

Package leaflet: Information for the user

GILENYA® 0.5 mg hard capsules Fingolimod

▼ This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What Gilenya is and what it is used for
2. What you need to know before you take Gilenya
3. How to take Gilenya
4. Possible side effects
5. How to store Gilenya
6. Contents of the pack and other information

1. What Gilenya is and what it is used for

What Gilenya is

The active substance of Gilenya is fingolimod.

What Gilenya is used for

Gilenya is used in adults to treat relapsing-remitting multiple sclerosis (MS), more specifically in: Patients who have failed to respond despite treatment with an MS treatment.

or

Patients who have rapidly evolving severe MS.

Gilenya does not cure MS, but it helps to reduce the number of relapses and to slow down the progression of physical disabilities due to MS.

What is multiple sclerosis

MS is a long-term condition that affects the central nervous system (CNS), comprised of the brain and spinal cord. In MS inflammation destroys the protective sheath (called myelin) around the nerves in the CNS and stops 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 stopping them from reaching the brain and spinal cord. This limits nerve damage caused by MS.

2. What you need to know before you take Gilenya

Do not take Gilenya

- if you have a **lowered immune response** (due to an immunodeficiency syndrome, a disease or to medicines that suppress the immune system).
- if you have a **severe active infection or active chronic infection** such as hepatitis or tuberculosis.
- if you have an **active cancer**.
- if you have **severe liver problems**.
- **if you are allergic** to fingolimod or any of the other ingredients of this medicine (listed in section 6).

If this applies to you, **tell your doctor without taking Gilenya**.

Warnings and precautions

Talk to your doctor before taking Gilenya:

- **if you have irregular, abnormal heart beat.**
- **if you suffer from symptoms of slow heart rate (e.g. dizziness, nausea, or palpitations).**
- **if you have any heart problems, blocked heart blood vessels, have had a heart attack, have a history of your heart having stopped or if you have angina.**
- **if you have had a stroke.**
- **if you suffer from heart failure.**
- **if you have severe breathing problems during sleep (severe sleep apnoea).**
- **if you have been told you have an abnormal electrocardiogram.**
- **if you are taking or have recently taken medicine for irregular heartbeat** such as quinidine, disopyramide, amiodarone or sotalol.
- **if you are taking or have recently taken medicines that slow your heart rate** (such as beta blockers, verapamil, diltiazem or ivabradine, digoxin, anticholinesteratic agents or pilocarpine).
- **if you have a history of sudden loss of consciousness or fainting (syncope).**
- **if you plan to get vaccinated.**
- **if you have never had chickenpox.**
- **if you have or have had visual disturbances** or other signs of swelling in the central vision area (macula) at the back of the eye (a condition known as macular oedema, see below), inflammation or infection of the eye (uveitis), **or if you have diabetes** (which can cause eye problems).
- **if you have liver problems.**
- if you have **high blood pressure that cannot be controlled by medicines.**
- if you have **severe lung problems** or smoker's cough.

If any of these applies to you, **tell your doctor before taking Gilenya**.

Slow heart rate (bradycardia) and irregular heartbeat: At the beginning of treatment, Gilenya causes the heart rate to slow down. As a result, you may feel dizzy or tired, or be consciously aware of your heartbeat, or your blood pressure may drop. **If these effects are pronounced, tell your doctor, because you may need treatment right away.** Gilenya can also cause an irregular heartbeat, especially after the first dose. Irregular heartbeat usually returns to normal in less than one day. Slow heart rate usually returns to normal within one month.

Your doctor will ask you to stay at the surgery or clinic for at least 6 hours, with hourly pulse and blood pressure measurements, after taking the first dose of Gilenya so that appropriate measures can be taken in the event of side effects that occur at the start of treatment. You should have an

electrocardiogram performed prior to the first dose of Gilenya and after the 6-hour monitoring period. Your doctor may monitor your electrocardiogram continuously during that time. If after the 6-hour period you have a very slow or decreasing heart rate, or if your electrocardiogram shows abnormalities, you may need to be monitored for a longer period (at least 2 more hours and possibly overnight) until these have resolved. The same may apply if you are resuming Gilenya after a break in treatment, depending on both how long the break was and how long you had been taking Gilenya before the break.

If you have, or if you are at risk for, an irregular or abnormal heartbeat, if your electrocardiogram is abnormal, or if you have heart disease or heart failure, Gilenya may not be appropriate for you.

If you have a history of sudden loss of consciousness or decreased heart rate, Gilenya may not be appropriate for you. You will be evaluated by a cardiologist (heart specialist) to advise how you should start treatment with Gilenya, including overnight monitoring.

If you are taking medicines that can cause your heart rate to decrease, Gilenya may not be appropriate for you. You will need to be evaluated by a cardiologist, who will check whether you can be switched to alternative medication that does not decrease your heart rate in order to allow treatment with Gilenya. If such a switch is impossible, the cardiologist will advise how you should start treatment with Gilenya, including overnight monitoring.

If you have never had chickenpox: If you have never had chickenpox, your doctor will check your immunity against the virus that causes it (varicella zoster virus). If you are not protected against the virus, you may need a vaccination before you start treatment with Gilenya. If this is the case, your doctor will delay the start of treatment with Gilenya until one month after the full course of vaccination is completed.

Infections: Gilenya lowers the white blood cell count (particularly the lymphocyte count). White blood cells fight infection. While you are taking Gilenya (and for up to 2 months after you stop taking it), you may get infections more easily. Any infection that you already have may get worse. Infections could be serious and life-threatening. If you think you have an infection, have fever, feel like you have the flu, or have a headache accompanied by stiff neck, sensitivity to light, nausea, and/or confusion (these may be symptoms of meningitis), contact your doctor right away. If you believe your MS is getting worse (e.g. weakness or visual changes) or if you notice any new symptoms, talk to your doctor as soon as possible, because these may be the symptoms of a rare brain disorder caused by infection and called progressive multifocal leukoencephalopathy (PML). PML is a serious condition that may lead to severe disability or death.

Macular oedema: Before you start Gilenya, if you have or have had visual disturbances or other signs of swelling in the central vision area (macula) at the back of the eye, inflammation or infection of the eye (uveitis) or diabetes, your doctor may want you to undergo an eye examination.

Your doctor may want you to undergo an eye examination 3 to 4 months after starting Gilenya treatment.

The macula is a small area of the retina at the back of the eye which enables you to see shapes, colours, and details clearly and sharply. Gilenya may cause swelling in the macula, a condition that is known as macular oedema. The swelling usually happens in the first 4 months of Gilenya treatment.

Your chance of developing macular oedema is higher if you have **diabetes** or have had an inflammation of the eye called uveitis. In these cases your doctor will want you to undergo regular eye examinations in order to detect macular oedema.

If you have had macular oedema, talk to your doctor before you resume treatment with Gilenya.

Macular oedema can cause some of the same vision symptoms as an MS attack (optic neuritis). Early on, there may not be any symptoms. Be sure to tell your doctor about any changes in your vision. Your doctor may want you to undergo an eye examination, especially if:

- the centre of your vision gets blurry or has shadows;
- you develop a blind spot in the centre of your vision;
- you have problems seeing colours or fine detail.

Liver function tests: If you have severe liver problems, you should not take Gilenya. Gilenya may affect your liver function. You will probably not notice any symptoms but if you notice yellowing of your skin or the whites of your eyes, abnormally dark urine or unexplained nausea and vomiting, **tell your doctor straight away.**

If you get any of these symptoms after starting Gilenya, **tell your doctor straight away.**

During the first twelve months of treatment your doctor will request blood tests to monitor your liver function. If your test results indicate a problem with your liver you may have to interrupt treatment with Gilenya.

High blood pressure

As Gilenya causes a slight elevation of blood pressure, your doctor may want to check your blood pressure regularly.

Lung problems

Gilenya has a slight effect on the lung function. Patients with severe lung problems or with smoker's cough may have a higher chance of developing side effects.

Blood count

The desired effect of Gilenya treatment is to reduce the amount of white blood cells in your blood. This will usually go back to normal within 2 months of stopping treatment. If you need to have any blood tests, tell the doctor that you are taking Gilenya. Otherwise, it may not be possible for the doctor to understand the results of the test, and for certain types of blood test your doctor may need to take more blood than usual.

Before you start Gilenya, your doctor will confirm whether you have enough white blood cells in your blood and may want to repeat a check regularly. In case you do not have enough white blood cells, you may have to interrupt treatment with Gilenya.

Posterior reversible encephalopathy syndrome (PRES)

A condition called posterior reversible encephalopathy syndrome (PRES) has been rarely reported in MS patients treated with Gilenya. Symptoms may include sudden onset of severe headache, confusion, seizures and vision changes. Tell your doctor, if you experience any of these symptoms during your treatment with Gilenya.

Basal cell carcinoma (BCC)

A type of skin cancer called basal cell carcinoma (BCC) has been reported in MS patients treated with Gilenya. Talk to your doctor if you notice any skin nodules (e.g. shiny pearly nodules), patches or open sores that do not heal within weeks (these may be signs of BCC). Before you start Gilenya, a skin examination is required to check whether you have any skin nodules. Your doctor will also carry out regular skin examinations during your treatment with Gilenya. If you develop problems with your skin, your doctor may refer you to a dermatologist, who after consultation may decide that it is important for you to be seen on a regular basis.

Elderly

Experience with Gilenya in elderly patients (over 65 years) is limited. Talk to your doctor if you have any concerns.

Children and adolescents

Gilenya is not intended to be used in children and adolescents below 18 years old as it has not been studied in MS patients below 18 years old.

Other medicines and Gilenya

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. Tell your doctor if you are taking any of the following medicines:

- **Medicines that suppress or modulate the immune system**, including **other medicines used to treat MS**, such as beta interferon, glatiramer acetate, natalizumab, mitoxantrone, teriflunomide, dimethyl fumarate or alemtuzumab. You must not use Gilenya together with such medicines as this could intensify the effect on the immune system (see also 'Do not take Gilenya').
- **Corticosteroids**, due to a possible added effect on the immune system.
- **Vaccines**. 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.
- **Medicines that slow the heartbeat** (for example beta blockers, such as atenolol). Use of Gilenya together with such medicines could intensify the effect on heartbeat in the first days after starting Gilenya.
- **Medicines for irregular heartbeat**, such as quinidine, disopyramide, amiodarone or sotalol. Your doctor may decide not to prescribe Gilenya if you are taking such a medicine because it could intensify the effect on irregular heartbeat.
- **Other medicines:**
 - protease inhibitors, anti-infectives such as ketoconazole,azole antifungals, clarithromycin or telithromycin.
 - carbamazepine, rifampicine, phenobarbital, phenytoin, efavirenz or St. John's Wort (potential risk of reduced efficacy).

Pregnancy and breast-feeding

Before you start treatment with Gilenya your doctor may ask you to do a pregnancy test in order to ensure that you are not pregnant. You should avoid becoming pregnant while taking Gilenya or in the two months after you stop taking it because there is a risk of harm to the baby. Talk with your doctor about reliable methods of birth control that you should use during treatment and for 2 months after you stop treatment.

If you do become pregnant while taking Gilenya, stop taking the medicine and tell your doctor straight away. You and your doctor will decide what is best for you and your baby.

You should not breast-feed while you are taking Gilenya. Gilenya can pass into breast milk and there is a risk of serious side effects for the baby.

Ask your doctor or pharmacist for advice before taking any medicine.

Driving and using machines

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

However, at initiation of treatment you will have to stay at the doctor's surgery or clinic for 6 hours after taking the first dose of Gilenya. Your ability to drive and use machines may be impaired during and potentially after this time period.

3. How to take Gilenya

Treatment with Gilenya will be overseen by a doctor who is experienced in the treatment of multiple sclerosis.

Always take this medicine exactly as your doctor has told you. Check with your doctor if you are not sure.

The dose is one capsule per day. Take Gilenya once a day with a glass of water. Gilenya can be taken with or without food.

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

Do not exceed the recommended dose.

Your doctor may switch you directly from beta interferon, glatiramer acetate or dimethyl fumarate to Gilenya if there are no signs of abnormalities caused by your previous treatment. Your doctor may have to do a blood test in order to exclude such abnormalities. After stopping natalizumab you may have to wait for 2-3 months before starting treatment with Gilenya. To switch from teriflunomide, your doctor may advise you to wait for a certain time or to go through an accelerated elimination procedure. If you have been treated with alemtuzumab, a thorough evaluation and discussion with your doctor is required to decide if Gilenya is appropriate for you.

If you have questions about how long to take Gilenya, talk to your doctor or your pharmacist.

If you take more Gilenya than you should

If you have taken too much Gilenya, call your doctor straight away.

If you forget to take Gilenya

If you have been taking Gilenya for less than 1 month and you forget to take 1 dose for a whole day, call your doctor before you take the next dose. Your doctor may decide to keep you under observation at the time you take the next dose.

If you have been taking Gilenya for at least 1 month and have forgotten to take your treatment for more than 2 weeks, call your doctor before you take the next dose. Your doctor may decide to keep you under observation at the time you take the next dose. However, if you have forgotten to take your treatment for up to 2 weeks, you can take the next dose as planned.

Never take a double dose to make up for a forgotten dose.

If you stop taking Gilenya

Do not stop taking Gilenya or change your dose without talking to your doctor first.

Gilenya will stay in your body for up to 2 months after you stop taking it. Your white blood cell count (lymphocyte count) may also remain low during this time and the side effects described in this leaflet may still occur. After stopping Gilenya you may have to wait for 6-8 weeks before starting a new MS treatment.

If you have to restart Gilenya more than 2 weeks after you stop taking it, the effect on heart rate normally seen when treatment is first started may re-occur and you will need to be monitored at the doctor's surgery or clinic for re-initiation of treatment. Do not restart Gilenya after stopping it for more than two weeks without seeking advice from your doctor.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Some side effects could be or could become serious

Common (may affect up to 1 in 10 people):

- Coughing with phlegm, chest discomfort, fever (signs of lung disorders)
- Herpes virus infection (shingles or herpes zoster) with symptoms such as blisters, burning, itching or pain of the skin, typically on the upper body or the face. Other symptoms may be fever and weakness in the early stages of infection, followed by numbness, itching or red patches with severe pain
- Slow heartbeat (bradycardia), irregular heart rhythm
- A type of skin cancer called basal cell carcinoma (BCC) which often appears as a pearly nodule, although it can also take other forms.

Uncommon (may affect up to 1 in 100 people):

- Pneumonia with symptoms such as fever, cough, difficulty breathing
- Macular oedema (swelling in the central vision area of the retina at the back of the eye) with symptoms such as shadows or blind spot in the centre of the vision, blurred vision, problems seeing colours or details
- Reduction in blood platelets which increases risk of bleeding or bruising

Rare (may affect up to 1 in 1,000 people):

- A condition called posterior reversible encephalopathy syndrome (PRES). Symptoms may include sudden onset of severe headache, confusion, seizures and/or vision disturbances.
- Lymphoma (a type of cancer that affects the lymph system).

Very rare (may affect up to 1 in 10,000 people):

- Electrocardiogram anomaly (T-wave inversion).

Isolated cases:

- 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.

Not known (frequency cannot be estimated from the available data):

- Allergic reactions, including symptoms of rash or itchy hives, swelling of lips, tongue or face, which are more likely to occur on the day you start Gilenya treatment.
- Risk of a rare brain infection called progressive multifocal leukoencephalopathy (PML). The symptoms of PML may be similar to an MS relapse. Symptoms might also arise that you might not become aware of by yourself, such as changes in mood or behaviour, memory lapses, speech and communication difficulties, which your doctor may need to investigate further to rule out PML. Therefore, if you believe your MS is getting worse or if you or those close to you notice any new or unusual symptoms, it is very important that you speak to your doctor as soon as possible.
- Tumour related to infection with human herpes virus 8 (Kaposi's sarcoma)

If you experience any of these, **tell your doctor straight away**.

Other side effects

Very common (may affect more than 1 in 10 people):

- Infection from flu virus with symptoms such as tiredness, chills, sore throat, aching in the joints or muscles, fever
- Feeling of pressure or pain in the cheeks and forehead (sinusitis)
- Headache
- Diarrhoea

- Back pain
- Blood testing showing higher levels of liver enzymes
- Cough

Common (may affect up to 1 in 10 people):

- Ringworm, a fungal infection of the skin (tinea versicolor)
- Dizziness
- Severe headache often accompanied by nausea, vomiting and sensitivity to light (migraine)
- Low level of white blood cells (lymphocytes, leucocytes)
- Weakness
- Itchy, red, burning rash (eczema)
- Itching
- Blood fat (triglycerides) level increased
- Hair loss
- Breathlessness
- Depression
- Blurred vision (see also the section on macular oedema under “Some side effects could be or could become serious”)
- Hypertension (Gilenya may cause a mild increase in blood pressure)

Uncommon (may affect up to 1 in 100 people):

- Low level of certain white blood cells (neutrophils)
- Depressed mood
- Nausea

Rare (may affect up to 1 in 1,000 people):

- Blood vessel disorders
- Nervous system disorders
- Cancer of the lymphatic system (lymphoma)

Not known (frequency cannot be estimated from the available data):

- Peripheral swelling

If any of these affects you severely, **tell your doctor**

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly (see details below). By reporting side effects you can help provide more information on the safety of this medicine.

United Kingdom:	Yellow Card Scheme Website: www.mhra.gov.uk/yellowcard
Ireland:	HPRA Pharmacovigilance Earlsfort Terrace IRL - Dublin 2 Tel: +353 1 6764971 Fax: +353 1 6762517 Website: www.hpra.ie e-mail: medsafety@hpra.ie
Malta:	ADR Reporting Website: www.medicinesauthority.gov.mt/adrportal

5. How to store Gilenya

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton and blister foil after “EXP”. The expiry date refers to the last day of that month.

Do not store above 25°C.

Store in the original package in order to protect from moisture.

Do not use any pack that is damaged or shows signs of tampering.

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 to protect the environment.

6. Contents of the pack and other information

What Gilenya contains

- The active substance is fingolimod. Each capsule contains 0.5 mg fingolimod (as hydrochloride).
- The other ingredients are:
Capsule core: magnesium stearate, mannitol
Capsule shell: yellow iron oxide (E172), titanium dioxide (E171), gelatin
Printing ink: 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 Gilenya looks like and contents of the pack

Gilenya 0.5 mg hard capsules have a white opaque body and bright yellow opaque cap. “FTY0.5mg” is imprinted on the cap with black ink and two bands are imprinted on the body with yellow ink.

Gilenya is available in packs containing 7, 28 or 98 capsules or in multipacks containing 84 capsules (3 packs of 28 capsules). Not all pack sizes may be marketed in your country.

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This leaflet was last revised in 12/2016

Other sources of information

Detailed information on this medicine is available on the European Medicines Agency website:
<http://www.ema.europa.eu>.