PATIENT LEAFLET IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) – 1986

The medicine is dispensed with a doctor's prescription only

Fingolimod Teva

Capsules

Composition

Each capsule contains:

Fingolimod (as HCl) 0.5 mg

For information regarding inactive ingredients and allergens, see section 2 "Important information about some of the ingredients of the medicine" and section 6 "Additional information".

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

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

In addition to the leaflet, the Fingolimod Teva preparation has a patient safety information card. This card contains important safety information that you must know before starting treatment with Fingolimod Teva and during the treatment, and act accordingly.
Please review the patient safety information card and the patient leaflet before starting to use the preparation. You should keep the card for further review, if necessary.

Taking the first dose:

After taking the first dose of Fingolimod Teva, observation by a healthcare professional is required for at least 6 hours.

This recommendation also applies if you are resuming treatment after interrupting treatment with Fingolimod Teva.

The full instructions for taking the first dose are detailed in section 2 "Special warnings regarding the use of the medicine".

1. WHAT IS THE MEDICINE INTENDED FOR?

Fingolimod Teva is intended for the treatment of relapsing forms of multiple sclerosis (MS), to reduce the number of relapses and to slow down the progression of physical problems (disability) caused by the disease.

Therapeutic group

Selective immunosuppressant

Sphingosine-1-phosphate receptor modulator

What is multiple sclerosis?

Multiple sclerosis is a chronic disease that affects the central nervous system, comprising the brain and spinal cord. In multiple sclerosis, the inflammatory process destroys the protective sheath (called myelin) that surrounds the nerves in the central nervous system, and prevents normal activity of the nerves (demyelination).

Relapsing-remitting multiple sclerosis is characterized by repeated attacks (relapses) of nervous system symptoms, that reflect inflammation within the central nervous system. Different patients may have different symptoms, but typical symptoms are: difficulty walking, numbness, vision problems or balance problems. The symptoms of a relapse may disappear completely when the attack is over, but some problems may remain.

How Fingolimod Teva works

Fingolimod Teva helps to protect the central nervous system from attack by the body's immune system, by reducing the ability of certain white blood cells (lymphocytes) to move freely within the body and preventing them from reaching the brain and spinal cord. This limits the damage to the nerves caused by multiple sclerosis. Fingolimod Teva also reduces some of the body's immune response.

2. BEFORE USING THE MEDICINE

Do not use this medicine if:

- You are allergic (hypersensitive) to fingolimod or to any of the additional ingredients the medicine contains, which are detailed in section 6 "Additional information". The symptoms of an allergic reaction may include: rash, itchy hives or swelling of the lips, tongue or face.
- You have had a heart attack, unstable angina, stroke or transient ischemic attack or certain types of heart failure in the last 6 months.
- You have, or have had in the past, certain types of irregular or abnormal heart rate (arrhythmias), including patients in whom a cardiac finding called long QT is seen on ECG before starting treatment with Fingolimod Teva.
- You have a heart rate problem that requires treatment with certain medicines.

Talk to your doctor before taking Fingolimod Teva if you have any of these conditions or if you do not know if you have them.

Special warnings regarding the use of the medicine

Taking the first dose:

Fingolimod Teva can cause your heart rate to slow down, especially after taking the first dose. You will undergo a test called an electrocardiogram (ECG) to check the electrical activity of the heart before taking the first dose of Fingolimod Teva.

All patients will remain under the observation of a healthcare professional for at least 6 hours after taking the first dose of Fingolimod Teva:

After taking the first dose of Fingolimod Teva:

- Your heart rate and blood pressure should be checked every hour
- You should be under the observation of a healthcare professional to see if you have any serious side effects. If your heart rate slows down too much, you may have symptoms such as: Dizziness, tiredness, feeling like your heart is beating slowly or skipping a beat, chest pain.
- If you have any of the symptoms of a slow heart rate, they will usually occur during the first 6 hours after taking the first dose of Fingolimod Teva. The symptoms can occur up to 24 hours after taking the first dose of Fingolimod Teva.
- 6 hours after taking the first dose of Fingolimod Teva, you will have another ECG. If the ECG shows any heart problems or if your heart rate is too low or continues to decrease, you will continue to be observed.
- If you have any serious side effects after taking the first dose of Fingolimod Teva, especially those that require treatment with other medicines, you will stay at the medical center for overnight observation. In addition, you will be observed for any serious side effects for at least 6 hours after taking the second dose of Fingolimod Teva on the next day.
- If you have certain types of heart problems or if you are taking certain types of medicines that can affect your heart, you will stay at the medical center for overnight observation by a healthcare professional after taking the first dose of Fingolimod Teva.

Your slow heart rate will usually return to normal within one month after you start taking Fingolimod Teva. Refer immediately to your doctor or to the emergency room of the nearest hospital if you have any symptoms of a slow heart rate.

If you miss one or more doses of Fingolimod Teva, you may need to be observed by a healthcare professional when taking the next dose. Refer to your doctor if you miss a dose of Fingolimod Teva. See also "How should you use the medicine?".

Tell your doctor about all your medical conditions before taking Fingolimod Teva, including if you have had or currently have:

- Irregular or abnormal heart rate (arrhythmia)
- History of stroke or transient ischemic attack
- Heart problems, including heart attack or angina
- History of repeated fainting (loss of consciousness)
- Fever or infection, or if you are unable to fight infections due to an illness or are taking or have taken in the past medicines that weaken your immune system
- You have recently been vaccinated or are about to be vaccinated
- Chickenpox or if you have been vaccinated for chickenpox. Your doctor may perform a blood test for the chickenpox virus. You may need to get the whole series of chickenpox vaccinations and then wait one month before starting the treatment with Fingolimod Teva
- Eye problems, especially an inflammation of the eye called uveitis
- Diabetes
- Breathing problems, including while sleeping
- Liver problems
- High blood pressure
- Types of skin cancer called basal cell carcinoma (BCC) or melanoma
- Please consult your doctor before becoming pregnant. You should avoid becoming pregnant while taking Fingolimod Teva or within two months after you stop taking it, due to the risk of harming the fetus. See the section "Pregnancy and breastfeeding" below

Elderly patients (over the age of 65)

Experience with Fingolimod Teva treatment in elderly people is limited.

Fingolimod Teva should be used with caution in patients 65 years of age and older.

Children and adolescents

Fingolimod Teva is not intended for treatment in children and adolescents under the age of 18.

Tests and follow-up

Before starting the treatment:

White blood cell test, vision test, liver function blood test – as detailed in the section "Side effects".

Pregnancy test – as detailed in the section "Pregnancy and breastfeeding".

Your doctor may perform a blood test for the chickenpox virus.

For the tests required when taking the first dose of Fingolimod Teva – see the section "Taking the first dose" above.

During the treatment:

Blood pressure tests, skin test, vision test 3 to 4 months after starting treatment, liver function blood test – as detailed in the section "Side effects".

You should consult regarding a routine examination of the cervix (Pap smear) – as detailed in the section "Side effects".

Drug interactions

Using Fingolimod Teva together with other medicines may cause serious side effects.

If you are taking or have recently taken other medicines including non-prescription medicines and nutritional supplements, tell the doctor or the pharmacist. Especially if you are taking:

- **Medicines that prolong the QT interval** such as citalopram, chlorpromazine, haloperidol, methadone and erythromycin, because starting treatment with Fingolimod Teva causes a decrease in heart rate and may prolong the QT interval.
- **Ketoconazole** – a medicine for the treatment of fungal infections. A patient using Fingolimod Teva and ketoconazole concomitantly should be closely monitored, as the risk of side effects is greater.
- **Vaccinations** – If you need to receive a vaccine, consult your doctor first. During the treatment and up to two months after the treatment with Fingolimod Teva, you will not be able to receive certain vaccines that contain a live virus (live attenuated vaccines) as they may cause the infection that the vaccine is meant to prevent. Other vaccines may also not work well if given during this period.
- **Antineoplastic medicines, medicines that suppress or modulate the immune system** (including corticosteroids) – are expected to increase the risk of immunosuppression, and the risk of added effect on the immune system must be considered if these medicines are co-administered with Fingolimod Teva. When switching the treatment from medicines that have a lasting effect on the immune system such as natalizumab, teriflunomide or mitoxantrone, the duration and mode of action of these medicines must be considered to avoid an additional and unintended immunosuppressive effect when starting to take Fingolimod Teva.
- **Medicines that slow down the heart rate and the atrioventricular conduction.** Such as beta-blockers, digoxin or calcium channel blockers such as diltiazem or verapamil. Before starting the treatment with Fingolimod Teva, consult the doctor who prescribed these medicines for you regarding the possibility of switching to medicines that do not slow down the heart rate and atrioventricular conduction.

Using Fingolimod Teva and Food

Fingolimod Teva can be taken with or without food.

Pregnancy and breastfeeding

Pregnancy

Fingolimod Teva may harm your fetus. Tell your doctor before taking Fingolimod Teva if you are pregnant or planning to become pregnant.

Tell your doctor immediately if you become pregnant during the treatment with Fingolimod Teva or if you become pregnant within two months of stopping the treatment with Fingolimod Teva.

- You should stop taking Fingolimod Teva two months before trying to become pregnant.
- If you can become pregnant, you must use effective contraception during the treatment with Fingolimod Teva and for at least two months after stopping the treatment.

See also the section "Severe worsening of multiple sclerosis after stopping Fingolimod Teva" in the "Side effects" section.

Breastfeeding

Tell your doctor before taking Fingolimod Teva if you are breastfeeding or if you are planning to breastfeed. It is not known whether Fingolimod Teva passes into breast milk. Consult your doctor regarding the best way to feed your baby if you are taking Fingolimod Teva.

Driving and operating machinery

Your doctor will tell you if your illness allows you to drive a vehicle, ride a bicycle and operate machinery safely. Fingolimod Teva is not expected to have an influence on your ability to drive and operate machinery.

However, after taking the first dose of Fingolimod Teva, you must stay for at least 6 hours under the observation of a healthcare professional. During this time, and possibly even later, your ability to drive and operate machinery may be impaired.

Important information about some of the ingredients of the medicine

The sodium content in one capsule is approximately 0.045 mg. This medicine contains less than 23 mg of sodium in each capsule, and is therefore considered sodium-free.

3. HOW SHOULD YOU USE THE MEDICINE?

Always use the preparation according to the doctor's instructions. Check with the doctor or pharmacist if you are uncertain about the dosage and how to use the preparation.

Dosage

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

The generally accepted dosage is:

One capsule per day (0.5 mg fingolimod).

Do not exceed the recommended dose.

How to take the medicine

For oral administration

Fingolimod Teva should be taken once a day with a glass of water.

Taking Fingolimod Teva at the same time each day will help you remember when to take the medicine.

No information is available regarding opening the capsule and dispersing its content.

If you accidentally took a higher dosage

If you took an overdose or by mistake a child swallowed this medicine, go to the doctor or the emergency room of the hospital immediately and take the package of the medicine with you.

If you have forgotten to take the medicine

If you forgot to take a dose of Fingolimod Teva, refer to your doctor immediately. You may need to be monitored by a healthcare professional for at least 6 hours when you take the next dose. If you need to be monitored by a healthcare professional when you take the next dose of Fingolimod Teva, you will undergo:

- An ECG test before taking the dose
- Hourly heart rate and blood pressure tests after taking the dose
- An ECG test 6 hours after taking the dose

Stopping treatment

Follow the treatment as recommended by the doctor. Even if there is an improvement in your health, do not stop treatment with the medicine without consulting the doctor.

If you stop taking the medicine, the symptoms of multiple sclerosis may return and become worse – see the section "Severe worsening of multiple sclerosis after stopping Fingolimod Teva" in the "Side effects" section.

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

If you have any other questions regarding use of the medicine, consult the doctor or the pharmacist.

4. SIDE EFFECTS

As with any medicine, using Fingolimod Teva may cause side effects in some users. Do not be alarmed when reading the list of side effects. You may not experience any of them.

Fingolimod Teva may cause serious side effects, including:

- **Slow heart rate (bradycardia or bradyarrhythmia) when you start taking Fingolimod Teva.** Fingolimod Teva can cause your heart rate to slow down, especially after you take the first dose. Refer immediately to the doctor or to the emergency room of the nearest hospital if you have any symptoms of a slow heart rate. See details in the section "Special warnings regarding the use of the medicine", under subsection "Taking the first dose".
- **Infections** – Fingolimod Teva can increase your risk of serious infections that may be life-threatening and cause death. Do not receive **live** vaccines during the treatment with Fingolimod Teva and for two months after you stop taking Fingolimod Teva. Talk to your doctor before you receive a vaccine during the treatment and for two months after the treatment with Fingolimod Teva. If you receive a live vaccine, you may get the infection that the vaccine was meant to prevent. Vaccines may be less effective when given during treatment with Fingolimod Teva. Human papillomavirus (HPV) – infections, including papilloma, dysplasia, warts and papillomavirus-related cancer have been reported in patients treated with Fingolimod Teva. Your doctor will consider whether you need to be vaccinated against papillomavirus before starting the treatment. Due to the risk of papillomavirus infection, you should consult your doctor regarding a routine examination of the cervix (Pap smear). Fingolimod Teva reduces the number of white blood cells (lymphocytes) in your blood. Levels usually return to normal within two months of stopping the treatment. Your doctor may perform a blood test to check your white blood cell level before you start taking Fingolimod Teva. Refer to your doctor immediately if you have any symptoms of infection during the treatment with Fingolimod Teva and for two months after the last dose of Fingolimod Teva:
  Fever, tiredness, body aches, chills, nausea, vomiting, headache accompanied by fever, stiffness in the neck, sensitivity to light, nausea or confusion (these may be symptoms of meningitis, an infection of the membranes around the brain and spine).
- **Progressive Multifocal Leukoencephalopathy (PML) -** PML is a rare brain infection that usually leads to death or severe disability. If PML occurs, it usually happens in people with a weakened immune system, but it has also happened in people whose immune system was not weakened. The symptoms of PML worsen over days to weeks. Refer to your doctor immediately if you have symptoms of PML, whether new or worsening, that last for several days, including:
  Weakness of one side of the body, loss of movement coordination in the arms and legs, decreased strength, balance problems, changes in vision, changes in thinking or memory, confusion, personality changes.
- **A vision problem called macular edema** – macular edema can cause some of the same vision symptoms as a multiple sclerosis attack (inflammation of the optic nerve). You may not notice any symptoms of macular edema. But if macular edema occurs, it usually begins during the first 3 to 4 months after starting the treatment with Fingolimod Teva. Your doctor should check your vision before starting the treatment with Fingolimod Teva and 3 to 4 months after starting the treatment, or whenever you notice changes in your vision during the treatment with Fingolimod Teva. Your risk of macular edema is higher if you have diabetes or if you have had an eye inflammation called uveitis. Refer to a doctor immediately if you have one or more of the following:
  Blurriness or shadows in the center of your vision, a blind spot in the center of your vision, sensitivity to light, abnormal color (shades) vision.

Additional serious side effects:

- **Swelling and narrowing of the blood vessels in your brain.** A condition called PRES (posterior reversible encephalopathy syndrome) has occurred rarely in patients taking Fingolimod Teva. The symptoms of PRES usually improve when you stop taking Fingolimod Teva. However, without treatment, they may lead to a stroke. Refer to a doctor immediately if you have one or more of the following symptoms:
  Sudden severe headache, sudden confusion, sudden loss of vision or other changes in your vision, convulsions.
- **Liver damage.** Fingolimod Teva may cause liver damage. Your doctor should perform blood tests to check your liver before you start taking Fingolimod Teva and periodically during the treatment. Refer to your doctor immediately if you have one or more of the following symptoms of liver damage: Nausea, vomiting, abdominal pain, tiredness, loss of appetite, yellowing of the skin or of the whites of the eye, dark urine.
- **Breathing problems.** Some people who take Fingolimod Teva have shortness of breath. Refer to a doctor immediately if you have new or worsening breathing problems.
- **Severe worsening of multiple sclerosis after stopping Fingolimod Teva.** After stopping Fingolimod Teva, multiple sclerosis symptoms may return and become worse compared to before or during the treatment. Many people who have worsening of multiple sclerosis symptoms that occurred after stopping Fingolimod Teva, do not return to the level of functioning they had before stopping Fingolimod Teva. This worsening usually occurs within 12 weeks after stopping Fingolimod Teva, but it may occur later. Always talk to your doctor before you stop taking Fingolimod Teva for any reason. Tell your doctor if there is a worsening of multiple sclerosis symptoms after stopping Fingolimod Teva.
- **Unusual brain lesions associated with a multiple sclerosis attack.** Rare cases of unusually large brain lesions associated with a multiple sclerosis attack have been reported in patients treated with Fingolimod Teva (a condition called tumefactive lesions). In case of a severe attack, your doctor will consider performing an MRI to evaluate the condition and will decide whether you need to stop taking Fingolimod Teva.
- **High blood pressure.** Your doctor should check your blood pressure during the treatment with Fingolimod Teva.
- **Types of skin cancer called basal cell carcinoma (BCC) and melanoma.** Tell your doctor if there are any changes in the appearance of your skin, including changes in a mole, a new dark area on your skin, a sore that does not heal or growths on your skin such as a bump that may be shiny, pearly white, skin-colored or pink. Your doctor should check your skin and see if there are any changes during the treatment with Fingolimod Teva. You should limit the amount of time you spend in sunlight and ultraviolet (UV) light. Wear protective clothing and use sunscreen with a high sun protection factor.
- **Allergic reactions.** Refer to your doctor if you have symptoms of an allergic reaction, including a rash, itchy hives, or swelling of the lips, tongue, or face.

Very common side effects (occur in more than one out of ten users):

- Headache
- Abnormal liver tests
- Diarrhea
- Cough
- Influenza
- Inflammation of the sinuses (sinusitis)
- Back pain
- Pain in the abdomen area
- Pain in the arms or legs

Common side effects (occur in 1-10 out of 100 users):

- Inflammation of the bronchi (bronchitis)
- Shingles (herpes zoster)
- Sun fungus
- Migraine
- Nausea
- Weakness
- Hair loss
- Actinic keratosis – a pre-cancerous growth
- Increased blood triglycerides levels
- Blurry vision
- Low level of lymphocytes (lymphopenia)
- Low level of white blood cells (leukopenia)
- Skin papilloma – a benign growth on the surface of the skin

Additional reported side effects include convulsions, dizziness, pneumonia, eczema and itching.

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

- Autoimmune hemolytic anemia – the autoimmune form of anemia (decreased amount of red blood cells) in which red blood cells are destroyed
- Thrombocytopenia – a decrease in platelets which increases the risk of bleeding or bruising
- Kaposi sarcoma – a tumor related to human herpesvirus 8 infection
- Cryptococcal infections (a type of fungal infection), including cryptococcal meningitis with symptoms such as headache accompanied by stiff neck, sensitivity to light, nausea and/or confusion
- Joint pain
- Muscle pain
- Squamous cell carcinoma (SCC) – a type of skin cancer which may look like a red hard tissue lump, a crusty sore or a new sore on an existing scar
- Merkel cell carcinoma (a type of skin cancer) – possible signs include a painless, bluish-red or skin colored tissue lump, often on the face, head or neck. Merkel cell carcinoma can also look like a tissue lump or a painless hard lump. Prolonged exposure to the sun and a weak immune system can affect the risk of developing Merkel cell carcinoma.
- Lymphoma – a type of cancer that affects the lymphatic system

If a side effect occurs, or if one of the side effects worsens, or if you suffer from a side effect not mentioned in the leaflet, consult with the doctor.

Reporting side effects

Side effects may be reported to the Ministry of Health by clicking on the link "Report side effects due to medicinal treatment" found on the Ministry of Health website homepage (www.health.gov.il), which will direct you to the online form for reporting side effects, or by clicking on the following link:
https://sideeffects.health.gov.il

5. HOW TO STORE THE MEDICINE?

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

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.

Storage conditions

The medicine should be stored below 25°C.

Do not discard medicines via wastewater or the trash. Ask your pharmacist how to dispose of medicines no longer in use. These measures will help to protect the environment.

6. ADDITIONAL INFORMATION

In addition to the active ingredient the medicine also contains:

Pregelatinized starch, gelatin, titanium dioxide (E171), sodium lauryl sulphate, iron oxide yellow (E172), printing ink (black).

What does the medicine look like and what are the contents of the package

Hard capsules containing a creamy white powder, with the white opaque body of the capsule imprinted with TEVA 7820 in black, and the yellow cap of the capsule imprinted with TEVA 7820 in black.

Size of the package: 28 or 30 capsules in trays (blisters).

Not all package sizes may be marketed.

Name and address of the manufacturer and license holder

Teva Israel Ltd.,
124 Dvora HaNevi'a St., Tel Aviv 6944020.

The leaflet was revised in August 2023 in accordance with the Ministry of Health guidelines.

Registration number of the medicine in the national drug registry of the Ministry of Health: 157-40-34718

FINGOLIMOD TABS PL MW0823

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