RYBREVANT *Faspro*™ (amivantamab and hyaluronidase-lpuj)
Subcutaneous injection | 160 mg/2,000 units per mL

+

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

Administration and Management Guide

Your guide to starting and keeping your patients on treatment with RYBREVANT *FASPRO*™–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 and 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®.

Table of contents

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 *FASPRO*™, RYBREVANT®, and LAZCLUZE®.

Overview[1]

Premedications

Administer antihistamine, antipyretic, and glucocorticoids*:

15 to 90 minutes prior to each injection according to the recommended premedications.

*Glucocorticoid administration is required for week 1, day 1 only and upon reinitiation after prolonged dose interruptions, then as necessary for subsequent injections.

Learn more >

Rapid injection(s)†

†Administration time only; actual clinic time may vary. If multiple dosing syringes are required, administer each injection consecutively in separate quadrants of the abdomen, with each injection taking ~5 minutes.

See details >

Proactive medications

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 >

About RYBREVANT *FASPRO*™

- **RYBREVANT *FASPRO*™ is contraindicated in patients with known hypersensitivity to hyaluronidase or to any of its excipients**
- **RYBREVANT *FASPRO*™ is intended for subcutaneous injection in the abdomen only**

Patients currently receiving RYBREVANT® (amivantamab-vmjw) may switch to RYBREVANT *FASPRO*™. See the intravenous to subcutaneous dosing conversion table on page 7

AR, adverse reaction; VTE, venous thromboembolism.

Premedications and observation time for RYBREVANT *FASPRO*™

ARR management[1]

Medication	Dose	Administration			Frequency
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) or equivalent	**IV** 15–30 minutes prior	OR	**Oral** 30–60 minutes prior	All doses
Glucocorticoid	Dexamethasone (20 mg) or equivalent	**IV** 45–60 minutes prior	OR	**Oral** At least 60 minutes prior	Initial dose (week 1, day 1)*
Glucocorticoid (optional)	Dexamethasone (10 mg) or equivalent	**IV** 45–60 minutes prior	OR	**Oral** 60–90 minutes prior	Optional for subsequent doses

PALOMA-3 study design: PALOMA-3 is a phase 3, randomized, open-label trial evaluating PK of RYBREVANT *FASPRO*™ vs RYBREVANT® (Q2W), both in combination with LAZCLUZE®. Patients with *EGFR*-mutated advanced NSCLC who progressed on or after osimertinib and platinum-based chemotherapy were randomly assigned 1:1 (N=418) to receive subcutaneous RYBREVANT *FASPRO*™ or intravenous RYBREVANT®, both combined with LAZCLUZE®.[1,2]

Observation time: ARRs occurred in 13% of patients in PALOMA-3 (n=206), 89% of which occurred on week 1, day 1. The median time to onset of ARR was ~2 hours. Monitor patients for any signs and symptoms of ARRs during injection in a setting where cardiopulmonary resuscitation medication and equipment are available. Patient monitoring time is up to healthcare provider discretion.[1]

*Glucocorticoid administration is also required after prolonged dose interruptions, then as necessary; or at a subsequent dose in the event of an ARR.[1]

ARR, administration-related reaction; EGFR, epidermal growth factor receptor; NSCLC, non–small cell lung cancer; PK, pharmacokinetics; Q2W, once every 2 weeks.

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 *FASPRO*™, ceramide-based moisturizer is recommended.

VTE concomitant medications

When initiating treatment with RYBREVANT *FASPRO*™ 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 for RYBREVANT *FASPRO*™ + LAZCLUZE®

Premedications[1]
Glucocorticoid required prior to initial injection (week 1, day 1).*
Antihistamine and antipyretic required prior to each injection.

RYBREVANT *FASPRO*™ ADMINISTRATION[1]

Q4W dosing
- Weeks 1–4: Weekly
- Weeks 5+: ~10 minutes† every 4 weeks

OR

Q2W dosing
- Weeks 1–4: Weekly
- Weeks 5+: ~5 minutes† every 2 weeks

	Month 1	2	3	4	5
LAZCLUZE® administration[4]	**LAZCLUZE® dose: 240 mg orally once daily**				

AT-HOME ORAL AND TOPICAL REGIMEN[1,3]

Medications
- **Oral doxycycline or minocycline** 100 mg twice daily for first 3 months of treatment
- **Topical clindamycin 1% lotion** on the scalp for next 9 months of treatment
- **Oral anticoagulant** for first 4 months of treatment

Daily skincare
- **Ceramide-based skin moisturizer** on the face and body (except scalp)
- **Chlorhexidine 4% wash** on the hands and feet (once daily)
- **Protective clothing and broad-spectrum UVA/UVB sunscreen** (SPF ≥30)

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

Month = month of treatment with RYBREVANT *FASPRO*™ and LAZCLUZE®.
*Glucocorticoid administration is also required upon reinitiation after prolonged dose interruptions, then as necessary; or at a subsequent dose in the event of an ARR.[1]
†Administration time only; actual clinic time may vary.
Q4W, once every 4 weeks; SPF, sun protection factor; UVA, ultraviolet A; UVB, ultraviolet B.

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

Switching from RYBREVANT® (amivantamab-vmjw) to RYBREVANT *FASPRO*™[1,5]*

For patients currently receiving Q2W RYBREVANT®:		<80 kg		≥80 kg	
		RYBREVANT®	RYBREVANT *FASPRO*™	RYBREVANT®	RYBREVANT *FASPRO*™
Switch to **Q2W RYBREVANT *FASPRO*™**	**From week 5 onward**	1,050 mg	1,600 mg	1,400 mg	2,240 mg
Switch to **Q4W RYBREVANT *FASPRO*™**	**From week 5 onward**	1,050 mg	3,520 mg	1,400 mg	4,640 mg

For patients currently receiving Q3W RYBREVANT®:		<80 kg		≥80 kg	
		RYBREVANT®	RYBREVANT *FASPRO*™	RYBREVANT®	RYBREVANT *FASPRO*™
Switch to **Q3W RYBREVANT *FASPRO*™**	**For week 4 only**	1,400 mg	2,400 mg	1,750 mg	3,360 mg
	From week 7 onward	1,750 mg	2,400 mg	2,100 mg	3,360 mg

For patients receiving a reduced dose of RYBREVANT®, please refer to the RYBREVANT *FASPRO*™ dose reduction tables when switching. If additional information is needed, please submit a Medical Information Request (MIR)

Regardless of whether patients initiated treatment with RYBREVANT *FASPRO*™ or switched from RYBREVANT®, those currently receiving RYBREVANT *FASPRO*™ must adhere to the RYBREVANT *FASPRO*™–specific premedication protocol.

*Based on pharmacokinetic data; reflective of patients receiving recommended starting dosage only.
Q3W, once every 3 weeks.

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

Vial selection and dose volume for RYBREVANT *FASPRO*™ with LAZCLUZE® or as a single agent (Q4W*)[1]

Q4W DOSING

STEP 1

Select the right vial for the starting dose based on patient weight at baseline

STEP 2

Determine dose volume needed

<80 kg	**WEEKS 1–4** (once weekly)	1,600 mg amivantamab	**ONE 10 mL VIAL**	**Administer 10 mL**
<80 kg	**SUBSEQUENT DOSES**† (Q4W from week 5)	3,520 mg amivantamab	**ONE 22 mL VIAL**	**Administer 22 mL**‡
≥80 kg	**WEEKS 1–4** (once weekly)	2,240 mg amivantamab	**ONE 14 mL VIAL**	**Administer 14 mL**
≥80 kg	**SUBSEQUENT DOSES**† (Q4W from week 5)	4,640 mg amivantamab	**ONE 14 mL VIAL** **ONE 15 mL VIAL**	**Administer 29 mL**§‖

Please read the full Prescribing Information for RYBREVANT *FASPRO*™ for units of hyaluronidase for each dose.

*Following weekly doses from weeks 1 to 4. For patients currently following a Q2W dosing regimen, switch to subcutaneous and/or Q4W dosing at their next scheduled dose after initial weekly dosing has been completed (on or after week 5).
†Dose adjustments not required for subsequent body weight changes.
‡Divide the 22 mL dose volume approximately equally into 2 syringes (each injection volume should not exceed 15 mL).
§Divide the 29 mL dose volume approximately equally into 2 syringes (each injection volume should not exceed 15 mL).
‖For the 29 mL dose volume, use one 2,240 mg amivantamab and 28,000 units hyaluronidase/14 mL vial and one 2,400 mg amivantamab and 30,000 units hyaluronidase/15 mL vial to minimize waste. If a different combination of vials is used, discard unused portion.

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

Vial selection and dose volume for RYBREVANT *FASPRO*™ with LAZCLUZE® or as a single agent (Q2W)[1]

Q2W DOSING

STEP 1

Select the right vial for the starting dose based on patient weight at baseline

STEP 2

Determine dose volume needed

<80 kg	**WEEKS 1–4** (once weekly)	1,600 mg amivantamab	ONE 10 mL VIAL		Administer 10 mL
	SUBSEQUENT DOSES* (Q2W from week 5)	1,600 mg amivantamab	ONE 10 mL VIAL		Administer 10 mL
≥80 kg	**WEEKS 1–4** (once weekly)	2,240 mg amivantamab	ONE 14 mL VIAL		Administer 14 mL
	SUBSEQUENT DOSES* (Q2W from week 5)	2,240 mg amivantamab	ONE 14 mL VIAL		Administer 14 mL

Please read the full Prescribing Information for RYBREVANT *FASPRO*™ for units of hyaluronidase for each dose.

*Dose adjustments not required for subsequent body weight changes.

Vial selection and dose volume for RYBREVANT *FASPRO*™ with chemotherapy (Q3W)[1]

Q3W DOSING

STEP 1

Select the right vial for the starting dose based on patient weight at baseline

STEP 2

Determine dose volume needed

<80 kg	WEEK 1 (Day 1)	1,600 mg amivantamab	ONE 10 mL VIAL	Administer 10 mL
	SUBSEQUENT DOSES*†	2,400 mg amivantamab	ONE 15 mL VIAL	Administer 15 mL
≥80 kg	WEEK 1 (Day 1)	2,240 mg amivantamab	ONE 14 mL VIAL	Administer 14 mL
	SUBSEQUENT DOSES*†	3,360 mg amivantamab	ONE 22 mL VIAL	Administer 21 mL‡§

Please read the full Prescribing Information for RYBREVANT *FASPRO*™ for units of hyaluronidase for each dose.

*Dose adjustments not required for subsequent body weight changes.
†Including week 2, day 1 and week 3, day 1 doses. Initiate Q3W dosing starting at week 4.
†Divide the 21 mL dose volume approximately equally into 2 syringes (each injection volume should not exceed 15 mL).
§For the 21 mL dose volume, the entire contents of the 3,520 mg amivantamab and 44,000 units hyaluronidase/22 mL vial will not be needed. Discard unused portion.

Preparation and storage[1]

STEP 1 Remove from fridge

Remove the appropriate number of RYBREVANT *FASPRO*™ vials from refrigerated storage

- During preparation and prior to administration, check the vial labels to ensure that the drug being prepared and administered is subcutaneous RYBREVANT *FASPRO*™ and not RYBREVANT® (amivantamab-vmjw)
- Do not substitute RYBREVANT *FASPRO*™ for or with RYBREVANT®

STEP 2 Bring to room temp

Wait at least 15 minutes to allow vial(s) to reach room temperature

- Do not warm any other way. Do not shake or dilute

STEP 3 Inspect visually

Once room temperature, inspect visually for particulate matter and discoloration prior to administration

- RYBREVANT *FASPRO*™ is a clear to opalescent and colorless to pale yellow solution
- Do not use if the solution is discolored or cloudy, or if foreign particles are present

STEP 4 Withdraw dose

Withdraw the required injection volume from the vial(s) into a syringe(s) using a transfer needle

- RYBREVANT *FASPRO*™ is compatible with stainless steel injection needles, PP and PC syringes, and PE, PU, and PVC subcutaneous infusion sets. Administer using a 21G to 23G needle or infusion set to ensure ease of administration
- Each injection volume should not exceed 15 mL. Divide doses requiring greater than 15 mL into approximately equal volumes in 2 syringes

Vial storage

Store RYBREVANT *FASPRO*™ vials in a refrigerator in original carton to protect from light. Do not freeze or shake.

Syringe storage

- RYBREVANT *FASPRO*™ does not contain an antimicrobial preservative. The prepared syringes should be administered immediately
- If immediate administration is not possible, replace the transfer needle with a syringe closing cap for transport, and store the prepared syringes of RYBREVANT *FASPRO*™ refrigerated at 36 °F to 46 °F (2 °C to 8 °C) for up to 24 hours followed by at room temperature of 59 °F to 86 °F (15 °C to 30 °C) for up to 24 hours
- Discard the prepared syringe(s) if stored for more than 24 hours refrigerated or more than 24 hours at room temperature
- If stored in the refrigerator, allow the solution to come to room temperature before administration

PC, polycarbonate; PE, polyethylene; PP, polypropylene; PU, polyurethane; PVC, polyvinyl chloride.

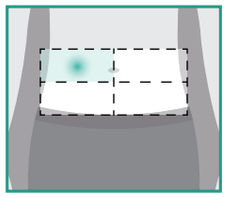
Administering subcutaneous RYBREVANT *FASPRO*™[1]

Administer premedications before each RYBREVANT *FASPRO*™ dose as recommended to reduce the risk of ARRs.

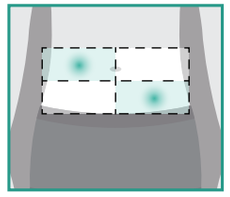
RYBREVANT *FASPRO*™ is for subcutaneous use only. Do not administer RYBREVANT *FASPRO*™ intravenously

- Do not substitute RYBREVANT *FASPRO*™ for or with intravenous amivantamab products because they have different recommended dosages. To reduce the risk of medication errors, prior to administration, check the vial labels to ensure that the drug being prepared and administered is subcutaneous RYBREVANT *FASPRO*™ and not intravenous amivantamab

Administer using a 21G to 23G needle or infusion set. Once the syringe(s) is prepped, prepare to administer the injection. RYBREVANT *FASPRO*™ must be administered by a healthcare professional.



- Administer each injection of RYBREVANT *FASPRO*™ subcutaneously in the abdomen over approximately 5 minutes to minimize injection site irritation



- If the total dose requires multiple injections of RYBREVANT *FASPRO*™, administer each injection consecutively in separate quadrants of the abdomen, with each injection taking approximately 5 minutes

- Do not inject into tattoos or scars or areas where the skin is red, bruised, tender, hard, not intact, or within 2 inches (5 cm) around the periumbilical area
- Rotate injection sites at the next scheduled dose
- If the patient experiences pain, pause or slow down delivery
  - If the pain is not alleviated by pausing or slowing down the delivery rate, deliver the rest of the dose in a second injection site on the opposite side of the abdomen
- If administering with a subcutaneous infusion set, ensure the full dose is delivered through the infusion set. A 0.9% sodium chloride solution may be used to flush the remaining liquid through the line
- Discard unused portion

Administering LAZCLUZE® with RYBREVANT *FASPRO*™[4]

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

- ✓ 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®

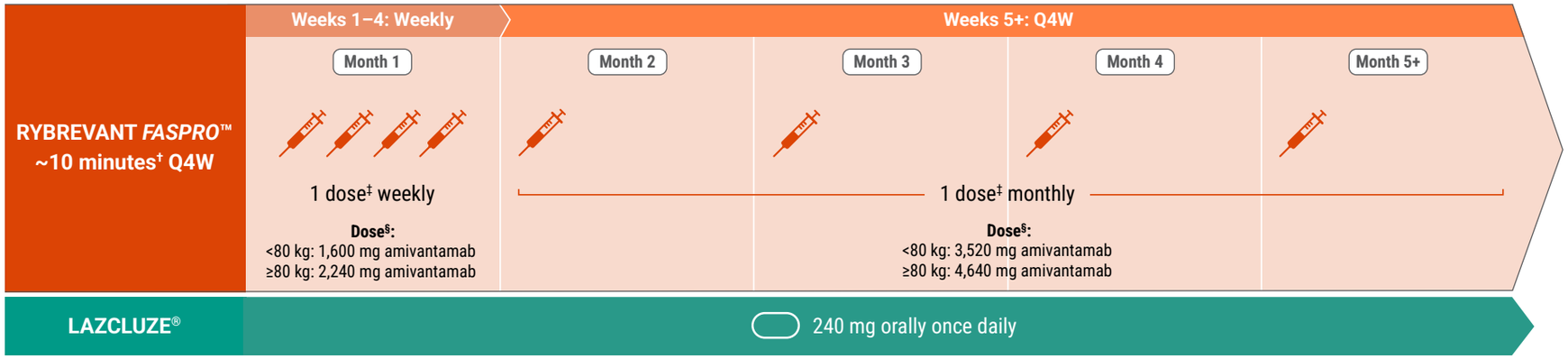
- ✗ Avoid concomitant use of LAZCLUZE® with strong and moderate CYP3A4 inducers. Consider an alternate concomitant medication with no potential to induce CYP3A4
- ✓ Monitor for adverse reactions associated with a CYP3A4 or BCRP substrate where minimal concentration changes may lead to serious adverse 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 *FASPRO*™ and LAZCLUZE®.

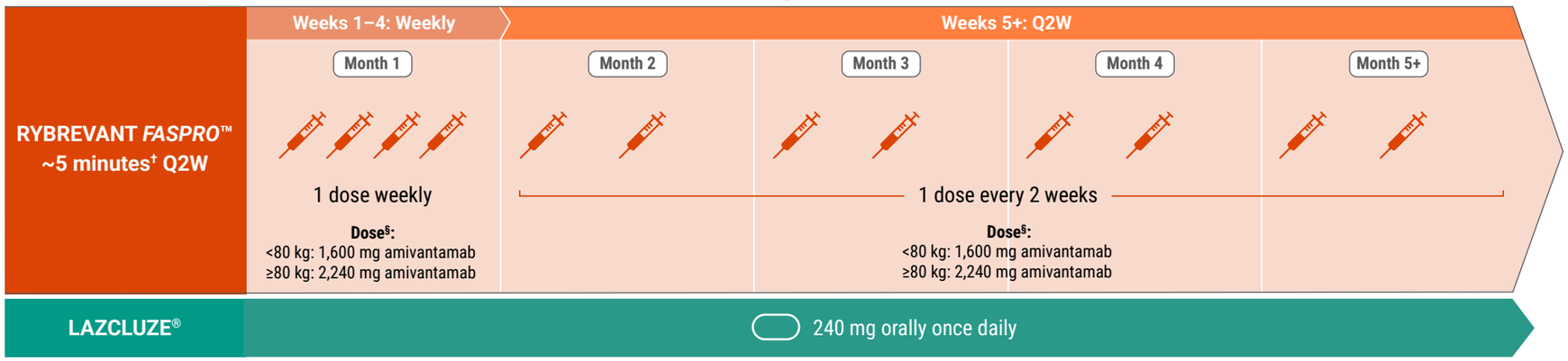
Recommended dosing schedule for RYBREVANT *FASPRO*™ + LAZCLUZE® (Q4W or Q2W)[1,4]

Q4W* dosing schedule



OR

Q2W dosing schedule



RYBREVANT *FASPRO*™

The recommended dosage of RYBREVANT *FASPRO*™ is based on baseline body weight and administered as a subcutaneous injection. Please read the full **Prescribing Information** for RYBREVANT *FASPRO*™ for units of hyaluronidase for each dose and administration guidance.[1]

Contraindications

RYBREVANT *FASPRO*™ is contraindicated in patients with known hypersensitivity to hyaluronidase or to any of its excipients.[1]

With LAZCLUZE®

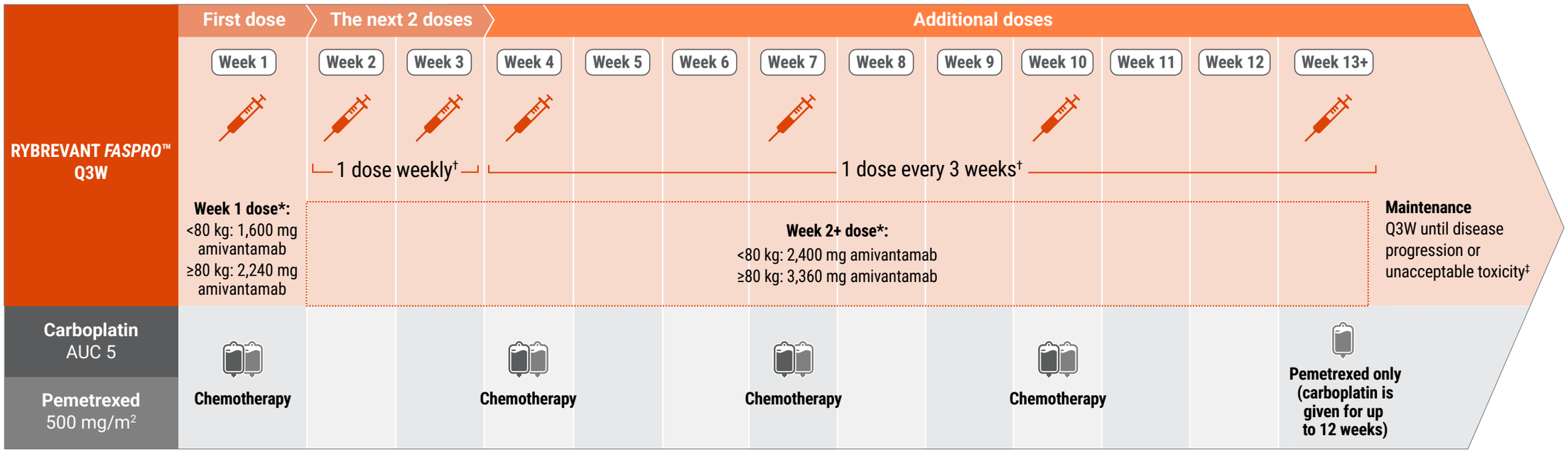
Administer RYBREVANT *FASPRO*™ any time after LAZCLUZE® when given on the same day. Refer to the full **Prescribing Information** for LAZCLUZE® for recommended LAZCLUZE® dosage and administration information.[1]

Patients currently receiving Q2W dosing (RYBREVANT® [amivantamab-vmjw] or RYBREVANT *FASPRO*™) may switch to RYBREVANT *FASPRO*™ Q4W dosing at their next scheduled dose on or after week 5

*Following weekly doses from weeks 1 to 4.[1]
†Administration time only; actual clinic time may vary.
‡Divide doses requiring greater than 15 mL into approximately equal volumes in 2 syringes. Each injection volume should not exceed 15 mL. If multiple dosing syringes are required, administer each injection consecutively in separate quadrants of the abdomen, with each injection taking ~5 minutes.[1]
§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®.

Recommended dosing schedule for RYBREVANT *FASPRO*™ + chemotherapy (Q3W)[1]



RYBREVANT *FASPRO*™

The recommended dosage of RYBREVANT *FASPRO*™ is based on baseline body weight and administered as a subcutaneous injection. Please read the full **Prescribing Information** for RYBREVANT *FASPRO*™ for units of hyaluronidase for each dose.

Contraindications

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

With chemotherapy

Administer RYBREVANT *FASPRO*™ after chemotherapy. Administer in the following order: pemetrexed, carboplatin, and then RYBREVANT *FASPRO*™. Refer to the full Prescribing Information for pemetrexed and carboplatin for the respective dosing information.

Patients currently receiving RYBREVANT® may switch to RYBREVANT *FASPRO*™

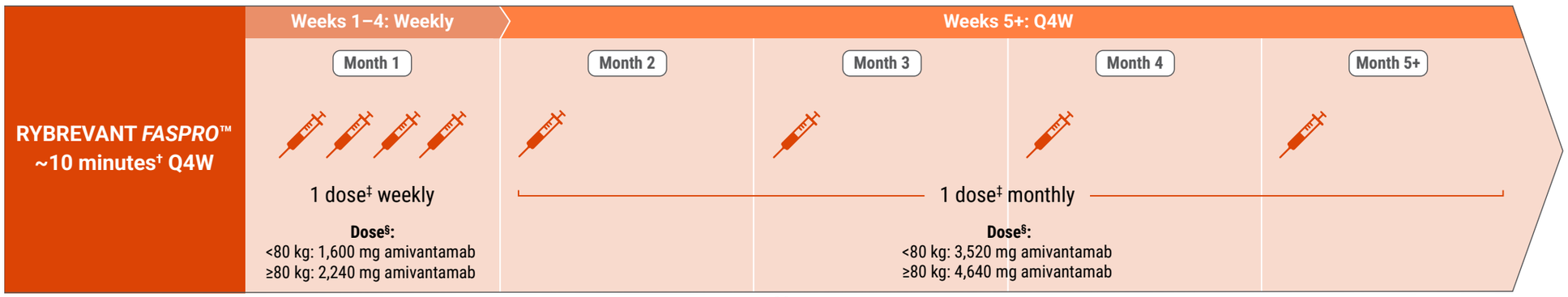
If switching from RYBREVANT® (amivantamab-vmjw) Q3W dosing to RYBREVANT *FASPRO*™ Q3W dosing, switch patients at their next scheduled dose on or after week 4

*Dose adjustments not required for subsequent body weight changes.
†Divide doses requiring greater than 15 mL into approximately equal volumes in 2 syringes and administer at separate injection sites. Each injection volume should not exceed 15 mL. Discard unused portion.
‡This refers only to RYBREVANT *FASPRO*™ and pemetrexed. Carboplatin should only be administered every 3 weeks for up to 12 weeks.
AUC, area under the curve.

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

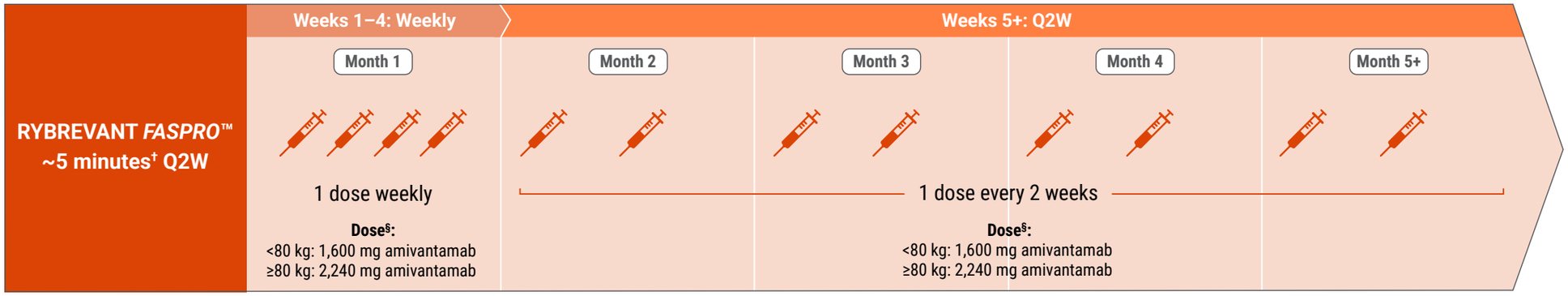
Recommended dosing schedule for RYBREVANT *FASPRO*™ as a single agent (Q4W or Q2W)[1]

Q4W* dosing schedule



OR

Q2W dosing schedule



The recommended dosage is based on baseline body weight and administered as a subcutaneous injection.
Please read the full **Prescribing Information** for RYBREVANT *FASPRO*™ for units of hyaluronidase for each dose.

Patients receiving Q2W dosing (RYBREVANT® [amivantamab-vmjw] or RYBREVANT *FASPRO*™) may switch to RYBREVANT *FASPRO*™ Q4W dosing at their next scheduled dose on or after week 5

*Following weekly doses from weeks 1 to 4.[1]
†Administration time only; actual clinic time may vary.
‡Divide doses requiring greater than 15 mL into approximately equal volumes in 2 syringes. Each injection volume should not exceed 15 mL. If multiple dosing syringes are required, administer each injection consecutively in separate quadrants of the abdomen, with each injection taking ~5 minutes.[1]
§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®.

Monitoring & managing ARs

Guide patients toward their goals with their optimal dose[1,4]

Dose modification steps to consider:

INITIATE	PAUSE	REDUCE	REEVALUATE
prophylactic strategies			

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 *FASPRO*™, treatment may be continued with LAZCLUZE®.[1,4]

Learn more about how dose modifications may help your patients stay on treatment

Monitoring & managing ARs (cont'd)

Recommended RYBREVANT *FASPRO*™ dose reductions for ARs[1]

Dose reductions for ARs			
Dose at which the AR occurred	**1st dose reduction**	**2nd dose reduction**	**3rd dose reduction**
1,600 mg amivantamab	1,050 mg amivantamab*	700 mg amivantamab†	Discontinue **RYBREVANT *FASPRO*™**
2,240 mg amivantamab	1,600 mg amivantamab‡	1,050 mg amivantamab*	
2,400 mg amivantamab	1,600 mg amivantamab‡	1,050 mg amivantamab*	
3,360 mg amivantamab	2,240 mg amivantamab§	1,600 mg amivantamab‡	
3,520 mg amivantamab	2,400 mg amivantamab‖	1,600 mg amivantamab‡	
4,640 mg amivantamab	3,360 mg amivantamab¶	2,240 mg amivantamab§	

*The dose volume should be 6.6 mL for 1,050 mg amivantamab and 13,200 units hyaluronidase.[1]
†The dose volume should be 4.4 mL for 700 mg amivantamab and 8,800 units hyaluronidase.[1]
‡The dose volume should be 10 mL for 1,600 mg amivantamab and 20,000 units hyaluronidase.[1]
§The dose volume should be 14 mL for 2,240 mg amivantamab and 28,000 units hyaluronidase.[1]
‖The dose volume should be 15 mL for 2,400 mg amivantamab and 30,000 units hyaluronidase.
¶The dose volume should be 21 mL for 3,360 mg amivantamab and 42,000 units hyaluronidase.

Please read the full Prescribing Information for RYBREVANT *FASPRO*™ for units of hyaluronidase for each dose.

Recommended LAZCLUZE® dose reductions for ARs[4]

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 *FASPRO*™ and LAZCLUZE®.

Monitoring & managing ARs (cont'd)

Adverse event severity scale[6]

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

Recommended dosage modifications and management for ARs for RYBREVANT *FASPRO*™ + LAZCLUZE®[1,4]

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

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

Table continues on next page

Severity	Dosage modifications		
Grade 2 or 3	**Withhold** Withhold **both drugs**	**Administer** Administer anticoagulant 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 *FASPRO*™** 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

*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.[6]
‡Self-care ADL refer to bathing, dressing and undressing, feeding self, using the toilet, taking medications, and not being bedridden.[6]

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

Monitoring & managing ARs (cont'd)

Recommended dosage modifications and management for ARs for RYBREVANT *FASPRO*™ + LAZCLUZE®[1,4]

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

Hypersensitivity and Administration-Related Reactions

Table continues on next page

Severity	Dosage modifications		
Grade 1 or 2	**Interrupt** Interrupt **RYBREVANT *FASPRO*™** injection if ARR is suspected and monitor patient until reaction symptoms resolve	**Resume** Resume injection upon resolution of symptoms	**Include prophylaxis** Include corticosteroid with premedications for subsequent dose of **RYBREVANT *FASPRO*™**
Grade 3	**Interrupt** Interrupt **RYBREVANT *FASPRO*™** injection and administer supportive care medications. Continuously monitor patient until reaction symptoms resolve	**Resume** Resume injection upon resolution of symptoms	**Include prophylaxis** Include corticosteroid with premedications for subsequent dose of **RYBREVANT *FASPRO*™** **Discontinue** For recurrent grade 3, discontinue **RYBREVANT *FASPRO*™** permanently
Grade 4	**Discontinue** Discontinue **RYBREVANT *FASPRO*™** permanently		

ILD/Pneumonitis

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

ILD, interstitial lung disease.

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

Monitoring & managing ARs (cont'd)

Recommended dosage modifications and management for ARs for RYBREVANT *FASPRO*™ + LAZCLUZE®[1,4]

For RYBREVANT *FASPRO*™ + LAZCLUZE®, refer to **both** the RYBREVANT *FASPRO*™ and LAZCLUZE® recommendations. For RYBREVANT *FASPRO*™ + chemotherapy or RYBREVANT *FASPRO*™ as a single agent, refer only to the RYBREVANT *FASPRO*™ 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 *FASPRO*™**	
Grade 2	**Initiate** Initiate supportive care management as clinically indicated	**Reassess** Reassess after 2 weeks; if rash does not improve, reduce **RYBREVANT *FASPRO*™** 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 *FASPRO*™** 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
Grade 4 (including severe bullous, blistering, or exfoliating skin conditions, including TEN for RYBREVANT *FASPRO*™)	**Discontinue** Discontinue **RYBREVANT *FASPRO*™** permanently	**Initiate** Initiate supportive care management as clinically indicated	**Withhold** Withhold **LAZCLUZE®** until recovery to grade ≤2 or baseline **Resume** Upon recovery to grade ≤2, resume **LAZCLUZE®** at a reduced dose at the discretion of the healthcare provider

TEN, toxic epidermal necrolysis.

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

Monitoring & managing ARs (cont'd)

Recommended dosage modifications and management for ARs for RYBREVANT *FASPRO*™ + LAZCLUZE®[1,4]

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

Other ARs

Severity	Dosage modifications		
Grade 3	**Withhold** Withhold **both drugs** until recovery to grade ≤1 or baseline	**Resume** 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** Discontinue **both drugs** permanently if recovery does not occur within 4 weeks
Grade 4	**Withhold** Withhold **both drugs** until recovery to grade ≤1 or baseline	**Resume** Resume **both drugs** at reduced dose or **LAZCLUZE®** alone if recovery occurs within 4 weeks	**Discontinue** Discontinue **both drugs** permanently if recovery does not occur within 4 weeks Discontinue **RYBREVANT *FASPRO*™** permanently for recurrent grade 4 reactions

Recommended dosage modifications for ARs for RYBREVANT *FASPRO*™ in combination with LAZCLUZE®[1]

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

Recommended dosage modifications for ARs for RYBREVANT *FASPRO*™ in combination with carboplatin and pemetrexed[1]

When administering RYBREVANT *FASPRO*™ in combination with carboplatin and pemetrexed, modify the dosage of one or more drugs. Withhold or discontinue RYBREVANT *FASPRO*™ as shown in the table on page 18. Refer to the Prescribing Information for carboplatin and pemetrexed for additional dosage modification information.

Patient counseling information[1,4]

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

Hypersensitivity and ARRs	RYBREVANT *FASPRO*™ can cause hypersensitivity and administration-related reactions, the majority of which may occur with the first injection. Advise patients to alert their healthcare provider immediately for any signs or symptoms of administration-related reactions during treatment with RYBREVANT *FASPRO*™.
ILD/pneumonitis	RYBREVANT *FASPRO*™ can cause interstitial lung disease (ILD)/pneumonitis. Advise patients to immediately contact their healthcare provider for new or worsening respiratory symptoms during treatment with RYBREVANT *FASPRO*™.
VTE events with concomitant use with LAZCLUZE®	When RYBREVANT *FASPRO*™ is used in combination with LAZCLUZE®, it can cause serious and life-threatening venous thromboembolic events (VTE), including deep venous thrombosis and pulmonary embolism. Advise patients that prophylactic anticoagulants are recommended to be used for the first four months of treatment. Advise patients to immediately contact their healthcare provider for signs and symptoms of VTE during treatment with RYBREVANT *FASPRO*™.
Dermatologic ARs	RYBREVANT *FASPRO*™ can cause dermatologic adverse reactions. 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	RYBREVANT *FASPRO*™ 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	RYBREVANT *FASPRO*™ can cause paronychia. Advise patients to contact their healthcare provider for signs or symptoms of paronychia.
Embryo-fetal toxicity	Advise females of reproductive potential of the potential risk to a fetus, to use effective contraception during treatment with RYBREVANT *FASPRO*™ and for 3 months after the last dose, and to inform their healthcare provider of a known or suspected pregnancy.
Lactation	Advise women not to breastfeed during treatment with RYBREVANT *FASPRO*™ and for 3 months after the last dose.
Infertility	Advise males and females of reproductive potential of the potential risk for impaired fertility with LAZCLUZE®.

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

References

1. RYBREVANT *FASPRO*™ [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc. **2.** Leighl NB, Akamatsu H, Lim SM, et al; PALOMA-3 Investigators. Subcutaneous versus intravenous amivantamab, both in combination with lazertinib, in refractory epidermal growth factor receptor-mutated non-small cell lung cancer: primary results from the phase III PALOMA-3 study. *J Clin Oncol.* 2024;42(30):3593-3605. doi:10.1200/JCO.24.01001 **3.** 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 **4.** LAZCLUZE® [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc. **5.** RYBREVANT® [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc. **6.** 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).

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

Important Safety Information (cont'd)

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 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.

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

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).

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

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*™, RYBREVANT® (amivantamab-vmjw), 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.

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

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 gamma-glutamyl 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).

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*™, RYBREVANT® (amivantamab-vmjw), 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 see full Prescribing Information for RYBREVANT *FASPRO*™, RYBREVANT® (amivantamab-vmjw), and LAZCLUZE®.

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