

PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS’ REGULATIONS (PREPARATIONS) - 1986

The medicine is dispensed with a doctor’s prescription only

GILENYA® 0.5 mg Hard capsules

The active ingredient

Each capsule contains:

Fingolimod (as hydrochloride) 0.5 mg

Inactive ingredients:

See section 6 'Further Information'

Read this leaflet carefully in its entirety before using the medicine. This leaflet contains concise information about the medicine. If you have further questions, refer to the doctor or pharmacist.

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

Taking the first dose:

After taking the first dose of Gilenya, 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 Gilenya. The full instructions regarding taking the first dose are detailed in the section 'Special warnings regarding use of the medicine'.

1. WHAT IS THE MEDICINE INTENDED FOR?

Gilenya 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 disabilities caused by the disease.

Therapeutic group:

Selective immunosuppressant

Sphingosine 1-phosphate receptor modulator

What is multiple sclerosis

Multiple sclerosis (MS) is a long-term condition that affects the central nervous system (CNS), comprising the brain and spinal cord. In MS, inflammation destroys the protective sheath (called myelin) around the nerves in the CNS and prevents the nerves from working properly. This is called demyelination.

Relapsing-remitting MS is characterised by repeated attacks (relapses) of nervous system symptoms that reflect inflammation within the CNS. Symptoms vary from patient to patient but typically involve walking difficulties, numbness, vision problems or disturbed balance. Symptoms of a relapse may disappear completely when the relapse is over, but some problems may remain.

How Gilenya works

Gilenya helps to protect against attacks on the CNS by the immune system by reducing the ability of some white blood cells (lymphocytes) to move freely within the body and by preventing them from reaching the brain and spinal cord. This limits nerve damage caused by MS. Gilenya also reduces some of the immune reactions of your body.

2. BEFORE USING THE MEDICINE

Do not use the medicine if:

- 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 heartbeat (arrhythmias), including patients in whom a heart finding called prolonged QT is seen on ECG before starting Gilenya.
- you have a heart rhythm problem that requires treatment with certain medicines.
- you are allergic (hypersensitive) to fingolimod or to any of the other ingredients the medicine contains, listed in section 6 'Further information'. The symptoms of an allergic reaction may include: rash, itchy hives or swelling of the lips, tongue or face.

Talk to your doctor before you take Gilenya if you have any of these conditions or if you do not know if you have any of them.

Special warnings regarding use of the medicine:

• Taking the first dose:

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

All patients will remain under observation by a healthcare professional for at least 6 hours after taking the first dose of Gilenya.

After you take your first dose of Gilenya:

- Your pulse and blood pressure should be checked every hour
- You should be observed by 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 beats
 - chest pain

If you have any of the symptoms of slow heart rate, they will usually happen during the first 6 hours after taking your first dose of Gilenya. The symptoms can happen up to 24 hours after you take your first Gilenya dose.

- 6 hours after you take your first dose of Gilenya, you will have another ECG. If your ECG shows any heart problems or if your heart rate is still 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 Gilenya, especially those that require treatment with other medicines, you will stay in the medical facility to be observed overnight. You will also be observed for any serious side effects for at least 6 hours after you take your second dose of Gilenya 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 in the medical facility to be observed overnight by a healthcare professional after taking your first dose of Gilenya.

Your slow heart rate will usually return to normal within 1 month after you start taking Gilenya. Refer to your doctor or go to the nearest hospital emergency room right away if you have any symptoms of a slow heart rate.

If you miss one or more doses of Gilenya, you may need to be observed by a healthcare professional when you take your next dose. Refer to your doctor if you miss a dose of Gilenya. Also see 'How should the medicine be used?'

Before you take Gilenya, tell your doctor about all your medical conditions, including if you had or now have:

- an irregular or abnormal heartbeat (arrhythmia)
- a history of stroke or mini-stroke
- heart problems, including heart attack or angina
- a history of repeated fainting (syncope)
- a fever or infection, or if you are unable to fight infections due to a disease or because you are taking, or have taken in the past, medicines that weaken your immune system
- you have recently received or are due to receive a vaccine
- chickenpox or you have received a vaccine for chickenpox. The doctor may conduct a blood test for the chickenpox virus. You may need to get the full course of chickenpox vaccinations and then wait one month before you start the treatment with Gilenya

- eye problems, especially an inflammation of the eye called uveitis
- diabetes
- breathing problems, including during your sleep
- liver problems
- high blood pressure
- types of skin cancer called basal cell carcinoma (BCC) or melanoma
- Please consult your doctor before getting pregnant. You should avoid becoming pregnant while taking Gilenya or in the two months after you stop taking it because of the risk of harm to the fetus. See section 'Pregnancy and breastfeeding'.

Elderly patients (over the age of 65)

Experience with Gilenya treatment in elderly people is limited. Gilenya should be used with caution in patients over the age of 65.

Children and adolescents

The medicine is not intended for children and adolescents under the age of 18.

Test and follow-up

Before starting treatment:

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

The doctor may do a blood test for the chickenpox virus.

For the tests required when taking the first dose of Gilenya - see section 'Taking the first dose' above.

During treatment:

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

You should consult about a routine Pap smear - as detailed in the side effects section.

Drug interactions

Using Gilenya together with other medicines may cause serious side effects.

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

- medicines that prolong the QT interval,** such as citalopram, chlorpromazine, haloperidol, methadone, erythromycin, since initiation of Gilenya treatment causes a decrease in heart rate and may prolong the QT interval.

- ketconazole** - a medicine to treat fungal infections. A patient who uses Gilenya and ketoconazole concomitantly should be closely monitored, as the risk of adverse reactions is greater.

- vaccinations** - If you need to receive a vaccine, seek your doctor’s advice first. During and for up to 2 months after treatment with Gilenya, you should not receive certain types of vaccine (live attenuated vaccines) as they could trigger the infection that they were supposed to prevent. Other vaccines may not work as well as usual 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 additive immune system effects must be considered if these therapies are coadministered with Gilenya. When switching treatment from drugs with prolonged immune effects, such as natalizumab, teriflunomide or mitoxantrone, the duration and mode of action of these drugs must be considered to avoid unintended additive immunosuppressive effects when initiating Gilenya.

- medicines that slow the heart rate and the atrioventricular conduction,** such as beta blockers, digoxin, or calcium channel blockers, such as diltiazem or verapamil. Before starting treatment with Gilenya, consult the doctor who prescribed these drugs regarding the possibility to switch to drugs that do not slow the heart rate and the atrioventricular conduction.

Taking Gilenya and food

Gilenya can be taken with or without food.

Pregnancy and breastfeeding

Before taking Gilenya, tell your doctor if you are pregnant or are planning to become pregnant.

Gilenya may harm your unborn baby.

Tell your doctor right away if you become pregnant while taking Gilenya or if you become pregnant within 2 months after stopping treatment with Gilenya.

- You should stop taking Gilenya 2 months before trying to become pregnant.

- If you can become pregnant, use an effective birth control during your treatment with Gilenya and for at least 2 months after stopping treatment.

Before taking Gilenya, tell your doctor if you are breastfeeding or if you are planning to breastfeed.

It is not known whether Gilenya passes into breast milk. Consult your doctor about the best way to feed your baby when you are taking Gilenya.

Driving and using machines

Your doctor will tell you whether your illness allows you to drive vehicles, including bicycle riding, and use machines safely. Gilenya is not expected to have an influence on your ability to drive and use machines.

However, after taking the first dose of Gilenya, you will have to stay under observation of a healthcare professional for at least 6 hours. Your ability to drive and use machines may be impaired during and potentially after this time period.

3. HOW SHOULD THE MEDICINE BE USED?

Always use the preparation according to the doctor’s instructions. Check with the doctor or pharmacist if you are uncertain about the dosage and treatment regimen of the preparation.

Dosage

The dosage and treatment regimen will be determined by the doctor only. The usual dosage is generally: One capsule per day (0.5 mg fingolimod).

Do not exceed the recommended dose.

How to take

For oral administration.

Take Gilenya once a day, with a glass of water.

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

There is no information about opening the capsule and dispersing its content.

Taking more Gilenya than required

If you took an overdose or if a child has accidentally swallowed the medicine, refer immediately to a doctor or proceed to a hospital emergency room and bring the package of the medicine with you.

If you forget to take Gilenya

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

- an ECG before taking the dose
- hourly pulse and blood pressure measurements after taking the dose
- an ECG 6 hours after taking the dose

Stopping treatment

Adhere to the treatment regimen 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 MS symptoms may recur and worsen - see section 'Severe worsening of multiple sclerosis after stopping Gilenya' in the side effects chapter.

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 further questions regarding use of the medicine, consult a doctor or pharmacist.

4. SIDE EFFECTS

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

Gilenya can cause serious side effects, including:

- Slow heart rate (bradycardia or bradyarrhythmia) when you start taking Gilenya**

Gilenya can cause your heart rate to slow down, especially after you take the first dose. See details in section 'Special warnings regarding use of the medicine' under subsection 'Taking the first dose'.

• Infections

Gilenya can increase your risk of serious infections that may be life-threatening and cause death. You should not receive **live** vaccines during treatment with Gilenya and for 2 months after you stop taking Gilenya. Talk to your doctor before you receive a vaccine during treatment and for 2 months after treatment with Gilenya. If you receive a live vaccine, you may get the infection that the vaccine was meant to prevent. Vaccines may not work as well when given during treatment with Gilenya.

Human Papilloma Virus (HPV). Due to risk of HPV infection, please consult your doctor regarding routine Pap smear.

Gilenya lowers the number of white blood cells (lymphocytes) in your blood. This will usually go back to normal within 2 months of stopping treatment. Your doctor may conduct a blood test to check your white blood cells before you start taking Gilenya. Refer to your doctor right away if you have any of the symptoms of an infection during treatment with Gilenya and for 2 months after the last dose of Gilenya:

- fever
- tiredness
- body aches
- chills
- nausea
- vomiting
- headache accompanied by fever, neck stiffness, sensitivity to light, nausea or confusion (these may be symptoms of meningitis, an infection of the membranes around your brain and spine).

• Progressive Multifocal Leukoencephalopathy (PML)

PML is a rare brain infection that usually leads to death or severe disability. If PML happens, it usually happens in people with a weakened immune system, but has also happened in people who do not have a weakened immune system. Symptomts of PML get worse over days to weeks. Refer to your doctor right away if you have any new or worsening symptoms of PML, that have lasted several days, including:

- weakness on one side of your body
- loss of coordination in the arms and legs
- decreased strength
- problems with balance
- changes in vision
- changes in thinking or memory
- confusion
- changes in personality

• A vision problem called macular edema:

Macular edema can cause some of the same vision symptoms as an MS attack (optic neuritis). You may not notice any symptoms with macular edema. If macular edema happens, it usually starts in the first 3 to 4 months after starting treatment with Gilenya. Your doctor should check your vision before you start treatment with Gilenya and 3 to 4 months after you start treatment, or any time you notice vision changes during treatment with Gilenya. Your risk of macular edema is higher if you have diabetes or have had an inflammation of your eye called uveitis.

Refer to a doctor right away if you have any 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 Gilenya. The symptoms of PRES usually get better when you stop taking Gilenya. However, if left untreated, it may lead to a stroke. Refer to a doctor right away if you have any of the following symptoms:

- sudden severe headache
- sudden confusion
- sudden loss of vision or other changes in your vision
- seizures

- Liver damage.** Gilenya may cause liver damage. Your doctor should conduct blood tests to check your liver before you start taking Gilenya and periodically during treatment. Refer to your doctor right away if you have any of the following symptoms of liver damage:

- nausea
- vomiting
- stomach pain
- tiredness
- loss of appetite
- yellowing of the skin or the whites of the eyes
- dark urine

- Breathing problems.** Some people who take Gilenya have shortness of breath. Call your doctor right away if you have new or worsening breathing problems.

- Severe worsening of multiple sclerosis after stopping Gilenya.**

When Gilenya is stopped, symptoms of MS can return and become worse compared to before or during treatment. Many people who have worsening of MS symptoms after stopping Gilenya do not return to the level of function that they had before stopping Gilenya. This worsening happens most often within 12 weeks after stopping Gilenya, but can happen later. Always talk to your doctor before you stop taking Gilenya for any reason. Tell your doctor if you have worsening symptoms of MS after stopping Gilenya.

- High blood pressure.** Your doctor should check your blood pressure during treatment with Gilenya.

- Types of skin cancer called basal cell carcinoma (BCC) and melanoma.** Tell your doctor if you have any changes in the appearance of your skin, including changes in a mole, a new darkened 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 for any changes during treatment with Gilenya. Limit the amount of time you spend in sunlight and ultraviolet (UV) light. Wear protective clothing and use a 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.

The most common side effects (occur in more than one user in 10) of Gilenya include:

- headache
- abnormal liver tests
- diarrhea
- cough
- flu
- inflammation of the sinuses (sinusitis)
- back pain
- abdominal pain
- pain in the arms or legs

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

- bronchitis
- shingles (herpes zoster)
- ringworm (tinea versicolor)
- migraine
- nausea
- weakness
- hair loss
- actinic keratosis - a precancerous growth
- an increase in blood triglyceride levels
- blurred vision
- low level of lymphocytes (lymphopenia)
- low level of white blood cells (leukopenia)
- skin papilloma - a benign skin tumor

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

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

Reporting side effects

Side effects can be reported to the Ministry of Health by clicking on the link "Report Side Effects of Drug Treatment" found on the Ministry of Health homepage (www.health.gov.il), that directs you to the online form for reporting side effects, or by entering the link: https://sideeffects.health.gov.il/

5. HOW SHOULD THE MEDICINE BE STORED?

Avoid poisoning! This medicine, and any other medicine, should be kept in a safe place out of the reach and sight of children and/ or infants in order to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by the doctor.

Do not use the medicine after the expiry date (exp. date) that appears on the package. The expiry date refers to the last day of that month.

Storage conditions

Store the medicine below 25°C; protect from moisture.

6. FURTHER INFORMATION

In addition to the active ingredient, the medicine also contains: Mannitol, magnesium stearate.

Ingredients of the empty capsule:

Gelatin, titanium dioxide (C.I. 77891, E171), yellow iron oxide (C.I. 77492, E172), printing ink black, printing ink yellow

Ingredients of the printing ink on the capsule:

Shellac (E904), dehydrated alcohol, isopropyl alcohol, butyl alcohol, propylene glycol, purified water, strong ammonia solution, potassium hydroxide, black iron oxide (E172), yellow iron oxide (E172), titanium dioxide (E171), dimethicone.

What the medicine looks like and the contents of the package

The medicine Gilenya is marketed as hard capsules for oral use (oral administration). The hard capsules have a white opaque body with two radial bands imprinted in yellow and a bright yellow opaque cap with FTY 0.5 mg imprinted in black. Contents of the capsules: white to almost white powder.

Package size: 7 or 28 capsules (Not all package sizes may be marketed).

Registration Holder and Importer and its address: Novartis Israel Ltd., P.O.B 7126, Tel Aviv.

Revised in November 2020.

Registration number of the medicine in the National Drug Registry of the Ministry of Health: Gilenya 0.5 mg – 145 78 33270