

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

The medicine is dispensed with a doctor's prescription only

Odefsey®

Film-Coated Tablets

Active ingredients and quantities per dosage unit:

emtricitabine 200 mg,

rilpivirine (as hydrochloride) 25 mg,

tenofovir alafenamide (as fumarate) 25 mg.

Inactive and allergenic ingredients in the preparation – see section 2 under “Important information about some of the ingredients of the medicine” and section 6 “Further Information”.

Read the 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 for the treatment of 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?

Odefsey is intended for adults and adolescents (aged 12 years and over, who weigh at least 35 kg), for the treatment of infection with the HIV-1 virus (Human Immunodeficiency Virus-1), without known mutations associated with resistance of the virus to non-nucleoside analog reverse transcriptase inhibitor – NNRTI, tenofovir or emtricitabine, and with a viral load that is less than or equal to 100,000 HIV-1 RNA copies per mL (viral load \leq 100,000 HIV-1 RNA copies/mL).

Odefsey contains three active ingredients – emtricitabine, rilpivirine and tenofovir alafenamide – in one tablet.

Each of these active ingredients impairs the function of an enzyme (a protein called “reverse transcriptase”) that is essential for the HIV virus to multiply.

Odefsey reduces the amount of HIV virus in the body, thus improving the immune system and reducing the risk of developing illnesses linked to HIV infection.

Therapeutic group

- Emtricitabine, nucleoside reverse transcriptase inhibitors (NRTI)
- Rilpivirine, non-nucleoside reverse transcriptase inhibitors (NNRTI)
- Tenofovir alafenamide, nucleotide reverse transcriptase inhibitors (NtRTI)

2. BEFORE USING THE MEDICINE

Do not use the medicine if:

- You are sensitive (allergic) to the active ingredients (**emtricitabine, rilpivirine, tenofovir alafenamide**) or to any of the additional ingredients contained in the

medicine. For a list of the additional ingredients, see section 6 “Further Information”.

- You are taking any of the following medicines:
 - **Carbamazepine, oxcarbazepine, phenobarbital and phenytoin** (medicines to treat epilepsy and prevent seizures)
 - **Rifabutin, rifampicin and rifapentine** (to treat certain bacterial infections such as tuberculosis)
 - **Omeprazole, dexlansoprazole, lansoprazole, rabeprazole, pantoprazole and esomeprazole** (to treat and prevent stomach ulcers, heartburn and reflux disease [gastroesophageal reflux])
 - **Dexamethasone** (a corticosteroid used to treat inflammations and suppress the immune system), whether taken by mouth or administered by injection (except as a single-dose treatment)
 - **Products that contain St. John’s wort (*Hypericum perforatum*)** (a herbal preparation used in conditions of depression and anxiety)

If you take any of the medicines mentioned, **do not take Odefsey and inform your attending doctor immediately.**

Special warnings regarding use of the medicine

During treatment with Odefsey, you must remain under the doctor’s continued medical monitoring.

This medicine does not cure HIV virus infection. During treatment with Odefsey, you may still develop infections or other related illnesses associated with HIV infection.

Before treatment with Odefsey, tell the doctor:

- **If you suffer from problems with liver function or have suffered in the past from a liver disease, including hepatitis.** Patients with liver diseases, including chronic hepatitis B or C, who are treated with antiretroviral medicines, have a higher risk of severe liver problems that could even be life-threatening. If you suffer from hepatitis B infection, the doctor will carefully consider the best treatment regimen for you.
- **If you suffer from hepatitis B infection.** Liver problems may become worse after you stop taking Odefsey. It is very important not to stop treatment without consulting your doctor (see section 3 “How Should the Medicine be Used?”).
- If you are taking other medicines that cause an irregular heartbeat that could be life-threatening (torsades de pointes).
- **If you have had kidney disease or if tests have shown kidney problems.** The doctor will refer you for blood tests at the initiation and during the course of treatment with Odefsey, to monitor kidney function.

While taking Odefsey

After you start taking Odefsey, look out for the following signs:

- **Signs of inflammation or infection**
- **Joint pain, stiffness or bone problems**

Tell your doctor immediately if you notice any of these signs. For additional

information, see section 4 “Side Effects”.

There is a possibility that you may experience kidney problems when taking Odefsey over a long period of time (see section “Special warnings regarding use of the medicine”).

Children and adolescents

The medicine is not intended for children under the age of 12, or for those weighing less than 35 kg. The use in children and adolescents under the age of 12 or weighing less than 35 kg has not been studied.

Drug interactions

If you are taking, or have recently taken, other medicines, including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist. Odefsey can interact with other medicines. As a result, the amount of Odefsey or other medicines in the blood may be affected. This may stop the proper action of the medicines you are taking or worsen the side effects. In certain cases, the attending doctor will need to adjust the dosage of the medicine or check the blood levels.

Medicines that must not be taken together with Odefsey:

- **Carbamazepine, oxcarbazepine, phenobarbital and phenytoin** (medicines to treat epilepsy and prevent seizures)
- **Rifabutin, rifampicin and rifapentine** (to treat certain bacterial infections such as tuberculosis)
- **Omeprazole, dexlansoprazole, lansoprazole, rabeprazole, pantoprazole and esomeprazole** (to treat and prevent stomach ulcers, heartburn and reflux disease [gastroesophageal reflux])
- **Dexamethasone** (a corticosteroid used to treat inflammations and suppress the immune system), whether taken by mouth or administered by injection (except as a single-dose treatment)
- **Products that contain St. John’s wort (*Hypericum perforatum*)** (a herbal preparation used in conditions of depression and anxiety)

If you take any of the aforementioned medicines, do not take Odefsey and tell the doctor immediately.

Tell the doctor if you are taking:

- **Medicines used to treat HIV infection**
- **Other medicines containing:**
 - Tenofovir alafenamide
 - Tenofovir disoproxil
 - Lamivudine
 - Adefovir dipivoxil
- **Antibiotics used to treat bacterial infections containing:**
 - Clarithromycin
 - Erythromycin

These medicines can increase the levels of rilpivirine and tenofovir alafenamide (the

active ingredients of Odefsey) in the blood. The doctor will prescribe an alternative medicine for you.

- **Antifungal medicines used to treat fungal infections:**
 - ketoconazole
 - fluconazole
 - itraconazole
 - posaconazole
 - voriconazole

These medicines can increase the levels of rilpivirine and tenofovir alafenamide (the active ingredients of Odefsey) in the blood.

The doctor will prescribe an alternative medicine for you.

- **Medicines for stomach ulcers, heartburn or reflux (gastroesophageal reflux),** such as:
 - **Antacids** (aluminium/magnesium hydroxide or calcium carbonate)
 - **H₂ antagonists** (famotidine, cimetidine, nizatidine or ranitidine)

These medicines can decrease the level of rilpivirine (one of the active ingredients in Odefsey) in the blood. If you are taking one of these medicines, the doctor will prescribe for you a different medicine, or alternatively, advise you how and when to take that medicine:

- **If you are taking an antacid,** take this medicine at least 2 hours before or 4 hours after taking Odefsey.
- **If you are taking medicines from the H₂ antagonists group,** these medicines should be taken at least 12 hours before or 4 hours after taking Odefsey. H₂ antagonists can be taken only once per day if you are taking Odefsey. Do not take H₂ antagonists twice per day. Consult with the attending doctor about an alternative treatment regimen (see section 3 “How Should the Medicine be Used?”).
- **Cyclosporin,** a medicine used to reduce the resistance of the body’s immune system: This medicine can increase the level of rilpivirine and tenofovir alafenamide (the active ingredients of Odefsey) in the blood. The doctor will prescribe an alternative medicine for you.
- **Methadone,** a medicine used to treat opiate addiction. The doctor may need to change the methadone dosage.
- **Dabigatran etexilate,** a medicine used to treat heart problems; the doctor may need to monitor the levels of this medicine in the blood.

Tell the doctor if you are taking any of these medicines. Do not stop the treatment without consulting the doctor.

Use of the medicine and food

Take the medicine together with a meal.

Pregnancy and breastfeeding

If you are pregnant or breastfeeding, think you are pregnant or are planning a pregnancy, consult with a doctor before using the medicine.

Use effective contraception while taking Odefsey.

Consult with a doctor or pharmacist before taking any medicine during pregnancy.

If you have taken Odefsey during pregnancy, the doctor may instruct you to perform blood tests and other diagnostic tests to monitor the development of the unborn baby. In children whose mothers took nucleoside reverse transcriptase inhibitors (NRTI) during pregnancy, the benefit from the protection against HIV outweighed the risk of side effects.

Do not breastfeed during treatment with Odefsey. This is because some of the active ingredients of the medicine pass into breast milk.

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 as soon as possible.**

Driving and operating machinery

Do not drive or operate dangerous machinery while using the medicine if you feel tired, sleepy or dizzy after taking the medicine.

Important information about some of the ingredients of the medicine

Lactose – Odefsey contains approximately 190 mg lactose monohydrate per tablet. If you are lactose-intolerant or if you have been told that you have an intolerance to certain sugars, **consult with the doctor before starting to take Odefsey.**

Sodium – This medicine contains less than 1 mmol (23 mg) sodium per tablet, i.e., it is considered to be 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 not sure about the dosage and treatment regimen of the preparation.

The dosage and treatment regimen will be determined by the doctor only. The usual dosage is generally:

Adults and adolescents aged 12 years and over, who weigh at least 35 kg: one tablet each day, with food.

Do not exceed the recommended dosage.

It is important to take Odefsey with a meal in order to get the right levels of the active ingredient in your body. A nutritional drink alone (e.g., protein-rich drink) does not replace a meal.

It is not recommended to crush, split or chew the tablet due to the bitter taste.

If you are taking an antacid, such as aluminium/magnesium hydroxide or calcium carbonate, take the antacid at least 2 hours before or 4 hours after taking Odefsey.

If you are taking medicines from the H₂ antagonist group, such as famotidine, cimetidine, nizatidine or ranitidine, take these medicines at least 12 hours before or 4 hours after taking Odefsey. H₂ antagonists can be taken only once per day if you are taking Odefsey. Do not take H₂ antagonists twice per day. Consult with the attending

doctor about an alternative treatment regimen.

If you are on dialysis treatment, take your daily dosage of Odefsey following completion of dialysis.

If you take a higher dosage of Odefsey than required

If you accidentally take too high a dosage, you may be at increased risk of experiencing side effects of the medicine (see section 4 “Side Effects”).

If you took an overdose, or if a child has accidentally swallowed the medicine, refer immediately to a doctor or proceed to a hospital emergency room, and bring the package of the medicine with you. Keep or take the tablet pack with you so that you can easily describe what you have taken.

If you forget to take Odefsey

It is very important not to forget to take the dose of Odefsey.

If you do forget a dose:

- **If you remember within 12 hours of the time you usually take Odefsey**, take Odefsey as soon as possible. Always take Odefsey with a meal. After that, take the next dose as usual at the planned time.
- **If you remember 12 hours or more after the time you usually take Odefsey**, do not take the forgotten dose. Wait until your next scheduled dose, and then take Odefsey with a meal.

If you vomit less than 4 hours after taking Odefsey, take another tablet with a meal.

If you vomit more than 4 hours after taking Odefsey, you do not need to take another tablet. Take the next tablet at the usual planned time.

Adhere to the treatment regimen as recommended by the doctor.

Do not stop taking Odefsey

Even if there is an improvement in your health, do not stop treatment with the medicine without consulting the doctor. Stopping treatment with Odefsey can seriously affect your response to future treatment. If treatment with Odefsey is stopped for any reason, consult with the doctor before you restart taking Odefsey.

When your supply of Odefsey starts running low, make sure to purchase an additional supply of the medicine.

This is extremely important because the amount of virus in your body may increase if treatment with the medicine is stopped, for even a short time. The disease may then become harder to treat.

If you have both HIV infection and hepatitis B, it is especially important not to stop your Odefsey treatment without consulting with the doctor first. You may be required to perform blood tests for several months after stopping treatment. In some patients with advanced liver disease or cirrhosis, stopping treatment is not recommended as this may lead to worsening of your hepatitis, even to the extent of being life-threatening.

Tell the attending doctor immediately about new or unusual symptoms upon stopping treatment with Odefsey, particularly about symptoms associated with hepatitis B.

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 Odefsey may cause side effects in some users. Do not be alarmed by reading the list of side effects. You may not suffer from any of them.

Possible side effects – Report immediately to a doctor:

- **Any signs of inflammation or infection.** In some patients with advanced HIV infection (AIDS) and a history of opportunistic infections (infections that occur in people with a weak immune system), signs and symptoms of inflammation from previous infections may occur immediately after starting treatment of HIV infection. It is thought that these symptoms are due to the improvement in the body's immune response, enabling the body to fight infections that may have been present with no obvious symptoms.
- **Autoimmune disorders**, when the immune system attacks healthy body tissue, may occur after you start taking medicines for the treatment of HIV. Autoimmune disorders may occur many months after the start of treatment. Look out for symptoms of infection or other symptoms such as:
 - Muscle weakness
 - Weakness beginning in the hands and feet and moving up towards the trunk of the body
 - Palpitations, tremor or hyperactivity

If you notice these symptoms or any symptoms of inflammation or infection, tell the attending doctor immediately.

Very common side effects – effects that occur in more than 1 user in 10:

- Sleeping difficulties (insomnia)
- Headache
- Dizziness
- Nausea

Laboratory tests may also detect:

- Increased levels of cholesterol and/or pancreatic amylase (an enzyme that helps with digestion) in the blood
- Increased levels of liver enzymes in the blood

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

- Decreased appetite
- Depression
- Abnormal dreams
- Sleep disorders
- Depressed mood
- Somnolence
- Tiredness
- Abdominal pain or discomfort
- Vomiting

- Feeling bloated
- Dry mouth
- Flatulence (in the abdomen)
- Diarrhea
- Rash

Laboratory tests may also detect:

- Low white blood cell count (a reduced white blood cell count can make you more prone to infections)
- Low platelet count (blood cells that participate in the blood clotting process)
- Decrease in hemoglobin in the blood
- Increased fatty acids (triglycerides), bilirubin or an enzyme called lipase in the blood

Uncommon side effects – effects that occur in 1-10 in 1,000 users:

- Signs or symptoms of inflammation or infection
- Low red blood cell count (anemia)
- Severe skin reaction including rash accompanied by fever, swelling and liver problems
- Problems with digestion resulting in discomfort after meals
- Swelling of the face, lips, tongue or throat
- Itching (pruritus)
- Hives (urticaria)
- Joint pain

Additional effects that may be seen during HIV treatment:

Side effects of unknown frequency (effects whose frequency has not been determined):

- **Bone problems** – Some patients taking combination antiretroviral medicines such as Odefsey may develop a bone disease called “osteonecrosis” (a disease in which bone tissue dies due to a loss of blood supply to the bone). Taking this type of medicine for a long time, taking corticosteroids, alcohol consumption, a very weak immune system and being overweight may be some of the many risk factors for developing this disease.

Signs of osteonecrosis:

- Joint stiffness
- Joint pain (especially of the hip, knee and shoulder)
- Movement difficulties

If you notice any of these symptoms, refer to the attending doctor.

During HIV treatment, there may be an increase in weight and in levels of blood lipids and glucose. This is partly linked to restored health and lifestyle, and in the case of increased blood lipids, is sometimes linked to the medicines themselves that are being taken to treat HIV. The doctor will test for these changes.

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 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 for reporting side effects, or by entering the link:

<https://sideeffects.health.gov.il>

5. HOW SHOULD THE MEDICINE BE STORED?

Avoid poisoning! This medicine, and any other medicine, should be kept in a safe place out of the reach and sight of children and/or infants in order 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 (exp. date) that appears on the package. The expiry date refers to the last day of that month.

Do not store at a temperature exceeding 30°C.

Shelf-life after opening: As the expiry date of the preparation.

Store the tablets in the original packaging in order to protect from moisture. Make sure to keep the bottle tightly closed.

Do not throw away medicines into the regular trash can. Consult with the pharmacist about how to discard medicines that are no longer needed.

6. FURTHER INFORMATION

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

Tablet core:

lactose monohydrate, microcrystalline cellulose, croscarmellose sodium, magnesium stearate, povidone, polysorbate 20.

Tablet film-coating:

polyvinyl alcohol, titanium dioxide, macrogol, talc, iron oxide black.

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

Odefsey is a film-coated, capsule-shaped, grey tablet debossed on one side with “GSI” and “255” on the other side.

The tablets are provided in a plastic bottle containing 30 tablets.

Each bottle contains a silica gel desiccant that must be kept in the bottle in order to protect the tablets. The desiccant comes in a separate sachet or canister. Do not swallow the sachet/canister.

Manufacturer: Janssen Cilag S.p.A., Via C. Janssen 04100, Borgo S.Michele, Latina, Italy.

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

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