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

GENDEVRA®
150 mg/150 mg/200 mg/10 mg film-coated tablets

Active ingredients: Each tablet contains –

elvitegravir	150 mg
cobicistat	150 mg
emtricitabine	200 mg
tenofovir alafenamide	10 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 is the same as yours. If you get 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, adolescents and children aged 6 years of age and older, who weigh at least 25 kg.

1. What is Gendevra intended for

Gendevra is a single tablet for the **treatment of human immunodeficiency virus 1 (HIV-1) infection** in adults, adolescents and in children aged 6 years and older who weigh at least 25 kg.

If Gendevra has been prescribed for your child, please note that all the information in this leaflet is addressed to your child (in this case please read "your child" instead of "you").

Therapeutic group:
Gendevra contains four active substances:

- **elvitegravir,** an antiretroviral medicine known as an integrase inhibitor
- **cobicistat,** a booster (enhancer) of the effects of elvitegravir
- **emtricitabine,** an antiretroviral medicine known as a nucleoside reverse transcriptase inhibitor (NRTI)
- **tenofovir alafenamide,** an antiretroviral medicine known as a nucleotide reverse transcriptase inhibitor (NtRTI)

Gendevra 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.

2. Before taking Gendevra

X **Do not take this medicine**

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

- **If you are taking one of these medicines:**
  - **alfuzosin** (used to treat an enlarged prostate gland)

- **dabigatran** (used to prevent and treat blood clots)
- **amiodarone, quinidine** (used to correct irregular heartbeats)
- **carbamazepine, phenobarbital, phenytoin** (used to prevent seizures)
- **rifampicin** (used to prevent and treat tuberculosis and other infections)
- **dihydroergotamine, ergometrine, ergotamine** (used to treat migraine headache)
- **cisapride** (used to relieve certain stomach problems)
- **St. John's wort** (*Hypericum perforatum*, a herbal remedy used for depression and anxiety) or products that contain it
- **lomitapide, lovastatin, simvastatin** (used to lower blood cholesterol)
- **lurasidone**, **pimozide** (used to treat abnormal thoughts or feelings)
- **sildenafil** (when used to treat pulmonary arterial hypertension – a lung disease that makes breathing difficult)
- orally administered **midazolam, triazolam** (used to help you sleep and/or relieve anxiety)

→ If any of these applies to you, **do not take Gendevra and tell your doctor immediately.**

! Special warnings relating to the use of this medicine

You must remain under the care of your doctor while taking Gendevra.

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

Talk to your doctor before taking Gendevra:

- **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 Gendevra. It is important not to stop taking Gendevra without talking to your doctor: see section 3, *Do not stop taking Gendevra*.

- **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 Gendevra.

While you are taking Gendevra

Once you start taking Gendevra, 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 Gendevra over a long period of time (see *Warnings and precautions*).

Children and adolescents

Do not give this medicine to children aged 5 years or under, or weighing less than 25 kg regardless of age. The use of Gendevra in children aged 5 years or under has not yet been studied.

Other medicines and Gendevra

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. Gendevra may interact with other medicines. As a result, the amounts of Gendevra or other medicines in your blood may be affected. 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 Gendevra:

- **alfuzosin** (used to treat an enlarged prostate gland)
- **amiodarone, quinidine** (used to correct irregular heartbeats)
- **carbamazepine, phenobarbital, phenytoin** (used to prevent seizures)
- **dabigatran** (used to prevent and treat blood clots)
- **rifampicin** (used to prevent and treat tuberculosis and other infections)
- **dihydroergotamine, ergometrine, ergotamine** (used to treat migraine headache)
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- **sildenafil** (when used to treat pulmonary arterial hypertension – a lung disease that makes breathing difficult)
- orally administered **midazolam, triazolam** (used to help you sleep and/or relieve anxiety)

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

Medicines used in treating hepatitis B infection:

You should not take Gendevra with medicines containing:

- **tenofovir alafenamide**
- **tenofovir disoproxil**
- **lamivudine**
- **adefovir dipivoxil**

→ **Tell your doctor** if you are taking any of these medicines.

Other types of medicine:

Talk to your doctor if you are taking:

- **antifungals,** used to treat fungal infections, such as:
  - ketoconazole, itraconazole, voriconazole, posaconazole and fluconazole
- **antibiotics,** used to treat bacterial infections including tuberculosis, containing:
  - rifabutin, clarithromycin and telithromycin
- **antidepressants,** used to treat depression:
  - medicines containing trazodone or escitalopram
- **sedatives and hypnotics,** used to treat anxiety:
  - buspirone, clorazepate, diazepam, estazolam, flurazepam, zolpidem and lorazepam
- **immunosuppressants,** used to control your body's immune response after a transplant, such as:
  - ciclosporin, sirolimus and tacrolimus
- **corticosteroids** including:
  - betamethasone, budesonide, fluticasone, mometasone, prednisone, triamcinolone.

  These medicines are used to treat allergies, asthma, inflammatory bowel diseases, inflammatory conditions of the skin, eyes, joints and muscles and other inflammatory conditions. These medicines are generally taken orally, inhaled, injected or applied to the skin or eye. If alternatives cannot be used, its use should only take place after medical evaluation and under close monitoring by your doctor for corticosteroid side effects.

- **medicines used to treat diabetes:**
  - metformin
- **contraceptive pill,** used to prevent pregnancy
- **erectile dysfunction medicines,** used to treat impotence, such as:
  - sildenafil, tadalafil and vardenafil
- **heart medicines,** such as:
  - digoxin, disopyramide, flecainide, lidocaine (injectable), mexiletine, propafenone, metoprolol, timolol, amlodipine, diltiazem, felodipine, nicardipine, nifedipine and verapamil
- **medicines used to treat pulmonary arterial hypertension:**
  - bosentan and tadalafil
- **anticoagulants,** used to prevent and treat blood clots, such as:
  - apixaban, edoxaban, rivaroxaban and warfarin
- **bronchodilators,** used to treat asthma and other lung-related problems:
  - salmeterol
- **cholesterol lowering medicines,** such as:
  - atorvastatin and pitavastatin
- **medicines used to treat gout:**
  - colchicine
- **antiplatelets,** used to reduce the risk of blood clots such as:
  - clopidogrel
- **medicines or oral supplements containing minerals (such as magnesium, aluminium, calcium, iron, zinc)**, such as:
  - mineral supplements, vitamins (including multivitamins), antacids and laxatives

  → **If you are taking medicines, oral supplements, antacids or laxatives containing minerals (such as magnesium, aluminium, calcium, iron, zinc),** take them at least 4 hours before or at least 4 hours after Gendevra.

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

Taking the medicine and food
Take 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 are pregnant, think you may be pregnant or are planning to have a baby.** Pregnant women should not take Gendevra. The amount of this medicine in your blood may decrease during pregnancy which may stop it from working properly.
- **Use effective contraception** while taking Gendevra.
- **Do not breast-feed during treatment with Gendevra.** 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

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

Important information on the inactive ingredients of the medicine

Gendevra contains sodium

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

Gendevra contains lactose

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

→ If any of these applies to you, **talk to your doctor before taking Gendevra.**

3. How to take Gendevra

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

The dosage and treatment regimen will be determined by the doctor only.

Usual dosage

Adults: one tablet each day with food
Adolescents and children 6 years of age and older, who weigh at least 25 kg: one tablet each day with food

Do not exceed the recommended dose.

Due to the bitter taste, it is recommended not to chew or crush the tablet.

If you have difficulty swallowing the tablet whole, you can split it in half. Take both halves of the tablet one after the other to get the full dose. Do not store the split tablet.

Always take the dose recommended by your doctor. This is to make sure that your medicine is fully effective, and to reduce the risk of developing resistance to the treatment. Do not change the dose unless your doctor tells you to.

Do not take antacids or multivitamins at the same time as Gendevra. If you are taking **medicines, oral supplements, antacids or laxatives containing minerals (such as magnesium, aluminium, calcium, iron, zinc),** take them at least 4 hours before or at least 4 hours after Gendevra.

If you are on dialysis, take your daily dose of Gendevra following completion of dialysis.

If you take more Gendevra than you should

If you accidentally take more than the recommended dose of Gendevra you may be at increased risk of experiencing possible side effects with this medicine (see section 4, *side effects*).

Immediately contact your doctor or nearest hospital emergency department and bring the tablet bottle with you.

If you forget to take Gendevra

It is important not to miss a dose of Gendevra.

If you do miss a dose:

- **If you notice within 18 hours** of the time you usually take Gendevra, take the tablet as soon as possible. Always take the tablet with food. Take the next dose as usual and consult with a doctor
- **If you notice 18 hours or more** after the time you usually take Gendevra, then do not take the missed dose. Wait and take the next dose, with food, at your usual time.

If you vomit less than 1 hour after taking Gendevra, take another tablet with food.

Do not stop taking Gendevra

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

When your supply of Gendevra starts to run low, get more from your doctor. 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 Gendevra 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, ask your doctor or pharmacist.

4. <u>Side effects</u>

Like all medicines, Gendevra 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.

In the following cases contact your doctor immediately

- **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 soon after anti-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 the side effects described above, tell your doctor immediately.**

Very common side effects
(*may affect more than 1 in 10 people*)
- feeling sick (*nausea*)

Common side effects
(*may affect up to 1 in 10 people*)
- abnormal dreams
- headache
- dizziness
- diarrhoea
- vomiting
- stomach pain
- wind (*flatulence*)
- rash
- tiredness (*fatigue*)

Uncommon side effects
(*may affect up to 1 in 100 people*)
- low red blood cell count (*anaemia*)
- suicidal thoughts and suicide attempt (in patients who have had depression or mental health problems before), depression
- problems with digestion resulting in discomfort after meals (*dyspepsia*)
- swelling of the face, lips, tongue or throat (*angioedema*)
- itching (*pruritus*)
- hives (*urticaria*)

→ 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 Gendevra 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.

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

5. How to store Gendevra

Prevent poisoning! Keep this medicine and any other 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. It is recommended to store at room temperature.
Store in the original package in order to protect from moisture. Keep the bottle tightly closed.

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 Gendevra contains

In addition to the active ingredients Gendevra contains:

Tablet core:
Microcrystalline cellulose (E460), silicon dioxide (E551). croscarmellose sodium, lactose (as monohydrate), magnesium stearate, sodium lauryl sulfate, hydroxypropyl cellulose (E463),

Film-coating:
Polyvinyl alcohol (E1203), titanium dioxide (E171), polyethylene glycol (E1521), talc (E553b), indigo carmine aluminium lake (E132), iron oxide yellow (E172).

What Gendevra looks like and contents of the pack

Gendevra film-coated tablets are green, capsule-shaped tablets, debossed on one side with "GSI" and the number "510" on the other side of the tablet. Gendevra comes in bottles of 30 tablets (with 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.

The product consists of an outer carton containing 1 bottle of 30 film-coated tablets.

Manufacturer
Gilead Sciences Ireland UC
IDA Business & Technology Park
Carrigtohill
County Cork
Ireland

Registration Holder
Gilead Sciences Israel Ltd.
4 HaHarash Street
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The medicine's registration no. in the national register of medicines at the Ministry of Health: 34742

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

Revised in March 2024.
Reference: EU SmPC from October 2022.

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