

This medicine can be sold with a physician's prescription only

Simvaxon® , caplets 10, 20, 40, 80 mg

Each caplet contains Simvastatin at a dose of 10, 20, 40 and 80 mg respectively.

Inactive ingredients and allergens in the medicine - see section 6 "Additional information" and in section 2 "Important information about some of the ingredients of this medicine".

Read this entire leaflet carefully before using this medicine. This leaflet contains concise information about the medicine. If you have any further questions, refer to the doctor or the pharmacist.

This medicine has been prescribed for the treatment of your illness. Do not pass it on to others. It may harm them, even if it seems to you that their medical condition is similar.

This medicine is not intended for children and adolescents under the age of 20 years.

1. What is the medicine intended for?

In patients with coronary heart disease and hypercholesterolemia, simvastatin reduces:

- The overall mortality risk by lowering mortality from heart disease.
- The risk of a non-fatal heart attack.
- The risk of invasive procedures to restore blood flow to the heart (such as balloon dilation or bypass surgery).
- The risk of stroke and Transient Ischemic Attack (TIA).

Simvastatin is indicated for lowering the levels of LDL and other fatty substances in the blood and raising HDL blood levels in patients with hyperlipidemia (high level of fats in the blood).

Therapeutic class: Statins, HMG-CoA reductase enzyme inhibitors.

How does simvastatin work:

Simvaxon contains the active ingredient simvastatin. Simvastatin is used to lower blood levels of total cholesterol, levels of the "bad" cholesterol (LDL cholesterol), and the levels of fatty compounds called triglycerides. In addition, simvastatin raises the levels of the "good" cholesterol (HDL cholesterol).

Cholesterol is one of the fatty components found in the blood. The total cholesterol is made up mainly of LDL and HDL cholesterol. LDL cholesterol is often called the "bad"

cholesterol, because it may build up on the walls of the arteries and form plaque. With time plaque buildup may cause narrowing of the arteries. This narrowing may slow or block blood flow to vital organs such as the heart or the brain. Blocking of the blood flow may lead to a heart attack or stroke. HDL cholesterol is often called the "good" cholesterol, because it helps prevent plaque buildup in the arteries and prevents heart disease. Triglycerides are another type of fat found in the blood that may increase the risk of heart disease.

You need to stick to a low cholesterol diet while taking this medicine.

2. Before using the medicine Do not use the medicine if:

- You are hypersensitive (allergic) to the active ingredient (simvastatin) or to any of the other ingredients this medicine contains (see section 6 - "Additional information" and in section 2 - "Important information about some of the ingredients of the medicine").
- You currently suffer from liver problems.
- You are pregnant or breastfeeding.
- You are taking medicines that contain one or more 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 infection).
 - Nefazodone (used to treat depression).
 - Cobicistat.
 - Gemfibrozil (used to lower cholesterol).
 - Ciclosporin (used in patients after organ transplant).
 - Danazol (artificial hormone used to treat endometriosis, a condition in which parts of the endometrial tissue grow outside the uterus).
- Do not take more than 40 mg of simvastatin if you are taking lomitapide (a medicine used to treat a severe and rare medical condition of genetic cholesterol).

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

Special warnings regarding the use of the medicine: Before the treatment with Simvaxon, tell the doctor:

- About all your medical problems including allergies.
- If you consume large amounts of alcohol.
- If you have suffered in the past from liver disease. The treatment with the medicine may not be right for you.
- If you are about to undergo surgery. You may need to stop taking the medicine for a short time.
- If you suffer from severe respiratory failure.
- If you are of Asian descent. You may need a different dosage.
- If you are taking or have taken in the last 7 days a medicine called fusidic acid (a medicine used to treat a bacterial infection) orally or by injection. Concomitant use of fusidic acid with simvastatin may lead to severe muscle problems (rhabdomyolysis).

Contact your doctor immediately if you experience unexplained muscle pain, tenderness or muscle weakness. This is because in rare cases, muscle problems may be severe, including muscle breakdown resulting in kidney damage, and in very rare cases death.

The risk of muscle breakdown is higher in patients taking high doses of simvastatin, particularly an 80 mg dosage. In addition, the risk of muscle breakdown is higher in certain patients. Talk to your doctor if any of the following applies to you:

- You consume large amounts of alcohol.
- You have kidney problems.
- You have thyroid problems.
- You are 65 years old or older.
- You are female.
- You had muscle problems in the past during treatment with cholesterol lowering medicines called "statins" or "fibrates".
- You or a family member has a hereditary muscle disease.

Furthermore, tell the doctor or pharmacist if you have constant muscle weakness. Additional tests and medicines may be required to diagnose and treat this.

Tests and follow-up

Before you start using the medicine and during the treatment period with the medicine, if you have any symptoms of liver problems, the doctor

will refer you to a blood test. This is to test your liver function.

After starting treatment with the medicine, you may be referred by your doctor to a liver function blood test.

Your doctor will monitor you closely, if you have diabetes or you are at risk of developing diabetes. You are at risk of developing diabetes if you have high levels of sugars and fats in your blood, excess weight and high blood pressure.

Drug interactions

If you are taking, or have recently taken other medicines, including non-prescription medicines and nutrition supplements, tell the doctor or pharmacist.

Taking simvastatin with one of the medicines listed below may increase the risk of muscle problems (some are mentioned in section 2 - "Do not use this medicine if"):

- **If you need to take fusidic acid orally to treat a bacterial infection, you will need to temporarily stop the treatment with simvastatin. Your doctor will instruct you when you can start taking the medicine safely again. Taking simvastatin concomitantly with fusidic acid may rarely cause muscle weakness, muscle tenderness or muscle pain (rhabdomyolysis). For more information about rhabdomyolysis see section 4 - "Side effects".**
- Ciclosporin (often given to patients after organ transplant).
- Danazol (artificial hormone used to treat endometriosis, a condition in which parts of the endometrial tissue grow outside the uterus).
- Medicines with active ingredients such as itraconazole, ketoconazole, fluconazole, posaconazole or voriconazole (used to treat fungal infections).
- Fibrates with active ingredients such as gemfibrozil or bezafibrate (used to lower cholesterol).
- Erythromycin, clarithromycin, telithromycin (used to treat bacterial infections).
- HIV protease inhibitors such as indinavir, nelfinavir, ritonavir or saquinavir (used to treat HIV).
- Antiviral medicines for the treatment of hepatitis C such as boceprevir, telaprevir, elbasvir or grazoprevir (used to treat hepatitis C viral infection).
- Nefazodone (used to treat depression).
- Medicines containing the active ingredient cobicistat.

- Amiodarone (used to treat irregular heartbeat).
- Verapamil, diltiazem or amlodipine (used to treat high blood pressure, chest pain attributed to heart disease or other heart conditions).
- Lomitapide (a medicine used to treat a severe and rare medical condition of genetic cholesterol).
- Daptomycin (a medicine used to treat complicated infections of the skin and skin tissues and bacteremia). It is possible that the side effects affecting the muscles will be stronger when taking this medicine during treatment with simvastatin. The doctor may decide that you should stop taking **Simvaxon** temporarily.
- Colchicine (used to treat gout).
- Ticagrelor (an anticoagulant).

In addition to the medicines listed above, tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including non-prescription medicines. Especially, tell your doctor if you are taking one of the following medicines:

- Medicines with an active ingredient to prevent blood clotting, such as warfarin, phenprocoumon or acenocoumarol (anticoagulants)
- Fenofibrate (also used to lower cholesterol)
- Niacin (also used to lower cholesterol)
- Rifampicin (used to treat tuberculosis)

Tell all doctors prescribing a new medicine for you that you are taking **Simvaxon**.

Use of this medicine and food

Grapefruit juice contains one or more compounds that affect the way in which the body breaks down certain medicines, including simvastatin. **Consuming grapefruit juice should be avoided.**

Pregnancy and breastfeeding

Do not use simvastatin if you are pregnant, trying to become pregnant or think you might be pregnant. If you become pregnant during treatment with the medicine, stop taking it and contact your doctor immediately.

Do not take simvastatin if you are breastfeeding, as it is not known if the medicine passes into breast milk.

Consult the doctor or pharmacist before taking any medicine.

Driving and using machines

The medicine is not expected to affect your ability to drive or operate machinery.

However, it should be taken into account that some people may feel dizzy after taking the medicine.

Important information about some of the ingredients of the medicine

This medicine contains 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 medicine.

3. How to use this medicine

Always use this medicine according to the doctor's instructions. Check with your doctor or pharmacist if you are not sure about the dosage and the manner of treatment with the medicine.

The dosage and manner of treatment will be determined by the doctor only. The usual dosage is: The recommended initial dose is 10 or 20 mg once a day, in the evening, with or without food.

How to take the medicine:

The tablet should be swallowed with some water.

Do not halve the caplet, because there is no score line. There is no information regarding crushing and chewing.

Due to the increased risk of muscle problems, the 80 mg dosage is only for patients who have chronically been taking a dosage of 80 mg (such as 12 months or more) without muscle damage and who do not need to take certain other medicines concomitantly with simvastatin, which may increase your risk for developing muscle damage.

Your doctor may prescribe you lower dosages, especially if you are taking certain medicines of those listed above or if you have certain kidney problems.

In case you also take medicines that bind bile acids (cholesterol-lowering medicines), such as cholestyramine, you should take simvastatin at least two hours before or four hours after taking these medicines.

Do not exceed the recommended dose.

If you have accidentally taken an overdose or if a child has accidentally swallowed the medicine, immediately proceed to a hospital emergency room and bring the package of the medicine with you.

If you forget to take the medicine at the designated time, do not take a double dose. Take the next dose at the usual time and consult a doctor.

Continue with the treatment as recommended by the doctor.

Even if there is an improvement in your health, do not stop taking the medicine without consulting your doctor.

If you stop taking the medicine

Continue taking simvastatin unless your doctor tells you to stop. If you stop taking the medicine, your cholesterol may rise again.

Do not take medicines in the dark! Check the label and the dose each time you take a medicine. Wear glasses if you need them.

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

4. Side effects

Like any medicine, the use of **Simvaxon** may cause side effects in some users. Do not be alarmed when reading the list of side effects. You may not suffer from any of them.

Rare and serious side effects (effects that appear in 1-10 out of 10,000 users):

Stop using this medicine and refer immediately to a doctor or to an emergency room at the appearance of any of the following side effects:

- Muscle pain, muscle tenderness, muscle weakness or muscle cramps, muscle rupture (very rare). In rare cases these muscle problems may be severe, including muscle breakdown resulting in kidney damage, and in very rare cases even death.
- Hypersensitivity (allergic) reactions including:
 - swelling of the face, tongue or throat that may cause difficulty breathing (angioedema).
- Severe muscle pain, usually in the shoulders or hips (polymyalgia rheumatica).
- Rash with weakness in the limbs and the neck muscles.
- Rash that may appear on the skin and sores in the mouth (lichenoid drug eruptions) (very rare).
- Pain or inflammation in the joints.
- Inflammation of blood vessels (vasculitis).
- Unusual bruising, rash and swelling of the skin (dermatomyositis), hives, skin sensitivity to the sun, fever, flushing.
- Shortness of breath (dyspnea) and generally feeling unwell.

- A condition similar to lupus (which includes a rash, joint problems and an effect on blood cells).
- Inflammation of the liver accompanied by the following symptoms: yellowing of the skin and the eyes, itching, dark colored urine or light-colored feces, feeling tired or weak, loss of appetite; fatal and non-fatal liver failure (very rare).
- Inflammation of the pancreas usually accompanied by severe abdominal pain.

Very rare serious side effects (effects that appear in less than 1 in 10,000 users):

- Severe allergic reaction that causes

breathing difficulties or dizziness (anaphylaxis).

- Gynecomastia (breast enlargement in men).

Rare side effects (effects that appear in 1-10 out of 10,000 users):

- Low red blood cell count (anemia).
- Numbness or weakness of the hands and feet.
- Headache, tingling sensation, dizziness.
- Blurred vision, impaired vision.
- Digestive system disturbances (abdominal pain, constipation, swelling, digestive difficulties, diarrhea, nausea, vomiting).
- Rash, itching, hair loss.
- Weakness.
- Sleeping problems (very rare).
- Poor memory (very rare), memory loss, confusion.

Side effects with an unknown frequency (effects for which frequency has not yet been determined):

- Erectile dysfunction.
- Depression.
- Tendon problems, sometimes with complications of tendon rupture.
- Constant muscle weakness.

Possible side effects when using statins:

- Sleep disturbances including nightmares.
- Difficulties in sexual functioning.
- Breathing problems including persistent cough and / or shortness of breath or fever.
- Diabetes. This is more likely if you have high levels of sugars and fats in your blood, excess weight and high blood pressure. Your doctor will monitor you during the course of treatment with this medicine.

Laboratory values results:

Elevations in certain laboratory blood tests of liver function and the muscle enzyme (creatine kinase) have been observed.

If a side effect appears, if one of the side effects worsens or if you suffer from a side effect not mentioned in this leaflet, consult your doctor.

Side effects can be reported to the Ministry of Health via the link "תווית" and "הוראת" קוב סיכור תרופות" that can be found on the home page of the Ministry of Health website (www.health.gov.il) directing to the online form of adverse events reporting or via the following link: <https://sideeffects.health.gov.il>

5. How to store the medicine Avoid poisoning!

This medicine and any other medicine must be stored in a closed place out of the reach and sight of children and/or infants to avoid poisoning. Do not induce vomiting

unless explicitly instructed to do so by your doctor.

Do not use the medicine after the expiry date (תאריך תפוגה) stated on the package. The expiry date refers to the last day of that month.

Storage conditions: Store below 25°C.

6. Additional information

In addition to the active ingredient, this medicine also contains:

- Lactose monohydrate, starch pregelatinised, microcrystalline cellulose, ascorbic acid, magnesium stearate, citric acid monohydrate, hydroxypropyl cellulose, hypromellose, titanium dioxide (E171), talc, butylhydroxyanisole, iron oxide (red, black, yellow) (E172), carnauba wax.

What the medicine looks like and what the package contains:

Simvaxon 10: elongated light pink coated caplets, imprinted with "SST" on one side and with "10" on the other.

Simvaxon 20: elongated beige coated caplets, imprinted with "SST" on one side and with "20" on the other.

Simvaxon 40: elongated pinkish-brown coated caplets, imprinted with "SST" on one side and with "40" on the other.

Simvaxon 80: elongated pinkish-brown coated caplets, imprinted with "SL" on one side.

Approved package sizes of **Simvaxon 10, 20, 40, 10, 14, 28, 30** caplets.

Approved package sizes of **Simvaxon 80:** 7, 10, 14, 28, 30 caplets.

Not all package sizes may be marketed.

Manufacturer and his address: Dexcel Ltd., 1 Dexcel St., Or Akiva 3060000, Israel

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Drug registration number at the national drug registry of the Ministry of Health:

Simvaxon 10 caplets: 132 83 31147 00

Simvaxon 20 caplets: 132 84 31148 00

Simvaxon 40 caplets: 132 85 31149 00

Simvaxon 80 caplets: 151 84 33890 00

SIMVAXON® Caplets 10, 20, 40, 80 mg PIL PB0422-03

Registration holder:
Dexcel Pharma Technologies Ltd.

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