

**Patient leaflet in accordance with
the Pharmacists' Regulations (Preparations) – 1986**

The medicine is dispensed
according to a physician's prescription only

Tivicay™

Film coated tablets.

Each tablet contains **dolutegravir 50 mg (as sodium)**

List of the additional ingredients detailed in section 6.

Read the entire leaflet carefully before using the medicine. This leaflet contains concise information about the medicine. If you have any other questions, refer to the physician or the pharmacist.

This medicine has been prescribed for you. Do not pass it on to others. It may harm them even if it seems to you that their medical condition is similar.

This medicine is not intended for adolescents and children under the age of 12.

1. What is the medicine intended for?

Tivicay is used to treat **HIV (human immunodeficiency virus) infection** in adults and adolescents over 12 years old and weighing at least 40 kg.

Tivicay does not cure HIV infection; it reduces the amount of virus in your body, and keeps it at a low level. As a result of that, it also increases the CD4 cell count in your blood. CD4 cells are a type of white blood cells that are important in helping your body to fight infection.

Not everyone responds to treatment with Tivicay in the same way. Your physician will monitor the effectiveness of your treatment.

Tivicay is always used in combination with other antiretroviral medicines (*combination therapy*). To control your HIV infection, and to stop your illness from getting worse, you must keep taking all your medicines, unless your physician tells you to stop taking any.

Therapeutic group

Tivicay contains the active ingredient dolutegravir. This medicine belongs to a group of antiretroviral medicines called *integrase inhibitors (INIs)*.

2. Before using the medicine

Do not use the medicine if:

- You are sensitive (allergic) to the active ingredient or to any of the other ingredients contained in the medicine (listed in section 6).
 - You are taking another medicine called dofetilide (to treat heart conditions).
- If you think any of these apply to you, tell your physician.

Special warnings regarding the use of the medicine

Look out for important symptoms

Some people taking medicines for HIV infection develop other conditions, which can be serious. These include:

- symptoms of infections and inflammation
- joint pain, stiffness and bone problems

You need to know about important signs and symptoms to look out for while you're taking Tivicay.

→ **Read the information 'Other possible side effects' in Section 4 of this leaflet.**

Protect other people

HIV infection is spread by sexual contact with someone who has the infection, or by transfer of infected blood (for example, by sharing injection needles). You can still pass on HIV when taking this medicine, although the risk is lowered by effective antiretroviral therapy. Discuss with your physician the precautions needed to avoid infecting other people.

Children

Do not give this medicine to children under the age of 12 and weighing less than 40 kg or with HIV infection that is resistant to other medicines similar to Tivicay. The use of Tivicay in children under the age of 12 has not yet been studied.

Other medicines and Tivicay

If you are taking, have recently taken or are planning to take any other medicines including non-prescription medicines and food supplements, tell the physician or the pharmacist.

Don't take Tivicay with the following medicines:

- dofetilide, used to treat **heart conditions**

Some medicines can affect how Tivicay works, or increase the risk of side effects. Tivicay can also affect how some other medicines work.

Tell your physician if you are taking any of the medicines *in the following list*:

- metformin, to treat **diabetes**
- medicines called **antacids**, to treat **indigestion** and **heartburn**. **Do not take an antacid** during the 6 hours before you take Tivicay, or for at least 2 hours after you take it (see also Section 3).
- calcium supplements, iron supplements and multivitamins. **Do not take a calcium supplement, iron supplement or multivitamin** during the 6 hours before you take Tivicay, or for at least 2 hours after you take it (see also Section 3).
- etravirine, efavirenz, fosamprenavir/ritonavir, nevirapine or tipranavir/ritonavir, to treat **HIV infection**
- rifampicin, to treat tuberculosis (TB) and other **bacterial infections**
- phenytoin and phenobarbital, to treat **epilepsy**
- oxcarbazepine and carbamazepine, to treat **epilepsy** or **bipolar disorder**
- **St. John's wort** (*Hypericum perforatum*), a herbal remedy to treat **depression**

→ **Tell your physician** if you are taking any of these medicines. Your physician may decide to adjust your dose or that you need extra checkups.

Pregnancy

If you are pregnant, if you become pregnant, or if you are planning to have a baby:

→ **Consult with your physician** about the risks and benefits of taking Tivicay.

Breast feeding

Women who are HIV-positive must not breast feed because HIV infection can be passed on to the baby in breast milk.

It is not known whether the ingredients of Tivicay can pass into your breast milk.

If you're breast feeding, or thinking about breast feeding:

→ **Talk to your physician immediately.**

Driving and using machines

Tivicay can make you dizzy and have other side effects that make you less alert.

→ Don't drive or operate machinery unless you are sure you're not affected.

3. How should you use the medicine?

Always use according to the physician's instructions. You should check with the physician or the pharmacist if you are unsure.

The dosage and treatment will be determined only by the physician.

The usual dosage is:

- The usual dosage is one 50 mg tablet **once a day**; if you are taking **certain other medicines** (see section 2, earlier in this leaflet), the dosage is one 50 mg tablet **twice a day**; or
- **For the treatment of HIV that is resistant** to other medicines similar to Tivicay, the usual dosage of Tivicay is one 50 mg tablet, **twice a day**.

Swallow the tablet with some liquid. Tivicay can be taken with or without food. When Tivicay is taken twice a day, your physician may advise you to take with food.

Use in children and adolescents

Children and adolescents aged between 12 and 17 years and weighing at least 40 kg can take the adult dose of one tablet (50 mg), once a day. Tivicay should not be used in children and adolescents with **HIV infection that is resistant** to other medicines similar to Tivicay.

Do not exceed the recommended dose

Antacid medicines

Antacids, to treat indigestion and heartburn, can stop Tivicay being absorbed into your body and make it less effective.

Do not take an antacid during the 6 hours before you take Tivicay, or for at least 2 hours after you take it. Other acid-lowering medicines like ranitidine and omeprazole can be taken at the same time as Tivicay.

→ Talk to your physician for further advice on taking acid-lowering medicines with Tivicay.

Calcium supplements, iron supplements or multivitamins

Calcium supplements, iron supplements or multivitamins can stop Tivicay being absorbed into your body and make it less effective. Do not take a calcium supplement, iron supplement or multivitamins during the 6 hours before you take Tivicay, or for at least 2 hours after you take it.

→ Talk to your physician for further advice on taking calcium supplements, iron supplements or multivitamins with Tivicay.

If you accidentally have taken a higher dosage

If you accidentally have taken too many tablets of Tivicay, **contact your physician or pharmacist for advice**. If possible, show them the Tivicay package. If a child has accidentally swallowed the medicine, refer immediately to a physician or to a hospital emergency room and bring the package of the medicine with you.

If you forgot to take the medicine

If you miss a dose, take it as soon as you remember. But if your next dose is due within 4 hours, skip the dose you missed and take the next dose at the usual time. Then continue your treatment as before.

→ **Don't take a double dose** to make up for a missed dose.

Don't stop taking Tivicay without consulting with your physician

Take Tivicay for as long as your physician recommends. Don't stop unless your physician advises you to.

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

4. Side effects

As with any medicine, use of Tivicay may cause side effects in some of the users. Do not be alarmed by reading the list of side effects. You may not experience any of them.

When you're being treated for HIV, it can be hard to tell whether a symptom is a side effect of Tivicay or other medicines you are taking, or an effect of the HIV infection itself. **So it is very important to inform your physician about any changes in your health.**

Allergic reactions

These are uncommon in people taking Tivicay. The signs include:

- skin rash
- a high temperature (*fever*)
- lack of energy (*fatigue*)
- swelling, sometimes of the face or mouth (*angioedema*), causing difficulty in breathing
- muscle or joint aches.

→ **See a physician straight away.** Your physician may decide to carry out tests on your liver, kidneys or blood, and may tell you to stop taking Tivicay.

Very common side effects

These may affect **more than 1 in 10 people**:

- headache
- diarrhoea
- nausea (*feeling sick*).

Common side effects

These may affect **up to 1 in 10 people**:

- rash
- itching (*pruritus*)
- vomiting (*being sick*)
- stomach pain (*abdominal pain*)
- stomach (*abdominal*) discomfort
- insomnia
- dizziness
- abnormal dreams
- depression (feelings of deep sadness and unworthiness)
- lack of energy (*fatigue*)
- wind (*flatulence*)
- increase in the level of liver enzymes
- increase in the level of enzymes produced in the muscles (*creatine phosphokinase*).

Uncommon side effects

These may affect **up to 1 in 100 people**:

- inflammation of the liver (*hepatitis*)
- suicidal thoughts and behaviours (mainly in patients who have had depression or mental health problems before)

Other possible side effects

People taking combination therapy for HIV may get other side effects.

Symptoms of infection and inflammation

People with advanced HIV infection (AIDS) have weak immune system, and are more likely to develop serious infections (*opportunistic infections*). Such infections may have been "silent" and not detected by the weak immune system before treatment was started. After starting treatment, the immune system becomes stronger, and may attack the infections, which can cause symptoms of infection or inflammation. The symptoms usually include **fever**, plus some of the following:

- headache
- stomach ache
- difficulty breathing

In rare cases, as the immune system becomes stronger, it can also attack healthy body tissue (*autoimmune disorders*). The symptoms of autoimmune disorders may develop many months after you start taking medicine to treat your HIV infection. The symptoms may include:

- palpitations (rapid or irregular heartbeat) or tremor
- hyperactivity (excessive restlessness and movement)
- weakness beginning in the hands and feet and moving up towards the trunk of the body.

If you get any symptoms of infection and inflammation or if you notice any of the symptoms above:

→ **Tell your physician immediately.** Don't take other medicines for the infection without your physician's advice.

Joint pain, stiffness and bone problems

Some people taking combination therapy for HIV develop a condition called *osteonecrosis*. With this condition, parts of the bone tissue die because of reduced blood supply to the bone. People may be more likely to get this condition:

- if they have been taking combination therapy for a long time
- if they are also taking anti-inflammatory medicines called corticosteroids
- if they drink alcohol
- if their immune system is very weak
- if they are overweight.

Signs of osteonecrosis include:

- stiffness in the joints
- aches and pains in the joints (especially in the hip, knee or shoulder)
- difficulty moving.

If you notice any of these symptoms:

→ **Tell your physician.**

If a side effect has appeared, if any of the side effects get worse or when you suffer from a side effect that has not been mentioned in the leaflet, you should consult the physician.

Adverse events can be reported to the Ministry of Health via the on-line form for adverse events reporting, that is located on the Ministry of Health home page www.health.gov.il

or by entering the link:

<https://forms.gov.il/globaldata/getsequence/getsequence.aspx?formType=AdversEffectMedic@moh.gov.il>

5. How to store the medicine?

• 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 the medicine after the expiry date (exp. date) appearing on the package. The expiry date refers to the last day of that month.

• Do not store above 30°C.

• Use within 30 days after opening.

6. Additional information

• In addition to the active ingredient the medicine also contains - D-mannitol (E421), microcrystalline cellulose, sodium starch glycolate, povidone K29/32, sodium stearyl fumarate, polyvinyl alcohol-partially hydrolyzed, titanium dioxide (E171), macrogol, talc and iron oxide yellow (E172).

• What does the medicine look like and what is the content of the package -

Tivicay film-coated tablets are yellow, round, biconvex and marked with the code 'SV 572' on one side and '50' on the other side. The film-coated tablets are provided in bottles containing 30 tablets.

• License Holder: GlaxoSmithKline (Israel) Ltd., 25 Basel St., Petach Tikva.

• Manufacturer: Glaxo Wellcome S.A., Burgos, Spain.

• This leaflet was checked and approved by the Ministry of Health in: August 2015.

• Registration number of the medicine in the National Drug Registry of the Ministry of Health: 151-40-33983-01.