LASTOLIP

COMPOSITION:

Lastolip 10mg Tablets
Each tablet contains:
Atorvastatin (as Calcium) U.S.P 10mg
Product conforms to the U.S.P Specifications.
Lastolip 20mg Tablets
Each tablet contains:
Atorvastatin (as Calcium) U.S.P 20mg
Product conforms to the U.S.P Specifications.
Lastolip 40mg Tablets
Each tablet contains:
Atorvastatin (as Calcium) U.S.P 40mg
Product conforms to the U.S.P Specifications
Lastolip 80mg Tablets
Each tablet contains:
Atorvastatin (as Calcium) U.S.P 80mg
Product conforms to the U.S.P Specifications

DESCRIPTION:

Atorvastatin (Lastolip) is an inhibitor of 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase. This enzyme catalyzes the conversion of HMG-CoA to mevalonate, an early and rate limiting step in cholesterol biosynthesis. Atorvastatin calcium is [R-®*, R*)]-2-(4-fluorophenyl)-β, δ-dihydroxy-5-(1-methylethyl)-3-phenyl-4-[(phenylamino)carbonyl]-1Hpyrrole-1-heptanoic acid, calcium salt (2:1) trihydrate. The empirical formula of atorvastatin calcium is (C33H34FN2O5) Ca.3H2O and its molecular weight is 1209.42.

MECHANISM OF ACTION:

Atorvastatin (Lastolip) 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. It 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 (Lastolip) also reduces LDL production and the number of LDL particles. Atorvastatin (Lastolip) reduces LDL-C in some patients with homozygous familial hypercholesterolemia (FH), a population that rarely responds to other lipid lowering medication(s).

PHARMACOKINETICS:

Absorption: Atorvastatin (Lastolip) is rapidly absorbed after oral administration, maximum plasma concentrations occur within 1 to 2 hours. Extent of absorption increases in proportion to Atorvastatin (Lastolip) dose. The absolute bioavailability of atorvastatin (parent drug) 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 (Lastolip) 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. Based on observations in rats, Atorvastatin is likely to be secreted in human milk.

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Metabolism: Atorvastatin is extensively metabolized to ortho and parahydroxylated derivatives and various beta oxidation products. In vitro inhibition of HMG-CoA reductase by ortho and parahydroxylated metabolites is equivalent to that of Atorvastatin. Approximately 70% of circulating inhibitory activity for HMG-CoA reductase is attributed to active metabolites. In vitro studies suggest the importance of Atorvastatin metabolism by cytochrome P450 3A4, consistent with increased plasma concentrations of Atorvastatin in humans following coadministration with erythromycin, a known inhibitor of this isozyme. In animals, the orthohydroxy metabolite undergoes further glucuronidation.
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 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:

Hyperlipidemia
Atorvastatin (Lastolip) is 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 (e.g. 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 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
Two or more other CVD risk factors are present in the pediatric patient
Prevention of Cardiovascular Disease
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 early coronary heart disease, Atorvastatin (Lastolip) is indicated to:
Reduce the risk of myocardial infarction.
Reduce the risk of stoke.
Reduce the risk for 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, Atorvastatin (Lastolip) is indicated to:
Reduce the risk of myocardial infarction.
Reduce the risk of stroke.

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In patients with clinically evident coronary heart disease, Atorvastatin (Lastolip) is indicated to:
Reduce the risk of non-fatal myocardial infarction.
Reduce the risk of fatal and non-fatal stroke.
Reduce the risk for revascularization procedures.
Reduce the risk of hospitalization for CHF.
Reduce the risk of angina.

DOSAGE & ADMINISTRATION:

Hyperlipidemia (Heterozygous Familial & Nonfamilial) and Mixed Dyslipidemia (Fredrickson Types IIa and Iib)
The recommended starting dose of Atorvastatin (Lastolip) is 10 or 20 mg once daily. Patients who require a large reduction in LDL-C (more than 45%) may be started at 40mg once daily. The dosage range of Atorvastatin (Lastolip) is 10 to 80mg once daily. Atorvastatin (Lastolip) can be administered as a single dose at any time of the day, with or without food. The starting dose and maintenance doses of Atorvastatin (Lastolip) should be individualized according to patient characteristics such as goal of therapy and response. After initiation and/or upon titration of Atorvastatin (Lastolip), lipid levels should be analyzed within 2 to 4 weeks and dosage adjusted accordingly.
Heterozygous Familial Hypercholesterolemia in Pediatric Patients
The recommended starting dose of Atorvastatin (Lastolip) is 10mg/day; the maximum recommended dose is 20mg/day (doses greater than 20mg have not been studied in this patient population). Doses should be individualized according to the recommended goal of therapy. Adjustments should be made at intervals of 4 weeks or more.
Homozygous Familial Hypercholesterolemia
The dosage of Atorvastatin (Lastolip) in patients with homozygous FH is 10 to 80mg daily. Atorvastatin (Lastolip) 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
Atorvastatin (Lastolip) may be used with bile acid resins. The combination of HMG-CoA reductase inhibitors (statins) and fibrates should generally be used with caution.
Dosage in Patients with Renal Impairment
Renal disease does not affect the plasma concentrations nor LDL-C reduction of Atorvastatin (Lastolip); thus, dosage adjustment in patients with renal dysfunction is not necessary.

CONTRAINDICATIONS:

Atorvastatin (Lastolip) is contraindicated in patients with hypersensitivity to any component of this medication and in active liver disease, which may include unexplained persistent elevations in hepatic transaminase levels.

PRECAUTIONS:

Rare cases of Rhabdomyolysis with acute Renal failure secondary to Myoglobinuria have been reported with Atorvastatin (Lastolip) and with other drugs in this class. A history of renal impairment may be a risk factor for the development of Rhabdomyolysis. Such patients merit closer monitoring for skeletal muscle effects. Statins, like some other lipid lowering therapies, have been associated with biochemical abnormalities of liver function.

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PREGNANCY & LACTATION:

Pregnancy

Atorvastatin (Lastolip) may cause fetal harm when administered to a pregnant woman. Serum cholesterol and triglycerides increase during normal pregnancy and cholesterol or cholesterol derivatives are essential for fetal development. Atherosclerosis is a chronic process and discontinuation of lipid lowering drugs during pregnancy should have little impact on the outcome of long term therapy of primary hypercholesterolemia. There are no adequate and well controlled studies of Atorvastatin (Lastolip) use during pregnancy; however in rare reports, congenital anomalies were observed following intrauterine exposure to statins. In rat and rabbit animal reproduction studies, atorvastatin revealed no evidence of teratogenicity. Atorvastatin (Lastolip) should be administered to women of childbearing age only when such patients are highly unlikely to conceive and have been informed of the potential hazards. If the patient becomes pregnant while taking this drug, Atorvastatin (Lastolip) should be discontinued immediately and the patient apprised of the potential hazard to the fetus.

Lactation

It is not known whether atorvastatin is excreted into human milk; however a small amount of another drug in this class does pass into breast milk. Because statins have the potential for serious adverse reactions in nursing infants, women who require Atorvastatin (Lastolip) treatment should not breast-feed their infants.

DRUG-DRUG INTERACTIONS:

The risk of myopathy during treatment with Statins is increased with concurrent administration of fibric acid derivatives, lipid modifying doses of niacin, cyclosporine or strong CYP 3A4 inhibitors (e.g. clarithromycin, HIV protease inhibitors and itraconazole).

Oral Contraceptives: Coadministration of Atorvastatin (Lastolip) and an oral contraceptive increased AUC values for norethindrone and ethinyl estradiol. These increases should be considered when selecting an oral contraceptive for a woman taking Atorvastatin (Lastolip).

Digoxin: When multiple doses of Atorvastatin (Lastolip) and digoxin were coadministered, steady state plasma digoxin concentrations increased by approximately 20%. Patients taking digoxin should be monitored appropriately.

Cyclosporine: Atorvastatin and atorvastatin metabolites are substrates of the OATP1B1 transporter. Inhibitors of the OATP1B1 (e.g. cyclosporine) can increase the bioavailability of atorvastatin. Atorvastatin AUC was significantly increased with concomitant administration of Atorvastatin (Lastolip) 10mg and cyclosporine 5.2 mg/kg/day compared to that of Atorvastatin (Lastolip) alone. The co-administration of Atorvastatin (Lastolip) with cyclosporine should be avoided.

SIDE EFFECTS:

··Unexplained muscle pain, tenderness or weakness
··Confusion, memory problems
· Fever, unusual tiredness and dark colored urine
· Swelling, weight gain
· Increased thirst, increased urination, hunger, dry mouth, fruity breath odor, drowsiness, dry skin, blurred vision, weight loss
· Nausea, upper stomach pain, itching, loss of appetite, dark urine, clay-colored stools, jaundice

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ADVERSE DRUG REACTIONS:

The most common adverse reactions with Atorvastatin (Lastolip) are:
Nasopharyngitis, Arthralgia, Diarrhea, Pain in extremity, Urinary tract infection, Dyspepsia, Nausea, Musculoskeletal pain, Muscle Spasms,Rhabdomyolysis, Myopathy, Myalgia, Insomnia, Liver enzyme abnormalities and Pharyngolaryngeal pain.

OVER DOSAGE:

There is no specific treatment for Atorvastatin (Lastolip) overdosage. In the event of an overdose, the patient should be treated symptomatically and supportive measures instituted as required. Due to extensive drug binding to plasma proteins, hemodialysis is not expected to significantly enhance Atorvastatin (Lastolip) clearance.

INSTRUCTIONS:

Store in a cool & dry place below 25ºC.
Protect from light, heat and moisture.
Keep out of reach of children.

PRESENTATION:

Lastolip 10mg tablets are available in a blister pack of 20's.
Lastolip 20mg tablets are available in a blister pack of 20's.
Lastolip 40mg tablets are available in a blister pack of 10's.
Lastolip 80mg tablets are available in a blister pack of 10's.