

PROPOSED PATIENT INFORMATION LEAFLET FOR EZESIM

PATIENT INFORMATION LEAFLET

SCHEDULING STATUS: S4

EZESIM 10/10, 10/20, 10/40 and 10/80 tablets

Ezetimibe and Simvastatin

EZESIM 10/10 contains sugar (lactose monohydrate, 51,48 mg)

EZESIM 10/20 contains sugar (lactose monohydrate, 112,95 mg)

EZESIM 10/40 contains sugar (lactose monohydrate, 235,90 mg)

EZESIM 10/80 contains sugar (lactose monohydrate, 481,80 mg)

Read all of this leaflet carefully before you start taking EZESIM.

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse or other health care provider.
- EZESIM has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

What is in this leaflet

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

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1. What EZESIM is and what it is used for

EZESIM contains ezetimibe and simvastatin, one of a group of medicines called serum-cholesterol reducers.

EZESIM is taken by patients who cannot control their cholesterol levels by diet alone. You should stay on a cholesterol-lowering diet while taking EZESIM.

EZESIM 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.

2. What you need to know before you take EZESIM

Do not take EZESIM:

- If you are hypersensitive (allergic) to ezetimibe, simvastatin, or any of the other ingredients of EZESIM (see section 6).
- If you have liver disease
- If you are pregnant or breastfeeding your baby.
- If you are a child
- 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),

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- 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).
- 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 EZESIM can lead to serious muscle problems (rhabdomyolysis).

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

Warnings and Precautions

Take special care with EZESIM:

- If you have moderate to severe liver problems
- If you are taking medicines containing danazol (to treat endometriosis), niacin (nicotinic acid), acipimox (also used to lower cholesterol)
- If you are taking medicine containing ciclosporin (used in organ transplant patients), as your doctor will want to monitor your progress
- If you are taking medicine to treat fungal or bacterial infections (e.g. itraconazole, ketoconazole, erythromycin, clarithromycin, telithromycin),
- If you are taking medicine to treat HIV or medicine to treat depression (nefazodone)

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- If you are taking fibrates (to lower cholesterol levels), especially gemfibrozil and bezafibrate
- If you are taking medicines to treat a heart condition (amiodarone or verapamil)
- **If you experience any unexplained muscle pain, tenderness, or weakness contact your doctor immediately.** This is because on rare occasions, muscle problems can be serious, including muscle breakdown resulting in kidney damage.
- The risk of muscle breakdown is greater at higher doses of EZESIM.

The risk of muscle breakdown is also greater in certain patients:

- if you have kidney problems
- if you have thyroid problems
- if you are 65 years or older
- if you are female
- if you have ever had muscle problems during treatment with cholesterol lowering medicines called “statins” (such as simvastatin, atorvastatin, and rosuvastatin)
- if you or close family members have a hereditary muscle disorder
- If you drink large amounts of alcohol
- If you are taking any medicines that may increase the risk of myopathy and rhabdomyolysis (disease of the muscle tissue)
- If you are taking medicines to thin your blood (e.g. warfarin)
- If you have diabetes or at risk of developing diabetes
- If you have severe lung disease
- If you have porphyria (a rare hereditary blood disease)
- If you are taking medicine that contains “statins”, such as **EZESIM**, you might be at risk of developing weakness of skeletal muscles that control body movement (arms and legs) and breathing (myasthenia gravis) or weakness of the muscles that control eye and

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eyelid movement (ocular myasthenia).

Children

EZESIM is not recommended in children under the age of 10 years.

Other medicines and EZESIM

Always tell your healthcare provider if you are taking any other medicine. (This includes all complementary or traditional medicines.)

Tell your doctor if you are taking, have recently taken or might take any other medicine(s) with any of the following active ingredients. Taking EZESIM 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 EZESIM**).

- 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)
- ciclosporin (often used in organ transplant patients)
- danazol (used to treat endometriosis, a condition in which the lining of the uterus grows outside the uterus)
- 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)
- fusidic acid (to treat a bacterial infection). If you need to take oral fusidic acid, you will need to temporarily stop using this medicine. Your doctor will tell you when it is safe to restart EZESIM. Taking EZESIM with fusidic acid may lead to muscle weakness, tenderness or pain (rhabdomyolysis). See more information regarding

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rhabdomyolysis in section 4.

- HIV protease inhibitors such as indinavir, nelfinavir, ritonavir, and saquinavir (used to treat AIDS)
- hepatitis C antiviral medicines 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
- erythromycin, clarithromycin, daptomycin or telithromycin (used to treat bacterial infections)
- cholestyramine (also used to lower cholesterol), because it affects the way EZESIM works
- medicines with an active ingredient to prevent blood clots, such as warfarin, fluindione (anticoagulants)
- lomitapide (used to treat a serious and rare genetic cholesterol condition)
- colchicine (used to treat gout)
- rifampicin (used to treat tuberculosis)
- large amounts (1 gram or more each day) of niacin or nicotinic acid (also used to lower cholesterol)

EZESIM with food, drink and alcohol

EZESIM can be taken with or without food.

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

Pregnancy, breastfeeding and fertility

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If you are pregnant or breastfeeding; think you may be pregnant or are planning to have a baby, please consult your doctor, pharmacist or other healthcare provider for advice before taking EZESIM.

Do not take EZESIM if you are pregnant, trying to get pregnant or are breastfeeding your baby (see **Do not take EZESIM**).

Driving and using machines

EZESIM can cause dizziness. It is not always possible to predict to what extent EZESIM may interfere with the daily activities of a patient. Patients should ensure that they do not engage in the above activities until they are aware of the measure to which EZESIM affects them.

EZESIM contains sugar (lactose monohydrate)

EZESIM contains lactose monohydrate. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking EZESIM.

3. How to take EZESIM

Do not share medicines prescribed for you with any other person. Always take this medicine exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure.

Before starting, and during treatment with EZESIM, you should be on a diet to lower your cholesterol.

Your doctor will determine the appropriate tablet strength for you, depending on your current condition and response.

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Adults

The usual starting dose, depending on your condition, is one EZESIM 10/20 mg tablet per day.

One tablet is to be taken in the evening, either with or without food. The dosage range is 10/10 mg to 10/80 mg per day.

If your doctor has prescribed EZESIM along with a bile acid sequestrant such as cholestyramine (a medicine to lower cholesterol), EZESIM should be taken at least 2 hours before or 4 hours after taking the bile acid sequestrant.

Children

EZESIM is not for use in children (see **Do not take EZESIM**).

Your doctor will tell you how long your treatment with EZESIM will last. Do not stop treatment early because cholesterol level may increase again. If you have the impression that the effect of EZESIM is too strong or too weak, tell your doctor or pharmacist.

If you take more EZESIM than you should

In the event of overdosage, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison control centre.

If you forget to take EZESIM

If you forget to take EZESIM, take a dose as soon as you remember, then continue to take EZESIM at the usual times. Do not take a double dose to make up for forgotten individual doses.

If you stop taking EZESIM

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If you stop taking EZESIM without consulting your doctor, your cholesterol levels may rise again.

4. Possible side effects

EZESIM can have side effects.

Not all side effects reported for EZESIM are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking EZESIM, please consult your health care provider for advice.

If any of the following happens, stop taking EZESIM and tell your doctor immediately or go to the casualty department at your nearest hospital:

- Swelling of your hands, feet, ankles, face, lips, mouth or throat, which may cause difficulty in swallowing or breathing
- Rash or itching
- Pain or inflammation of the joints, unusual bruising, skin eruptions and swelling, skin sensitivity to the sun, fever, flushing, feeling unwell.

These are all very serious side effects. If you have them, you may have had a serious reaction to EZESIM. You may need urgent medical attention or hospitalisation.

Tell your doctor immediately or go to the casualty department at your nearest hospital if you notice any of the following:

- muscle breakdown (with symptoms such as muscle pain, tenderness, weakness, swollen muscles, tendon rupture/tear, kidney disorder with reddish-brown urine)
- liver problems (you may experience jaundice – yellowing of the skin and eyes - stomach pain and swelling, dark coloured urine)
- an increase in blood sugar which could lead to problems if you are a diabetic (your diabetic medicine may need to be adjusted).

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These are all serious side effects. You may need urgent medical attention.

Tell your doctor if you notice any of the following:

Frequent side effects:

- Headache
- Cough
- Viral infections, sore throat (pharyngitis), sinusitis, chest infections
- Stomach pain/disturbances, flatulence diarrhoea
- Muscle pain, back pain
- Extreme tiredness, chest pain
- Elevations in laboratory blood tests of liver (transaminases) and/or muscle (CK) function

Less frequent side effects:

- Low red blood cell count (anaemia); reduction in blood cell counts, which may cause bruising/bleeding (thrombocytopenia), increased blood clotting time (longer than normal bleeding)
- Weight loss
- Sleep disorder, trouble sleeping, depression
- Dizziness, pins and needles, poor memory, weakness/numbness/pain (peripheral neuropathy)
- Inflammation of the pancreas often with severe abdominal pain, pain that worsens with deep breathing or pain that travels to the right shoulder or back
- Gastrointestinal problems such as wind, discomfort or bloating, indigestion or heartburn, nausea, vomiting, dry mouth, constipation
- Itchy or red skin, rash, hair loss, skin or mouth lesions that have a pink-red centre surrounded by a pale ring border and an outer pink-red ring (erythema multiforme)

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- Pain in the joints or neck, back pain, muscle pain and weakness with skin rash, muscle cramps, muscle spasm, inflammation of the muscle
- Abnormal lack of energy, feeling generally unwell, swelling of the hands or feet
abnormal liver function test results.

Frequency unknown:

- Difficulty breathing, chest infection
- Decrease in appetite
- Changes to the content of your urine which will be seen in a test performed by your doctor, kidney failure.
- Trouble remembering, learning new things, concentrating, or making decisions, nightmares, weakness in the arm, leg and eye muscles, sleep disturbances
- Hot flush, high blood pressure
- Gall stones, inflammation of the gall bladder
- Erectile dysfunction, sexual dysfunction, decreased sex drive, testicular pain, Impotence.

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

Reporting of side effects

If you get side effects, talk to your doctor or pharmacist.

You can also report side effects to SAHPRA via the “**6.04 Adverse Drug Reaction**

Reporting Form”, found online under SAHPRA’s publications:

<https://www.sahpra.org.za/Publications/Index/8>. By reporting side effects, you can help provide more information on the safety of EZESIM.

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5. How to store EZESIM

Store all medicines out of reach of children.

Store at or below 25 °C.

Keep container tightly closed.

Store in the original packaging.

Do not take after the expiry date stated on the package.

Return all unused medicine to your pharmacist.

Do not dispose of unused capsules in drains or sewerage systems (e.g. toilets).

6. Contents of the pack and other information

What EZESIM contains

EZESIM 10/10: The active substance is 10 mg ezetimibe and 10 mg simvastatin.

EZESIM 10/20: The active substance is 10 mg ezetimibe and 20 mg simvastatin.

EZESIM 10/40: The active substance is 10 mg ezetimibe and 40 mg simvastatin.

EZESIM 10/80: The active substance is 10 mg ezetimibe and 80 mg simvastatin.

The other ingredients are butylated hydroxy anisole, citric acid monohydrate, croscarmellose sodium, hypromellose, lactose monohydrate, magnesium stearate, microcrystalline cellulose, propyl gallate, sodium lauryl sulfate.

What EZESIM looks like and contents of the pack

EZESIM 10/10: White to off-white capsule shaped uncoated tablets debossed with "G" on one side and "321", on other side.

EZESIM 10/20: White to off-white capsule shaped uncoated tablets debossed with "G" on one side and "322" on other side.

EZESIM 10/40: White to off-white capsule shaped uncoated tablets debossed with "G" on one side and "323" on other side.

Ezetimibe/Simvastatin Tablets 10/10, 10/20, 10/40, 10/80
Forrester Pharma (Pty) Ltd

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EZESIM 10/80: White to off-white capsule shaped uncoated tablets de bossed with "G" on one side and "324" on other side.

Bottles: White high-density polyethylene (HDPE) containers containing 30 tablets.

Pack size: 30 tablets.

Holder of certificate of registration

Forrester Pharma (Pty) Ltd

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Waterford Place

Century City

7441

Cape Town

South Africa

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EZESIM 10/10: 51/7.5/0949

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EZESIM 10/40: 51/7.5/0951

EZESIM 10/80: 51/7.5/0952