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

The medicine is dispensed with a doctor's prescription only

REKAMBYS®

Prolonged-release suspension for injection

Active ingredient:
Each 1 ml suspension for injection contains:
rilpivirine 300 mg
The 2 ml Rekambys vial contains rilpivirine 600 mg.
The 3 ml Rekambys vial contains rilpivirine 900 mg.

Inactive and allergenic ingredients in the preparation: see chapter 2 section "Important information about some of the ingredients in the medicine" and chapter 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 ailment is similar.

1. WHAT IS THE MEDICINE INTENDED FOR?

Rekambys is indicated for the treatment of human immunodeficiency virus type 1 (HIV-1) infection in adults. Rekambys is always given together with another HIV-1 medicine called cabotegravir. The two medicines are used together in adults from the age of 18 years and over, whose HIV-1 infection is already under control.

Therapeutic group: Rekambys belongs to a group of medicines called non-nucleoside reverse transcriptase inhibitors (NNRTIs), which are used to treat human immunodeficiency virus type 1 (HIV-1) infection.
Rekambys is indicated together with cabotegravir injection to treat HIV-1 infection in adults whose HIV-1 infection is under control with antiretroviral therapy, with no evidence of resistance to, or treatment failure with medicines of the NNRI and INI group.

2. BEFORE USING THE MEDICINE

Do not use the medicine if:

- you are sensitive (allergic) to rilpivirine or to any of the additional ingredients contained in the medicine (see chapter 6).
- you are taking one of the following medicines, since they may affect the way Rekambys works or the way other medicines work:
  - carbamazepine, oxcarbazepine, phenobarbital, phenytoin (medicines to treat epilepsy and prevent seizures).
  - rifabutin, rifampicin, rifapentine (medicines to treat certain bacterial infections, such as tuberculosis).
  - dexamethasone (a corticosteroid used for a variety of medical conditions, such as inflammation and allergic reactions), administered orally or by injection.
  - preparations containing St. John's wort (*Hypericum perforatum*, a herbal preparation to treat depression).

If you are taking any of the listed medicines, ask the doctor about alternatives.

Special warnings regarding use of the medicine
Speak to the doctor or pharmacist before using Rekambys.
Rekambys does not cure HIV infection. It is part of a treatment to reduce the amount of virus in the blood.

Before treatment with Rekambys, tell the doctor if any of these conditions apply to you:

- You must attend all appointments scheduled for you to receive injections; do not skip any appointments. This is very important for the success of the treatment. If you cannot attend a scheduled appointment, inform the doctor as soon as possible.
- Tell the doctor if you have had **liver problems**, including hepatitis B or hepatitis C, or **kidney problems** in the past. The doctor may check how well your liver and kidneys work to decide whether you can use Rekambys. See signs of liver damage under “Uncommon side effects” in chapter 4 of this leaflet.
- Inform the doctor immediately if you notice any **symptoms of infection** (e.g., fever, chills, sweating). In some patients with HIV, inflammation from previous infections may develop soon after starting HIV treatment. It is believed that these symptoms are caused by the improved immune response of the body, which enables the body to fight infections that were already present but did not cause any noticeable symptoms.
- Also tell the doctor immediately if you notice symptoms such as muscle weakness, weakness that starts in the palms of the hands and soles of the feet and moves up toward the trunk of the body, noticeable heart pounding, tremor or hyperactivity. This is because autoimmune disorders (conditions in which the immune system mistakenly attacks healthy body tissue) may also occur after starting to take medicines to treat HIV infection. Autoimmune disorders may develop many months after starting treatment.
- Tell the doctor if you are taking medicines that you have been told may cause life-threatening irregular heart rate (torsade de pointes).

Additional warnings

Reactions to injections: Some people who received a rilpivirine injection developed symptoms of a post-injection reaction within minutes of the injection. Most of the symptoms disappeared within a few minutes after the injection. Symptoms of post-injection reaction may include: difficulty breathing, stomach cramps, rash, sweating, numbness of the mouth, feeling anxious, feeling warm, feeling dizzy or feeling that you are going to faint, changes in blood pressure and pain (e.g., back and chest pain). Tell the doctor if you developed these symptoms after receiving injections.

Regular appointments are important: To control the HIV infection and prevent worsening of your disease, it is important that you attend appointments scheduled for you to receive Rekambys. Do not skip any appointments; this is very important for the success of the treatment. If you cannot attend a scheduled appointment, inform your doctor as soon as possible. Speak to the doctor if you are thinking of stopping the treatment. If you are late receiving a Rekambys injection or if you stopped receiving Rekambys, you must take other medicines to treat the HIV infection and reduce the risk of the virus developing resistance, since the levels of the medicine in your body will be too low to treat the HIV infection.

Children and adolescents

This medicine is not intended for children and adolescents under 18 years of age.

There is no information about the safety and efficacy of use of this medicine in children and adolescents under 18 years of age.

Drug interactions

If you are taking, or have recently taken, other medicines, including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist. Some medicines can affect the levels of Rekambys in the blood if taken during the course of treatment with Rekambys, or Rekambys can affect the effectiveness of other medicines.

Do not use Rekambys if you are taking any of the following medicines since they may affect the way Rekambys or other medicines work:

- carbamazepine, oxcarbazepine, phenobarbital, phenytoin (medicines to treat epilepsy and prevent seizures).
- rifabutin, rifampicin, rifapentine (medicines to treat certain bacterial infections, such as tuberculosis).
- dexamethasone (a corticosteroid used for a variety of medical conditions, such as inflammation and allergic reactions), as a course of treatment by mouth or by injection.
- preparations containing St. John’s wort (*Hypericum perforatum*, a herbal preparation to treat

depression).

If you are taking any of the listed medicines, ask the doctor about alternatives.

The effects of Rekambys or other medicines can change if you use Rekambys together with any of the following medicines:

- clarithromycin, erythromycin (antibiotic).
- methadone (used to treat narcotic withdrawal and addiction).

Pregnancy and breastfeeding

If you are pregnant, planning to become pregnant or are breastfeeding, do not use this medicine without consulting a doctor before starting treatment.

Pregnancy

Tell the doctor immediately if you are pregnant or are planning to become pregnant. The doctor will consider the benefits and the risks of use of Rekambys to you and your baby during pregnancy. If you are planning to become pregnant, speak to your doctor in advance, since rilpivirine can stay in the body for up to 4 years after the last injection of Rekambys.

Breastfeeding

Breastfeeding is not recommended in women living with HIV because HIV infection can be passed on to the baby through breast milk.

If you are breastfeeding, or thinking about breastfeeding, consult with the doctor or pharmacist as soon as possible.

Driving and operating machinery

Some patients may feel tired, dizzy or sleepy during the course of treatment with Rekambys. Do not drive and do not operate machinery if you have these side effects.

Important information about some of the ingredients in the medicine

This medicine contains less than 1 mmol sodium (23 mg) per vial, and is therefore considered essentially “sodium-free”.

3. HOW SHOULD THE MEDICINE BE USED?

Always use the preparation according to the doctor’s instructions. Check with the doctor or pharmacist if you are uncertain about the preparation dosage and treatment regimen. The dosage and treatment regimen will be determined by the doctor only.

The usual dosage is generally:

You will receive an injection once a month or once every two months, together with another medicine given by injection, which is called cabotegravir. The doctor will explain how often the medicine will be given to you.

Do not exceed the recommended dosage.

Before commencing treatment with Rekambys, the doctor will give you a prescription for daily treatment with rilpivirine and cabotegravir tablets for one month. This treatment is called the ***lead-in period*** – taking tablets before receiving rilpivirine and cabotegravir injections will enable the doctor to check how suitable these medicines are for you.

If you are due to receive Rekambys once a month, the treatment will be given as follows:

	When		
Medicine	**Month 1 (at least 28 days)**	**Month 2 (after 1 month of tablets)**	**Month 3 and on**
Rilpivirine	One 25 mg tablet, once a day	One 900 mg injection	600 mg, by injection, once a month
Cabotegravir	One 30 mg tablet, once a day	One 600 mg injection	400 mg, by injection, once a month

If you are due to receive Rekambys once in two months, the treatment will be given as follows:

	When		
Medicine	**Month 1 (at least 28 days)**	**Month 2 (after 1 month of tablets) and Month 3**	**Month 5 and on**
Rilpivirine	One 25 mg tablet, once a day	One 900 mg injection	900 mg, by injection, once in two months
Cabotegravir	One 30 mg tablet, once a day	One 600 mg injection	600 mg, by injection, once in two months

Mode of administration
A nurse or doctor will inject Rekambys into your buttock muscle (intramuscular injection).

If you received too much Rekambys
A doctor or nurse will give you this medicine. Therefore, it is unlikely that you will receive too much. If you are concerned, talk to the doctor or nurse.

If you missed a Rekambys injection
It is important that you attend your regular appointments scheduled for you to receive the injection. If you skipped an appointment, refer to the doctor immediately to schedule a new appointment.

Speak to the doctor if you think you will not be able to receive the Rekambys injection at the usual time. The doctor may recommend that you take tablets instead until you will be able to receive the Rekambys injection again.
Adhere to the treatment as recommended by the doctor.

Do not stop using Rekambys without advice from the doctor
Use Rekambys for the duration of time recommended by the doctor. Do not stop unless the doctor has advised you to do so.
Small amounts of rilpivirine (the active ingredient in Rekambys) can remain in the body for up to 4 years after discontinuation of treatment. However, as soon as you receive the last Rekambys injection, the small amounts of rilpivirine that remain will not work well enough against the virus, which may then develop resistance. To keep the HIV-1 infection under control and prevent the virus from developing resistance, you should start another anti-HIV treatment at the time when you were supposed to get your next Rekambys injection.

Do not take medicines in the dark! Check the label and the dose each time you take medicine. Wear glasses if you need them.
If you have further questions regarding use of the medicine, consult the doctor or pharmacist.

4. SIDE EFFECTS

As with any medicine, use of Rekambys may cause side effects in some users. Do not be alarmed by the list of side effects. You may not suffer from any of them.
Side effects that were reported with the use of Rekambys together with cabotegravir injection

Very common side effects (occur in at least 1 user in 10):
- headache
- injection site reactions – usually mild to moderate and their frequencies decline with time. The symptoms may include:
  - Very common: pain and discomfort, a hardened mass or lump
  - Common: redness, itching, swelling, feeling warm or bruising (which may include discoloration or a collection of blood under the skin)

- Uncommon: numbness, minor bleeding, an abscess (a build-up of pus) or cellulitis (fever, swelling or redness)
- feeling hot/fever which may occur within one week after an injection

Common side effects (occur in less than 1 user in 10):
- depression
- anxiety
- unusual dreams
- sleeping difficulty (insomnia)
- dizziness
- feeling sick (nausea)
- vomiting
- abdominal pain
- flatulence (wind)
- diarrhea
- rash
- muscle pain
- tiredness
- weakness
- malaise
- weight gain

Uncommon side effects (occur in less than 1 user in 100):
- feeling drowsy
- feeling lightheaded during or after the injection. This may lead to fainting
- liver damage (signs can include yellowing of the skin and whites of the eyes, loss of appetite, itching, tenderness in the stomach, light-colored stools or unusually dark urine)
- changes in liver function blood tests (increase in transaminases)
- an increase in bilirubin (a substance produced by the liver) in the blood

Other side effects:
- severe stomachache caused by inflammation of the pancreas (pancreatitis)

<u>The following side effects that can occur when taking rilpivirine tablets can also occur with the Rekambys injection:</u>

Very common side effects (occur in at least 1 user in 10):
- increased blood cholesterol and/or amylase produced by the pancreas

Common side effects (occur in less than 1 user in 10):
- decreased appetite
- sleep disorders
- depressed mood
- stomach discomfort
- dry mouth
- low white blood cell and/or platelet count, decreased blood hemoglobin, increased blood triglycerides and/or lipase

Uncommon side effects (occur in less than 1 user in 100):
- signs or symptoms of inflammation or infection, e.g., fever, chills, sweating (immune reactivation syndrome; see further details in chapter 2)

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.
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 (<u>www.health.gov.il</u>), which directs you to an online form for reporting side effects. Or by entering the link:
<u>https://sideeffects.health.gov.il</u>

5. HOW SHOULD THE MEDICINE BE STORED?

Avoid poisoning! This medicine and any other medicine must be kept in a safe place out of the reach and sight of children and/or infants to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by the doctor.

Do not use the medicine after the expiry date that appears on the carton package/label after the word “EXP”. The expiry date refers to the last day of that month.

Storage conditions

Store in a refrigerator (2°C-8°C). Do not freeze.

Do not discard medicines in wastewater or household waste. Consult the pharmacist as to how to dispose of medicines that are no longer in use. This will help protect the environment.

6. FURTHER INFORMATION

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

poloxamer 338, glucose monohydrate, sodium dihydrogen phosphate monohydrate, citric acid monohydrate, sodium hydroxide to adjust pH and water for injections.

What the medicine looks like and the contents of the package:

White to off-white suspension for injection. Rekambys is provided in a glass vial. The package also contains one syringe, one vial adaptor and one injection needle.

The 2 ml vial contains 600 mg rilpivirine, the 3 ml vial contains 900 mg rilpivirine.

Registration Holder: J-C Health Care Ltd., Kibbutz Shefayim, 6099000, Israel.

Manufacturer: Cilag AG, Hochstrasse 201, 8200 Schaffhausen Switzerland.

Revised in December 2022 according to MOH guidelines.

Registration number of the medicine in the National Drug Registry of the Ministry of Health:
170-12-36949-99

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