Package leaflet: Information for the patient

ZETIVASIM 10 mg/10 mg, tabletten
ZETIVASIM 10 mg/20 mg, tabletten
ZETIVASIM 10 mg/40 mg, tabletten
ZETIVASIM 10 mg/80 mg, tabletten
ezetimibe/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 ZETIVASIM is and what it is used for

ZETIVASIM contains the active substances ezetimibe and simvastatin. ZETIVASIM is a medicine used to lower levels of total cholesterol, "bad" cholesterol (LDL cholesterol), and fatty substances called triglycerides in the blood. In addition, ZETIVASIM raises levels of "good" cholesterol (HDL cholesterol).

ZETIVASIM 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.

ZETIVASIM 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.

ZETIVASIM 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, ZETIVASIM reduces the risk of heart attack, stroke, surgery to increase heart blood flow, or hospitalization for chest pain.

ZETIVASIM does not help you lose weight.

2. What you need to know before you take ZETIVASIM

Do not take ZETIVASIM if:
- you are allergic to ezetimibe, simvastatin, or any of the other ingredients of this medicine (listed in Section 6: Contents of the pack and other information)
- you currently have liver problems
- you are pregnant or breast-feeding
- 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)
  - boceprevir or telaprevir (used to treat hepatitis C virus infections)
  - nefazodone (used to treat depression)
  - cobicistat
  - 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)
- 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 ZETIVASIM can lead to serious muscle problems (rhabdomyolysis)

Do not take more than 10/40 mg ZETIVASIM 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 ZETIVASIM:
- about all your medical conditions including allergies.
- if you drink large amounts of alcohol or have ever had liver disease. ZETIVASIM may not be right for you.
- if you are due to have an operation. You may need to stop taking ZETIVASIM tablets for a short time.
- if you are Asian, because a different dose may be applicable to you.
- If you have or have had myasthenia (a disease with general muscle weakness including in some cases muscles used when breathing), or ocular myasthenia (a disease causing eye muscle weakness) as statins may sometimes aggravate the condition or lead to the occurrence of myasthenia (see section 4).

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

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

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.

Tell your doctor if you have severe lung disease.

The combined use of ZETIVASIM and fibrates (certain medicines for lowering cholesterol) should be avoided since the combined use of ZETIVASIM 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 ZETIVASIM, particularly the 10/80 mg dose. The risk of muscle breakdown is also greater in certain patients. Talk with 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

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 and adolescents
ZETIVASIM is not recommended for children under age 10.

Other medicines and ZETIVASIM
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

Taking ZETIVASIM with any of the following medicines can increase the risk of muscle problems (some of these have already been listed in the above section "Do not take ZETIVASIM if").

- **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 ZETIVASIM. Taking ZETIVASIM 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 AIDS)
- Hepatitis C antiviral agents such as boceprevir, telaprevir, elbasvir, or grazoprevir (used to treat

hepatitis C virus infection)
- nefazodone (used to treat depression)
- medicines with the active ingredient cobicistat
- 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. ZETIVASIM). Your doctor may decide that you stop taking ZETIVASIM 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, tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including those obtained without prescription. In particular, tell your doctor if you are taking any of the following:
- medicines with an active ingredient to prevent blood clots, such as warfarin, fluindione, phenprocoumon or acenocoumarol (anticoagulants)
- cholestyramine (also used to lower cholesterol), because it affects the way ZETIVASIM works
- fenofibrate (also used to lower cholesterol)
- rifampicin (used to treat tuberculosis)
- ticagrelor (antiplatelet medicine)

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

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

Pregnancy and breast-feeding
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

Do not take ZETIVASIM if you are pregnant, are trying to get pregnant or think you may be pregnant. If you get pregnant while taking ZETIVASIM, stop taking it immediately and tell your doctor. Do not take ZETIVASIM if you are breast-feeding, because it is not known if the medicine is passed into breast milk.

Driving and using machines
ZETIVASIM is not expected to interfere with your ability to drive or to use machinery. However, it should be taken into account that some people get dizzy after taking ZETIVASIM.

ZETIVASIM contains lactose
ZETIVASIM tablets contain a sugar called lactose. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.

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

3. How to take ZETIVASIM

Your doctor will determine the appropriate tablet strength for you, depending on your current treatment and your personal risk status.

The tablets are not scored and should not be divided.

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

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

Adults: The recommended dose is **1 tablet** ZETIVASIM by mouth once a day.

Use in adolescents (10 to 17 years of age): The recommended dose is **1 tablet** ZETIVASIM by mouth once a day (a maximum dose of 10 mg/40 mg once daily must not be exceeded).

The ZETIVASIM 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.

Take ZETIVASIM in the evening. You can take it with or without food.

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

If you take more ZETIVASIM than you should
Please contact your doctor or pharmacist

If you forget to take ZETIVASIM
Do not take a double dose to make up for a forgotten tablet, just take your normal amount of ZETIVASIM at the usual time the next day.

If you stop taking ZETIVASIM
Talk to your doctor or pharmacist 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 (See section 2, *What you need to know before you take ZETIVASIM*).

The following common side effects were reported (may affect up to 1 in 10 people):

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

The following uncommon side effects were reported (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; nausea; vomiting; abdominal bloating; diarrhoea; dry mouth; heartburn
- rash; itching; hives
- joint pain; muscle pain, 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

Additionally, the following side effects have been reported in people taking either ZETIVASIM or medicines containing the active ingredients ezetimibe or simvastatin:
- 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
- breathing problems including persistent cough and/or shortness of breath or fever
- constipation
- inflammation of the pancreas often with severe abdominal pain
- inflammation of the liver with the following symptoms: yellowing of the skin and eyes, itching, dark coloured urine or pale coloured stool, feeling tired or weak, loss of appetite; liver failure; gallstones or inflammation of the gallbladder (which may cause abdominal pain, nausea, vomiting)
- hair loss; raised red rash, sometimes with target-shaped lesions (erythema multiforme)
- blurred vision and impaired vision (which each may affect up to 1 in 1000 people)
- rash that may occur on the skin or sores in the mouth (lichenoid drug eruptions) (which each may affect up to 1 in 10000 people)
- hypersensitivity reactions including some of the following: allergic reactions including swelling of the face, lips, tongue and/or throat which may cause difficulty in breathing or swallowing and requires treatment immediately, (angioedema), 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). A serious very rare allergic reaction (which may affect up to 1 in 10000 people) may occur that causes difficulty in breathing or dizziness and requires immediate treatment (anaphylaxis)
- muscle pain, tenderness, weakness or cramps; muscle breakdown; muscle rupture (which may affect up to 1 in 10000 people); tendon problems, sometimes complicated by rupture of the tendon
- gynaecomastia (breast enlargement in men) (which may affect up to 1 in 10000 people)
- decreased appetite
- hot flush; high blood pressure
- pain
- erectile dysfunction
- depression
- alterations in some laboratory blood tests for liver function

Additional possible side effects reported with some statins:
- sleep disturbances, including nightmares
- sexual difficulties
- 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
- muscle pain, tenderness, or weakness that is constant that may not go away after stopping ZETIVASIM (frequency not known)

Adverse reactions with frequency not known:
- Myasthenia gravis (a disease causing general muscle weakness including in some cases muscles used when breathing).
- Ocular myasthenia (a disease causing eye muscle weakness).

Talk to your doctor if you experience weakness in your arms or legs that worsens after periods of activity, double vision or drooping of your eyelids, difficulty swallowing, or shortness of breath.

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.

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
Bijwerkingen Centrum Lareb
Website: www.lareb.nl
By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store ZETIVASIM

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 bottle after EXP. The expiry date refers to the last day of that month.

Do not store above 25°C.
Blisters: Keep the blister in the outer carton in order to protect from moisture.
Bottles: Keep the bottles tightly closed and in the outer carton in order to protect from moisture.

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 ZETIVASIM contains

- The active substances are ezetimibe and simvastatin. Each tablet contains 10 mg ezetimibe and 10 mg, 20 mg, 40 mg, or 80 mg simvastatin.
- The other ingredients are: lactose monohydrate, cellulose, microcrystalline (E 460), hypromellose (E 464), croscarmellose sodium (E 468), propyl gallate (E 310), butyl hydroxyl anisole (E 320), citric acid monohydrate (E 330), sodium lauryl sulfate (E 487), magnesium stearate (E 470b). See also section 2 *'What you need to know before you take ZETIVASIM'*.

What ZETIVASIM looks like and contents of the pack

10 mg/10 mg:
White to Off white capsule shaped uncoated tablets debossed with "G" on one side and "321" on other side, approx.8.5 mm in length and 4.25 mm in width.
10 mg/20 mg:
White to Off white capsule shaped uncoated tablets debossed with "G" on one side and "322" on other side, approx.10.7 mm in length and 5.3 mm in width.
10 mg/40 mg:
White to Off white capsule shaped uncoated tablets debossed with "G" on one side and "323" on other side, approx.14.0 mm in length and 6.0 mm in width.
10 mg/80 mg:
White to Off white capsule shaped uncoated tablets debossed with "G" on one side and "324" on other side, approx.17.5 mm in length and 7.5 mm in width.

ZETIVASIM 10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, or 10 mg/80 mg tablets are available in PVC-Aluminium-OPA / Aluminium blisters of 7, 10, 14, 28, 30, 49, 50, 56, 84, 90, 98, multi-pack containing 98 (2 cartons of 49), 100, 196, 300 or 392 tablets and HDPE bottles of 90 ZETIVASIM

10 mg/80 mg tablets only), 100 tablets (10 mg/10 mg 10 mg/20 mg, and 10 mg/40 mg tablets only).The tablets packed in HDPE bottles include a desiccant protecting the tablets from moisture. The desiccant should not be swallowed.

Not all pack sizes may be marketed.

Marketing Authorisation Holder
ANFARM HELLAS S.A.
4 Achaias Str. & Trizinias,
14564 Kifissia Attiki
Greece

Manufacturer
Glenmark Pharmaceuticals s.r.o.
Fibichova 143
56617 Vysoke Myto
Czech Republic

In het register ingeschreven onder:
ZETIVASIM 10 mg/10 mg, tabletten - RVG 126375
ZETIVASIM 10 mg/20 mg, tabletten - RVG 126376
ZETIVASIM 10 mg/40 mg, tabletten - RVG 126377
ZETIVASIM 10 mg/80 mg, tabletten - RVG 126378

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

Netherlands	ZETIVASIM 10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, 10 mg/80 mg tabletten
Greece	ZETIVASIM
Cyprus	ZETIVASIM 10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, 10 mg/80 mg tablets

Deze bijsluiter is voor het laatste goedgekeurd in april 2023.