Patient leaflet in accordance with the Pharmacists' Regulations (Preparations) - 1986
This medicine is dispensed with a doctor's prescription only

Rybrevant® 160 mg/ml S.C.
Solution for injection

Active ingredient and its concentration
1 ml of solution contains 160 mg of amivantamab.
1 vial of 10 ml contains 1600 mg of amivantamab.
1 vial of 14 ml contains 2240 mg of amivantamab.

Inactive ingredients and allergens in this medicine: see section 2 under 'Important information about some of this medicine's ingredients', and section 6 'Additional information'.
Read the entire leaflet carefully before you start using this medicine. This leaflet contains concise information about this medicine. If you have any further questions, consult your doctor or pharmacist.
This medicine has been prescribed to treat your illness. Do not pass it on to others. It may harm them, even if it seems to you that their illness is similar to yours.

1. What is this medicine intended for?
- Rybrevant 160 mg/ml S.C. is indicated for the treatment of adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) exon 20 insertion mutation, as detected by an approved test, whose disease has progressed on or after platinum based chemotherapy.
- Rybrevant 160 mg/ml S.C., in combination with lazertinib, is indicated for the first-line treatment of adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 L858R substitution mutations, as detected by an approved test.

Therapeutic group: Anti-cancer medicines of the class of monoclonal antibodies and antibody-drug conjugates.

Rybrevant 160 mg/ml S.C. is a cancer medicine. It contains the active substance amivantamab, which is an antibody (type of protein) designed to recognise and attach to specific target proteins in the body.
The active substance in Rybrevant 160 mg/ml S.C., amivantamab, targets two proteins found on cancer cells:
- epidermal growth factor receptor (EGFR)
- mesenchymal-epithelial transition factor (MET).

This medicine works by attaching to these proteins. This may help to slow or stop your lung cancer from growing. It may also help to reduce the size of the tumour.

2. Before using this medicine
Do not use this medicine if:

You are sensitive (allergic) to the active ingredient (amivantamab) or to any of the other ingredients in this medicine. For the list of the other ingredients, see section 6 'Additional information'.

Special warnings about using this medicine
Before treatment with Rybrevant 160 mg/ml S.C., tell your doctor if:
- You have suffered from inflammation of your lungs (interstitial lung disease or inflammation of the lung tissue (pneumonitis)).

Tell your doctor or nurse straight away while using this medicine if you experience any of the following side effects (see section 4 'Side effects' for more information):

- Any side effect while the medicine is injected.
- Sudden difficulty in breathing, cough, or fever that may suggest inflammation of the lungs. The condition may be life-threatening; therefore, healthcare professionals will monitor you for potential symptoms.
- When used with another drug containing lazertinib, life-threatening side effects (due to blood clots in the veins) may occur. Your doctor will give you additional medicine to help prevent blood clots during the course of your treatment and will monitor you for potential symptoms.
- Skin and nail problems. To reduce the risk of skin problems, avoid sun exposure, wear protective clothing, apply sunscreen, and use moisturisers regularly on your skin and nails while taking this medicine. You will need to continue doing this for 2 months after you stop treatment. Your doctor may recommend that you start treatment with a medicine(s) to prevent skin problems, may treat you with a medicine(s), or refer you to a skin specialist (dermatologist) if you get skin reactions during treatment.
- Eye problems. If you have vision problems or eye pain, contact your doctor or nurse straight away. If you use contact lenses and experience any new eye symptoms, stop using contact lenses and tell your doctor straight away.

Children and adolescents
There is no information about the safety and efficacy of using this medicine in children and adolescents below 18 years of age. Do not give this medicine to children or adolescents below 18 years of age.

Interactions with other medicines
If you are taking or have recently taken other medicines, including nonprescription medicines and dietary supplements, tell your doctor or pharmacist.

Pregnancy, breastfeeding, and fertility
Pregnancy
Before using this medicine, tell your doctor if you are pregnant, may be pregnant, or are planning to become pregnant. Rybrevant 160 mg/ml S.C. may harm the foetus. No data are available regarding the use of Rybrevant 160 mg/ml S.C. in pregnant women for evaluation of its effect during pregnancy.

Women who are able to become pregnant:

- Your doctor will refer you for a pregnancy test before you start treatment with Rybrevant 160 mg/ml S.C.
- You should use effective birth control during treatment and for 3 months after your last dose of Rybrevant 160 mg/ml S.C.
- Tell your doctor right away if you become pregnant or think you might be pregnant during treatment with Rybrevant 160 mg/ml S.C.

Breastfeeding
Tell your doctor if you are breastfeeding or plan to breastfeed. It is not known if Rybrevant 160 mg/ml S.C. passes into your breast milk, if it affects the breastfed baby or milk production.
Due to the potential of severe side effects of Rybrevant 160 mg/ml S.C. in breastfed babies, you should not breastfeed during treatment and for 3 months after your last dose of Rybrevant 160 mg/ml S.C.

Driving and using machines
Rybrevant 160 mg/ml S.C. may have a moderate influence on the ability to drive and operate machines (e.g.: dizziness, fatigue, visual impairment). If you experience treatment-related symptoms, including vision-related side effects, which may affect your ability to concentrate and react, it is recommended to refrain from driving or operating machines until the effect subsides.

Important information about some of this medicine's ingredients
Rybrevant 160 mg/ml S.C. contains sodium:
This medicine contains less than 23 mg sodium per dose, that is to say essentially 'sodium-free'.
Rybrevant 160 mg/ml S.C. contains polysorbate:
This medicine contains 0.6 mg of polysorbate 80 in each ml, which is equivalent to 6 mg per 10 ml vial, or 8.4 mg per 14 ml vial.
Polysorbates may cause allergic reactions. Tell your doctor if you have any known allergies.

3. How to use this medicine?
Always use this medicine according to your doctor's instructions. Check with your doctor or pharmacist if you are not sure about your dose or about how to take this medicine.
Only your doctor will determine your dose, dose regimen and manner of treatment with Rybrevant 160 mg/ml S.C.

The dose of this medicine will depend on your body weight at the start of your therapy.
The recommended dose is usually 1600 mg for patients weighing less than 80 kg and 2240 mg for patients weighing 80 kg or above.
Once a week for the first 4 weeks.
Once every 2 weeks starting at week 5, for as long as you keep getting benefit from the treatment.
Do not exceed the recommended dose.

How the medicine is given
- Rybrevant 160 mg/ml S.C. is given by a doctor or nurse as an injection under your skin (subcutaneous injection) over approximately 5 minutes.
- It is given in the stomach area (abdomen), not in other sites of the body, and not into areas of the abdomen where the skin is red, bruised, tender, hard or where there are tattoos or scars.
- If you experience pain during the injection, the doctor or nurse will interrupt the injection and inject the remaining medicine in another area of your abdomen.

Medicines given during treatment with Rybrevant 160 mg/ml S.C.
Before each injection of Rybrevant 160 mg/ml S.C., you will be given medicines which help lower the chance of administration-related reactions.
These medicines may include:
- medicines for an allergic reaction (antihistamines)
- anti-inflammatory medicines (corticosteroids)
- medicines for fever (such as paracetamol)

You may also be given additional medicines based on any symptoms you may experience.

If you have accidentally taken a higher dose
This medicine will be given to you by your doctor or nurse. In the unlikely event that you are given too much (an overdose), your doctor will check you for side effects.

If you forget your appointment to receive Rybrevant 160 mg/ml S.C.
It is very important to go to all your scheduled appointments. If you miss an appointment, contact your healthcare team as soon as possible to schedule a new appointment.
Adhere to the treatment as recommended by your doctor.
Even if your health improves, do not stop treatment with this medicine without consulting your doctor.

Do not take medicines in the dark! Check the label and dose <u>every time</u> you take medicine. Wear glasses if you need them.
If you have any further questions about using this medicine, consult your doctor, pharmacist or nurse.

4. Side effects
As with any medicine, using Rybrevant 160 mg/ml S.C. may cause side effects in some users. Do not be alarmed by this list of side effects; you may not experience any of them.

Serious side effects (see also section 2 under 'Special warnings about using this medicine')
Tell your doctor or nurse straight away if you notice the following serious side effects:

Very common side effects – may affect more than one in ten users:
- Signs of a reaction to the injection - such as chills, feeling short of breath, feeling sick (nausea), flushing, chest discomfort, and fever. These effects may happen especially with the first dose injection. Your doctor may give you other medicines, or the injection may need to be stopped.
- Skin problems - such as rash (including acne), infected skin around the nails, dry skin, itching, pain, and redness. Tell your doctor if your skin or nail problems get worse.
- When given together with lazertinib, a blood clot in the veins, especially in the lungs or legs, may occur. Signs may include sharp chest pain, shortness of breath, rapid breathing, leg pain, and swelling of your arms or legs.
- Eye problems - such as dry eye, swollen eyelid, and itchy eyes.

Common side effects – may affect up to one in ten users:
- Signs of an inflammation in the lungs - such as sudden difficulty in breathing, cough, or fever. This effect could lead to permanent damage (interstitial lung disease). Your doctor may wish to stop treatment with Rybrevant 160 mg/ml S.C. if you get this side effect.
- Eye problems - such as problems with vision and growth of eyelashes.
- Inflamed cornea (front part of the eye).

<u>The following side effects have been reported in clinical studies with Rybrevant when given alone as an infusion into a vein:</u>

<u>Additional side effects</u>
Tell your doctor if you notice any of the following side effects:

Very common side effects – may affect more than one in ten users:
- low level of the protein albumin in the blood
- swelling caused by fluid build up in the body
- feeling very tired
- sores in the mouth
- nausea
- vomiting
- constipation or diarrhoea
- decreased appetite
- increased levels of the liver enzymes alanine aminotransferase and aspartate aminotransferase in the blood
- feeling dizzy
- increased level of the enzyme alkaline phosphatase in the blood
- muscle aches
- fever
- low level of calcium in the blood

Common side effects – may affect up to one in ten users:
- stomach pain
- low level of potassium in the blood
- low level of magnesium in the blood
- haemorrhoids

Uncommon side effects – may affect up to one in 100 users:
- ulcers (sores) on the skin

The following side effects have been reported in clinical studies with Rybrevant (either as an infusion into a vein or as an injection under the skin) in combination with lazertinib:

Additional side effects
Tell your doctor if you notice any of the following side effects:

Very common side effects – may affect more than one in ten users:
- low level of the protein albumin in the blood
- sores in the mouth
- liver toxicity
- swelling caused by fluid build up in the body
- feeling very tired
- unusual feeling in the skin (such as tingling or a crawling feeling)
- constipation
- diarrhoea
- decreased appetite
- nausea
- low level of calcium in the blood
- vomiting
- muscle aches
- low level of potassium in the blood
- muscle spasms
- feeling dizzy
- fever
- stomach pain

Common side effects – may affect up to one in ten users:
- haemorrhoids
- irritation or pain at the injection site
- low level of magnesium in the blood
- redness, swelling, peeling or tenderness, mainly on the hands or feet (palmar-plantar erythrodysaesthesia syndrome)
- itchy rash (hives)
- ulcers (sores) on the skin.

If you experience any side effect, if any side effect gets worse, or if you experience a side effect not mentioned in this leaflet, consult your doctor.

You can report side effects to the Ministry of Health by following the 'Reporting Side Effects of Drug Treatment' link on the Ministry of Health home page (www.health.gov.il), which opens an online form for reporting side effects, or you can also use this link: https://sideeffects.health.gov.il

5. How to store the medicine?
- Prevent poisoning! To prevent poisoning, keep this and all other medicines in a closed place, out of the reach and sight of children and/or infants. Do not induce vomiting unless explicitly instructed to do so by your doctor.
- Do not use the medicine after the expiry date (exp. date) which is stated on the package. The expiry date refers to the last day of that month.
- **Storage conditions**
  Store the medicine in a refrigerator at 2-8°C. Do not freeze.

Store the medicine in the original package in order to protect from light.
Chemical and physical in-use stability of the prepared syringe has been demonstrated up to 24 hours at 2-8°C followed by up to 24 hours at 15-30°C. From a microbiological point of view, unless the method of dose preparation excludes the risk of microbial contamination, the product should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user.

6. Additional information

In addition to the active ingredient, this medicine also contains:
recombinant human hyaluronidase (rHuPH20), sucrose, sodium acetate trihydrate, L-methionine, polysorbate 80, glacial acetic acid, EDTA disodium salt dihydrate and water for injection.

What the medicine looks like and contents of the pack:

- Colourless to pale yellow liquid, intended for subcutaneous injection.
- Pack size: 1 glass vial of 10 ml or 1 glass vial of 14 ml in a carton pack.

Manufacturer's name and address: Janssen Cilag International NV, Turnhoutseweg 30, Beerse, 2340, Belgium.

Registration holder's name and address: J-C Health Care Ltd., Kibbutz Shefayim 6099000, Israel.

Registration number of the medicine in the Ministry of Health National Drug Registry:
181-91-38501-00

Revised in June 2026.

The following information is intended for healthcare professionals only:

Rybrevant 160 mg/ml S.C. should be administered by a healthcare professional.

To prevent medication errors, it is important to check the vial labels to ensure that the appropriate formulation (intravenous or subcutaneous formulation) and dose is being given to the patient as prescribed. Rybrevant 160 mg/ml S.C. should be given by subcutaneous injection only, using the dose specified. Rybrevant 160 mg/ml S.C. is not intended for intravenous administration.

This medicinal product must not be mixed with other medicinal products except those mentioned below.
Prepare the solution for subcutaneous injection using aseptic technique as follows:

Preparation

- Determine the dose required and the appropriate Rybrevant 160 mg/ml S.C. vial needed based on patient's baseline weight.
- Patients < 80kg receive 1600 mg and patients ≥ 80 kg receive 2240 mg weekly from Weeks 1 to 4 and then every 2 weeks starting at Week 5 onward.
- Remove the appropriate Rybrevant 160 mg/ml S.C. vial from refrigerated storage (2°C to 8°C).

- Check that the solution is colourless to pale yellow. Do not use if opaque particles, discolouration or other foreign particles are present.
- Equilibrate Rybrevant 160 mg/ml S.C. to room temperature (15°C to 30°C) for at least 15 minutes. Do not warm Rybrevant 160 mg/ml S.C. in any other way. Do not shake.
- Withdraw the required injection volume of Rybrevant 160 mg/ml S.C. from the vial into an appropriately sized syringe using a transfer needle. Smaller syringes require less force during preparation and administration.
- Rybrevant 160 mg/ml S.C. is compatible with stainless steel injection needles, polypropolene and polycarbonate syringes, and polyethylene, polyurethan, and polyvinylchloride subcutaneous infusion sets. A sodium chloride 9 mg/mL (0.9%) solution may also be used to flush an infusion set if needed.
- Replace the transfer needle with the appropriate ancillaries for transport or administration. Use of a 21G to 23G needle or infusion set is recommended to ensure ease of administration.

Storage of prepared syringe

The prepared syringe should be administered immediately. If immediate administration is not possible, store the prepared syringe refrigerated at 2°C to 8°C for up to 24 hours followed by at room temperature of 15°C to 30°C for up to 24 hours. The prepared syringe should be discarded 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.

Traceability

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

Disposal

This medicinal product is for single use only. Any unused medicinal product or waste material should be disposed of in accordance with local requirements.