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1. WHAT SIMVASTATIN IS AND WHAT IT IS USED FOR

Simvastatin belongs to a group of medicines known as statins. These work by reducing the amount of cholesterol and certain fatty substances called triglycerides in your blood.

Simvastatin is used:
- to lower cholesterol and triglycerides in the blood when a low fat diet and other measures (such as exercise, weight loss) have failed. You should stay on the low fat diet while taking this medicine.
- to lower inherited high levels of cholesterol in your blood (homozygous familial hypercholesterolemia), together with dieting and other treatments (e.g. LDL-apheresis), or when such treatments are not appropriate.
- to reduce the risk of coronary heart disease if you have hardening of the arteries (arteriosclerosis) or diabetes, even if your cholesterol levels are normal, together with dieting and other treatments.

2. BEFORE YOU TAKE SIMVASTATIN

Do not take Simvastatin:
- if you are allergic (hypersensitive) to simvastatin or to any of the other ingredients of the tablet
- if you have liver problems or a continuous high level of certain liver enzymes (serum transaminases)
- if you are pregnant or breast-feeding
- if you are taking the following medicines (see also the section “Taking other medicines” below):
  - certain antifungals (ketoconazole or itraconazole)
  - certain medicines for the treatment of AIDS (HIV-protease inhibitors)
  - certain antibiotics (erythromycin, clarithromycin or telithromycin)
  - the antidepressant nefazodone

Take special care with Simvastatin:
- if while being treated with simvastatin you experience unexplained muscle pain, sensitivity to pressure or muscle weakness. Simvastatin may cause muscle problems and sometimes muscle breakdown with muscle cramps, fever and red-brown discolouration of urine. The risk of muscle breakdown is greater at higher doses. Contact your doctor immediately if you experience muscle pain, tenderness or weakness.
- if any of the following applies to you, as you may have a greater risk of muscle breakdown:
  - you are more than 70 years old
- you have kidney problems
- you have thyroid problems (and are not taking medicine for it)
- you or close family members have a hereditary muscle disorder
- you have ever had muscle problems during treatment with simvastatin or other statins or fibrates
  (other cholesterol lowering medicines).
- if you are taking certain other medicines; see the section “Taking other medicines” below.
- if you consume large amounts of alcohol or have had liver problems or liver disease in the past.
  Simvastatin can affect your liver without you noticing it directly. Your doctor may conduct some blood
  tests to check your liver before and after starting treatment.

Consult your doctor if any of the above applies to you or has applied to you in the past.

Taking other medicines

Please note that the following statements may also apply to products you took some time ago or may
take at some time in the future.

You may know the medicines mentioned below by a different name, usually the brand name. In this
section, the brand name of the medicine is not mentioned, only the name of the active substance or the
group of active substances. Therefore, always check the box and package leaflet of the medicine you are
taking carefully to find out what the active substance is.

The risk of muscle problems can be greater if simvastatin is taken with the following medicines: (some of
these have already been listed in the above section “Do not take the tablets”)
- Fibrates (other cholesterol-lowering medicines, such as gemfibrozil, bezafibrate)
- Niacin or nicotinic acid (other cholesterol-lowering medicines) in large doses (greater than or equal to
  1 g per day)
- Ciclosporin (medicine used to suppress the immune system, often used in organ transplant patients)
- Certain antifungals (such as itraconazole or ketoconazole)
- The antibiotics erythromycin, clarithromycin and telithromycin
- Certain medicines for the treatment of AIDS (HIV protease inhibitors)
- Danazol (medicine used to treat endometriosis and breast cysts in women)
- The antidepressant nefazodone
- Amiodarone, a medicine used for irregular heart beat
- Verapamil and diltiazem (medicine used to treat high blood pressure, chest pain associated with heart
disease, or other heart conditions)
- Fusidic acid as a tablet or infusion (a medicine used to treat bacterial infections)

You should also tell your doctor if you take:
- medicines that prevent blood clots (anticoagulants, such as acenocoumarol and warfarin). Simvastatin
  may increase the effect of these medicines.
- fenofibrate (another medicine for lowering cholesterol)

Please inform your doctor or pharmacist if you are taking, or have recently taken any other medicines,
including medicines obtained without a prescription.

Taking Simvastatin with food and drink:
Grapefruit juice contains one or more components which may increase the amount of simvastatin in the
blood. Therefore, you should not drink grapefruit juice as it could increase the risk of muscle damage.
You can take the tablets with or without food.

Pregnancy and breast-feeding

Do not take simvastatin if you are pregnant, trying to become pregnant or suspect you may be pregnant,
as the safety in pregnant women has not been established. If you become pregnant while using
simvastatin, you must stop taking the tablets immediately and contact your doctor.
No data on the excretion of simvastatin in breast milk are available. Because many medicinal products
are excreted in human milk and because of the potential for serious side effects, you must not breast-
feed your infant while taking simvastatin.
Ask your doctor or pharmacist for advice before taking any medicine.

Driving and using machines:
Simvastatin has no effect or only a negligible effect on the ability to drive or use machines. However, there have been rare cases of dizziness reported in patients taking simvastatin tablets (see section 4 “Possible side effects”). Do not drive vehicles or operate machines that require attention if you experience this side-effect.

Important information about some of the ingredients of Simvastatin:
Amongst other ingredients, Simvastatin tablets contain a sugar called lactose. If your doctor has informed you that you cannot tolerate certain sugars, contact your doctor before taking this medicine.

3. HOW TO TAKE SIMVASTATIN?

Always take your tablets exactly as your doctor has instructed you. You should check with your doctor or pharmacist if you are unsure. The usual dose is 5 mg to 80 mg simvastatin per day as a single dose in the evening. If needed, your doctor can increase the dose at intervals of at least 4 weeks to a maximum of 80 mg per day as a single dose in the evening. The dose of 80 mg is only recommended in patients with very high cholesterol levels and high-risk cardiovascular complications.

Instructions for use
Simvastatin tablets should be taken with water. You can take the tablets with or without food.

Duration of treatment:
You will have to take simvastatin over a long period of time. Your doctor will tell you how long you need to take simvastatin.

If you have the impression that the effect of simvastatin is too strong or too weak, talk to your doctor or pharmacist.

If you take more Simvastatin than you should:
If you take too many tablets by mistake, contact a doctor or pharmacist immediately.

If you forget to take Simvastatin:
If you realise you have forgotten to take a dose soon after its due time, take it as soon as possible. However, if it is almost time to take the next dose, omit the forgotten dose and take the next one when it is due. Ask your doctor or pharmacist in case of doubt. Do not take a double dose to make up for a forgotten tablet.

If you stop taking Simvastatin:
If you suddenly stop taking this medicine, your cholesterol may rise again. It is therefore important that you consult a doctor before stopping treatment, even if you suffer from physical complaints. He/she can tell you if you can stop and the best way to do so.

If you have any further questions on the use of this product, ask your doctor or pharmacist.

4. POSSIBLE SIDE EFFECTS

Like all medicines, Simvastatin can have side effects, although not everybody will have them. For the most part side effects have been mild and short-lived. The following side effects were reported rarely (more than 1 in 10,000, but less than 1 in 1000 users):
Anaemia, stomach upsets (such as feeling unwell, constipation, abdominal pain, flatulence, nausea, indigestion, diarrhoea, vomiting), inflammation of the pancreas (severe abdominal pain radiating to the back, nausea and vomiting), weakness, headache, dizziness, numbness or loss of sensation in the arms and legs, hair loss, rash, itchiness, liver disease (possibly presenting as yellowing of the eyes and/or skin), itchiness of the skin, dark coloured urine, pale coloured stools, muscle damage (see below), abnormal blood tests or an allergic reaction to simvastatin. The allergic reaction may include some of the following symptoms: sudden swelling of face, tongue or throat (angioedema, see below), a certain skin disease (lupus-like syndrome) with rash, fever and joint pain, joint and blood vessel inflammation, joint pains, unusual bruising, skin eruptions, swelling, hives, skin sensitivity to the sun, a high temperature, flushing, difficulty in breathing or tiredness.

The following side effect was reported very rarely (<1/10,000): liver failure.

Contact your doctor promptly if you experience muscle aches and pains, tenderness, weakness or cramps. This is because on rare occasions, muscle damage can be serious (see section 2 “Take special care with Simvastatin”). Also, contact your doctor immediately if a rapid swelling of the face, tongue or throat occurs (angioedema), which may cause great difficulty in breathing. Hives can develop simultaneously and the swelling can be itchy.

*If you notice any side effects not mentioned in this leaflet, or if you experience one of the listed side effects as serious, please inform your doctor or pharmacist.*

5. HOW TO STORE SIMVASTATIN?

*Keep Simvastatin out of the reach and sight of children.*

Store the tablets in the original package in order to protect from light and moisture. Do not store above 25°C.

Do not use the tablets after the "do not use after" or "exp". date stated on the packaging. The wording "exp" means: "expiry date". The first 2 digits denote the month, the last digits the year.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. FURTHER INFORMATION

**Composition of Simvastatin 10, 20 and 40 mg:**

The active substance is: Simvastatin.

Each Simvastatin 10 mg, 20 mg and 40 mg, film-coated tablet contains 10 mg, 20 mg and 40 mg simvastatin, respectively.

The other ingredients are:

**Tablet core:** Lactose, microcrystalline cellulose (E460), pregelatinised maize starch, butylhydroxyanisole (E320), ascorbic acid (E300), citric acid (E330), colloidal anhydrous silica (E551), talc (E553b), magnesium stearate (E470b).

**Film-coating:** hypromellose (E464), red iron oxide (E172), yellow iron oxide (E172), triethylicitrate (E1505), titanium dioxide (E171), povidone. Red and yellow iron oxide (E172) are used as colorants.

**Product appearance and pack size**

Simvastatin 10 mg is a peach-coloured, oval, biconvex, film-coated tablet, scored on one side; Simvastatin 20 mg is a tan-coloured, oval, biconvex, film-coated tablet, scored on one side; Simvastatin 40 mg is a brick red-coloured, oval, biconvex, film-coated tablet.

The tablets are packed in blisters in a carton box, containing 10, 14, 20, 28, 30, 50, 56, 60, 84, 90, 98 or 100 tablets. Not all pack sizes may be marketed.
Marketing Authorisation Holder and Manufacturer

<NL>: Marketing authorisation holder:
Farmaprojects S.A.
Santa Eulàlia 240-242
08902 L’Hospitalet de Llobregat (Barcelona)
Spain.

<DE>: Marketing authorisation holder:
S-P Projekt GmbH & Co. KG
Bismarckstrasse 22
80803 München
Germany

<FR>: Marketing authorisation holder:
Laboratoires Alter
3, avenue de la Baltique
Z.A de Courtaboef
91140 VILLEBON-SUR-YVETTE

<NL/DE/FR>: Manufacturers:
Laboratorios Belmac S.A.
Polígono Industrial Malpica, Calle C.4
50016 Zaragoza
Spain

Atlantic Pharma - Produções Farmacêuticas, S.A.
Rua da Tapada Grande No.2
2710-089 Sintra
Portugal

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