

Package leaflet: Information for the patient

Ezetimibe/Simvastatin 10 mg/20 mg Tablets
Ezetimibe/Simvastatin 10 mg/40 mg Tablets
Ezetimibe/Simvastatin 10 mg/80 mg Tablets

ezetimibe and simvastatin

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

1. What Ezetimibe/Simvastatin is and what it is used for

Ezetimibe/Simvastatin contains two active substances ezetimibe and simvastatin.

Ezetimibe/Simvastatin is a medicine used to lower levels of total cholesterol, “bad” cholesterol (LDL cholesterol), and fatty substances called triglycerides in the blood. In addition, Ezetimibe/Simvastatin raises levels of “good” cholesterol (HDL cholesterol).

Ezetimibe/Simvastatin works to reduce your cholesterol in two ways. The active ingredient ezetimibe reduces the cholesterol absorbed in your digestive tract. The active ingredient simvastatin, belonging to the class of “statins,” inhibits the production of the cholesterol your body makes by itself.

Cholesterol is one of several fatty substances found in the bloodstream. Your total cholesterol is made up mainly of LDL and HDL cholesterol.

LDL cholesterol is often called “bad” cholesterol because it can build up in the walls of your arteries forming plaque. Eventually this plaque build-up can lead to a narrowing of the arteries. This narrowing can slow or block blood flow to vital organs such as the heart and brain. This blocking of blood flow can result in a heart attack or stroke.

HDL cholesterol is often called “good” cholesterol because it helps keep the bad cholesterol from building up in the arteries and protects against heart disease.

Triglycerides are another form of fat in your blood that may increase your risk for heart disease.

Ezetimibe/Simvastatin is used for patients who cannot control their cholesterol levels by diet alone. You should stay on a cholesterol-lowering diet while taking this medicine.

Ezetimibe/Simvastatin is used in addition to your cholesterol-lowering diet if you have:

- a raised cholesterol level in your blood (primary hypercholesterolaemia [heterozygous familial and non-familial]) or elevated fat levels in your blood (mixed hyperlipidaemia):
 - that is not well controlled with a statin alone
 - for which you have used a statin and ezetimibe as separate tablets
- a hereditary illness (homozygous familial hypercholesterolaemia) that increases the cholesterol level in your blood. You may also receive other treatments.
- heart disease, Ezetimibe/Simvastatin reduces the risk of heart attack, stroke, surgery to increase heart blood flow, or hospitalisation for chest pain.

Ezetimibe/Simvastatin does not help you lose weight.

2. What you need to know before you take Ezetimibe/Simvastatin

Do not take Ezetimibe/Simvastatin:

- if you are allergic to ezetimibe or to simvastatin or any of the other ingredients of this medicine (listed in section 6)
- if you currently have liver problems
- if you are pregnant or breast-feeding
- if you are taking medicine(s) with one or more than one of the following active ingredients:
 - itraconazole, ketoconazole, posaconazole or voriconazole (used to treat fungal infections)
 - erythromycin, clarithromycin or telithromycin (used to treat infections)
 - HIV protease inhibitors such as indinavir, nelfinavir, ritonavir and saquinavir (HIV protease inhibitors are used to treat HIV infections) or medicines which contain cobicistat (that are also used to treat HIV infections).
 - boceprevir or telaprevir (used to treat hepatitis C virus infections)
 - nefazodone (used to treat depression)
 - gemfibrozil (used to lower cholesterol)
 - ciclosporin (often used in organ transplant patients)
 - danazol (a man-made hormone used to treat endometriosis, a condition in which the lining of the uterus grows outside the uterus).
- if you are taking or have taken, in the last 7 days, a medicine called fusidic acid (a medicine for bacterial infection) orally or by injection. The combination of fusidic acid and Ezetimibe/Simvastatin can lead to serious muscle problems (rhabdomyolysis).

Do not take more than 10 mg/40 mg Ezetimibe/Simvastatin if you are taking lomitapide (used to treat a serious and rare genetic cholesterol condition).

Ask your doctor if you are not sure if your medicine is listed above.

Warnings and precautions

Talk to your doctor or pharmacist before taking Ezetimibe/Simvastatin:

- about all your medical conditions including allergies.
- if you drink large amounts of alcohol or have ever had liver disease. Ezetimibe/Simvastatin may not be right for you.
- if you are due to have an operation. You may need to stop taking Ezetimibe/Simvastatin tablets for a short time.
- if you are of Asian origin, because a different dose may be applicable to you.

Your doctor should do a blood test before you start taking Ezetimibe/Simvastatin and if you have any symptoms of liver problems while you take Ezetimibe/Simvastatin. This is to check how well your liver is working.

Your doctor may also want you to have regular blood tests to check how well your liver is working after you start taking Ezetimibe/Simvastatin.

While you are on this medicine your doctor will monitor you closely if you have diabetes or are at risk of developing diabetes. You are likely to be at risk of developing diabetes if you have high levels of sugars and fats in your blood, are overweight and have high blood pressure.

Talk to your doctor if you have severe lung disease.

The combined use of Ezetimibe/Simvastatin and fibrates (certain medicines for lowering cholesterol) should be avoided since the combined use of Ezetimibe/Simvastatin and fibrates has not been studied.

Contact your doctor immediately if you experience unexplained muscle pain, tenderness, or weakness. This is because on rare occasions, muscle problems can be serious, including muscle breakdown resulting in kidney damage; and very rare deaths have occurred.

The risk of muscle breakdown is greater at higher doses of ezetimibe/simvastatin, particularly the 10 mg/80 mg dose. The risk of muscle breakdown is also greater in certain patients.

Talk to your doctor if any of the following applies:

- you have kidney problems
- you have thyroid problems
- you are 65 years or older
- you are female
- you have ever had muscle problems during treatment with cholesterol lowering medicines called “statins” (like simvastatin, atorvastatin, and rosuvastatin) or fibrates (like gemfibrozil and bezafibrate)
- you or close family members have a hereditary muscle disorder.
- you are of Asian origin.

Also tell your doctor or pharmacist if you have a muscle weakness that is constant. Additional tests and medicines may be needed to diagnose and treat this.

Children

Ezetimibe/Simvastatin is not recommended for children under the age of 10.

Other medicines and Ezetimibe/Simvastatin

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines including any of the following medicines. Taking Ezetimibe/Simvastatin with any of these medicines can increase the risk of muscle problems.

Do not take Ezetimibe/Simvastatin with:

- **fusidic acid. If you need to take oral fusidic acid to treat a bacterial infection you will need to temporarily stop using this medicine. Your doctor will tell you when it is safe to restart Ezetimibe/Simvastatin. Taking Ezetimibe/Simvastatin with fusidic acid may rarely lead to muscle weakness, tenderness or pain (rhabdomyolysis). See more information regarding rhabdomyolysis in section 4.**
- ciclosporin (often used in organ transplant patients)
- danazol (a man-made hormone used to treat endometriosis, a condition in which the lining of the uterus grows outside the uterus)
- medicines with an active ingredient like itraconazole, ketoconazole, fluconazole, posaconazole or voriconazole (used to treat fungal infections)
- fibrates with active ingredients like gemfibrozil and bezafibrate (used to lower cholesterol)

- erythromycin, clarithromycin or telithromycin (used to treat bacterial infections)
- HIV protease inhibitors such as indinavir, nelfinavir, ritonavir and saquinavir (used to treat HIV infections)
- Hepatitis C antiviral agents such as boceprevir, telaprevir, elbasvir, grazoprevir or glecaprevir/pibrentasvir (used to treat hepatitis C virus infection)
- nefazodone (used to treat depression)
- medicines which contain cobicistat (that are also used to treat HIV infections)
- amiodarone (used to treat an irregular heartbeat)
- verapamil, diltiazem or amlodipine (used to treat high blood pressure, chest pain associated with heart disease or other heart conditions)
- lomitapide (used to treat a serious and rare genetic cholesterol condition)
- daptomycin (a drug used to treat complicated skin and skin structure infections and bacteraemia). It is possible that side effects affecting the muscles may be higher when this medicine is taken during treatment with simvastatin (e.g. Ezetimibe/Simvastatin). Your doctor may decide that you stop taking Ezetimibe/Simvastatin for a while
- large amounts (1 gram or more each day) of niacin or nicotinic acid (also used to lower cholesterol)
- colchicine (used to treat gout)

As well as the medicines listed above, talk to your doctor or pharmacist if you are taking or have recently taken any other medicines, including those obtained without prescription. In particular, talk to your doctor if you are taking any of the following:

- medicines with an active ingredient to prevent blood clots, such as warfarin, fludione, phenprocoumon acenocoumarol (anticoagulants)
- cholestyramine (also used to lower cholesterol), because it affects the way Ezetimibe/Simvastatin works
- fenofibrate (also used to lower cholesterol)
- rifampicin (used to treat tuberculosis)
- ticagrelor (antiplatelet medicine)

Also talk to your doctor if you are taking niacin (nicotinic acid) or a niacin-containing product or niacin related products such as acipimox (used to lower cholesterol) and you are of Asian origin.

You should also tell any doctor who is prescribing a new medicine for you that you are taking Ezetimibe/Simvastatin.

Ezetimibe/Simvastatin with food and drink

Grapefruit juice contains one or more components that alter the metabolism of some medications, including Ezetimibe/Simvastatin. Consuming grapefruit juice should be avoided as it may increase the risk of muscle problems.

Pregnancy and breast-feeding

Do not take Ezetimibe/Simvastatin if you are pregnant, are trying to get pregnant or think you may be pregnant. If you get pregnant while taking Ezetimibe/Simvastatin, stop taking it immediately and tell your doctor.

Do not take Ezetimibe/Simvastatin if you are breast-feeding, because it is not known if the medicine is passed into breast milk.

Driving and using machines

Ezetimibe/Simvastatin is not expected to interfere with your ability to drive or to use machinery. However, some people may get dizzy after taking Ezetimibe/Simvastatin, if this happens do not drive or use machinery.

Ezetimibe/Simvastatin contains lactose monohydrate

If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicine.

This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially ‘sodium-free’.

3. How to take Ezetimibe/Simvastatin

Always take this medicine exactly as your doctor or pharmacist has told you. Your doctor will determine the appropriate tablet strength for you, depending on your current treatment and your personal risk status.

Check with your doctor or pharmacist if you are not sure.

- Before starting Ezetimibe/Simvastatin, you should be on a diet to lower your cholesterol.
- You should keep on this cholesterol-lowering diet while taking Ezetimibe/Simvastatin.

Adults

The recommended dose is one Ezetimibe/Simvastatin tablet by mouth once a day in the evening.

The Ezetimibe/Simvastatin 10 mg/80 mg dose is only recommended for adult patients with very high cholesterol levels and at high risk of heart disease problems who have not reached their cholesterol goal on lower doses.

Use in adolescents (10 to 17 years of age)

The recommended dose is one Ezetimibe/Simvastatin tablet by mouth once a day in the evening (a maximum dose of 10 mg/40 mg once daily must not be exceeded).

- Take Ezetimibe/Simvastatin in the evening.
- You can take it with or without food.
- The tablets are not scored and should not be divided.

If your doctor has prescribed Ezetimibe/Simvastatin along with another medicine for lowering cholesterol containing the active ingredient cholestyramine or any other bile acid sequestrant, you should take Ezetimibe/Simvastatin at least 2 hours before or 4 hours after taking these medicines.

If you take more Ezetimibe/Simvastatin than you should

If you take more Ezetimibe/Simvastatin than you have been told to, contact your doctor.

If you forget to take Ezetimibe/Simvastatin

Do not take a double dose to make up for a forgotten dose, just take your next dose of Ezetimibe/Simvastatin at the usual time the next day.

If you stop taking Ezetimibe/Simvastatin

Talk to your doctor before you stop taking this medicine, because your cholesterol may rise again.

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

Tell your doctor or go to your nearest hospital casualty department straight away if you have any of the following serious side effects; these effects are not known (frequency cannot be estimated from the available data) but you may need medical attention:

- unexplained muscle pain, tenderness, or weakness, especially muscle weakness that is constant, muscle rupture, (which may affect up to 1 in 10,000 people). This is because on rare occasions, muscle problems, including muscle breakdown resulting in kidney damage, can be serious and may become a potentially life-threatening condition
- allergic reactions, including swelling of the face, lips, tongue, and/or throat that may cause difficulty in breathing or swallowing (which requires treatment right away) (angioedema)
- inflammation of the pancreas often with severe abdominal pain
- gallstones or inflammation of the gallbladder (which may cause abdominal pain, feeling or being sick)
- raised red rash, sometimes with target shaped lesions (erythema multiforme), rash that may occur on the skin or sores in the mouth (lichenoid drug eruptions), (which each may affect up to 1 in 10,000 people)
- inflammation of the liver (which may cause yellowing of the skin and eyes, itching, dark coloured urine or pale coloured stool, feeling tired or weak, loss of appetite)
- liver failure
- breathing problems including persistent cough and/or shortness of breath or fever
- a hypersensitivity reaction including some of the following: hypersensitivity (a serious allergic reactions which causes difficulty in breathing or dizziness and requires immediate treatment (anaphylaxis, which may affect up to 1 in 10,000 people), pain or inflammation of the joints, inflammation of blood vessels, unusual bruising, skin eruptions and swelling, hives, skin sensitivity to the sun, fever, flushing, shortness of breath and feeling unwell, lupus-like disease picture (including rash, joint disorders, and effects on white blood cells))
- diabetes. This is more likely if you have high levels of sugars and fats in your blood, are overweight and have high blood pressure. Your doctor will monitor you while you are taking this medicine.
- gynecomastia (breast enlargement in men), (which may affect up to 1 in 10,000 people)

Other possible side effects:

Common: may affect up to 1 in 10 people:

- muscle pains
- elevations in laboratory blood tests of liver (transaminases) and/or muscle function.

Uncommon: may affect up to 1 in 100 people:

- elevations in blood tests of liver function; elevations in blood uric acid; elevations in the time it takes for blood to clot; protein in urine; weight decreased
- dizziness; headache; tingling sensation
- abdominal pain; indigestion; flatulence; feeling sick; being sick, abdominal bloating; diarrhoea; dry mouth; heartburn
- rash; itching; hives
- joint pain, muscle tenderness, weakness or spasms; neck pain; pain in arms and legs; back pain
- unusual tiredness or weakness; feeling tired; chest pain; swelling, especially in the hands and feet
- sleep disorder; trouble sleeping.

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

- blurred vision; impaired vision

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

- low red blood cell count (anaemia); reduction in blood cell counts, which may cause bruising/bleeding (thrombocytopenia)
- numbness or weakness of the arms and legs; poor memory, memory loss, confusion
- constipation
- hair loss
- muscle cramps; muscle inflammation; tendon problems, sometimes complicated by rupture of the tendon
- decreased appetite
- hot flush; high blood pressure
- pain
- erectile dysfunction
- depression
- alterations in some laboratory blood tests for levels of sugar in the blood
- inflammation of the stomach lining
- shortness of breath
- cough.

Further side effects reported with use of some statins:

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

- sleep disturbances, including nightmares
- sexual difficulties.

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 via HPRA Pharmacovigilance, website: www.hpra.ie. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Ezetimibe/Simvastatin

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 blister, carton or bottle after EXP. The expiry date refers to the last day of that month.

This medicine does not require any special storage conditions.

Bottles: Use within 100 days of opening.

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.

6. Contents of the pack and other information

What Ezetimibe/Simvastatin contains

- The active substances are ezetimibe and simvastatin. Each tablet contains 10 mg ezetimibe and 20 mg, 40 mg or 80 mg simvastatin.

- The other ingredients are: lactose monohydrate (see section 2 “Ezetimibe/Simvastatin contains lactose monohydrate”); citric acid monohydrate, butylhydroxyanisole (E320), ascorbic acid (E300), sodium laurilsulfate (E487), croscarmellose sodium, hypromellose (E464), cellulose, microcrystalline, magnesium stearate.

What Ezetimibe/Simvastatin looks like and contents of the pack

Ezetimibe/Simvastatin 10 mg/20 mg Tablets are white to off-white, oval, biconvex tablets marked with M on one side of the tablet and ES2 on the other side.

Ezetimibe/Simvastatin 10 mg/40 mg Tablets are white to off-white, oval, biconvex tablets marked with M on one side of the tablet and ES3 on the other side.

Ezetimibe/Simvastatin 10 mg/80 mg Tablets are white to off-white, oval, biconvex tablets marked with M on one side of the tablet and ES4 on the other side.

Ezetimibe/Simvastatin Tablets are available in:

Blister packs:

10 mg/20 mg and 10 mg/40 mg: 14, 28, 30, 98, 100 tablets and calendar blisters of 28 tablets

10 mg/80 mg: 28, 30, 98 and 100 tablets

Perforated unit dose blister packs:

10 mg/20 mg and 10 mg/40 mg: 14 x 1, 28 x 1, 30 x 1 and 90 x 1 tablets

10 mg/80 mg: 30 x 1 and 90 x 1 tablets

Plastic bottle, with screw cap closure with aluminium wad along with absorbent cotton, containing:
30, 100, 250 and 500 tablets

Not all pack sizes may be marketed.

Marketing Authorisation Holder

McDermott Laboratories Limited t/a Gerard Laboratories, 35/36 Baldoyle Industrial Estate, Grange Road, Dublin 13, Ireland

Manufacturers

McDermott Laboratories Limited t/a Gerard Laboratories, 35/36 Baldoyle Industrial Estate, Grange Road, Dublin 13, Ireland

Mylan Hungary Kft, H-2900 Komárom, Mylan utca 1, Hungary

This medicinal product is authorised in the Member States of the EEA under the following names:

Belgium	Ezetimibe/Simvastatine Mylan 10 mg/20 mg, 10 mg/40 mg, 10 mg/80 mg tabletten
Cyprus	Ezetimibe + Simvastatin / Mylan 10 mg/10 mg, 10mg/20mg, 10 mg/40 mg Tablets
France	EZETIMIBE/SIMVASTATINE MYLAN 10/20 mg, 10/40 mg, comprimé
Germany	Ezetimib/Simvastatin Mylan 10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, 10 mg/80 mg Tabletten
Greece	Ezetimibe/Simvastatin Mylan 10 mg/10 mg, 10 mg/20mg, 10 mg/40 mg Tablets
Ireland	Ezetimibe/Simvastatin 10 mg/20 mg, 10 mg/40 mg, 10 mg/80 mg Tablets
Italy	Ezetimibe e Simvastatina Mylan
Luxembourg	Ezetimibe/Simvastatine Mylan 10 mg/20 mg, 10 mg/40 mg, 10 mg/80 mg comprimés
Portugal	Sinvastatina + Ezetimiba Mylan
Spain	Ezetimiba/Simvastatina Mylan 10 mg/10 mg, 10 mg/ 20 mg, 10 mg/40 mg, 10 mg/ 80 mg comprimidos
The Netherlands	Ezetimibe/Simvastatine Mylan 10 mg/20 mg, 10 mg/40 mg, 10 mg/80 mg, tabletten

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