PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) – 1986

The medicine is dispensed with a doctor's prescription only

Joenja

Tablets

Active ingredient and its quantity:
Leniolisib (as phosphate) 70 mg.

Inactive ingredients and allergens in the product: see section 2 "Before using the medicine" and section 6 "Further information".

Read this leaflet carefully in its entirety before using the medicine. This leaflet contains concise information about the medicine. If you have further questions, refer to the doctor or pharmacist.

This medicine has been prescribed to treat your ailment. Do not pass it on to others. It may harm them, even if it seems to you that their medical condition is similar.

1. WHAT IS THE MEDICINE INTENDED FOR?

Joenja is indicated for the treatment of activated phosphoinositide 3-kinase delta syndrome (APDS) in adults and adolescents 12 years of age and older and weighing 45 kg or more.

Therapeutic group: other immunostimulants (medicines that increase the ability of the immune system, the body's natural defences, to fight infections and diseases). In people with APDS, the immune system does not work properly, leaving them unable to fight infections. The active substance in Joenja, leniolisib, blocks the activation of a protein known as phosphoinositide 3-kinase delta (PI3Kδ), which is involved in the regulation of the immune system. In people with APDS, there is excessive activity of PI3Kδ. By blocking the excessive activity of PI3Kδ, leniolisib helps to normalize the immune system, thereby potentially slowing the progression of the disease.

2. BEFORE USING THE MEDICINE

Do not use the medicine if:

- you are sensitive (allergic) to leniolisib or any of the other ingredients of this medicine (listed in section 6)

Before using Joenja inform the doctor if:

- **You suffer from liver problems.** The use of Joenja in patients with moderate to severe hepatic impairment is not recommended.

Additional warning:

Special warnings before using the medicine

- Use in pregnancy - Embryo-Fetal Toxicity: Joenja may cause harm to the fetus. Consult your doctor about the use of effective contraception due to the potential risk to the fetus. Your doctor will conduct a test to determine if you are pregnant before initiating treatment. For additional information see section "Pregnancy, breast-feeding and fertility" later in this section.
- Vaccinations: live, attenuated vaccinations may be less effective if administered during Joenja treatment. Consult a doctor before receiving a vaccination.
- Risk of hypersensitivity reactions, including anaphylaxis: serious allergic reactions including itching, skin redness, hives, rash, difficulty breathing or swallowing have been reported. If hypersensitivity reactions occur, discontinue Joenja and seek immediate medical attention.

Children and adolescents:

- Do not give Joenja to children under 12 years of age and/or weighing under 45 kg, as the safety and efficacy have not been established and the product is not intended for this population.

Geriatric use:

- Because clinical studies of Joenja did not include any patients 65 years of age and older, it cannot be determined whether they respond differently from younger adult patients.

Drug interactions

If you are taking, or have recently taken other medicines including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist. Especially if you are taking:

Products that may affect how Joenja works; avoid concomitant use:

- Strong inhibitors of CYP3A4 liver enzymes; these medicines may increase the risk of side effects with Joenja by increasing the levels of Joenja in the blood, e.g., itraconazole, used to treat fungal infections.
- Moderate inhibitors of CYP3A4 liver enzymes, e.g., erythromycin (a type of antibiotics).
- Strong or moderate inducers of CYP3A4 liver enzymes; these medicines may reduce the effectiveness of Joenja by lowering its levels in the blood, e.g., efavirenz, used to treat HIV (human immunodeficiency virus) infection, rifampin, for bacterial infections.

Also, tell your doctor or pharmacist if you are taking any of the following medicines, as Joenja may affect their action; avoid concomitant use:

- BCRP, OATP1B1 and OATP1B3 substrates; Joenja may increase the risk of side effects by increasing the levels of these medicines in the blood, e.g., rosuvastatin, used to lower the cholesterol levels.

Use of the medicine and food

This medicine can be taken with or without food.

Pregnancy, breast-feeding and fertility

- **Pregnancy**
  - Joenja is not recommended for use during pregnancy. Joenja may cause harm to the fetus.
  - For women who could become pregnant, Joenja is not recommended if not using highly effective methods of contraception during treatment. Continue contraception for at least 1 week after the last dose of Joenja. Ask your doctor about suitable methods of contraception.
  - If you are pregnant or think you may be pregnant before starting treatment with Joenja or during the treatment, tell your doctor immediately.
- **Breast-feeding**

  Do not breast-feed during treatment with Joenja and up to a week after taking the last dose. If you are breast-feeding or are planning to breast-feed, inform your doctor before taking the medicine. It is unknown whether Joenja can pass into breast milk or if it could affect your baby or milk production.
- **Fertility**

  No human data on the effect of Joenja on fertility are available. Animal studies suggest a possible risk of Joenja affecting male fertility. Inform your doctor before taking the medicine.

Driving and using machines:

This medicine has no or negligible influence on your ability to drive or use machines.

Important information about some of the ingredients of the medicine

Joenja contains lactose

If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking the medicine.

Joenja contains sodium

This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium-free'.

3. HOW SHOULD YOU USE THE MEDICINE?

Always take this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are unsure about the dosage and treatment regimen. The dosage and treatment regimen will be determined by the doctor only.

The usual dosage is generally: 1 tablet twice daily, approximately 12 hours apart in adult and adolescent patients, from 12 years or older weighing more than 45 kg.

This medicine can be taken with or without food.

Do not exceed the recommended dose.

If you vomit within an hour after taking the tablet, take another tablet right away. If you vomit more than an hour after taking the tablet, wait and take the next dose, as usual, at the scheduled time.

Form of administration - Swallow the tablet.

There is no data regarding splitting, crushing, or chewing the tablets.

If you have accidentally taken a higher dose or if a child has accidentally swallowed the medicine, immediately proceed to a doctor or a hospital emergency room and bring the package of this medicine with you.

If you forget to take the medicine

If you forget to take a dose, take it as soon as you remember, but if more than 6 hours have passed from the time you were supposed to take the medicine, do not take another tablet, wait and take the next dose at your usual scheduled time.

Adhere to the treatment as recommended by the doctor.

Even if your health improves, do not stop taking the medicine without consulting the doctor.

If you stop taking the medicine

Do not stop taking the medicine unless your doctor tells you to.

If you have any further questions about the use of this medicine, contact your doctor or pharmacist.

Do not take medicines in the dark! Check the label and the dose each time you take a medicine. Wear glasses if you need them.

If you have further questions regarding the use of the medicine, consult a doctor or pharmacist.

4. SIDE EFFECTS

As with any medicine, the use of Joenja may cause side effects in some users. Do not be alarmed when reading the list of side effects. You may not experience any of them.

Very common side effects - effects that occur in more than 1 in 10 users:

headache, sinusitis, atopic dermatitis (including eczema), increased weight, decrease in levels of neutrophils – a type of white blood cell (neutropenia).

Common side effects - effects that occur in 1-10 out of 100 users:

accelerated heartbeat (tachycardia, including sinus tachycardia), diarrhea, fatigue, fever (pyrexia), back pain, neck pain, hair loss (alopecia).

Side effects with unknown frequency (the frequency has not yet been determined):

allergic reaction (hypersensitivity) including itching, skin redness, hives, rash, difficulty breathing or swallowing.

If a side effect occurs, if one of the side effects worsens or if you suffer from a side effect not mentioned in the leaflet, consult with the doctor.

Reporting of side effects

Side effects can be reported to the Ministry of Health by clicking on the link "Report Side Effects of Drug Treatment", found on the Ministry of Health homepage (www.health.gov.il) that directs you to the online form, or by entering the link:
https://sideeffects.health.gov.il

Additionally, you may report to Kamada Ltd. by email: pharmacovigilance@kamada.com

5. HOW SHOULD THE MEDICINE BE STORED?

Avoid poisoning! This medicine and any other medicine must be kept in a closed place out of the reach and sight of children and/or infants, to avoid poisoning. Do not induce vomiting without explicit instruction from the doctor.

Do not use the medicine after the expiry date (exp. date) that appears on the package. The expiry date refers to the last day of that month.

Store up to 25°C. Do not refrigerate.

Store in the original container.

Shelf life after first opening – until the expiry date, at temperature up to 25°C.

Do not dispose of medicines via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer used. These measures will help protect the environment.

6. FURTHER INFORMATION

In addition to the active ingredient, the medicine also contains:

Lactose monohydrate, microcrystalline cellulose, sodium starch glycolate (Type A), hydroxypropyl methylcellulose, magnesium stearate, colloidal silicon dioxide.

The coating (Opadry® 00F220015 yellow) ingredients are:

Hypromellose/hydroxypropyl methylcellulose (HPMC 2910), titanium dioxide (E171), talc, macrogol/polyethylene glycol, iron oxide yellow (E172) and iron oxide red (E172).

What the medicine looks like and the contents of the pack

Joenja is a yellow, oval-shaped, biconvex, bevelled edge film-coated tablet debossed with "70" on one side and "LNB" on the other side.

Each pack contains 1 white polyethylene bottle with 60 tablets.

Marketing Authorisation Holder

Kamada Ltd., Beit Kama, MP Negev, 8532500

Manufacturer

Pharming Technologies B.V., Leiden, The Netherlands

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Registration number of the medicine in the National Drug Registry of the Ministry of Health:

176-19-37785-99