

**PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS REGULATIONS
(PREPARATIONS) 1986**

This medicine can be sold under doctor's prescription only

SIMOVIL[®] 10 mg SIMOVIL[®] 20 mg SIMOVIL[®] 40 mg
Tablets Tablets Tablets

Each tablet contains:

Simvastatin 10 mg

Simvastatin 20 mg

Simvastatin 40 mg

For a list of inactive ingredients see section 6.1 "What **SIMOVIL** contains". See also section 2.7 "**Important information about some of the ingredients of SIMOVIL**".

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

- This leaflet contains concise information about **SIMOVIL**. If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their medical condition seems similar to yours.
- This medicine is not intended for children and adolescents under 20 years of age.

1. WHAT SIMOVIL IS AND WHAT IT IS USED FOR?

SIMOVIL reduces levels of LDL and other lipid components in the blood, and raises HDL levels - in patients with hyperlipidemia (high blood lipid levels). In patients with coronary heart disease and hypercholesterolemia, **SIMOVIL** reduces the risk of total mortality by reducing coronary death; reduces the risk of non-fatal myocardial infarction; reduces the risk for undergoing myocardial revascularization procedures (CABG & PTCA), and reduces the risk of stroke and transient ischemic attacks (TIAs).

Therapeutic group: Statins, HMG-CoA reductase inhibitors.

2. Before you TAKE SIMOVIL

2.1 Do not take SIMOVIL if you:

- are hypersensitive (allergic) to Simvastatin or any of the other ingredients of **SIMOVIL** (for a list of inactive ingredients, see section 6.1).
- are diagnosed with active liver disease.
- are pregnant. **SIMOVIL** should not be used in women who are pregnant, trying to become pregnant or suspect that they are pregnant. If you become pregnant while taking **SIMOVIL**, stop taking it and contact your doctor immediately.
- are breast-feeding. Women taking **SIMOVIL** should not breast-feed.
- are taking any of the following medicines:
 - certain antifungal medicines (such as itraconazole, ketoconazole, posaconazole or voriconazole)
 - HIV protease inhibitors (such as indinavir, nelfinavir, ritonavir and saquinavir)
 - certain hepatitis C virus protease inhibitors (such as boceprevir or telaprevir)
 - certain antibiotics (such as erythromycin, clarithromycin or telithromycin)
 - antidepressant nefazodone
 - any medicines containing cobicistat including those for the treatment of HIV infection.
 - gemfibrozil (a fibric acid medicine for lowering cholesterol)

- cyclosporine
- danazol

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

2.2 Special warnings concerning use of SIMOVIL

- **Before starting treatment with SIMOVIL, tell your doctor if:**
 - you are suffering or have suffered in the past from any medical problems or any allergies
 - you consume substantial quantities of alcohol or have a past history of liver disease
 - you are to undergo an elective major surgery
 - you have kidney problems
 - you have severe lung disease
 - you have muscle pain, tenderness or unexplained muscle weakness.
 - you or a close family member have a hereditary muscle disorder or a previous history of muscle problems with other cholesterol lowering drugs called statins or fibrates.
 - you have thyroid problems
 - you are older than 65
 - you are a female
 - you are Asian

2.3 Taking other medicines

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

You should also tell your doctor who is prescribing a new medication for you that you are taking **SIMOVIL**.

Because taking **SIMOVIL** with any of the following drugs or substances can increase the risk of muscle problems (see "SIDE EFFECTS"), it is particularly important to tell your doctor if you are taking:

- antifungal agents (such as itraconazole, ketoconazole, fluconazole, posaconazole or voriconazole)
- HIV protease inhibitors (such as indinavir, nelfinavir, ritonavir and saquinavir)
- boceprevir or telaprevir (drugs used to treat hepatitis C virus infection)
- the antibiotics erythromycin, clarithromycin, telithromycin and fusidic acid
- the antidepressant nefazodone
- medicines containing cobicistat
- cyclosporine
- danazol
- fibric acid derivatives (such as gemfibrozil and bezafibrate)
- amiodarone or dronedarone (drugs used to treat an irregular heartbeat)
- verapamil, diltiazem, amlodipine or ranolazine (drugs used to treat high blood pressure, angina or other heart conditions)
- grapefruit juice (which should be avoided while taking **SIMOVIL**)
- lomitapide (a drug used to treat a serious and rare genetic cholesterol condition)

Especially inform your doctor or pharmacist if you are taking:

- anticoagulants (drugs that prevent blood clots, such as warfarin, phenprocoumon or acenocoumarol)
- digoxin
- colchicine (a medicine used for gout)
- niacin
- fenofibrate, another fibric acid derivative.
- Also tell your doctor if you are taking niacin or a niacin-containing product and are Chinese.

2.4 Taking SIMOVIL with food and drink

Do not take **SIMOVIL** with grapefruit juice.

During treatment with this medicine, ensure that a low fat diet is followed.

2.5 Pregnancy and breast-feeding

SIMOVIL should not be used in women who are pregnant, trying to become pregnant or suspect that they are pregnant. If you become pregnant while taking **SIMOVIL**, stop taking it and contact your doctor immediately.

Women taking **SIMOVIL** should not breast-feed.

2.6 Driving and using machines

SIMOVIL is not expected to interfere with the ability to drive or to use machinery. However, it should be taken into account that some people get dizzy after taking **SIMOVIL**.

2.7 Important information about some of the ingredients of SIMOVIL

SIMOVIL contains lactose. If you have been told by your doctor that you have an intolerance to some sugars, consult the doctor before taking this medicinal product.

3. HOW TO TAKE SIMOVIL?

Always take **SIMOVIL** as instructed by the doctor. You should check with your doctor or pharmacist if you are not sure.

The dosage and method of treatment will be determined by the doctor only.

The usually recommended dose is:

The usual recommended starting dose is 10 or 20 mg once a day in the evening, with or without food.

Swallow the medicine with a small amount of water.

Because of the increased risk of muscle problems, the 80 mg dose is only for patients who have been taking the 80 mg dose chronically (such as 12 months or more) without having muscle damage and do not need to take certain other medicines with **SIMOVIL** that would increase your chance of getting muscle damage.

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

If you are also taking bile acid sequestrants medicines (medicines for lowering cholesterol) such as: cholestyramine, you should take **SIMOVIL** at least 2 hours before or 4 hours after taking the bile acid sequestrants medicines.

Do not exceed the recommended dose.

Examinations and monitoring

- During treatment with **SIMOVIL** liver function tests should be performed.
- 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.
- See your doctor regularly to check your cholesterol level and to check for side effects. Your doctor should do blood tests to check your liver before you start taking **SIMOVIL** and if you have any symptoms of liver problems while you take **SIMOVIL**.

If you take more SIMOVIL than you should

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

If you forget to take SIMOVIL

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

Complete the full course of treatment as instructed by the doctor.

Even if there is an improvement in your health, do not discontinue use of this medicine before consulting your doctor.

If you stop taking SIMOVIL

Keep taking **SIMOVIL** unless your doctor tells you to stop. If you stop taking **SIMOVIL**, your cholesterol may rise again.

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

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

4. SIDE EFFECTS

Like all medicines, **SIMOVIL** can cause side effects, in some of the users.

Do not be alarmed by reading the list of side effects, you may not suffer from any of them.

SIMOVIL is generally well tolerated. For the most part side effects have been mild and short-lived.

Stop taking the medicine and refer to the doctor immediately if you develop any of the following rare signs (affect 1 to 10 of 10,000 patients):

- muscle pain, tenderness, cramps or weakness, particularly if accompanied by malaise or fever or if muscle signs and symptoms persist after discontinuing **SIMOVIL**. This is because on rare occasions, muscle problems can be serious, including muscle breakdown resulting in kidney damage that can lead to death.
This risk of muscle breakdown is greater for patients taking higher doses of **SIMOVIL**, particularly the 80 mg dose. This risk of muscle breakdown is also greater for older patients (65 years of age and older), female patients, patients with abnormal kidney function, and patients with thyroid problems.
- hypersensitivity (allergy) which may include:
 - swelling of the face, tongue and throat- which may cause difficulty in breathing
 - severe muscle pain usually in the shoulders and hips
 - rash with weakness of limbs and neck muscles
 - pain or inflammation of the joints
 - inflammation of the blood vessels (vasculitis)
 - unusual bruising, skin eruptions and swelling, hives, skin sensitivity to the sun light, fever, flushing
 - shortness of breath and feeling unwell
 - chills, flushing, malaise
 - lupus- like disease picture (including rash, joint disorders, and changes in blood cells)
 - severe skin reactions (toxic epidermal necrolysis, erythema multiforme, including Stevens-Johnson syndrome).

- 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 (pancreatitis), often with severe abdominal pain.

Additional side effects

Rare (affects 1 to 10 patients in 10,000)

- digestive disturbances (abdominal pain, constipation, flatulence, indigestion, diarrhoea, nausea, vomiting)
- muscle pain, tenderness or weakness (that in very rare cases may not go away after stopping **SIMOVIL**)
- headache, dizziness, tingling, numbness or weakness of the arms and legs (paresthesia, peripheral neuropathy), memory loss, confusion
- rash, itching (pruritus), hair loss (alopecia)
- low red blood cell count (anaemia)
- weakness

Very rare (affects less than 1 of 10,000 patients)

- memory impairment (poor memory)
- trouble sleeping

Unknown (side effects for which frequency has not been determined yet)

- upper respiratory infections, a variety of skin changes (e.g., nodules, discoloration, dryness of skin/mucous membranes, changes to hair/nails), muscle cramps, erectile dysfunction, interstitial lung disease (breathing problems including persistent cough and/or shortness of breath or fever), and depression.

Diabetes or increases in blood sugar levels have been reported with statins. This is more likely if you have high levels of sugars or fats in your blood, are overweight and have high blood pressure. Your doctor will monitor you while you are taking this medicine.

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

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

5. HOW TO STORE SIMOVIL?

- Avoid Poisoning! This medicine, as all other medicines, must be stored in a safe place out of the reach and sight of children and/or infants, in order to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by a doctor!
- Do not use **SIMOVIL** after the expiry date (exp. date) which is stated on the pack. The expiry date refers to the last day of the indicated month.
- **Storage conditions:** store this medicine below 30°C.
- 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

6.1 What SIMOVIL contains?

- In addition to the active ingredient the medicine also contains inactive ingredients: Ascorbic acid, citric acid monohydrate, hydroxypropyl cellulose, hydroxypropyl methylcellulose, red ferric oxide, yellow ferric oxide, lactose hydrous, magnesium stearate, microcrystalline cellulose, pregelatinized starch, talc, and titanium dioxide. Butylated hydroxyanisole is added as a preservative.

Each 10 mg tablet contains 70.7 mg of lactose monohydrate.

Each 20 mg tablet contains 141.5 mg of lactose monohydrate.

Each 40 mg tablet contains 283.0 mg of lactose monohydrate.

6.2 What SIMOVIL looks like and contents of the pack

Simovil 10 mg are peach-coloured, oval-shaped tablets marked 'MSD 735' on one side and plain on the other.

Simovil 20 mg are tan-coloured, oval-shaped tablets marked 'MSD 740' on one side and plain on the other.

Simovil 40 mg are brick-red coloured, oval-shaped tablets marked 'MSD 749' on one side and plain on the other.

Pack sizes:

SIMOVIL 10 mg Tablets and **SIMOVIL** 20 mg Tablets:

10, 30, 60 or 100 tablets in blisters.

SIMOVIL 40 mg Tablets:

30, 60 or 100 tablets in blisters.

Not all pack sizes may be marketed.

Marketing authorization holder:

Merck, Sharp & Dohme (Israel-1996) Company Ltd., P.O.Box 7121, Petah-Tikva 49170.

Manufacturer: Merck Sharp & Dohme B.V., Haarlem, Holland.

This Leaflet was checked and approved by the Ministry of Health in January 2015.

Drug registration no. listed in the official registry of the Ministry of Health:

SIMOVIL 10 mg Tablets: 127 53 26694 00

SIMOVIL 20 mg Tablets: 127 52 26695 00

SIMOVIL 40 mg Tablets: 127 51 26696 00