Simvast

Lipid-Regulating Agent
Film-Coated Tablets

Composition

Each tablet contains:

Active ingredient: Simvastatin sodium equivalent to simvastatin 10mg or 20mg.

Excipients: Lactose, starch, butylated hydroxyanisole, ascorbic acid, citric acid, cellulose, magnesium stearate, hypromellose, polyethylene glycol, titanium dioxide, talc, iron oxide red, and iron oxide yellow.

Properties

Simvastatin, the active ingredient of **Simvast**, is a competitive inhibitor of 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase, the enzyme catalyzing the early rate-limiting step in cholesterol biosynthesis. Simvastatin has been shown to be tissue selective and the inhibitory activity is highest in those tissues (e.g. liver, ileum) with the highest rates of cholesterol synthesis. Unlike other HMG-CoA reductase inhibitors, **Simvast** has little effect on cholesterol synthesis in other tissues (e.g. lens, adrenal glands). *In vitro* studies demonstrated that simvastatin is transported into hepatocytes with substantially less uptake into other cells.

Simvastatin produces its lipid-lowering effect in two ways. First, it affects modest reductions in intracellular pools of cholesterol which results in an increased number of LDL-receptors in the liver, enhanced receptor-mediated catabolism and clearance of circulating low density lipoprotein cholesterol (LDL-C). Second, simvastatin inhibits LDL-C production by inhibiting hepatic synthesis of very low-density lipoprotein (VLDL-C), the precursor of LDL-C. These effects result in a reduction of total cholesterol (Total-C), LDL-C, VLDL-C, apolipoprotein B and triglycerides, whilst increasing high density lipoprotein cholesterol (HDL-C) and apolipoprotein A. **Simvast** monotherapy has been shown to be effective in reducing both the progression of coronary atherosclerosis and clinical cardiac events rates in patients with moderate hypercholesterolaemia and documented atherosclerotic coronary artery disease.

Simvastatin is administered orally in the active form. Simvastatin undergoes extensive first-pass extraction in the liver, which is its primary site of action, and the primary site of cholesterol synthesis and of LDL-C clearance.

Indications

Simvast is indicated for the treatment of primary hypercholesterolaemia (hyperlipidaemia Type IIa) in patients who have not responded adequately to diet and other appropriate measures.

Simvast is also indicated to reduce the incidence of clinical coronary events and slow the progression of coronary atherosclerosis in patients with coronary heart disease and cholesterol concentration of 5.5mmol/L or greater.

Dosage

Prior to initiating **Simvast** therapy, secondary causes of hypercholesterolaemia should be excluded and the patient should be placed on a standard cholesterol-lowering diet, which should be continued during treatment. Periodic lipid determinations should be performed and dosage adjusted according to the patient's response.

The general dosage regimen is:

- Hypercholesterolaemia: The initial recommended dose is 10mg daily administered at bedtime, and it may be adjusted at intervals of not less than 4 weeks. The usual range is 10-40mg once daily at night.
- Coronary heart disease: The recommended initial dose is 20mg once daily at bedtime.

If you miss a dose

- Take the medicine as soon as you remember.
- If it is almost time for your next dose, wait until then to take the medicine and skip the missed dose.
- Do not take two doses at one time.

Contraindications

It is contraindicated in individuals with a known hypersensitivity to any of its components.

Simvastatin is also contraindicated in patients with active liver disease or unexplained persistent elevations in serum transaminases as well as in those with porphyria.

Pregnancy: As cholesterol and other products of cholesterol biosynthesis are essential components for foetal development, simvastatin is contraindicated during pregnancy and in women of childbearing potential unless protected by appropriate contraception. In addition to this, congenital anomalies have been reported with the use of simvastatin during pregnancy. Therefore, an interval of one month should elapse between the end of therapy with simvastatin and planned conception.

Lactation: Although no information is are available on the use of simvastatin during lactation, it is advisable to avoid the use of simvastatin.

Precautions

General

As with other lipid-lowering therapy, simvastatin is not indicated when hypercholesterolaemia is due to elevated HDL-C.

Simvastatin has not been evaluated in patients with the rare homozygous familial hypercholesterolaemia. In this group of patients, it has been reported that HMG-CoA reductase inhibitors are less effective because the patients lack functional LDL receptors.

Liver functions

As with other lipid-lowering agents, including HMG-CoA reductase inhibitors and nonabsorbable bile acid-binding resins, simvastatin should be used with caution in patients with a history of liver disease or with high alcohol intake. Increases in liver enzymes occurred during therapy with simvastatin. However, the significance of these changes, which usually appear during the first few months of treatment, is not known. In the majority of patients treated with simvastatin, these increased values declined to pretreatment levels despite continuation of therapy at the same dose. Liver function tests should be performed before and within 1 - 3 months of starting treatment and thereafter at intervals of 6 months for 1 year, unless indicated sooner by symptoms and signs suggestive of hepatotoxicity. Special attention should be given to patients who develop increased transaminase levels and treatment should be discontinued if increases in alanine aminotransferase (ALT) and aspartate aminotransferase (AST) exceed, and persist at, three times the upper limit of normal.

Skeletal Muscles

As with other HMG-CoA reductase inhibitors, sporadic elevations of creatine phosphokinase levels (CPK [MM fraction]) have been observed. If a markedly elevated (greater than 10 times upper limit of normal) serum CPK develops, discontinuation of simvastatin therapy is recommended. There have been rare reports of rhabdomyolysis with acute renal dysfunction secondary to myoglobinuria. An increase in the incidence of myositis and myopathy has been seen in patients receiving HMG-CoA reductase inhibitors, especially those being treated concomitantly with cyclosporin (see Drug Interaction), fibric acid derivatives and, nicotinic acid. Therefore, such combinations should continue to be used with caution.

The combined use of simvastatin and fibric acid derivatives may be useful in selected patients requiring further lipid level reductions. However, since the occurrence of myopathy cannot be excluded, concomitant use of simvastatin and fibric acid derivatives should generally be avoided.

Side Effects

The commonest adverse effects of simvastatin therapy are headache, skin rashes, and gastrointestinal disorders including abdominal pain, nausea, and vomiting. Other adverse effects reported include dizziness, anaemia, alopecia, or depression. Alteration in liver function tests, hepatitis, jaundice, or pancreatitis have infrequently been reported. Rarely, hypersensitivity syndrome (including angioedema) has been reported.

Occasionally, some neurological side effects were reported with the use of simvastatin including paraesthesia and peripheral neuropathy.

As with other statins, reversible myositis, myalgia, and myopathy have rarely been reported with the use of simvastatin. Treatment should be discontinued if the creatine kinase concentration is markedly elevated (> 10 times upper limit of normal) and myopathy is suspected or diagnosed. Patients should be advised to report promptly unexplained muscle pain, tenderness, or weakness.

Overdosage

Until now, no specific treatment for simvastatin overdose is recommended; therefore, symptomatic and supportive measures should be established as needed.

Drug Interactions

The effects of oral anticoagulants (e.g. nicoumalone and warfarin) may be enhanced by simvastatin; prothrombin time should be monitored upon concurrent administration of these medications.

Concurrent use of itraconazole with simvastatin should be avoided, as this may increase the risk of myopathy.

Increased risk of myopathy may also occur upon concurrent administration of simvastatin with other lipid-regulating drugs (e.g clofibrate group and nicotinic acid in lipid-lowering doses) as well as with immunosuppressants such as cyclosporin; close monitoring of liver function and, if symptomatic, of creatine kinase is required in patients receiving these drugs concurrently.

Presentation

Simvast tablets: Pack of 28 tablets.

* *Store at a temperature of 15-25°C, in a dry place.*

THIS IS A MEDICAMENT

- **Medicament is a product which affects your health, and its consumption contrary to instructions is dangerous for you.**
- **Follow strictly the doctor's prescription, the method of use and the instructions of the phamacist who sold the medicament.**
- **The doctor and the phamacist are experts in medicines, their benefits and risks.**
- **Do not by yourself interrupt the period of treatment prescribed for you.**
- **Do not repeat the same prescription without consulting your doctor.**
- **Keep all medicaments out of reach of the children.**

Council of Arab Health Ministers,
Union of Arab Phamacists

***Any information? Call Our Toll Free No.* (971) 800-4994**

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