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

STRIBILD®
Film-coated tablets

Active ingredients: Each capsule contains -

Elvitegravir	150 mg
Cobicistat	150 mg
Emtricitabine	200 mg
Tenofovir disoproxil	245 mg

Equivalent to tenofovir disoproxil fumarate 300 mg or 136 mg of tenofovir

Inactive agents and allergens: 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).

The medicine is intended for adults above the age of 18.

1. What is Stribild intended for

Stribild is indicated for the treatment of human immunodeficiency virus-1 (HIV-1) infection in adults aged 18 years and over who are antiretroviral treatment-naïve or are infected with HIV-1 without known mutations associated with resistance to any of the three antiretroviral agents in Stribild.

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

Stribild 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 Stribild

X Do not take this medicine if:

- You are sensitive **(**allergic**)** to the active agents **elvitegravir, cobicistat, emtricitabine, tenofovir, tenofovir disoproxil,** or any of the other ingredients of this medicine (listed in section 6 of this leaflet).
- You stopped treatment with any medicine containing **tenofovir disoproxil** on the advice of your doctor following problems with your kidney function.
- **You are taking one of these medicines:**
  - **alfuzosin** (used to treat an enlarged prostate gland)
  - **amiodarone, quinidine** (used to correct irregular heartbeats)
  - **dabigatran** (used to prevent and treat blood clots)
  - **carbamazepine, phenobarbital, phenytoin** (used to prevent seizures)
  - **rifampicin** (used to prevent and treat tuberculosis and other infections)
  - **dihydroergotamine, ergotamine, ergometrine** (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
  - **lovastatin, simvastatin** (used to lower blood cholesterol)
  - **pimozide, lurasidone** (used to treat abnormal thoughts or feelings)
  - **sildenafil** (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, you should not take Stribild and you should tell your doctor immediately.**

! Special warnings regarding the use of Stribild

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

You can still pass on HIV when taking this medicine, although the risk is lowered by effective antiretroviral therapy. Discuss with your doctor the precautions needed to avoid infecting other people.

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

Talk to your doctor before taking Stribild:

- **If you have kidney problems,** or have had kidney problems, or if tests have shown problems with your kidneys. Your doctor will carefully consider whether to treat you with Stribild.

  Stribild may affect your kidneys. Before starting treatment, your doctor will order blood tests to assess your kidney function. Your doctor will also order blood tests during treatment to monitor your kidneys.

  Stribild is not usually taken with other medicines that can damage your kidneys (see Other medicines and Stribild). If this is unavoidable, your doctor will monitor your kidney function more frequently.

- **Bone problems** (manifesting as persistent or worsening bone pain and sometimes resulting in fractures) may also occur due to damage to kidney tubule cells (see section 4, *Possible side effects*). Tell your doctor if you have bone pain or fractures.

  Tenofovir disoproxil may also cause loss of bone mass.

Overall, the effects of tenofovir disoproxil on long term bone health and future fracture risk in adult and paediatric patients are uncertain.

Tell your doctor if you know you suffer from osteoporosis. Patients with osteoporosis are at a higher risk of fractures.

- **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 Stribild. It's important not to stop taking Stribild without talking to your doctor: see section 3, Do not stop taking Stribild.

- **If you are over 65.** Stribild has not been studied in patients over 65 years of age. If you are older than this and are prescribed Stribild, your doctor will monitor you carefully.

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

While you are taking Stribild

Once you start taking Stribild, look out for:

- any **signs of inflammation or infection**
- **bone problems**

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

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

Other medicines and Stribild

There are some medicines that should never be taken with Stribild.
These are mentioned above under the heading "Do not take Stribild - If you are taking one of these medicines".

If you are taking, or have recently taken any other medicines including non prescription medicines and food supplements, tell your doctor or pharmacist. Stribild may interact with other medicines. As a result, the amounts of Stribild 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.

It is especially important to talk to your doctor if you are taking any of the following:

- **any other medicines containing:**
  - **tenofovir disoproxil**
  - **tenofovir alafenamide**
  - **lamivudine**
  - **adefovir dipivoxil**

- **medicines that may damage your kidneys,** examples include:
  - aminoglycosides (such as streptomycin, neomycin and gentamicin), vancomycin (for bacterial infections)
  - foscarnet, ganciclovir, cidofovir (for viral infections)
  - amphotericin B, pentamidine (for fungal infections)
  - interleukin-2, also called aldesleukin (to treat cancer)

- non-steroidal anti-inflammatory drugs (NSAIDs, to relieve bone or muscle pains)

It is also important to tell your doctor if you are taking any of the following types of medicines:

- **antifungals,** used to treat fungal infections, such as:
  - ketoconazole, itraconazole, voriconazole, fluconazole and posaconazole
- **antivirals,** used to treat hepatitis C infection:
  - ledipasvir/sofosbuvir, sofosbuvir/velpatasvir and sofosbuvir/velpatasvir/voxilaprevir
- **antibiotics,** used to treat bacterial infections including tuberculosis, containing:
  - rifabutin, clarithromycin or telithromycin
- **antidepressants,** used to treat depression:
  - medicines containing trazodone or escitalopram
- **sedatives and hypnotics,** used to treat anxiety:
  - buspirone, clorazepate, diazepam, estazolam, flurazepam and zolpidem
- **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, mexiletine, propafenone, metoprolol, timolol, amlodipine, diltiazem, felodipine, nicardipine, nifedipine and verapamil
- **medicines used to treat pulmonary arterial hypertension:**
  - bosentan
- **anticoagulants,** used to prevent and treat blood clots, such as:
  - warfarin, edoxaban, apixaban and rivaroxaban
- **bronchodilators,** used to treat asthma and other lung-related problems:
  - salmeterol
- **cholesterol lowering medicines,** such as:
  - rosuvastatin, atorvastatin, pravastatin, fluvastatin 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 Stribild.

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

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

Do not breast-feed during treatment with Stribild. This is because some of the active substances in this medicine pass into human breast milk. If you are a woman with HIV it is recommended that you do not breast-feed to avoid passing the virus to the baby in breast milk.

Driving and using machines
Stribild can cause dizziness, tiredness or insomnia. If you are affected while taking Stribild, do not drive and do not use any tools or machines.

Important information about some ingredients of the medicine

Stribild 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.

Stribild 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 Stribild

Always take this medicine exactly as your doctor has told you. Check with your 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 dose:
One tablet each day by mouth, with food. There is no information available regarding the crushing/splitting of the product. Do not chew, crush or split the tablet.

Do not exceed the recommended dose.

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.

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 Stribild.

If you take more Stribild than you should

If you accidentally take more than the recommended dose of Stribild or if a child has accidentally swallowed the medicine, you/they may be at increased risk of experiencing possible side effects with this medicine (see section 4, Side effects).

Contact your doctor or nearest emergency department immediately for advice. Keep the tablet bottle with you so that you can easily describe what you have taken.

If you forget to take Stribild

It is important not to miss a dose of Stribild.

If you do miss a dose:
- **and you notice within 18 hours** of the time you usually take Stribild, you must take the tablet as soon as possible. Always take the tablet with food. Then take the next dose as usual.
- **and you notice 18 hours or more** after the time you usually take Stribild, 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 Stribild, take another tablet with food.

Do not stop taking Stribild

Do not stop taking Stribild without talking to your doctor. Stopping Stribild can seriously affect your response to future treatment. If Stribild is stopped for any reason, speak to your doctor before you restart taking Stribild tablets.

When your supply of Stribild 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 HIV infection and hepatitis B, it is especially important not to stop your Stribild 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 (such as yellowing of your skin or the white part of your eyes, dark "tea-coloured" urine, light-coloured stools, loss of appetite for several days or longer, feeling or being sick, or stomach-area pain).

Do not take medicines in the dark!
Check the label and the dose <u>each 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>

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.

Like all medicines, this medicine can cause side effects, although not everybody gets them. Do not be alarmed by reading the list of side effects. You may not experience any of them. When treating HIV infection, it is not always possible to tell whether some of the unwanted effects are caused by Stribild or by other medicines that you are taking at the same time, or by the HIV disease itself.

Possible serious side effects: tell a doctor immediately

- **Lactic acidosis** (excess lactic acid in the blood) is a rare but potentially life-threatening side effect of some HIV medicines. Lactic acidosis occurs more often in women – particularly if they are overweight and in people with liver disease. The following may be signs of lactic acidosis:
  - deep, rapid breathing
  - tiredness or drowsiness
  - feeling sick (nausea), being sick (vomiting)
  - stomach pain

→ **If you think you may have lactic acidosis, tell 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. In addition to the opportunistic infections, autoimmune disorders (a condition that occurs when the immune system attacks healthy body tissue) may also occur after you start taking medicines for the treatment of your HIV infection. Autoimmune disorders may occur many months after the start of treatment. If you notice 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, please inform your doctor immediately to seek necessary treatment.

→ If you notice any symptoms of inflammation or infection, tell your doctor immediately.

Very common side effects
(*may affect at least 1 in every 10 patients treated*)
- diarrhoea
- vomiting
- feeling sick (nausea)
- weakness
- headache, dizziness
- rash

Tests may also show:
- decreased phosphate in your blood
- increased levels of creatine kinase in the blood that may result in muscle pain and weakness

Common side effects
(*may affect 1 to 10 in every 100 patients treated*)
- decreased appetite
- difficulty sleeping (*insomnia*), abnormal dreams
- pain, stomach pain
- problems with digestion resulting in discomfort after meals (*dyspepsia*)
- feeling bloated
- constipation, wind (*flatulence*)
- rashes (including red spots or blotches sometimes with blistering and swelling of the skin), which may be allergic reactions, itching, changes in skin colour including darkening of the skin in patches
- other allergic reactions
- tiredness

Tests may also show:
- low white blood cell count (which can make you more prone to infection)
- increased sugar, fatty acids (triglycerides), bilirubin in your blood
- liver and pancreas problems
- increased levels of creatinine in your blood

Uncommon side effects
(*may affect up to 1 in every 100 patients treated*)
- suicidal ideation and suicide attempt (in patients who have had depression or mental health problems before), depression
- back pain caused by kidney problems, including kidney failure. Your doctor may do blood tests to see if your kidneys are working properly
- damage to kidney tubule cells
- swelling of the face, lips, tongue or throat
- pain in the abdomen (tummy) caused by inflammation of the pancreas (*pancreatitis*)

- breakdown of muscle, muscle pain or weakness

Tests may also show:
- anaemia (low red blood cell count)
- decreased levels of potassium in the blood
- changes to your urine

Rare side effects
(*may affect up to 1 in every 1,000 patients treated*)
- lactic acidosis (see Possible serious side effects: tell a doctor immediately)
- yellow skin or eyes, itching, or pain in the abdomen (tummy) caused by inflammation of the liver (*hepatitis*)
- fatty liver
- inflammation of the kidney (*nephritis*)
- passing a lot of urine and feeling thirsty (*nephrogenic diabetes insipidus*)
- softening of the bones (with bone pain and sometimes resulting in fractures)

The breakdown of muscle, softening of the bones (with bone pain and sometimes resulting in fractures), muscle pain, muscle weakness and decreases in potassium or phosphate in the blood may occur due to damage to kidney tubule cells.

→ 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 Stribild 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.

→ 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 to the registration holder at the following: DrugSafety.Israel@gilead.com.
By reporting side effects, you can help provide more information on the safety of this medicine.

5. How to store Stribild

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

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

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.

Store below 30°C.

6. Additional information

What Stribild contains

In addition to the active ingredients, Stribild contains:

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

Film-coating:
Polyvinyl alcohol (E1203), indigo carmine (FD&C Blue #2) aluminium lake (E132), polyethylene glycol (E1521), titanium dioxide (E171), talc (E553b), yellow iron oxide (E172).

What Stribild looks like and contents of the pack

Stribild film-coated tablets are green, capsule-shaped tablets, debossed on one side with "GSI" and the number "1" surrounded by a square box on the other side of the tablet. Stribild 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 following pack size is available: outer cartons containing 1 bottle of 30 film-coated tablets.

Registration Holder
Gilead Sciences Israel Ltd.
4 HaHarash Street, Hod Hasharon
4524075, Israel

Manufacturer
Gilead Sciences Ireland UC
IDA Business & Technology Park
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Registration number of the medicine in the National Drug Registry of the Ministry of Health: 33963

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

Revised in January 2022 in accordance with MoH guidelines.
Reference: EU SmPC from October 2021.

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