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PRO-STATIN

Atorvastatin Tablet USP

COMPOSITION:
PRO-STATIN Tablet 10 mg:
Each film coated tablet contains:
Atorvastatin Calcium Trihydrate USP equivalent to
Atorvastatin ..... 10 mg.

Product Specs.: USP

PRO-STATIN Tablet 20 mg:
Each film coated tablet contains:
Atorvastatin Calcium Trihydrate USP equivalent to
Atorvastatin ..... 20 mg.

Product Specs.: USP

DESCRIPTION:
Atorvastatin, the active ingredient of Pro-Statin, is a synthetic lipid regulating agent intended for oral administration.

CLINICAL PHARMACOLOGY:
MECHANISM OF ACTION:
Atorvastatin is a competitive inhibitor of 3-hydroxy-3-methyl-glutaryl-coenzyme A (HMG-CoA) reductase enzyme. The enzyme catalyzes the conversion of HMG-CoA to mevalonate, an early and rate limiting step in the synthesis of cholesterol. The primary site of action of HMG-CoA reductase inhibition is the liver. Inhibition of cholesterol synthesis in the liver leads to upregulation of LDL-receptors and an increase in LDL-catabolism. There is also some reduction of LDL-production as a result of inhibition of hepatic synthesis of very low density lipoprotion (VLDL), the precursor of LDL-cholesterol.

PHARMACOKINETICS:
Absorption: Atorvastatin is rapidly absorbed after oral administration; maximum plasma concentrations occur within 1 to 2 hours. The absolute bioavailability of Atorvastatin is approximately 14% and the systemic availability of HMG-CoA reductase inhibitory activity is approximately 30%.
Distribution: Mean volume of distribution of Atorvastatin is approximately 381 liters. Atorvastatin is 98% bound to plasma proteins.
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. Mean plasma elimination half-life of Atorvastatin in humans 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:
The drug is indicated in following conditions:
- 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 (FredricksonType IV);
- For the treatment of patients with primary dysbetalipoproteinemia (FredricksonType 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 (eg, LDL apheresis) 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;
- For the reduction ofthe risk of myocardial infarction;
- For the reduction of therisk of stroke;
- For the reduction of the risk for revascularization procedures and angina.

Lipid altering agents should be used in addition to diet restricted in saturated fat and cholesterol only when the response to diet and other nonpharmacological measures has been inadequate [see National Cholesterol Education Program (NCEP) Guidelines, summarized in the Table given below]. At the time of hospitalization for an acute coronary event, consideration can be given to initiating drug therapy at discharge if the LDL-C levels is > 130 mg/dL.

NCEP GUIDELINES FOR LIPID MANAGEMENT

Definite Atherosclerotic Disease*	Two or More Other Risk Factors **	LDL-C mg/dL (mmol/L)	LDL-C mg/dL(mmol/L)
		Initiation Level	Minimum Goal
No	No	≥ 190 (≥ 4.9)	< 160 (< 4.1)
No	No	≥ 160 (≥ 4.1)	< 130 (< 3.4)
Yes	Yes or No	≥ 130 (≥ 3.4)	< 100 (< 2.6)

***Coronary heart disease or peripheral vascular disease (including symptomatic carotid artery disease). Other risk factors for coronary heart disease (CHD) include age (males > 45 years. Females > 55 years or premature menopause without estrogen replacement therapy); family history of premature CHD; current cigarette smoking; hypertension, confirmed HDL-C < 35 mg/dL (< 0.91mmol/L); and diabetes mellitus. Subtract 1 risk factor if HDL-C is 60 mg/dL (> 1.6 mmol/L).

CONTRAINDICATIONS:
- Hypersensitivity to any component of this medication.
- Active liver disease or unexplained persistent elevations of serum transaminases exceeding three times the upper limit of normal.

DOSAGE AND ADMINISTRATION:
Hypercholesterolemia (Heterozygous Familial and Nonfamilial) and mixed:
Dyslipidemia (Fredrickson Types IIa and IIb): The recommended starting dose of Pro-Statinis 10 or 20 mg once daily. Patients who require a large reduction in LDL-C may be started at 40 mg once daily. The dosage range of Pro-Statinis 10 to 80 mg once daily. The starting dose and maintenance doses of Pro-Statinshould be individualized according to patient characteristics such as goal of therapy.

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Heterozygous Familial Hypercholesterolemia in Pediatric Patients (10-17 years of age):
The recommended starting dose of Pro-Statinis 10 mg/day; the maximum recommended dose is 20 mg/day.
Homozygous Familial Hypercholesterolemia:
The dosage of Pro-Statinin patients with homozygous Familial Hypercholesterolemia is 10 to 80 mg daily. Pro-Statinshould be used as an adjunct to other lipid-lowering treatments (eg, LDL apheresis) in these patients or if such treatments are unavailable.

WARNINGS:
Liver function abnormalities:
Like some other lipid-lowering therapies, Pro-Statinhas been associated with biochemical abnormalities of liver function. Liver function tests shouldbe 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. Should an increase in ALT or AST of >3 times ULN persist, reduction of dose or withdrawal of Atorvastatin is recommended.
Myopathy/Rhabdomyolysis/Elevation of creatine kinase:
Atorvastatin therapy should be temporarily withheld or discontinued in any patient with an acute, serious condition suggestive of a myopathy of having a risk factor predisposing to the development of renal failure secondary to (e.g. rhabdomyolysis severe acute infection, hypotension, major surgery, trauma, severe metabolic, endocrine and electrolyte disorders, and uncontrolled seizures). Atorvastatin therapy be discontinued if markedly should elevated CPK levels occur or myopathy is diagnosed or suspected.

PRECAUTIONS:
Pregnancy/Lactation: Safety of Atorvastatin in pregnancy has not been established. HMG-CoA reductase inhibitors are not recommended for use during pregnancy. An interval of 1 month should be allowed from stopping Atorvastatin treatment to conception in the event of planning a pregnancy. Use of HMG-CoA reductase inhibitors during breast feeding is not recommended, because of the potential for serious adverse effects in nursing infants
Pediatric use: Safety and efficacy of Atorvastatin has not been established in children.
Patients with hepatic dysfunction: In patients with moderate to severe hepatic dysfunction, the therapeutic response to Atorvastatin is unaffected but exposure to the drug is greatly increased. C_{max} increases by approximately 16-fold and AUC(0-24) by approximately 11-fold. Therefore caution should be exercised in patients who consume substantial quantities of alcohol and/or have a history of liver disease.
Patients with renal insufficiency: Renal disease has no influence on the plasma concentrations or lipid effects of Atorvastatin; hence no adjustment of dose is required. Haemodialysis is not expected to significantly enhance the clearance at Atorvastatin since the drug is extensively bound to plasma proteins.

SIDE EFFECTS:
Atorvastatin is generally well tolerated. Adverse effects reported commonly include constipation, flatulence, dyspepsia, abdominal pain, headache, nausea, myalgia, diarrhoea, asthenia and insomnia.
concurrent Dose-related and reversible elevated serum ALT levels have been reported in approximately 1.3% of patients receiving Atorvastatin. Elevated serum CPK levels have been reported in some patients on Atorvastatin but rarely patients havemuscle pain, tenderness or weakness.

DRUG INTERACTIONS:
Erythromycin: Concurrent administration with erythromycin may result in higher plasma concentrations of Atorvastatin.
Oral contraceptives: Coadministration of Atorvastatin with an oral contraceptive result in increased AUC values of norethindrone and ethinyl oestradiol.
Colestipol:
Plasma concentrations of Atorvastatin decreasedwhen colestipol and Atorvastatin are coadministered.
Digoxin:
Administration of multiple doses of Atorvastatin with digoxin increases the steady state plasma digoxin concentration by approximately 20%; patients taking digoxin should be monitored appropriately.
Cyclosporine, fibric acid derivatives, erythromycin, azole antifungals or niacin:
The risk of myopathy during treatment with drugs belonging to the class of HMG-CoA reductase inhibitors is increased with concurrent administration of these agents.
Antacids:
Decreased plasma concentrations of Atorvastatin may occur when administered along with an oral antacids suspension containing magnesium and aluminium hydroxides, however LDL-cholesterol reduction is not altered.
Warfarin:
Minimal decrease in prothrombin time may occur when warfarin and Atorvastatin are administered concurrently, patients receiving warfarin should be closely monitored when Atorvastatin is added to their therapy.
Cimetidine:
Atorvastatin plasma concentrations and LDL-cholesterol reduction are not altered bycoadministration of cimetidine.

OVERDOSAGE:
There is no specific treatment available for Atorvastatin overdosage. General supportive measures should be adopted as required. Liver function tests and serum CPK levels should be monitored. Due to extensive drug binding to plasma proteins, haemodialysis is not expected to significantly enhance Atorvastatin clearance.

INSTRUCTIONS:
Store below 30ºC. Protect from heat, sunlight and moisture. Keep out of the reach of children. To be sold on the prescription of a registered medical practitioner only.

PRESENTATION:
Pro-Statin tablet 10 mg : Pack of 1 x 10 tablets.
Pro-Statin tablet 10 mg : Pack of 10 x 10 tablets.
Pro-Statin tablet 20 mg : Pack of 1 x 10 tablets.
Pro-Statin tablet 20 mg : Pack of 10 x 10 tablets.

FOR FURTHER INFORMATIONS PLEASE CONTACT:

CCL
Manufactured by:
CCL Pharmaceuticals (Pvt.) Ltd.
62 Industrial Estate, Kot Lakhpat, Lahore, Pakistan.

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