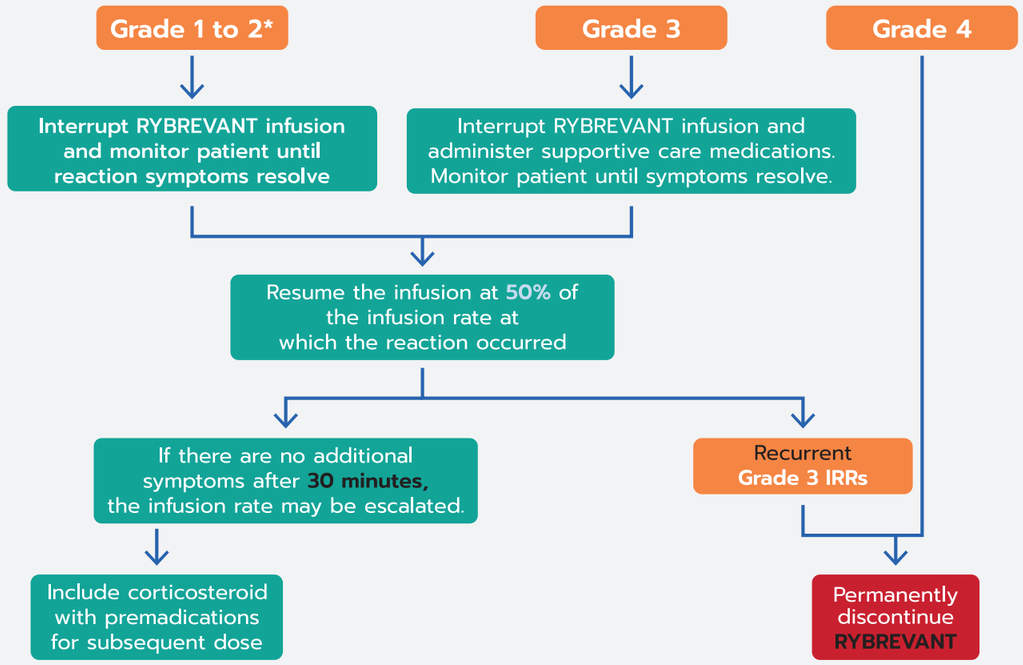
IRRs Management guideline

Stop infusion, if IRRs are suspected and notify doctors immediately.



*Include corticosteroid with pre-medications for subsequent dose

Warnings and Precautions[1]

Dermatologic Adverse Reactions:
RYBREVANT can cause rash (including dermatitis acneiform), pruritus and dry skin. Withhold, dose reduce or permanently discontinue RYBREVANT based on severity.

Advise patients of the risk of dermatologic adverse reactions. Advise patients to limit direct sun exposure, to use broad spectrum UVA/UVB sunscreen, and to wear protective clothing during treatment with RYBREVANT. Advise patients to apply alcohol free emollient cream to dry skin.

Interstitial Lung Disease (ILD)/Pneumonitis:
Monitor for new or worsening symptoms indicative of ILD. Immediately withhold RYBREVANT in patients with suspected ILD/pneumonitis and permanently discontinue if ILD/pneumonitis is confirmed.

Advise patients to immediately contact their healthcare provider for new or worsening respiratory symptoms.

Ocular Toxicity:
RYBREVANT can cause ocular toxicity including keratitis, dry eye symptoms, conjunctival redness, blurred vision, visual impairment, ocular itching, and uveitis. Promptly refer patients presenting with eye symptoms to an ophthalmologist. Withhold, dose reduce or permanently discontinue RYBREVANT based on severity

Advise patients to contact their ophthalmologist if they develop eye symptoms and advise discontinuation of contact lenses until symptoms are evaluated.

Embryo-Fetal Toxicity:
Based on its mechanism of action and findings from animal models, RYBREVANT can cause fetal harm when administered to a pregnant woman. Administration of other EGFR inhibitor molecules to pregnant animals has resulted in an increased incidence of impairment of embryo-fetal development, embryo lethality, and abortion.

Advise 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 final dose, and to inform their healthcare provider of a known or suspected pregnancy.

RYBREVANT®

Drug administration and managements

Amivantamab injection
for patients with
advanced NSCLC with EGFR exon20 insertion mutation,
whose disease has progressed on or after platinum-based chemotherapy

Johnson&Johnson

RYBREVANT™
(amivantamab) Injection

Indication[1]

RYBREVANT as monotherapy is indicated for treatment of adult patients with locally advanced or metastatic **NSCLC** with activating **EGFR** exon 20 insertion mutations, whose disease has progressed on or after platinum-based chemotherapy.

Mechanism of action[1,2]

Amivantamab, a fully human bispecific antibody targeting EGFR and MET, employs 3 distinct potential mechanisms of action (MOAs) including ligand blocking, receptor degradation, and immune cell-directing activity

Dosing and Preparing for Administration[1]

- One **7 mL vial** contains **350 mg** of amivantamab.
- Check that the RYBREVANT solution is **colorless to pale yellow**. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. **Do not use if discoloration or visible particles are present.**
- Determine the **dose required** and the **number of vials** needed, based on patient's baseline weight.
- Withdraw and discard a volume of either **5% glucose solution** or **0.9% sodium chloride solution** for injection from the **250 mL** infusion bag that is equal to the required volume of RYBREVANT solution to be added.
  Infusion bags must be made of PVC, PP, PE or PP+PE
- Withdraw **7 mL** of RYBREVANT from each vial and add to the infusion bag. The final volume in the infusion bag should be **250 mL**. Discard any unused portion left in the vial.
- Gently invert the bag to mix the solution. **Do not shake.**

<10h

After dilution, the solutions should be administered ***within 10 hours*** *(including infusion time) at room temperature (15–25°C) and in room light.*

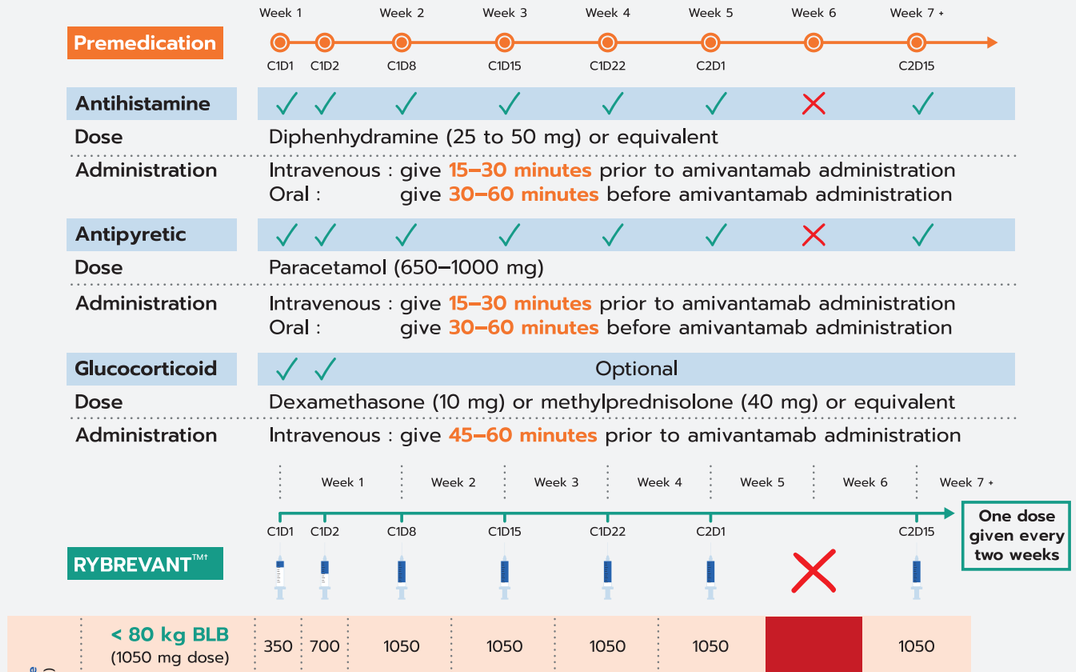
Administer the diluted solution by IV infusion using an ***infusion set*** fitted with a flow regulator and with an in-line, sterile, non-pyrogenic, low protein-binding ***PES filter*** *(pore size 0.22 or 0.2 micrometer).*

RYBREVANT sets must be made of either PU, PBD, PVC, PP, or PE.

Do not infuse RYBREVANT concomitantly in the same IV line with other agents.

1. Rybrevant (amivantamab) [Package Insert]. Available at: http://ndi.fda.moph.go.th/. Last updated November 2022. 2. Cho, Byoung Chul, et al. Clinical lung cancer 24.2 (2023): 89-97. 3. Dougherty, Lindsay, et al. ONS 47th Annual Congress. ONS, 2022.

Dosing schedule of Premedication and RYBREVANT[1]



† One 7 mL vial contains 350 mg of amivantamab.
* Initial infusion rate is increased to the subsequent infusion rate after 2 hours in the absence of IRRs.

RYBREVANT Dose Modifications[1]

Body Weight at Baseline	Initial Dose	1st Dose Reduction	2nd Dose Reduction	3rd Dose Reduction
<80 kg	1050 mg	700 mg	350 mg	Discontinue RYBREVANT
≥80 kg	1400 mg	1050 mg	700 mg	