Oscar Tablets*

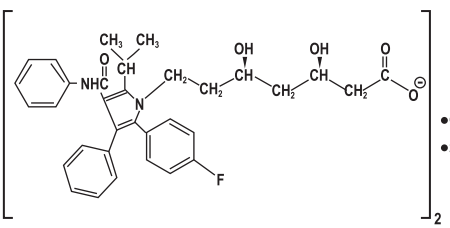
آسکر ٹیبلٹس

COMPOSITION

Each tablet contains: Atorvastatin (as Calcium trihydrate) BP/USP.....10, 20 & 40 mg tablets, respectively.

DESCRIPTION

Atorvastatin calcium is a white to off-white crystalline powder that is insoluble in aqueous solutions of pH 4 and below. Atorvastatin calcium is very slightly soluble in distilled water, pH 7.4 phosphate buffer, and acetonitrile; slightly soluble in ethanol; and freely soluble in methanol. Atorvastatin calcium is [R-(R*, R*)]-2-(4-fluorophenyl)-ß,•-dihydroxy-5- (1-methylethyl)-3-phenyl-4-[(phenylamino) carbonyl]-1H-pyrrole-1-heptanoic acid, calcium salt (2:1) trihydrate. The empirical formula of atorvastatin calcium is $(C_{33}H_{34}FN_2O_5)_2Ca•3H_2O$ and its molecular weight is 1209.42. Its structural formula is:



PHARMACOLOGY

Mechanism of action: Atorvastatin is a selective, competitive inhibitor of HMG-CoA reductase, the rate-limiting enzyme that converts 3-hydroxy-3 methylglutaryl-coenzyme A to mevalonate, a precursor of sterols, including cholesterol. Atorvastatin lowers plasma cholesterol and lipoprotein levels by inhibiting HMG-CoA reductase and cholesterol synthesis in the liver and by increasing the number of hepatic LDL receptors on the cell surface to enhance uptake and catabolism of LDL; atorvastatin also reduces LDL production and the number of LDL particles. Atorvastatin reduces LDL-C in some patients with homozygous familial hypercholesterolemia (FH), a population that rarely responds to other lipid-lowering medication(s). Atorvastatin reduces total-C, LDL-C, and apo B in patients with homozygous and heterozygous FH, nonfamilial forms of hypercholesterolemia, and mixed dyslipidemia. Atorvastatin also reduces VLDL-C and TG and produces variable increases in HDL-C and apolipoprotein A-1. Atorvastatin reduces total-C, LDL-C, VLDL-C, apo B, TG, and non-HDL-C, and increases HDL-C in patients with isolated hypertriglyceridemia. Atorvastatin reduces intermediate density lipoprotein cholesterol (IDL-C) in patients with dysbetalipoproteinemia.

Pharmacodynamics: Atorvastatin, as well as some of its metabolites, are pharmacologically active in humans. The liver is the primary site of action and the principal site of cholesterol synthesis and LDL clearance. Drug dosage, rather than systemic drug concentration, correlates better with LDL-C reduction. Individualization of drug dosage should be based on therapeutic response.

Pharmacokinetics: ***Absorption:*** Atorvastatin is rapidly absorbed after oral administration; maximum plasma concentrations occur within 1 to 2 hours. Extent of absorption increases in proportion to atorvastatin dose. The absolute bioavailability of atorvastatin is approximately 14% and the systemic availability of HMG-CoA reductase inhibitory activity is approximately 30%. The low systemic availability is attributed to presystemic clearance in gastrointestinal mucosa and/or hepatic first-pass metabolism. Although food decreases the rate and extent of drug absorption by approximately 25% and 9%, respectively, as assessed by Cmax and AUC, LDL-C reduction is similar whether atorvastatin is given with or without food. Plasma atorvastatin concentrations are lower (approximately 30% for Cmax and AUC) following evening drug administration compared with morning. However, LDL-C reduction is the same regardless of the time of day of drug administration.

Distribution: Mean volume of distribution of atorvastatin is approximately 381 liters. Atorvastatin is ≥98% bound to plasma proteins. A blood/plasma ratio of approximately 0.25 indicates poor drug penetration into red blood cells.

Metabolism: Atorvastatin is extensively metabolized to ortho- and parahydroxylated derivatives and various beta-oxidation products. Approximately 70% of circulating inhibitory activity for HMG-CoA reductase is attributed to active metabolites.

Excretion: Atorvastatin and its metabolites are eliminated primarily in bile following hepatic and/or extra-hepatic metabolism; however, the drug does not appear to undergo enterohepatic recirculation. Mean plasma elimination half-life of atorvastatin is approximately 14 hours, but the half-life of inhibitory activity for HMG-CoA reductase is 20 to 30 hours due to the contribution of active metabolites. Less than 2% of a dose of atorvastatin is recovered in urine following oral administration.

INDICATIONS AND USAGE

Therapy with lipid-altering agents should be only one component of multiple risk factor intervention in individuals at significantly increased risk for atherosclerotic vascular disease due to hypercholesterolemia. Drug therapy is recommended as an adjunct to diet when the response to a diet restricted in saturated fat and cholesterol and other nonpharmacologic measures alone has been inadequate. In patients with CHD or multiple risk factors for CHD, OSCAR can be started simultaneously with diet.

Prevention of Cardiovascular Disease: OSCAR Tablets are indicated:

- In adult patients without clinically evident coronary heart disease, but with multiple risk factors for coronary heart disease such as age, smoking, hypertension, low HDL-C, or a family history of an early coronary heart disease, to reduce the risk of myocardial infarction, stroke, revascularization procedures and angina.
- In patients with type 2 diabetes, and without clinically evident coronary heart disease, but with multiple risk factors for coronary heart disease such as retinopathy, albuminuria, smoking, or hypertension, to reduce the risk of myocardial infarction and stroke.
- In patients with clinically evident coronary heart disease, to reduce the risk of non-fatal myocardial infarction, fatal & non-fatal stroke, revascularization procedures, hospitalization for CHF and angina.

Hypercholesterolemia: OSCAR Tablets are indicated:

- As an adjunct to diet to reduce elevated total-C, LDL-C, apo B, and TG levels and to increase HDL-C in patients with primary hypercholesterolemia (heterozygous familial and nonfamilial) and mixed dyslipidemia (Fredrickson Types IIa and IIb);
- As an adjunct to diet for the treatment of patients with elevated serum TG levels (Fredrickson Type IV);
- For the treatment of patients with primary dysbetalipoproteinemia (Fredrickson Type III) who do not respond adequately to diet;
- To reduce total-C and LDL-C in patients with homozygous familial hypercholesterolemia as an adjunct to other lipid-lowering treatments or if such treatments are unavailable;
- As an adjunct to diet to reduce total-C, LDL-C, and apo B levels in boys and postmenarchal girls, 10 to 17 years of age, with heterozygous familial hypercholesterolemia if after an adequate trial of diet therapy the following findings are present: a. LDL-C remains ≥ 190 mg/dL or b. LDL-C remains

≥ 160 mg/dL and there is a positive family history of premature cardiovascular disease or two or more other CVD risk factors are present inthe pediatric patient.

CONTRAINDICATIONS

Atorvastatin is contraindicated in patients, who are hypersensitive to any content of the formulation, who have active liver disease or unexplained persistent elevated serum transaminase level exceeding three times the upper limit of normal, pregnant and breast feeding mothers or in women with child bearing potential, who are not using adequate contraceptive measures.

POSSIBLE ADVERSE EFFECTS

Atorvastatin is generally well tolerated. Adverse reactions reported commonly include constipation, flatulence, dyspepsia, abdominal pain, headache, dizziness, nausea, diarrhea, myalgia, asthenia & insomnia, skin rashes and infection. The following additional adverse effects have been reported very rarely: pancreatitis, hepatitis, hypersensitivity syndrome including angioedema, muscle pain or weakness associated with elevated serum CPK levels.

DRUG INTERACTIONS

Fibric Acid Derivatives, Lipid-Modifying Doses of Niacin or Cytochrome P450 3A4 Inhibitors (e.g. Cyclosporine, Erythromycin, Clarithromycin, and Azole Antifungals): The risk of myopathy during treatment with HMG-CoA reductase inhibitors is increased with concurrent administration of these agents. **Antacid:** When Atorvastatin and aluminium containing compounds are coadministered, plasma concentrations of atorvastatin decrease approximately 35%. However, LDL-C reduction is not altered. **Digoxin:** When multiple doses of atorvastatin and digoxin are co-administered, steady-state plasma digoxin concentrations increase by approximately 20%. Patients taking digoxin should be monitored appropriately. **Oral Contraceptives:** Co-administration of atorvastatin and an oral contraceptive increase AUC values for norethindrone and ethinyl estradiol by approximately 30% and 20%. These increases should be considered when selecting an oral contraceptive for a woman taking atorvastatin.

WARNINGS

General: Before instituting therapy with atorvastatin, an attempt should be made to control hypercholesterolemia with appropriate diet, exercise, and weight reduction in obese patients, and to treat other underlying medical problems. **Liver Function Abnormalities:** HMG-CoA reductase inhibitors, like some other lipid-lowering therapies, have been associated with biochemical abnormalities of liver function. It is recommended that liver function tests be performed prior to and at 12 weeks following both the initiation of therapy and any elevation of dose, and periodically (e.g., semiannually) thereafter. Liver enzyme changes generally occur in the first 3 months of treatment with atorvastatin. Patients who develop increased transaminase levels should be monitored until the abnormalities resolve. If an increase in ALT or AST of >3 times ULN persist, reduction of dose or withdrawal of atorvastatin is recommended. Atorvastatin should be used with caution in patients who consume substantial quantities of alcohol and/or have a history of liver disease. Active liver disease or unexplained persistent transaminase elevations are contraindications to the use of atorvastatin. **Skeletal Muscle:** Atorvastatin therapy should be temporarily withheld or discontinued in any patient with an acute, serious condition suggestive of a myopathy or having a risk factor predisposing to the development of renal failure secondary to rhabdomyolysis (e.g., severe acute infection, hypotension, major surgery, trauma, severe metabolic, endocrine & electrolyte disorders, and uncontrolled seizures). Patients should be advised to report promptly unexplained muscle pain, tenderness or weakness, particularly if accompanied by malaise or fever. **Pregnancy:** Atorvastatin should be administered to women of child-bearing potential only when such patients are highly unlikely to conceive and have been informed of the potential hazards. If the woman becomes pregnant while taking atorvastatin, it should be discontinued and the patient advised again as to the potential hazards to the fetus. **Lactation:** Because of the potential for adverse reactions in nursing infants, women taking atorvastatin should notbreast-feed. **Pediatric Use:** No data available for pre-pubertal patients or patients younger than 10 years of age.

DOSAGE & ADMINISTRATION

The patient should be placed on a standard cholesterol-lowering diet before receiving OSCAR Tablets and should continue on this diet during treatment with OSCAR Tablets. **Hypercholesterolemia (Heterozygous Familial & Nonfamilial) & Mixed Dyslipidemia (Fredrickson Types IIa and IIb):** The recommended starting dose of OSCAR Tablets is 10 or 20 mg once-daily. Patients who require a large reduction in LDL-C (more than 45%) may be started at 40 mg once-daily. The dosage range of OSCAR Tablets is 10 to 80 mg once-daily. OSCAR Tablets can be administered as a single dose at any time of the day, with or without food. The starting and maintenance doses of OSCAR Tablets should be individualized according to patient characteristics such as goal of therapy and response. After initiation and/or upon titration of OSCAR Tablets, lipid levels should be analyzed within 2 to 4 weeks and dosage adjusted accordingly. Since the goal of treatment is to lower LDL-C, the NCEP (National Cholesterol Education Programme) recommends that LDL-C levels be used to initiate and assess treatment response. Only if LDL-C levels are not available, total-C should be used to monitor therapy. **Heterozygous Familial Hypercholesterolemia in Pediatric Patients (10-17 years of age):** The recommended starting dose of OSCAR Tablets is 10 mg/day; the maximum recommended dose is 20 mg/day. Adjustments should be made at intervals of 4 weeks or more. **Homozygous Familial Hypercholesterolemia:** The dosage of OSCAR Tablets in patients with homozygous FH is 10 to 80 mg daily. OSCAR Tablets should be used as an adjunct to other lipid-lowering treatments (e.g., LDL apheresis) in these patients or if such treatments are unavailable. **Concomitant Lipid Lowering Therapy:** OSCAR Tablets may be used in combination with a bile acid binding resin for additive effect. The combination of HMG-CoA reductase inhibitors and fibrates should generally be avoided. **Dosage in Patients with Renal Insufficiency:** No dosage adjustment is necessary in patients with renal dysfunction. The drug should be used under strict medical supervision/advice.

SPECIAL INSTRUCTIONS TO THE PHYSICIAN

Overdosage: There is no specific overdosage treatment. It should be treated symptomatically and supportive measures initiated as required.

STORAGE/PRECAUTIONS

Store in a cool, dry and dark place between 15-30 °C. Keep all the medicines out of the reach of children. To be used on the prescription of Registered Medical Practitioners.

PRESENTATION

OSCAR 10, 20 & 40 mg Tablets are available in packing containing 10 tablets, respectively.

*Scotmann Specs.

خوراک: ڈاکٹر کی ہدایت کے مطابق۔
احتیاط: روشنی، نمی اور گرمی سے بچائیں۔
15 سے 30 ڈگری سینٹی گریڈ کے درمیان محفوظ کریں۔
تمام ادویات بچوں کی پہنچ سے دور رکھیں۔
مستند ڈاکٹر کے نسخہ پر استعمال کریں۔

Complete Medical Information available only for doctors on request.

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