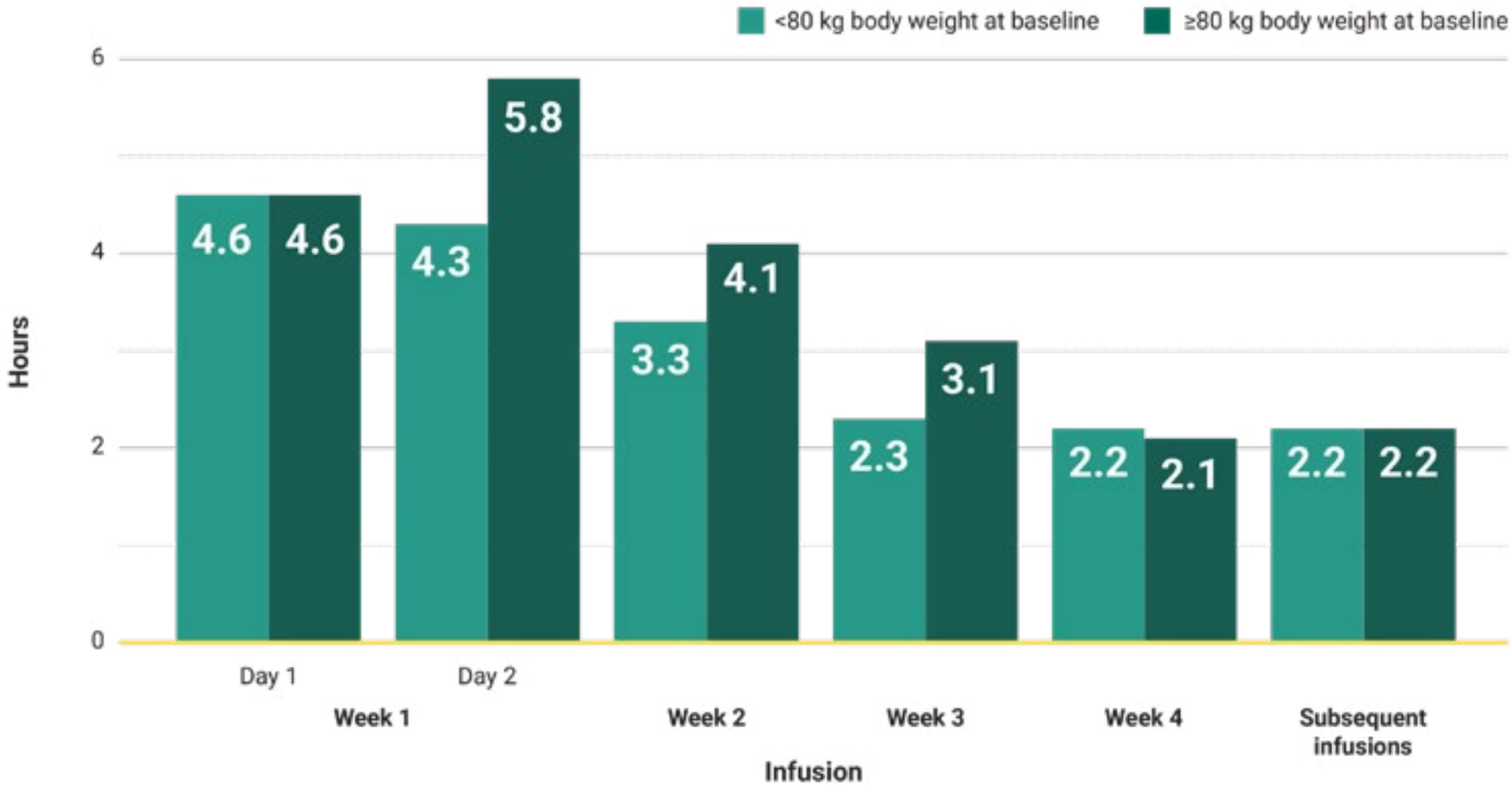
Body weight ≥80 kg			
Week	**Dose (per 250 mL bag)**	**Initial infusion rate**	**Subsequent infusion rate***
Week 1 (split dose infusion)			
Week 1, day 1	350 mg	50 mL/hr	75 mL/hr
Week 1, day 2	1,050 mg	35 mL/hr	50 mL/hr
Week 2	1,400 mg	65 mL/hr	
Week 3	1,400 mg	85 mL/hr	
Week 4	1,400 mg	125 mL/hr	
Week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

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

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

MARIPOSA infusion times

Clinical trial median infusion times by hours[2]*



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]

MARIPOSA is a clinical trial comparing RYBREVANT® + LAZCLUZE® to osimertinib in patients with untreated locally advanced or metastatic *EGFR*+† NSCLC.[1]

*Data reflect results from 2-week dosing in the MARIPOSA trial.[1]
†Ex19del/L858R.[1]

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

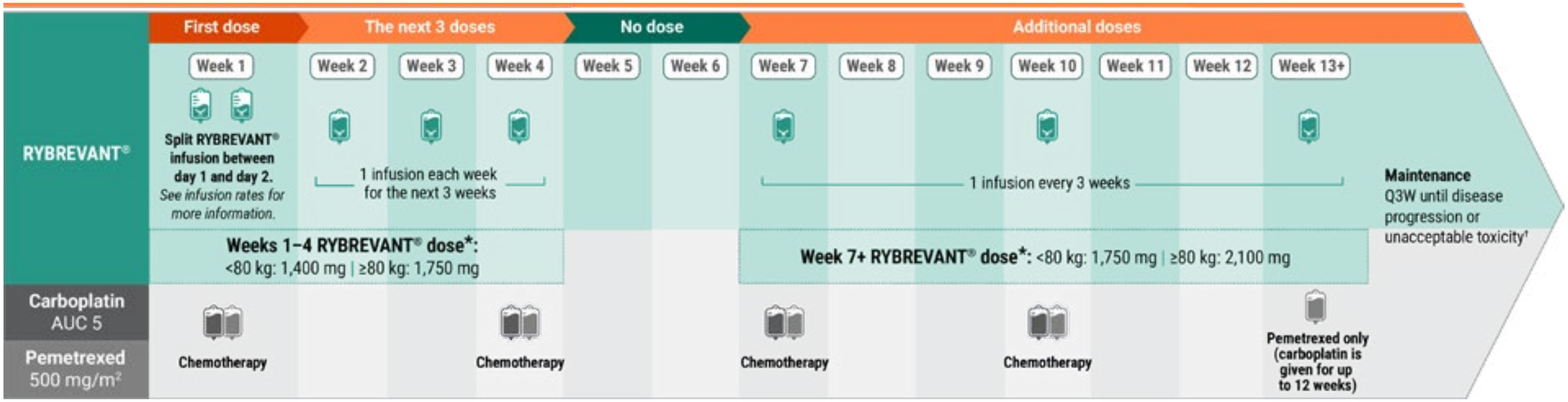
Administering RYBREVANT® infusions with chemotherapy[1]

- ✓ 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 the pemetrexed infusion first, carboplatin infusion second, and the RYBREVANT® infusion last
- ✓ 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 premedications before each RYBREVANT® dose as recommended to reduce the risk of IRRs.

- Administer the diluted RYBREVANT® solution by IV 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 IV line with other agents

Recommended dosing schedule for RYBREVANT® + chemotherapy (Q3W)[1]



RYBREVANT®

The recommended dosage is based on baseline body weight and can be administered as an intravenous infusion after dilution.

With chemotherapy

Administer RYBREVANT® after chemotherapy. Administer in the following order: pemetrexed, carboplatin, and then RYBREVANT®.

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

Appropriate patients may switch from RYBREVANT® Q3W dosing to RYBREVANT *FASPRO*™ (amivantamab and hyaluronidase-lpuj) Q3W dosing at their next scheduled dose on or after week 4.[3]

*Dose adjustments not required for subsequent body weight changes.[1]
†This refers only to RYBREVANT® and pemetrexed. Carboplatin should only be administered every 3 weeks for up to 12 weeks.[1]
AUC, area under the curve; Q3W, every 3 weeks.

Infusion rates for RYBREVANT® + carboplatin and pemetrexed by body weight[1]

Body weight <80 kg			
Week	**Dose (per 250 mL bag)**	**Initial infusion rate**	**Subsequent infusion rate***
Week 1 (split dose infusion)			
Week 1, day 1	350 mg	50 mL/hr	75 mL/hr
Week 1, day 2	1,050 mg	33 mL/hr	50 mL/hr
Week 2	1,400 mg	65 mL/hr	
Week 3	1,400 mg	85 mL/hr	
Week 4	1,400 mg	125 mL/hr	
Weeks 5 and 6	No dose		
Week 7 and every 3 weeks thereafter	1,750 mg	125 mL/hr	

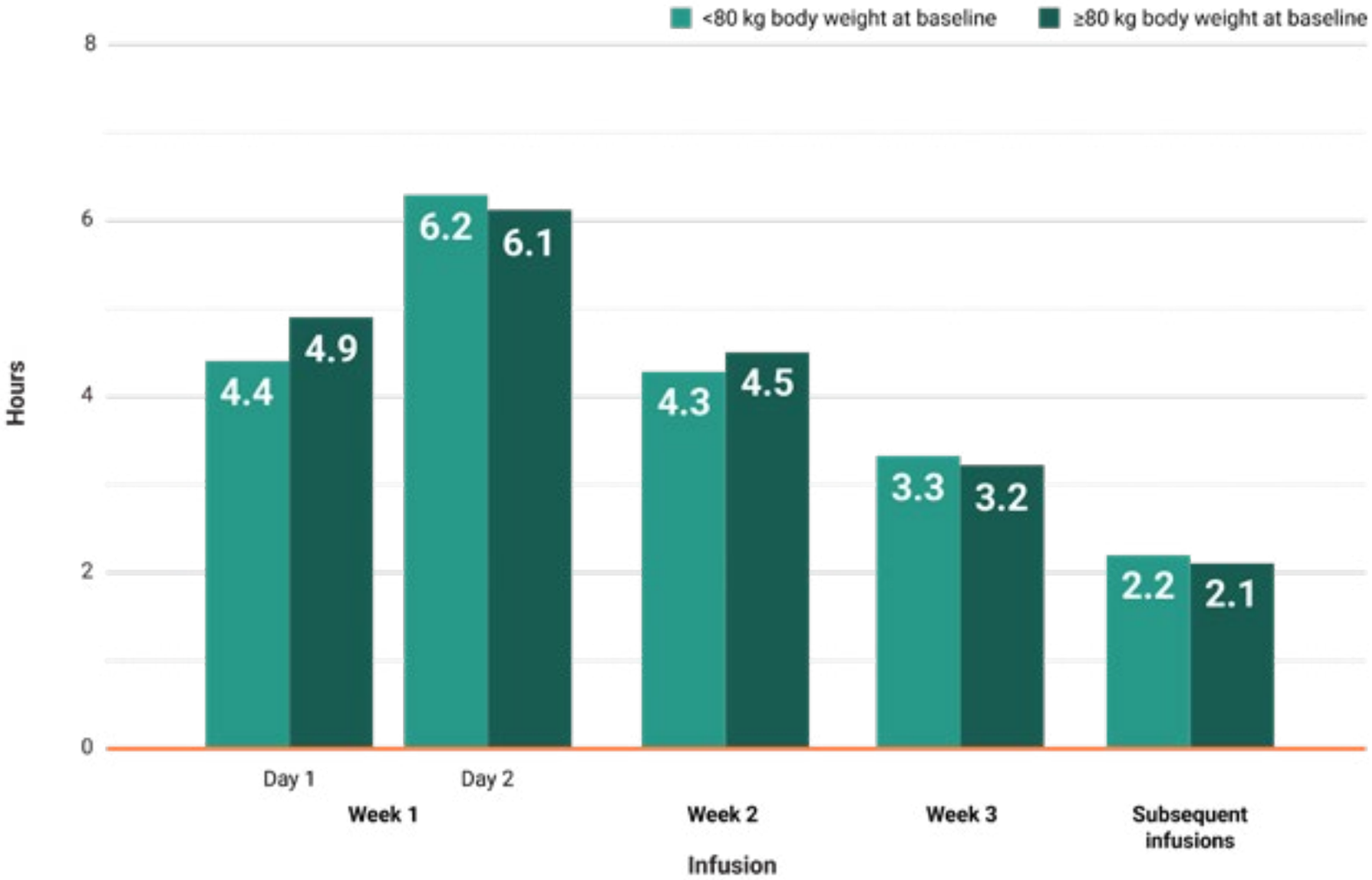
Body weight ≥80 kg			
Week	**Dose (per 250 mL bag)**	**Initial infusion rate**	**Subsequent infusion rate***
Week 1 (split dose infusion)			
Week 1, day 1	350 mg	50 mL/hr	75 mL/hr
Week 1, day 2	1,400 mg	25 mL/hr	50 mL/hr
Week 2	1,750 mg	65 mL/hr	
Week 3	1,750 mg	85 mL/hr	
Week 4	1,750 mg	125 mL/hr	
Weeks 5 and 6	No dose		
Week 7 and every 3 weeks thereafter	2,100 mg	125 mL/hr	

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

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

MARIPOSA-2 infusion times for RYBREVANT®

Clinical trial median infusion times by hours[2]*



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]

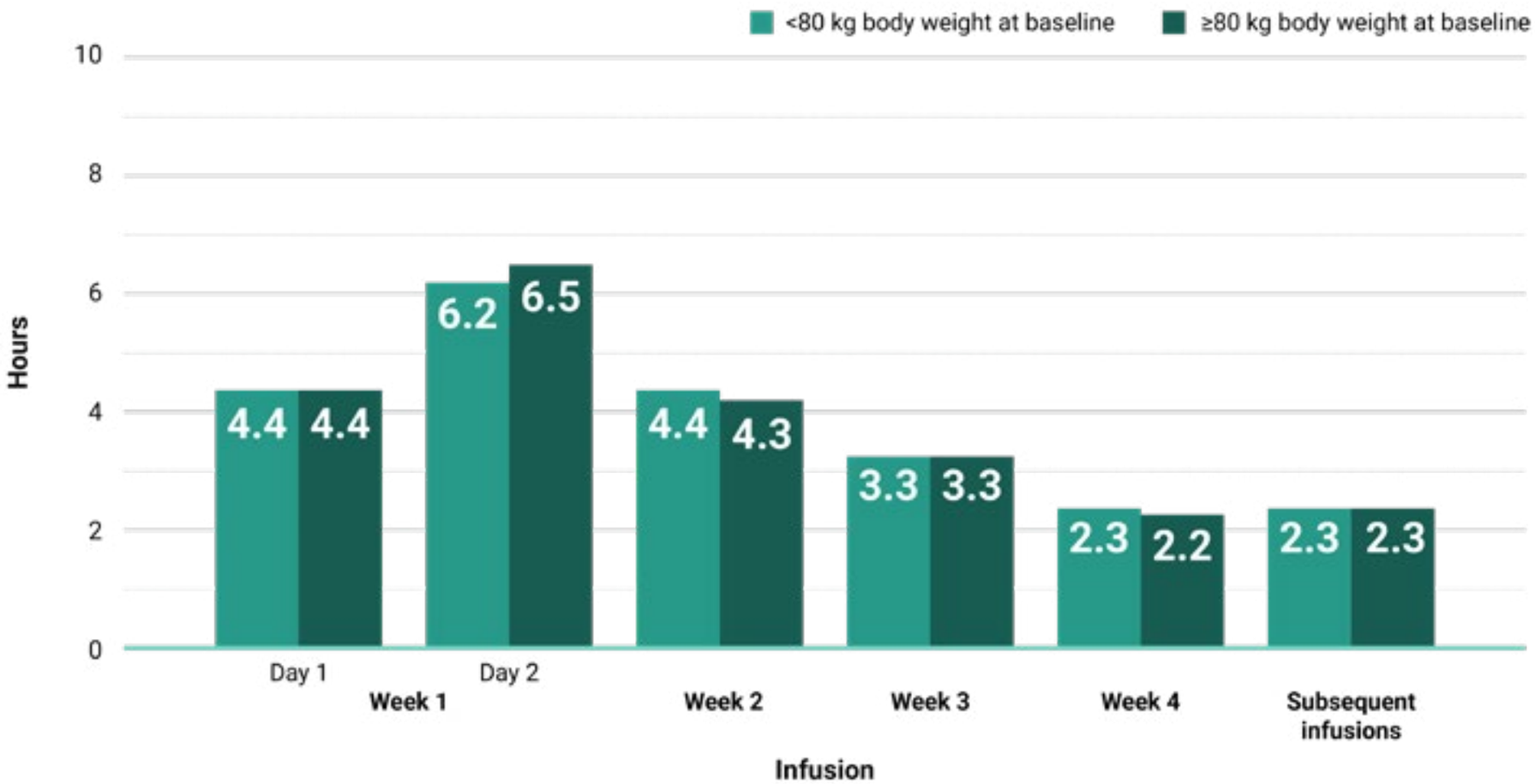
MARIPOSA-2 is a clinical trial evaluating the efficacy of RYBREVANT® in combination with carboplatin and pemetrexed in patients with previously treated locally advanced or metastatic *EGFR*+[†] NSCLC.[1]

*Data reflect results from 3-week dosing in the MARIPOSA-2 trial.[1]
[†]Ex19del/L858R.[1]

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

PAPILLON infusion times for RYBREVANT®

Clinical trial median infusion times by hours[2]*



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]

PAPILLON is a clinical trial evaluating the efficacy of RYBREVANT® in patients with previously untreated locally advanced or metastatic NSCLC with *EGFR* exon 20 insertion mutations.[1]

*Data reflect results from 3-week dosing in the PAPILLON trial.[1]

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

Administering RYBREVANT® infusions as a single agent[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

Administer premedications before each RYBREVANT® dose as recommended to reduce the risk of IRRs.

- Administer the diluted solution by IV 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 IV line with other agents

Recommended dosing for RYBREVANT® as a single agent[1]

The recommended dosage is based on baseline body weight and can be administered as an intravenous infusion after dilution.

Appropriate patients may switch from RYBREVANT® Q3W dosing to RYBREVANT *FASPRO*™ (amivantamab and hyaluronidase-lpuj) Q3W dosing at their next scheduled dose on or after week 5.[3]

*Dose adjustments not required for subsequent body weight changes.[1]

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

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

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

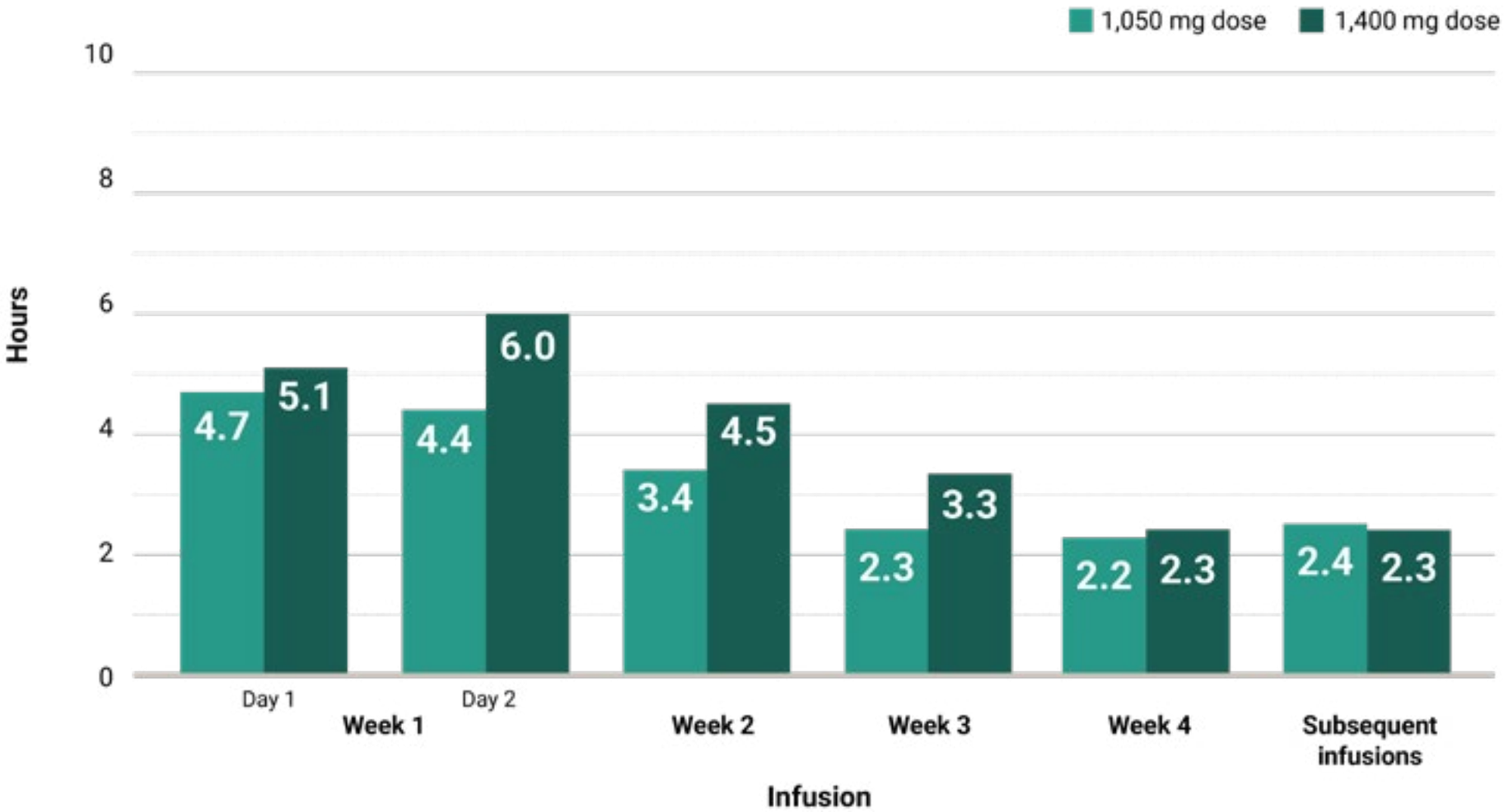
Body weight ≥80 kg			
Week	**Dose (per 250 mL bag)**	**Initial infusion rate**	**Subsequent infusion rate***
Week 1 (split dose infusion)			
Week 1, day 1	350 mg	50 mL/hr	75 mL/hr
Week 1, day 2	1,050 mg	35 mL/hr	50 mL/hr
Week 2	1,400 mg	65 mL/hr	
Week 3	1,400 mg	85 mL/hr	
Week 4	1,400 mg	125 mL/hr	
Week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

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

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

CHRYSALIS infusion times for RYBREVANT®

Clinical trial median infusion times by hours[2]*



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]

CHRYSALIS is a clinical trial evaluating the efficacy of RYBREVANT® in patients with previously treated locally advanced or metastatic NSCLC with *EGFR* exon 20 insertion mutations.[1]

*Data reflect results from 2-week dosing in the CHRYSALIS trial.[1]

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

Monitoring & managing ARs

Guide patients toward their goals with their optimal dose[1,6]

Based on severity and/or recurrence, certain ARs require discontinuation.[1] See specific guidance for dose modifications on the next pages.

Note: If a dose modification is needed for RYBREVANT®, treatment may be continued with LAZCLUZE®.[1,6]

Monitoring & managing ARs (cont'd)

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[6]

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

Monitoring & managing ARs (cont'd)

Adverse event 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 activities of daily living (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.

Monitoring & managing ARs (cont'd)

Recommended dosage modifications for ARs for RYBREVANT® + LAZCLUZE®[1]

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.

Infusion-Related Reactions

Table continues on next page

Severity	Dosage modifications		
Grade 1 or 2	**Interrupt** Interrupt **RYBREVANT®** infusion if suspected and monitor patient until symptoms resolve	**Resume** 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 prophylaxis** Include corticosteroid with premedications for subsequent dose of **RYBREVANT®**
Grade 3	**Interrupt** Interrupt **RYBREVANT®** infusion and administer supportive care medications. Continuously monitor patient until reaction symptoms resolve	**Resume** 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 prophylaxis** Include corticosteroid with premedications for subsequent dose **Discontinue** For recurrent grade 3, discontinue **RYBREVANT®** permanently
Grade 4 (or any grade anaphylaxis/ anaphylactic reactions)	**Discontinue** Discontinue **RYBREVANT®** permanently		

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

Monitoring & managing ARs (cont'd)

Recommended dosage modifications for ARs for RYBREVANT® + LAZCLUZE®[1,6]

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.

ILD/Pneumonitis

Table continues on next page

Severity	Dosage modifications	
Any grade	**Withhold** Withhold **both drugs** if suspected	**Discontinue** Discontinue **both drugs** permanently if confirmed

VTE Events (applies to RYBREVANT® + LAZCLUZE® combination only)

Severity	Dosage modifications		
Grade 2 or 3	**Withhold** Withhold **both drugs**	**Administer** Administer anticoagulation treatment as clinically indicated	**Resume** Once anticoagulant treatment has been initiated, resume **both drugs** at the same dose level, at the discretion of the treating physician
Grade 4 or recurrent grade 2 or 3 despite therapeutic level anticoagulation	**Discontinue** Discontinue **RYBREVANT®** permanently **Withhold** Withhold **LAZCLUZE®**	**Administer** Administer anticoagulant treatment as clinically indicated	**Resume** Once anticoagulant treatment has been initiated, treatment can continue with **LAZCLUZE®** at the same dose level, at the discretion of the treating physician

ILD, interstitial lung disease.

Monitoring & managing ARs (cont'd)

Recommended dosage modifications for ARs for RYBREVANT® + LAZCLUZE®[1,6]

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.

Dermatologic ARs (including dermatitis acneiform, pruritus, dry skin)

Table continues on next page

Severity	Dosage modifications		
Grade 1	**Initiate** Initiate supportive care management as clinically indicated	**Reassess** Reassess after 2 weeks; if rash does not improve, consider dose reduction of **RYBREVANT®**	
Grade 2	**Initiate** Initiate supportive care management as clinically indicated	**Reassess** Reassess after 2 weeks; if rash does not improve, reduce **RYBREVANT®** dose and continue **LAZCLUZE®** at the same dose	**Reassess** 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	**Withhold** Withhold **both drugs** and initiate supportive care management as clinically indicated	**Reassess** Upon recovery to grade ≤2, resume **RYBREVANT®** at a reduced dose; resume **LAZCLUZE®** at the same dose or consider dose reduction	**Discontinue** If there is no improvement within 2 weeks, discontinue **both drugs** permanently

Monitoring & managing ARs (cont'd)

Recommended dosage modifications for ARs for RYBREVANT® + LAZCLUZE®[1,6]

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.

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Dermatologic ARs (including dermatitis acneiform, pruritus, dry skin) (cont'd)

Severity	Dosage modifications			
	Discontinue	**Initiate**	**Withhold**	**Resume**
Grade 4 (including severe bullous, blistering, or exfoliating skin conditions, including TEN for RYBREVANT®)	Discontinue **RYBREVANT®** permanently	Initiate supportive care management as clinically indicated	Withhold **LAZCLUZE®** until recovery to grade ≤2 or baseline	Upon recovery to grade ≤2, resume **LAZCLUZE®** at a reduced dose at the discretion of the healthcare provider

Other ARs

Severity	Dosage modifications		
	Withhold	**Resume**	**Discontinue**
Grade 3	Withhold **both drugs** until recovery to grade ≤1 or baseline	Resume **both drugs** at the same dose if recovery occurs within 1 week Resume **both drugs** at reduced dose, or **LAZCLUZE®** alone, if recovery occurs after 1 week but within 4 weeks	Discontinue **both drugs** permanently if recovery does not occur within 4 weeks

TEN, toxic epidermal necrolysis.

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

Monitoring & managing ARs (cont'd)

Recommended dosage modifications for ARs for RYBREVANT® + LAZCLUZE®[1,6]

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.

Other ARs (cont'd)

Severity	Dosage modifications		
	Withhold	**Resume**	**Discontinue**
Grade 4	Withhold **both drugs** until recovery to grade ≤1 or baseline	Resume **both drugs** at reduced dose, or **LAZCLUZE®** alone, if recovery occurs within 4 weeks	Discontinue **both drugs** permanently if recovery does not occur within 4 weeks Discontinue **RYBREVANT®** permanently for recurrent grade 4 reactions

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® as shown in the tables on pages 25-29. Refer to Prescribing Information for carboplatin and pemetrexed for additional dosage modification information.

Patient counseling information

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

IRRs[1,6]	RYBREVANT® can cause IRRs, including anaphylaxis. Instruct patients to take glucocorticoids 48 hours prior to the first RYBREVANT® infusion to reduce the risk of IRR. The majority of IRRs occurred with the first infusion. Advise patients to alert their healthcare provider immediately for any signs or symptoms of IRRs.
ILD/pneumonitis[1,6]	RYBREVANT® can cause ILD/pneumonitis. Advise patients to immediately contact their healthcare provider for new or worsening respiratory symptoms.
VTE events with concomitant use with LAZCLUZE®[1,6]	When RYBREVANT® is used in combination with LAZCLUZE®, there is a risk of serious and life-threatening VTE events, including DVT and PE. 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 ARs[1,6]	RYBREVANT® can cause dermatologic ARs. Advise patients that prophylactic oral antibiotics are recommended starting on day 1 for the first 12 weeks of treatment and, after completion of oral antibiotic treatment, topical antibiotic lotion to the scalp for the next 9 months of treatment. Advise patients to use a non-comedogenic skin moisturizer (ceramide-based or other formulations that provide long-lasting skin hydration and exclude drying components) on the face and whole body (except scalp) and 4% chlorhexidine solution to wash hands and feet, while on treatment. Advise patients to limit direct sun exposure during and for 2 months after treatment, to wear protective clothing, and to use broad-spectrum UVA/UVB sunscreen to reduce the risk and severity of dermatologic adverse reactions.
Ocular toxicity[1,6]	RYBREVANT® can cause 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[1,6]	RYBREVANT® can cause paronychia. Advise patients to contact their healthcare provider for signs or symptoms of paronychia.
Embryo-fetal toxicity[1,6]	Advise females of reproductive potential of the potential risk to a fetus, to use effective contraception during treatment with RYBREVANT® and for 3 months after the last dose, and to inform their healthcare provider of a known or suspected pregnancy.
Lactation[1,6]	Advise women not to breastfeed during treatment with RYBREVANT® and for 3 months after the last dose.
Infertility[6]	Advise males and females of reproductive potential of the potential risk for impaired fertility with LAZCLUZE®.

DVT, deep vein thrombosis; FDA, US Food and Drug Administration; PE, pulmonary embolism; UVA, ultraviolet A; UVB, ultraviolet B.

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

References

References: 1. RYBREVANT® [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc. **2.** Data on file. Janssen Biotech, Inc. **3.** RYBREVANT *FASPRO*™ [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc. **4.** Cho BC, Li W, Spira AI, et al. Enhanced versus standard dermatologic management with amivantamab-lazertinib in *EGFR*-mutated advanced NSCLC: the COCOON global randomized controlled trial. *J Thorac Oncol*. 2025;20(10):1517-1530. doi:10.1016/j.jtho.2025.07.117 **5.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Cancer-Associated Venous Thromboembolic Disease V.3.2025. © National Comprehensive Cancer Network, Inc. 2025. All rights reserved. Accessed November 6, 2025. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way. **6.** LAZCLUZE® [Prescribing Information]. Horsham, PA: 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 December 10, 2025. https://dctd.cancer.gov/research/ctep-trials/for-sites/adverse-events/ctcae-v5-5x7.pdf

Indications and Important Safety Information

INDICATIONS

RYBREVANT *FASPRO*™ (amivantamab and hyaluronidase-lpuj) and RYBREVANT® (amivantamab-vmjw) are indicated:

- in combination with LAZCLUZE® (lazertinib) for the first-line treatment of adult patients with locally advanced or metastatic NSCLC with 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

CONTRAINDICATIONS

RYBREVANT *FASPRO*™ is contraindicated in patients with known hypersensitivity to hyaluronidase or to any of its excipients.

WARNINGS AND PRECAUTIONS

Hypersensitivity and Administration-Related Reactions with RYBREVANT *FASPRO*™

RYBREVANT *FASPRO*™ can cause hypersensitivity and administration-related reactions (ARR); signs and symptoms of ARR include dyspnea, flushing, fever, chills, chest discomfort, hypotension, and vomiting. The median time to ARR onset is approximately 2 hours.

RYBREVANT FASPRO™ *with LAZCLUZE®*

In PALOMA-3 (n=206), all Grade ARR occurred in 13% of patients, including 0.5% Grade 3. Of the patients who experienced ARR, 89% occurred with the initial dose (Week 1, Day 1).

Premedicate with antihistamines, antipyretics, and glucocorticoids and administer RYBREVANT *FASPRO*™ as recommended. Monitor patients for any signs and symptoms of administration-related reactions during injection in a setting where cardiopulmonary resuscitation medication

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

Important Safety Information (cont'd)

and equipment are available. Interrupt RYBREVANT *FASPRO*™ injection if ARR is suspected. Resume treatment upon resolution of symptoms or permanently discontinue RYBREVANT *FASPRO*™ based on severity.

Infusion-Related Reactions with RYBREVANT®

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

RYBREVANT® with LAZCLUZE®

In MARIPOSA (n=421), IRRs occurred in 63% of patients, including Grade 3 in 5% and Grade 4 in 1% of patients. IRR-related infusion modifications occurred in 54%, dose reduction in 0.7%, and permanent discontinuation of RYBREVANT® in 4.5% of patients.

RYBREVANT® with Carboplatin and Pemetrexed

Based on the pooled safety population (n=281), IRRs occurred in 50% of patients including Grade 3 (3.2%) adverse reactions. IRR-related infusion modifications occurred in 46%, and permanent discontinuation of RYBREVANT® in 2.8% of patients.

RYBREVANT® as a Single Agent

In CHRYSALIS (n=302), IRRs occurred in 66% of patients. IRRs occurred in 65% of patients on Week 1 Day 1, 3.4% on Day 2 infusion, 0.4% with Week 2 infusion, and were cumulatively 1.1% with subsequent infusions. 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. IRR-related infusion modifications occurred in 62%, and permanent discontinuation of RYBREVANT® in 1.3% of patients.

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 signs and symptoms of IRRs in a setting where cardiopulmonary resuscitation medication and equipment are available. Interrupt infusion if IRR is suspected. Reduce the infusion rate or permanently discontinue RYBREVANT® based on severity. If an anaphylactic reaction occurs, permanently discontinue RYBREVANT®.

Interstitial Lung Disease/Pneumonitis

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

Important Safety Information (cont'd)

RYBREVANT FASPRO™ *with LAZCLUZE®*

In PALOMA-3, ILD/pneumonitis occurred in 6% of patients, including Grade 3 in 1%, Grade 4 in 1.5%, and fatal cases in 1.9% of patients. 5% of patients permanently discontinued RYBREVANT *FASPRO*™ and LAZCLUZE® due to ILD/pneumonitis.

RYBREVANT® with LAZCLUZE®

In MARIPOSA, ILD/pneumonitis occurred in 3.1% of patients, including Grade 3 in 1.0% 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.

RYBREVANT® with Carboplatin and Pemetrexed

Based on the pooled safety population, ILD/pneumonitis occurred in 2.1% of patients 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, 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). Immediately withhold RYBREVANT *FASPRO*™ or RYBREVANT® and LAZCLUZE® (when applicable) in patients with suspected ILD/pneumonitis and permanently discontinue if ILD/pneumonitis is confirmed.

Venous Thromboembolic (VTE) Events with Concomitant Use with LAZCLUZE®

RYBREVANT *FASPRO*™ and RYBREVANT® in combination with LAZCLUZE® can cause serious and fatal venous thromboembolic (VTE) events, including deep vein thrombosis and pulmonary embolism. Without prophylactic anticoagulation, the majority of these events occurred during the first four months of treatment.

RYBREVANT FASPRO™ *with LAZCLUZE®*

In PALOMA-3 (n=206), all Grade VTE occurred in 11% of patients and 1.5% were Grade 3. 80% (n=164) of patients received prophylactic anticoagulation at study entry, with an all Grade VTE incidence of 7%. In patients who did not receive prophylactic anticoagulation (n=42), all Grade VTE occurred in 17% of patients. In total, 0.5% of patients had VTE leading to dose reductions of RYBREVANT *FASPRO*™ and no patients required permanent discontinuation. The median time to onset of VTEs was 95 days (range: 17 to 390).

Important Safety Information (cont'd)

RYBREVANT® with LAZCLUZE®

In MARIPOSA (n=421), VTEs occurred in 36% of patients including Grade 3 in 10% and Grade 4 in 0.5% of patients. On-study VTEs occurred in 1.2% of patients (n=5) while receiving anticoagulation therapy. There were two fatal cases of VTE (0.5%), 9% of patients had VTE leading to dose interruptions of RYBREVANT®, and 7% of patients had VTE leading to dose interruptions of LAZCLUZE®; 1% of patients had VTE leading to dose reductions of RYBREVANT®, and 0.5% of patients had VTE leading to dose reductions of LAZCLUZE®; 3.1% of patients had VTE leading to permanent discontinuation of RYBREVANT®, and 1.9% of patients had VTE leading to permanent discontinuation of LAZCLUZE®. The median time to onset of VTEs was 84 days (range: 6 to 777).

Administer prophylactic anticoagulation for the first four months of treatment. The use of Vitamin K antagonists is not recommended.

Monitor for signs and symptoms of VTE events and treat as medically appropriate. Withhold RYBREVANT *FASPRO*™ or RYBREVANT® and LAZCLUZE® based on severity. Once anticoagulant treatment has been initiated, resume RYBREVANT *FASPRO*™ or 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 *FASPRO*™ or 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

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

RYBREVANT FASPRO™ *with LAZCLUZE®*

In PALOMA-3, rash occurred in 80% of patients, including Grade 3 in 17% and Grade 4 in 0.5% of patients. Rash leading to dose reduction occurred in 11% of patients, and RYBREVANT *FASPRO*™ was permanently discontinued due to rash in 1.5% of patients.

RYBREVANT® with LAZCLUZE®

In MARIPOSA, rash occurred in 86% of patients, 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®.

Please see full Important Safety Information. Please read full Prescribing Information for RYBREVANT *FASPRO*™ (amivantamab and hyaluronidase-lpuj), RYBREVANT®, and LAZCLUZE®.

Important Safety Information (cont'd)

RYBREVANT® with Carboplatin and Pemetrexed

Based on the pooled safety population, rash occurred in 82% of patients, 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, including Grade 3 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% and permanent discontinuation due to rash occurred in 0.7% of patients. Toxic epidermal necrolysis occurred in one patient (0.3%).

When initiating treatment with RYBREVANT *FASPRO*™ or RYBREVANT® and LAZCLUZE®, prophylactic and concomitant medications are recommended to reduce the risk and severity of dermatologic adverse reactions. Instruct patients to limit sun exposure during and for 2 months after treatment. Advise patients to wear protective clothing and use broad spectrum UVA/UVB sunscreen.

If skin reactions develop, administer supportive care including 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 *FASPRO*™ or RYBREVANT® in combination with LAZCLUZE®, withhold, reduce the dose, or permanently discontinue both drugs based on severity. For patients receiving RYBREVANT *FASPRO*™ or RYBREVANT® as a single agent or in combination with carboplatin and pemetrexed, withhold, dose reduce or permanently discontinue RYBREVANT *FASPRO*™ or RYBREVANT® based on severity.

Ocular Toxicity

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

RYBREVANT FASPRO™ *with LAZCLUZE®*

In PALOMA-3, all Grade ocular toxicity occurred in 13% of patients, including 0.5% Grade 3.

RYBREVANT® with LAZCLUZE®

In MARIPOSA, ocular toxicity occurred in 16%, including Grade 3 or 4 ocular toxicity in 0.7% of patients.

Important Safety Information (cont'd)

RYBREVANT® with Carboplatin and Pemetrexed

Based on the pooled safety population, ocular toxicity occurred in 16% of patients. 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. All events were Grade 1-2.

Promptly refer patients presenting with new or worsening eye symptoms to an ophthalmologist. Withhold, dose reduce or permanently discontinue RYBREVANT *FASPRO*™ or RYBREVANT® and continue LAZCLUZE® based on severity.

Embryo-Fetal Toxicity

Based on animal models, RYBREVANT *FASPRO*™, RYBREVANT® and LAZCLUZE® can cause fetal harm when administered to a pregnant woman. Verify pregnancy status of females of reproductive potential prior to initiating RYBREVANT *FASPRO*™ and RYBREVANT®. Advise pregnant women and females 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 *FASPRO*™ or RYBREVANT®, and for 3 weeks after the last dose of LAZCLUZE®.

ADVERSE REACTIONS

RYBREVANT FASPRO™ *with LAZCLUZE®*

In PALOMA-3 (n=206), the most common adverse reactions (≥20%) were rash (80%), nail toxicity (58%), musculoskeletal pain (50%), fatigue (37%), stomatitis (36%), edema (34%), nausea (30%), diarrhea (22%), vomiting (22%), constipation (22%), decreased appetite (22%), and headache (21%). The most common Grade 3 or 4 laboratory abnormalities (≥2%) were decreased lymphocyte count (6%), decreased sodium (5%), decreased potassium (5%), decreased albumin (4.9%), increased alanine aminotransferase (3.4%), decreased platelet count (2.4%), increased aspartate aminotransferase (2%), increased gammaglutamyl transferase (2%), and decreased hemoglobin (2%).

Serious adverse reactions occurred in 33% of patients, with those occurring in ≥2% of patients including ILD/pneumonitis (6%); and pneumonia, VTE and fatigue (2.4% each). Death due to adverse reactions occurred in 5% of patients treated with RYBREVANT *FASPRO*™, including ILD/pneumonitis (1.9%), pneumonia (1.5%), and respiratory failure and sudden death (1% each).

Please see full Important Safety Information. Please read full Prescribing Information for RYBREVANT *FASPRO*™ (amivantamab and hyaluronidase-lpuj), RYBREVANT®, and LAZCLUZE®.

Important Safety Information (cont'd)

RYBREVANT® with LAZCLUZE®

In MARIPOSA (n=421), the most common adverse reactions (ARs) (≥20%) were rash (86%), nail toxicity (71%), infusion-related reactions (IRRs) (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%), and nausea (21%). 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 ARs occurred in 49% of patients, with those occurring in ≥2% of patients including VTE (11%), pneumonia (4%), ILD/pneumonitis and rash (2.9% each), COVID-19 (2.4%), and pleural effusion and IRRs (RYBREVANT®) (2.1% each). Fatal ARs occurred in 7% of patients 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

In MARIPOSA-2 (n=130), the most common ARs (≥20%) were rash (72%), IRRs (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 ARs occurred in 32% of patients, with those occurring in >2% of patients including dyspnea (3.1%), thrombocytopenia (3.1%), sepsis (2.3%), and PE (2.3%). Fatal ARs occurred in 2.3% of patients; these included respiratory failure, sepsis, and ventricular fibrillation (0.8% each).

In PAPILLON (n=151), the most common ARs (≥20%) were rash (90%), nail toxicity (62%), stomatitis (43%), IRRs (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%).

Please see full Important Safety Information. Please read full Prescribing Information for RYBREVANT *FASPRO*™ (amivantamab and hyaluronidase-lpuj), RYBREVANT®, and LAZCLUZE®.

Important Safety Information (cont'd)

In PAPILLON, serious ARs occurred in 37% of patients, with those occurring in ≥2% of patients including rash, pneumonia, ILD, PE, 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

In CHRYSALIS (n=129), the most common ARs (≥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 ARs occurred in 30% of patients, with those occurring in ≥2% of patients including PE, 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 *FASPRO*™ (amivantamab and hyaluronidase-lpuj), RYBREVANT®, and LAZCLUZE®.

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