Simvastatin is a drug that was developed back in 1988 and today is one of the most widely used drugs for lowering high cholesterol. It is an inhibitor of metilglutaril- hydroxy-coenzyme A reductase (the enzyme which acts by increasing the number of LDL receptors and this means an increase in degradation of LDL cholesterol). In this way, simvastatin reduces the concentration of cholesterol in the blood (especially LDL cholesterol).

**Warnings and precautions**

The only serious adverse effect reported in studies during the application of this drug is myopathy, which can be develop into a more serious problem - rhabdomyolysis. Rhabdomyolysis is a sudden and serious muscle damage, or the disintegration of skeletal muscles. The disintegration of skeletal muscle causes a large increase in myoglobin in the blood which leads to kidney failure. This condition is life threatening, and you need to inform your physician if you notice any changes in the muscles. Change of urine color in dark brown or red, means that disintegration of muscle tissue has already started. However, before changed urine color, you should feel pain in the muscles.

This side effect is characteristic of all statins, but in one study that followed hundreds of cases of statin-induced rhabdomyolysis, simvastatin is reported as a drug that most frequently causes rhabdomyolysis. Rhabdomyolysis mortality rate is 15%. The same study reported that the average time from the start of simvastatin therapy to the occurrence of rhabdomyolysis was 9 days, so frequent monitoring of the patient during the first 30-60 days of initiation of simvastatin therapy is necessary. Rhabdomyolysis is diagnosed if creatine kinase levels (CK) are 10-25 times
higher than the normal range (38-176 U/L).

The incidence of rhabdomyolysis when using statins is 0.44 per 10,000 patients, and the vast majority of patients do not experience the side effects on the muscles.

Simvastatin should not be used in patients who have liver damage, as there is a risk of liver damage. In studies, the incidence of liver damage caused by the application of simvastatin is 1 in 100,000 patients while for acute liver failure is 1 in 1,000,000 patients. However, although small, the risk still exists, and it is important to consult your doctor if you notice any symptoms of liver damage (*pain in the upper right upper abdomen, loss of appetite, nausea and jaundice*).

Certain medications can raise the level of simvastatin in the blood, which significantly increases the risk of rhabdomyolysis and liver damage, since the higher concentration of the Simvastatin in the blood means greater risk of side effects. You can found more information in the section Interaction.

Simvastatin should be applied with caution in patients who have hypothyroidism, or in patients who are older than 65 years.

**Simvastatin use during pregnancy and lactation**

According to the FDA, simvastatin must not be used during pregnancy because it inhibits certain biochemical processes necessary for the fetal development. This leads to malformation.

Given the potential impact on the metabolism of lipids in infants, simvastatin should not be used during breastfeeding or the breastfeeding should be discontinued during treatment with this drug.

**Dosage**

Simvastatin should be taken as a single dose in the evening before you go to sleep, because its efficacy is much better at night.

The recommended dosage is given in the table below.

**Table 1: Recommended dosage of the Simvastatin**

<table>
<thead>
<tr>
<th>Indication</th>
<th>Recommended dosage regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>High cholesterol</td>
<td>The usual starting dose is 10-20 mg once a day, in the evening. If the level of LDL cholesterol in the blood is very high, an initial dose may be larger (20-40 mg per day). The dose may be increased once every month until the proper effect is achieved.</td>
</tr>
<tr>
<td>Prevention of heart disease</td>
<td>The usual dose is 20 to 40 mg once a day, in the evening.</td>
</tr>
<tr>
<td>Inherited high cholesterol (<em>the so-called familial hypercholesterolemia</em>)</td>
<td>40 mg once a day, in the evening.</td>
</tr>
</tbody>
</table>
Bearing in mind that this drug is metabolized by CYP3A4 enzyme (many other drugs are metabolized via this enzyme), simvastatin can interact with a large number of drugs. These interactions mostly result in increased concentration of simvastatin in the blood which increases the risk of myopathy, rhabdomyolysis and liver damage. Simultaneous use of simvastatin with the following medicines should be avoided:

- Drugs used for the fungal infections treatment (e.g., fluconazole, voriconazole, itraconazole, ketoconazole and others).
- Drugs used to treat HIV (e.g. nelfinavir, cobicistat, atazanavir, ritonavir, indinavir and saquinavir).
- Drugs for the endometriosis treatment (e.g. danazol).
- Drugs used to treat high cholesterol and triglycerides (niacin, atorvastatin, cerivastatin, rosuvastatin, lovastatin, fluvastatin, clofibrate and fenofibrate).
- Drugs used to treat depression (e.g. nefazodone).
- Medicines used to treat gout (colchicine).
- Drugs that kill bacteria (erythromycin, fusidic acid, clarithromycin (Klacid) and azithromycin).

These are just some of the drugs which may interact with Simvastatin. Tell your doctor about all the medicines you are taking.

Co-administration of this drug with alcoholic beverages is strictly prohibited.

Rare side effects of Simvastatin include:

- Impaired digestion
- Alopecia (hair loss)
- Malaise
- Sleep problems
- Impaired memory or memory loss
- Tingling
- Dizziness

Very rare side effects of Simvastatin include:

- Insomnia
- Severe hepatic impairment

Other side effects of Simvastatin include:

- Lung disorders
- Depression
- Erectile dysfunction
- Loss of appetite
- Inflammation of the pancreas
- Shortness of breath
- Pain or inflammation of the joints
References

1. NCBI link 1
2. NCBI link 2