

ZOCOR[®]

(SIMVASTATIN)

PLEASE READ THIS SUMMARY CAREFULLY, THEN ASK YOUR DOCTOR ABOUT ZOCOR. NO ADVERTISEMENT CAN PROVIDE ALL THE INFORMATION NEEDED TO PRESCRIBE A DRUG. THIS ADVERTISEMENT DOES NOT TAKE THE PLACE OF CAREFUL DISCUSSIONS WITH YOUR DOCTOR. ONLY YOUR DOCTOR HAS THE TRAINING TO WEIGH THE RISKS AND BENEFITS OF A PRESCRIPTION DRUG FOR YOU.

USES OF ZOCOR

ZOCOR is a prescription drug that is indicated as an addition to diet for many patients with high cholesterol. For patients at high risk of coronary heart disease (CHD) because of existing heart disease, diabetes, vascular disease, or history of stroke, ZOCOR is indicated along with diet to reduce the risk of death by reducing coronary death; reduce the risk of heart attack and stroke; and reduce the need for revascularization procedures.

WHEN ZOCOR SHOULD NOT BE USED

Some people should not take ZOCOR. Discuss this with your doctor.

ZOCOR should not be used by patients who are allergic to any of its ingredients. In addition to the active ingredient simvastatin, each tablet contains the following inactive ingredients: cellulose, lactose, magnesium stearate, iron oxides, talc, titanium dioxide, and starch. Butylated hydroxyanisole is added as a preservative.

Patients with liver problems: ZOCOR should not be used by patients with active liver disease or repeated blood test results indicating possible liver problems. (See WARNINGS.)

Women who are or may become pregnant: Pregnant women should not take ZOCOR because it may harm the fetus. **Women of childbearing age should not take ZOCOR unless it is highly unlikely that they will become pregnant.** If a woman does become pregnant while on ZOCOR, she should stop taking the drug and talk to her doctor at once.

Women who are breast-feeding should not take ZOCOR.

WARNINGS

Muscle: Tell your doctor right away if you experience any unexplained muscle pain, tenderness, or weakness at any time during treatment with ZOCOR so your doctor can decide if ZOCOR should be stopped. Some patients may have muscle pain or weakness while taking ZOCOR. Rarely, this can include muscle breakdown resulting in kidney damage. The risk of muscle breakdown is greater in patients taking certain other drugs along with ZOCOR:

- Cyclosporine, itraconazole, ketoconazole, erythromycin, clarithromycin, telithromycin, HIV protease inhibitors, the antidepressant nefazodone, or large quantities of grapefruit juice (>1 quart daily), particularly with higher doses of ZOCOR.
- Gemfibrozil particularly with higher doses of ZOCOR.
- Other lipid lowering drugs (other fibrates or ≥ 1 g/day of niacin) that can cause myopathy when given alone.
- Danazol particularly with higher doses of ZOCOR.
- Amiodarone or verapamil with higher doses of ZOCOR.

The risk of muscle breakdown is greater at higher doses of simvastatin.

Because the risk of muscle side effects is greater when ZOCOR is used with the products listed above, the combined use of these products should be avoided unless your doctor determines the benefits are likely to outweigh the increased risks.

The dose of ZOCOR should not exceed 10 mg daily in patients receiving gemfibrozil. The combined use of ZOCOR and gemfibrozil should be avoided, unless your doctor determines that the benefits outweigh the increased risks of muscle problems. Caution should be used when using ZOCOR with other fibrates or niacin because these can cause muscle problems when taken alone.

No more than 10 mg/day of ZOCOR should be taken with cyclosporine or danazol.

The combined use of verapamil or amiodarone with doses above ZOCOR 20 mg should be avoided unless your doctor determines the benefits outweigh the increased risk of muscle breakdown.

Your doctor should also carefully monitor for any muscle pain, tenderness, or weakness, particularly during the initial months of therapy and if the dose of either drug is increased. Your doctor also may monitor the level of certain muscle enzymes in your body, but there is no assurance that such monitoring will prevent the occurrence of severe muscle disease.

The risk of muscle breakdown is greater in patients with kidney problems or diabetes.

If you have conditions that can increase your risk of muscle breakdown, which in turn can cause kidney damage, your doctor should temporarily withhold or stop ZOCOR. Also, since there are no known adverse consequences of briefly stopping therapy with ZOCOR, treatment should be stopped a few days before elective major surgery and when any major acute medical or surgical condition occurs. Discuss this with your doctor, who can explain these conditions to you.

Liver: About 1% of patients who took ZOCOR in clinical trials developed elevated levels of some liver enzymes. Patients who had these increases usually had no symptoms. Elevated liver enzymes usually returned to normal levels when therapy with ZOCOR was stopped.

In the ZOCOR Survival Study, the number of patients with more than 1 liver enzyme level elevation to greater than 3 times the normal upper limit was no different between the ZOCOR and placebo groups. Only 8 patients on ZOCOR and 5 on placebo discontinued therapy due to elevated liver enzyme levels. Patients were started on 20 mg of ZOCOR, and one third had their dose raised to 40 mg.

Your doctor should perform routine blood tests to check these enzymes before you start treatment with ZOCOR and thereafter when clinically indicated. Patients titrated to the 80-mg dose should receive an additional test at 3 months and periodically thereafter (eg, semiannually) for the first year of treatment. If your enzyme levels increase, your doctor should order more frequent tests. If your liver enzyme levels remain unusually high, your doctor should discontinue your medication.

Tell your doctor about any liver disease you may have had in the past and about how much alcohol you consume. ZOCOR should be used with caution in patients who consume large amounts of alcohol.

PRECAUTIONS

Drug Interactions: Because of possible serious drug interactions, it is important to tell your doctor what other drugs you are taking, including those obtained without a prescription. You should also tell other doctors

who are prescribing a new medicine for you that you are taking ZOCOR[®] (simvastatin). ZOCOR can interact with the following:

- Itraconazole
- Ketoconazole
- Erythromycin
- Clarithromycin
- Telithromycin
- HIV protease inhibitors
- Nefazodone
- Cyclosporine
- Large quantities of grapefruit juice (>1 quart daily)

The risk of myopathy is also increased by gemfibrozil and to a lesser extent other fibrates and niacin (nicotinic acid) (≥ 1 g/day).

The risk of muscle breakdown is increased with other drugs:

- Danazol
- Amiodarone
- Verapamil

Some patients taking lipid-lowering agents similar to ZOCOR and coumarin anticoagulants (a type of blood thinner) have experienced bleeding and/or increased blood clotting time. Patients taking these medicines should have their blood tested before starting therapy with ZOCOR and should continue to be monitored.

Central Nervous System Toxicity; Cancer, Mutations, Impairment of Fertility: Like most prescription drugs, ZOCOR was required to be tested on animals before it was marketed for human use. Often these tests were designed to achieve higher drug concentrations than humans achieve at recommended dosing. In some tests, the animals had damage to the nerves in the central nervous system. In studies of mice with high doses of ZOCOR, the likelihood of certain types of cancerous tumors increased. No evidence of mutations or damage to genetic material has been seen. In 1 study with ZOCOR, there was decreased fertility in male rats.

Pregnancy: Pregnant women should not take ZOCOR because it may harm the fetus.

Safety in pregnancy has not been established. In studies with lipid-lowering agents similar to ZOCOR, there have been rare reports of birth defects of the skeleton and digestive system. Therefore, women of childbearing age should not take ZOCOR unless it is highly unlikely they will become pregnant. If a woman does become pregnant while taking ZOCOR, she should stop taking the drug and talk to her doctor at once. The active ingredient of ZOCOR did not cause birth defects in rats at 3 times the human dose or in rabbits at 3 times the human dose.

Nursing Mothers: Drugs taken by nursing mothers may be present in their breast milk. Because of the potential for serious adverse reactions in nursing infants, a woman taking ZOCOR should not breast-feed. (See WHEN ZOCOR SHOULD NOT BE USED.)

Pediatric Use: ZOCOR is not recommended for children or patients under 10 years of age.

Geriatric Use: Higher blood levels of active drug were seen in elderly patients (70–78 years of age) compared with younger patients (18–30 years of age) in 1 study. In other studies, the cholesterol-lowering effects of ZOCOR were at least as great in elderly patients as in younger patients, and there were no overall differences in safety between elderly and younger patients over the 20–80 mg/day dosage range. Of the 7 cases of myopathy/rhabdomyolysis among 10,269 patients on ZOCOR in another study, 4 were aged 65 or more (at baseline), 1 of whom was over 75.

SIDE EFFECTS

Most patients tolerate treatment with ZOCOR well; however, like all prescription drugs, ZOCOR can cause side effects, and some of them can be serious. Side effects that do occur are usually mild and short-lived. Only your doctor can weigh the risks versus the benefits of any prescription drug. In clinical studies with ZOCOR, less than 1.5% of patients dropped out of the studies because of side effects. In 2 large, 5-year studies, patients taking ZOCOR experienced similar side effects to those patients taking placebo (sugar pills). Some of the side effects that have been reported with ZOCOR or related drugs are listed below. This list is not complete. Be sure to ask your doctor about side effects before taking ZOCOR and to discuss any side effects that occur.

Digestive System: Constipation, diarrhea, upset stomach, gas, heartburn, stomach pain/cramps, anorexia, loss of appetite, nausea, inflammation of the pancreas, hepatitis, jaundice, fatty changes in the liver, and, rarely, severe liver damage and failure, cirrhosis, and liver cancer.

Muscle, Skeletal: Muscle cramps, aches, pain, and weakness; joint pain; muscle breakdown.

Nervous System: Dizziness, headache, insomnia, tingling, memory loss, damage to nerves causing weakness and/or loss of sensation and/or abnormal sensations, anxiety, depression, tremor, loss of balance, psychic disturbances.

Skin: Rash, itching, hair loss, dryness, nodules, discoloration.

Eye/Senses: Blurred vision, altered taste sensation, progression of cataracts, eye muscle weakness.

Hypersensitivity (Allergic) Reactions: On rare occasions, a wide variety of symptoms have been reported to occur either alone or together in groups (referred to as a syndrome) that appeared to be based on allergic-type reactions, which may rarely be fatal. These have included 1 or more of the following: a severe generalized reaction that may include shortness of breath, wheezing, digestive symptoms, and low blood pressure and even shock; an allergic reaction with swelling of the face, lips, tongue, and/or throat with difficulty swallowing or breathing; symptoms mimicking lupus (a disorder in which a person's immune system may attack parts of his or her own body); severe muscle and blood vessel inflammation, sometimes including rash; bruises; various disorders of blood cells (that could result in anemia, infection, or blood clotting problems) or abnormal blood tests; inflamed or painful joints; hives; fatigue and weakness; sensitivity to sunlight; fever, chills; flushing; difficulty breathing; and severe skin disorders that vary from rash to a serious burn-like shedding of skin all over the body, including mucous membranes such as the lining of the mouth.

Other: Loss of sexual desire, breast enlargement, impotence.

Laboratory Tests: Liver function test abnormalities including elevated alkaline phosphatase and bilirubin; thyroid function abnormalities.

NOTE: This summary provides important information about ZOCOR. If you would like more information, ask your doctor or pharmacist to let you read the prescribing information and then discuss it with them.



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