Patient leaflet in accordance with the Pharmacists' (Products) Regulations - 1986
This medicine is to be supplied by doctor's prescription only

Biktarvy®
Film-coated tablets

Active ingredients: Each tablet contains –

Bictegravir (as sodium)	50 mg
emtricitabine	200 mg
tenofovir alafenamide (as fumarate)	25 mg

Inactive and allergenic substances: see section 6 *"Additional information*".

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you. This leaflet contains essential information about this medicine. If you have any further questions, ask your doctor or pharmacist. Keep this leaflet. You may need to read it again. This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if it seems to you that their illness issimilar to yours. If you experience any side effects, talk to your doctor or pharmacist. Even if you experience any side effects that are not listed in this leaflet (see section 4).

This medicine is intended for adults aged 18 years and over.

1. What is the medicine intended for

Biktarvy is indicated for the treatment of human immunodeficiency virus 1 (HIV-1) infection in adults without present or past evidence of viral resistance to the integrase inhibitor class, emtricitabine or tenofovir.

Therapeutic group: Antiviral for systemic use; antivirals for treatment of HIV infections, combinations.

Biktarvy reduces the amount of HIV in your body. This will improve your immune system and reduce the risk of developing illnesses linked to HIV infection.

Biktarvy contains three active substances:

bictegravir, an antiretroviral medicine known as an integrase strand transfer inhibitor (INSTI)
emtricitabine, an antiretroviral medicine of a type known as a nucleoside reverse transcriptase inhibitor (NRTI)
tenofovir alafenamide, an antiretroviral medicine of a type known as a nucleotide reverse transcriptase inhibitor (NtRTI)

2. Before taking the medicine

X Do not take this medicine

- **If you are allergic to bictegravir, emtricitabine, tenofovir alafenamide** or any of the other ingredients of the medicine (listed in section 6 of this leaflet).

- **If you are currently taking any of the following medicines:**
  - **Rifampicin** used to treat some bacterial infections such as tuberculosis
  - **St. John's wort** (*Hypericum perforatum*), a herbal remedy used for depression and anxiety, or products that contain it.

→ If any of these apply to you, **tell your doctor immediately.**

! Special warnings relating to the use of the medicine

Talk to your doctor before taking Biktarvy:

- **If you have liver problems or a history of liver disease, including hepatitis.** Patients with liver disease including chronic hepatitis B or C, who are treated with antiretrovirals, have a higher risk of severe and potentially fatal liver complications. If you have hepatitis B infection, your doctor will carefully consider the best treatment regimen for you.

- **If you have hepatitis B infection**. Liver problems may become worse after you stop taking Biktarvy.

→ Do not stop taking Biktarvy if you have hepatitis B. Talk to your doctor first. For more details, see section 3, *Do not stop taking Biktarvy*.

- **If you have had kidney disease or if tests have shown problems with your kidneys.** Your doctor may order blood tests to monitor how your kidneys work when starting and during treatment with Biktarvy.

While you are taking Biktarvy

Once you start taking Biktarvy, look out for:

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

→ **If you notice any of these symptoms, tell your doctor immediately.** For more information see section 4, *Side effects*.

There is a possibility that you may experience kidney problems when taking Biktarvy over a long period of time (see *Warnings and precautions*).

This medicine is not a cure for HIV infection. While taking Biktarvy you may still develop infections or other illnesses associated with HIV infection.

Children and adolescents

Do not give this medicine to children and adolescents under 18 years of age. The use of Biktarvy in children and adolescents under 18 years of age has not yet been studied.

Drug-Drug Interactions:

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. This includes non-prescription medicines and dietary supplements. Biktarvy may interact with other medicines. As a result, the amounts of Biktarvy or other medicines in your blood may change. This may stop your medicines from working properly, or may make any side effects worse. In some cases, your doctor may need to adjust your dose or check your blood levels.

Medicines that must never be taken with Biktarvy:
- **rifampicin** used to treat some bacterial infections such as tuberculosis
- **St. John's wort** (*Hypericum perforatum)*, a herbal remedy used for depression and anxiety, or products that contain it.

→ If you are taking any of these medicines, **do not take Biktarvy and tell your doctor immediately.**

Talk to your doctor if you are taking:
- **medicines used for treating HIV and/or hepatitis B, containing:**
  - adefovir dipivoxil, atazanavir, bictegravir, emtricitabine, lamivudine, tenofovir alafenamide, or tenofovir disoproxil
- **antibiotics used to treat bacterial infections, containing:**
  - azithromycin, clarithromycin, rifabutin or rifapentine
- **anticonvulsants** used to treat epilepsy, containing:
  - carbamazepine, oxcarbazepine, phenobarbital or phenytoin
- **immunosuppressants** used to control your body's immune response after a transplant, containing ciclosporin
- **ulcer-healing medicines** containing sucralfate

→ **Tell your doctor if you are taking any of these medicines.** Do not stop your treatment without contacting your doctor.

Get advice from a doctor or pharmacist if you are taking:
- **antacids** to treat stomach ulcers, heartburn, or acid reflux, containing aluminium and/or magnesium hydroxide
- **mineral supplements** or **vitamins** containing magnesium or iron

→ **Get advice from your doctor or pharmacist before taking Biktarvy** if you are taking any of these medicines.
Antacids and magnesium supplements: you will need to take Biktarvy at least 2 hours **before** antacids or supplements containing aluminium and/or magnesium. Or you can take Biktarvy with food at least 2 hours **after.**
Iron supplements: you will need to take Biktarvy at least 2 hours **before** iron supplements, or you can take them together with food.

Pregnancy and breast-feeding

- If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.
- Tell your doctor immediately if you become pregnant and ask about the potential benefits and risks of your antiretroviral therapy to you and your child.

If you have taken Biktarvy during your pregnancy, your doctor may request regular blood tests and other diagnostic tests to monitor the development of your child. In children whose mothers took nucleoside reverse transcriptase inhibitors (NRTIs) during pregnancy, the benefit from the protection against HIV outweighed the risk of side effects.

Do not breast-feed during treatment with Biktarvy. This is because some of the active substances in this medicine pass into human breast milk. Breast-feeding is not recommended in women living with HIV because HIV infection can be passed on to the baby in breast milk. If you are breast-feeding, or thinking about breast-feeding, you should **discuss it with your doctor as soon as possible.**

Driving and using machines

Biktarvy can cause dizziness. If you feel dizzy when taking Biktarvy, do not drive or ride a bicycle and do not use any tools or machines.

Biktarvy contains sodium

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

3. How to take the medicine

Always take this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure regarding the dose and treatment regimen.

The dose and treatment regimen will be determined by a doctor.

The usual dose of Biktarvy usually is:

Adults: one tablet each day with or without food

It is not recommended to chew, crush or split the tablet as it has a very bitter taste. No information available regarding tablet effectiveness after splitting, chewing or crushing it.

Do not exceed the recommended dose.

The Biktarvy 30-day blister pack contains four 7-blister strips and one 2-blister strip. To help track taking your medication over 30 days, the 7-blister strips have days of the week printed and you can write the relevant days of the week on the 2-blister strip.
The 90-day multipack contains three 30-day packs together.

→ **Get advice from a doctor or pharmacist if you are taking:**
- **antacids** to treat stomach ulcers, heartburn, or acid reflux, containing aluminium and/or magnesium hydroxide
- **mineral supplements** or **vitamins** containing magnesium or iron

→ **See section 2 for more information** on taking these medicines with Biktarvy.

If you take more Biktarvy than you should

If you accidentally take more than the recommended dose of Biktarvy you may be at higher risk of side effects of this medicine (see section 4, *Side effects*).

If you take more than you should or if a child has accidentally swallowed some of the medicine, contact your doctor or nearest hospital emergency department immediately and bring the tablet bottle or carton with you.

If you forget to take Biktarvy

It is important not to miss a dose of Biktarvy.

If you do miss a dose:
- **If you notice within 18 hours** of the time you usually take Biktarvy, you must take the tablet as soon as possible. Then take the next dose as usual.
- **If you notice 18 hours or more** after the time you usually take Biktarvy, then do not take the missed dose. Wait and take the next dose at your usual time.

If you vomit less than 1 hour after taking Biktarvy, take another tablet**.** If you vomit more than 1 hour after taking Biktarvy you do not need to take another tablet until your next regularly scheduled tablet.

You should adhere to the treatment as recommended by your doctor.

Do not stop taking Biktarvy

Even if your health improves, do not stop taking Biktarvy without talking to your doctor. Stopping Biktarvy can seriously affect your response to future treatment. If Biktarvy is stopped for any reason, speak to your doctor before you restart taking Biktarvy tablets.

When your supply of Biktarvy starts to run low, get more from your doctor or pharmacist. This is very important because the amount of virus may start to increase if 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 Biktarvy treatment without talking to your doctor first. You may require 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, which may be life-threatening.

→ **Tell your doctor immediately** about new or unusual symptoms after you stop treatment, particularly symptoms you associate with hepatitis B infection.

Do not take medicines in the dark!
Check the label and the dose <u>every time</u> you take a medicine.
Wear glasses if you need them.

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

4. Side Effects

Like all medicines, Biktarvy can cause side effects for some users.
Do not be alarmed by reading the list of side effects. You may not experience any of them.

Possible side effects: tell a doctor immediately

- **Any signs of inflammation or infection.** In some patients with advanced HIV infection (acquired immunodeficiency syndrome (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 soon after HIV treatment is started. It is thought that these symptoms are due to an 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 also occur after you start taking medicines for HIV infection. Autoimmune disorders may occur many months after the start of treatment. Look out for any 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 or any symptoms of inflammation or infection, tell your doctor immediately.

Common side effects
(*may affect up to 1 in 10 people*)
- depression
- abnormal dreams
- headache
- dizziness
- diarrhoea
- feeling sick (*nausea*)
- tiredness (*fatigue*)

Uncommon side effects
(*may affect up to 1 in 100 people*)
- anaemia
- vomiting
- stomach pain
- problems with digestion resulting in discomfort after meals (*dyspepsia*)
- wind (*flatulence*)
- swelling of the face, lips, tongue or throat (*angioedema*)
- itching (*pruritus*)
- rash
- hives (*urticaria*)
- joint pain (*arthralgia*)
- suicidal thoughts and suicide attempt (particularly in patients who have had depression or mental health problems before)
- anxiety
- sleep disorders

Blood tests may also show:
- higher levels of substances called bilirubin and/or serum creatinine in the blood

Rare side effects
(may affect up to 1 in 1000 people)
- Stevens-Johnson syndrome (SJS) is a serious life-threatening condition which usually starts with flu- like symptoms. A few days later other symptoms appear including:
  - Painful red or purple skin that looks burned and peels off
  - Blisters on your skin, mouth, nose, and genitals
  - Red, painful, watery eyes

→ If you have any of these symptoms, stop your medicine immediately and tell your doctor straight away.

→ If any of the side effects get serious, tell your doctor.

Other effects that may be seen during HIV treatment

The frequency of the following side effects is not known (frequency cannot be estimated from the available data).

- **Bone problems.** Some patients taking combination antiretroviral medicines such as Biktarvy may develop a bone disease called *osteonecrosis* (death of bone tissue caused by loss of blood supply to the bone). Taking this type of medicine for a long time, taking corticosteroids, drinking alcohol, having a very weak immune system, and being overweight, may be some of the many risk factors for developing this disease. Signs of osteonecrosis are:
  - joint stiffness
  - joint aches and pains (especially of the hip, knee and shoulder)
  - difficulty with movement

→ If you notice any of these symptoms tell your doctor.

During HIV therapy there may be an increase in weight and in levels of blood lipids and glucose. This is partly linked to restored health and life style, and in the case of blood lipids sometimes to the HIV medicines themselves. Your doctor will test for these changes.

→ If a side effect has appeared, if any of the side effects worsen or if you suffer from a side effect not mentioned in the leaflet, consult the doctor.

Reporting of side effects

You can report any side effects to the Ministry of Health by clicking on the link "Report side effects due to medical treatment" that is located on the Ministry of Health homepage (www.health.gov.il) which redirects to the online form for reporting side effects or by clicking on the link: https://sideeffects.health.gov.il .

You can also report any side effects directly to the registration holder via email: DrugSafety.Israel@gilead.com.

By reporting side effects, you can help provide more information on the safety of this medicine.

5. How to store the medicine

Prevent poisoning! Keep this medicine out of the sight and reach of children and/or babies. In this way you will prevent poisoning. Do not induce vomiting without a doctor's express instruction.

Do not use this medicine after the expiry date which is stated on the carton and bottle after {EXP}. The expiry date refers to the last day of that month.

There are no special storage conditions. Recommended to store at room temperature.

Bottle
Store in the original package in order to protect from moisture. Keep the bottle tightly closed. Do not use if the seal over the bottle opening is broken or missing.

Blister
Store in the original package in order to protect from moisture. Do not use if foil over blister is broken or pierced.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Additional Information

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

Tablet core:
Microcrystalline cellulose (E460), croscarmellose sodium (E468), magnesium stearate (E470b).

Film-coating:
Polyvinyl alcohol (E203), titanium dioxide (E171), polyethylene glycol (E1521), talc (E553b), iron oxide red (E172), iron oxide black (E172).

What the medicine looks like and contents of the pack

Biktarvy film-coated tablets are purplish-brown, capsule-shaped, film-coated tablets debossed on one side with “GSI” and “9883” on the other side.

The tablets may be supplied either in a bottle or in a blister pack. Not all pack sizes may be marketed.

Bottle
Biktarvy comes in bottles of 30 tablets. Each bottle contains a silica gel desiccant that must be kept in the bottle to help protect your tablets. The silica gel desiccant is contained in a separate sachet or canister and should not be swallowed.

Blister
Biktarvy also comes in blister packs of 30 tablets and in multipacks comprising 3 cartons, each containing 30 tablets. Each individual pack contains 4 x blister strips containing 7 tablets and 1 x blister strip containing 2 tablets.

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Registration Holder
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Revised in January 2023 according to MoH guidelines.

The medicine’s registration no. in the national register of medicines at the Ministry of Health: 35648

For simplicity and ease of reading, this leaflet was phrased in the masculine. Nevertheless, the medicine is intended for both sexes.

Reference: EU SmPC November 2022.
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