

Package leaflet: Information for the user

SIMTAN 5 mg film-coated tablets
SIMTAN 10 mg film-coated tablets
SIMTAN 20 mg film-coated tablets
SIMTAN 40 mg film-coated tablets

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

1. What Simtan is and what it is used for

Simtan contains the active substance simvastatin. 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, simvastatin raises levels of “good” cholesterol (HDL cholesterol). Simvastatin is a member of the class of medicines called statins.

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.

You should stay on a cholesterol-lowering diet while taking this medicine.

Simtan is used in addition to your cholesterol-lowering diet if you have:

- a raised cholesterol level in your blood (primary hypercholesterolaemia) or elevated fat levels in your blood (mixed hyperlipidaemia),
- a hereditary illness (homozygous familial hypercholesterolaemia) that increases the cholesterol level in your blood. You may also receive other treatments,
- coronary heart disease (CHD) or are at high risk of CHD (because you have diabetes, history of stroke, or other blood vessel disease). Simtan may prolong your life by reducing the risk of heart disease problems, regardless of the amount of cholesterol in your blood.

In most people, there are no immediate symptoms of high cholesterol. Your doctor can measure your cholesterol with a simple blood test. Visit your doctor regularly, keep track of your cholesterol, and discuss your goals with your doctor.

2. What you need to know before you take Simtan

DO NOT take Simtan

- if you are allergic 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 for HIV infections),
 - boceprevir or telaprevir (used to treat hepatitis C virus infection),
 - nefazodone (used to treat depression),
 - cobicistat
 - gemfibrozil (used to lower cholesterol),
 - ciclosporin (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 Simtan can lead to serious muscle problems (rhabdomyolysis).

Do not take more than 40 mg 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 Simtan.

- 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).

Tell your doctor:

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

Your doctor should do a blood test before you start taking Simtan and if you have any symptoms of liver problems while you take Simtan. 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 Simtan.

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.

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 Simtan, particularly the 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 consume large amounts of alcohol,
- 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” or fibrates,
- you or a close family member 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

Safety and effectiveness of Simtan have been studied in 10-17 year old boys and in girls who had started their menstrual period (menstruation) at least one year before (see section 3: “How to take Simtan”). Simtan has not been studied in children under the age of 10 years. For more information, talk to your doctor.

Other medicines and Simtan

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

It is particularly important to tell your doctor if you are taking medicine(s) with any of the following active ingredients. Taking Simtan 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 Simtan”).

- **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 Simtan. Taking Simtan 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 an active ingredient 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. Simtan). Your doctor may decide that you stop taking Simtan for a while,

- 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 a prescription. In particular, tell your doctor if you are taking medicines(s) with any of the following active ingredients:

- medicines with an active ingredient to prevent blood clots, such as warfarin, phenprocoumon or acenocoumarol (anticoagulants),
- fenofibrate (also used to lower cholesterol),
- niacin (also used to lower cholesterol),
- rifampicin (used to treat tuberculosis),
- ticagrelor (antiplatelet agent).

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

Simtan with food and drink

Grapefruit juice contains one or more components that alter how the body uses some medicinal products, including Simtan. Consuming grapefruit juice should be avoided.

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

Driving and using machines

Simtan 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 Simtan.

Simtan contains lactose

Simtan 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.

3. How to take Simtan

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

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

You should stay on a cholesterol-lowering diet while taking Simtan.

Dosage:

The recommended dose is simvastatin 5 mg, 10 mg, 20 mg, 40 mg or 80 mg by mouth once a day.

Adults:

The usual starting dose is 10, 20 or, in some cases, 40 mg a day. Your doctor may adjust your dose after at least 4 weeks to a maximum of 80 mg a day. **Do not take more than 80 mg a day.**

Your doctor may prescribe lower doses, particularly if you are taking certain medicinal products listed above or have certain kidney conditions.

The 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 children and adolescents:

For children (10-17 years old), the recommended usual starting dose is 10 mg a day in the evening. The maximum recommended dose is 40 mg a day.

Method and duration of administration:

Take Simtan in the evening. You can take it with or without food. Keep taking Simtan unless your doctor tells you to stop.

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

If you take more Simtan than you should

- please contact your doctor or pharmacist.

If you forget to take Simtan

- do not take a double dose to make up for a forgotten tablet. Just take your normal amount of Simtan at the usual time the next day.

If you stop taking Simtan

- 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.

The following terms are used to describe how often side effects have been reported:

- Rare (may affect up to 1 of 1 000 people).
- Very rare (may affect up to 1 of 10 000 people).
- Not known (frequency cannot be estimated from the available data).

The following rare serious side effects were reported:

If any of these serious side effects happen, stop taking the medicine and tell your doctor immediately or go to the emergency room at your nearest hospital.

- muscle pain, tenderness, weakness, or cramps. On rare occasions, these muscle problems can be serious, including muscle breakdown resulting in kidney damage; and very rare deaths have occurred.
- hypersensitivity (allergic) reactions including:
 - swelling of the face, tongue and throat which may cause difficulty in breathing (angioedema),
 - severe muscle pain usually in the shoulders and hips,
 - rash with weakness of limbs and neck muscles,
 - pain or inflammation of the joints (polymyalgia rheumatica),
 - inflammation of the blood vessels (vasculitis),
 - unusual bruising, skin eruptions and swelling (dermatomyositis), hives, skin sensitivity to the sun, fever, flushing,
 - shortness of breath (dyspnoea) and feeling unwell,
 - lupus-like disease picture (including rash, joint disorders, and effects on blood cells),
- 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 (very rare),
- inflammation of the pancreas often with severe abdominal pain.

The following very rare serious side effect was reported:

- a serious allergic reaction which causes difficulty in breathing or dizziness (anaphylaxis)

The following side effects have also been reported rarely:

- low red blood cell count (anaemia),

- numbness or weakness of the arms and legs,
- headache, tingling sensation, dizziness,
- digestive disturbances (abdominal pain, constipation, flatulence, indigestion, diarrhoea, nausea, vomiting),
- rash, itching, hair loss,
- weakness, blurred vision and impaired vision.

The following side effects have also been reported very rarely:

- rash that may occur on the skin or sores in the mouth (lichenoid drug eruptions),
- gynecomastia (breast enlargement in men),
- muscle rupture,
- trouble sleeping,
- poor memory, memory loss, confusion.

The following side effects have also been reported but the frequency cannot be estimated from the available data (frequency not known):

- erectile dysfunction,
- depression,
- inflammation of the lungs causing breathing problems including persistent cough and/or shortness of breath or fever,
- tendon problems, sometimes complicated by rupture of the tendon,
- myasthenia gravis (a disease causing general muscle weakness including in some cases muscles used when breathing) ¹,
- ocular myasthenia (a disease causing eye muscle weakness) ¹.

¹ 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 simvastatin (frequency not known).

Laboratory Values

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

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 the national reporting system:

HPRRA 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 Simtan

Keep this medicine out of the sight and reach of children.

5 mg: Do not store above 25°C.

Do not use this medicine after the expiry date which is stated on the carton and blister pack after "EXP". The expiry date refers to the last day of that month.

Commented [JCB1]: Applicant's comment: The applicant proposes to use footnotes to clearly indicate that this information belongs to the side effects "myasthenia gravis" and "ocular myasthenia".

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 Simtan contains

The active substance is simvastatin.

Simtan 5/10/20/40 mg film-coated tablets

One film-coated tablet contains either 5 mg, 10 mg, 20 mg or 40 mg of simvastatin.

The other ingredients are:

Tablet core:

- lactose
- microcrystalline cellulose
- pregelatinised maize starch
- butylhydroxyanisole
- magnesium stearate
- talc

Tablet coat:

- hydroxypropylcellulose
- hypromellose
- talc
- titanium dioxide (E171)

Simtan 5 mg tablets also contain the colourant iron oxide yellow (E172).

What Simtan looks like and contents of the pack

Simtan 5 mg tablets are yellow, oblong, biconvex, film-coated tablets, scored on one side and embossed with “SVT” and “5”.

Simtan 10 mg tablets are white, oblong, biconvex, film-coated tablets, scored on one side and embossed with “SVT” and “10”.

Simtan 20 mg tablets are white, oblong, biconvex, film-coated tablets, scored on one side and embossed with “SVT” and “20”.

Simtan 40 mg tablets are white, oblong, biconvex, film-coated tablets, scored on one side and embossed with “SVT” and “40”.

5 mg:

Blister packs, PVC / PE / PVDC / Al blister:

10, 14, 20, 28, 30, 40, 49, 50, 56, 60, 84, 90, 98, 100, 112, 120, 250 film-coated tablets.

Blister packs within aluminium sachets, PVC / PE / PVDC / Al blister in Al sachet:

10, 14, 20, 28, 30, 40, 49, 50, 56, 60, 84, 90, 98, 100, 112, 120, 250 film-coated tablets.

10 mg:

Blister packs, PVC / PE / PVDC / Al blister:

10, 14, 20, 28, 30, 40, 49, 50, 56, 60, 84, 90, 98, 100, 112, 120, 250 film-coated tablets.

Blister packs within aluminium sachets, PVC / PE / PVDC / Al blister in Al sachet:

10, 14, 20, 28, 30, 40, 49, 50, 56, 60, 84, 90, 98, 100, 112, 120, 250 film-coated tablets.

20 mg:

Blister packs, PVC / PE / PVDC / Al blister:

10, 14, 20, 28, 30, 40, 48, 49, 50, 56, 60, 84, 90, 98, 100, 110, 112, 120, 250 film-coated tablets.

Blister packs within aluminium sachets, PVC / PE / PVDC / Al blister in Al sachet:
10, 14, 20, 28, 30, 40, 48, 49, 50, 56, 60, 84, 90, 98, 100, 110, 112, 120, 250 film-coated tablets.

40 mg:

Blister packs, PVC / PE / PVDC / Al blister:
10, 14, 20, 28, 30, 40, 48, 49, 50, 56, 60, 84, 90, 98, 100, 105, 110, 112, 120, 250 film-coated tablets.

Blister packs within aluminium sachets, PVC / PE / PVDC / Al blister in Al sachet:
10, 14, 20, 28, 30, 40, 48, 49, 50, 56, 60, 84, 90, 98, 100, 110, 112, 120, 250 film-coated tablets.

Simtan is also available in a HDPE container with a child-resistant PP closure and aluminium seal containing 100, 300, 500 or 1000 tablets “for hospital use only”.

20 mg

Simtan is also available in a HDPE container (30 ml) with polypropylene tamper evident closure with integrated silica gel containing 30 or 100 tablets.

40mg

Simtan is also available in a HDPE container (75 ml) with polypropylene tamper evident closure with integrated silica gel containing 30 or 100 tablets.

20 mg

Simtan is also available in a HDPE container (150 ml) with polypropylene tamper evident closure with integrated silica gel containing 500 tablets for hospital use and for dose-dispensing in pharmacies only.

40 mg

Simtan is also available in a HDPE container (250 ml) with polypropylene tamper evident closure with integrated silica gel containing 500 tablets for hospital use and for dose-dispensing in pharmacies only.

Not all pack sizes may be marketed.

Marketing authorisation holder and manufacturer:

Marketing authorisation holder:
Clonmel Healthcare Ltd, Waterford Road, Clonmel, Co. Tipperary, Ireland

Manufacturer:
Synthon Hispania SL, Polígono Las Salinas, 08830 Sant Boi de Llobregat, Spain
Centrafarm Services B.V., Van de Reijtstraat 31-E, 4814 NE Breda, The Netherlands
STADA Arzneimittel AG, Stadastrasse 2-18, D-61118, Bad Vilbel, Germany

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

BE: Simvastatine EG 20mg/40mg filmomhulde tabletten
DE: Simvastatin STADA 5mg/10mg/20mg/40mg Filmtabletten
DK: Simvastatin STADA 5mg/10mg/20mg/40mg
IE: Simtan 5mg/10mg/20mg/40mg Film-coated Tablets
LU: Simvastatine EG 20mg/40mg comprimés pelliculés
NL: Simvastatine CF 5mg/10mg/20mg/40mg, filmomhulde tabletten
PT: Sinvastatina Stada 10mg/20mg/40mg Comprimidos Revestidos
SE: Simvastatin STADA 10mg/20mg/40mg

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