Package leaflet: Information for the user

Ezetimibe/Simvastatin Krka 10 mg/10 mg tablets
Ezetimibe/Simvastatin Krka 10 mg/20 mg tablets
Ezetimibe/Simvastatin Krka 10 mg/40 mg tablets
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 Ezetimibe/Simvastatin Krka is and what it is used for

Ezetimibe/Simvastatin Krka contains the active substances ezetimibe and simvastatin. Ezetimibe/Simvastatin Krka 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 Krka raises levels of "good" cholesterol (HDL cholesterol).

Ezetimibe/Simvastatin Krka 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 Krka 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 Krka 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 Krka reduces the risk of heart attack, stroke, surgery to increase heart blood flow or hospitalization for chest pain.

Ezetimibe/Simvastatin Krka does not help you lose weight.

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

Do not take Ezetimibe/Simvastatin Krka:
- if you are allergic to ezetimibe, 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)
    - 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 Ezetimibe/Simvastatin Krka can lead to serious muscle problems (rhabdomyolysis).

Do not take more than 10/40-mg Ezetimibe/Simvastatin Krka 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 Krka.
Tell your doctor:
- about all your medical conditions including allergies.
- if you drink large amounts of alcohol or have ever had liver disease. Ezetimibe/Simvastatin Krka may not be right for you.
- if you are due to have an operation. You may need to stop taking Ezetimibe/Simvastatin Krka 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 Ezetimibe/Simvastatin Krka and if you have any symptoms of liver problems while you take Ezetimibe/Simvastatin Krka. 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 Ezetimibe/Simvastatin Krka.

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 Ezetimibe/Simvastatin Krka and fibrates (certain medicines for lowering cholesterol) should be avoided since the combined use of Ezetimibe/Simvastatin Krka 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 Krka, 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
Ezetimibe/Simvastatin Krka is not recommended for children under age 10.

Other medicines and Ezetimibe/Simvastatin Krka
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicine(s) with any of the following active ingredients. Taking Ezetimibe/Simvastatin Krka 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 Ezetimibe/Simvastatin Krka ").
- 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 Krka. Taking Ezetimibe/Simvastatin Krka 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. Ezetimibe/Simvastatin Krka). Your doctor may decide that you stop taking Ezetimibe/Simvastatin Krka 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),
- colestyramine (also used to lower cholesterol), because it affects the way Ezetimibe/Simvastatin Krka 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 Ezetimibe/Simvastatin Krka.

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

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

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

Driving and using machines
Ezetimibe/Simvastatin Krka 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 Ezetimibe/Simvastatin Krka.

Ezetimibe/Simvastatin Krka contains lactose and sodium
If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.
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 Krka

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

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

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

Adults: The dose is 1 tablet Ezetimibe/Simvastatin Krka by mouth once a day.

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

The 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.

Not all recommended dosages are possible with these products; however, other products with a different dosage strength (10 mg/80 mg) are also available.

Take Ezetimibe/Simvastatin Krka in the evening. You can take it with or without food.

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

If you take more Ezetimibe/Simvastatin Krka than you should
Please contact your doctor or pharmacist.

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

If you stop taking Ezetimibe/Simvastatin Krka
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.

If you experience any of the following, stop taking the medicinal product at once and tell your doctor immediately:
- muscle aches (common: may affect up to 1 in 10 people)
- signs indicating disorders of the blood, e.g. tiredness, unexplained bruising bleeding, mouth ulcers (not known: cannot be estimated from the available data)
- inflamed pancreas which may cause severe abdominal and back pain accompanied with feeling very unwell (not known: cannot be estimated from the available data)
- signs indicating liver problems, gallstones or inflammation of the gallbladder, e.g. yellowing of the skin, nausea, stomach pain, itching, dark coloured urine or pale coloured stool (not known: cannot be estimated from the available data)
- angio-oedema (stop using Ezetimibe/Simvastatin Krka and immediately contact a doctor if you

experience any of the following symptoms: swelling of face, tongue or throat, difficulty swallowing, hives and breathing difficulties) (rare: may affect up to 1 in 1,000 people)

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 following common side effects were reported (may affect up to 1 in 10 people):
- 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 Ezetimibe/Simvastatin Krka or medicines containing the active ingredients ezetimibe or simvastatin:
- 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
- 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
- gynecomastia (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
- 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.

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 Ezetimibe/Simvastatin Krka (frequency not known)

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 Krka

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

This medicine does not require any special temperature storage conditions.
Store in the original package in order to protect from light and 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 Ezetimibe/Simvastatin Krka contains
- The active substances are ezetimibe and simvastatin.
  Each tablet contains 10 mg ezetimibe and 10 mg simvastatin.
  Each tablet contains 10 mg ezetimibe and 20 mg simvastatin.
  Each tablet contains 10 mg ezetimibe and 40 mg simvastatin.
- The other ingredients are lactose monohydrate, microcrystalline cellulose, croscarmellose sodium, magnesium stearate, hypromellose 2910, yellow iron oxide (E172) – only for 10 mg/10 mg tablets and red iron oxide (E172) – only for 10 mg/20 mg tablets. See section 2 "Ezetimibe/Simvastatin Krka contains lactose and sodium".

What Ezetimibe/Simvastatin Krka looks like and contents of the pack
10 mg/10 mg tablets appear as yellowish white, round, slightly biconvex tablets with bevelled edges. Tablet diameter 6 mm.
10 mg/20 mg tablets appear as pinkish white, oval, biconvex tablets. Tablet length 11 mm, width 5.5 mm.
10 mg/40 mg tablets appear as white to almost white, biconvex capsule shape tablets. Tablet dimensions 14 x 6 mm.

Ezetimibe/Simvastatin Krka is available in boxes containing:
- 14, 28, 30, 50, 56, 60, 90, 98 or 100 tablets in blisters,
- 14 x 1, 28 x 1, 30 x 1, 56 x 1, 60 x 1, 90 x 1, 98 x 1 or 100 x 1 tablet in perforated unit dose blisters.

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer
KRKA, d.d., Novo mesto, Šmarješka cesta 6, 8501 Novo mesto, Slovenia

This medicine is authorised in the Member States of the European Economic Area under the following names:

Name of the Member State	Name of the medicine
Sweden, Denmark, Norway, Iceland	Ezetimib/Simvastatin Krka
Austria	Ezetimib/Simvastatin HCS
Belgium, Ireland	Ezetimibe/Simvastatin Krka
Croatia, Greece, Slovenia	Vasitimb
Germany	Ezesimin
France, Netherlands	Ezetimibe/Simvastatine Krka
Italy	Ezetimibe e Simvastatina Krka
Portugal	Sinvastatina + Ezetimiba Krka
Spain	Ezetimiba/Simvastatina Krka

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