

Lipid Lowering Agents

LIPOREST Tablets

Composition

LIPOREST-10

Each film-coated tablet contains Atorvastatin Calcium equivalent to Atorvastatin 10 mg

Description

Atorvastatin is a synthetic lipid-lowering agent. It is an inhibitor of 3-hydroxy-3-methyl-glutaryl-coenzyme A (HMG-CoA) reductase enzyme. This enzyme catalyzes the conversion of HMG-CoA to mevalonate, an early and rate limiting step in the synthesis of cholesterol.

Atorvastatin reduces total cholesterol, LDL-cholesterol and apo B in patients with homozygous and heterozygous familial hypercholesterolemia, non familial forms of hypercholesterolemia and mixed dyslipidemias. Atorvastatin also reduces VLDL-cholesterol and triglycerides and produces variable increases in HDL-cholesterol and apolipoprotein A1.

Indications

- As an adjunct to diet to reduce elevated total cholesterol, LDL-cholesterol, apo B and triglyceride levels in patients with primary hypercholesterolemia (heterozygous familial and non familial) and mixed dyslipidemia (Fredrickson Types IIa and IIb).
- As adjunctive therapy to diet for the treatment of patients with elevated serum triglyceride 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 cholesterol and LDL-cholesterol in patients with homozygous familial hypercholesterolemia as an adjunct to other lipid lowering treatments (e.g. LDL apheresis) or if such treatments are unavailable.
- 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 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 level is ≥ 130 mg/dL.

NCEP Guidelines for Lipid Management

| Definite Atherosclerotic | Two or more Other Risk Factors** | LDL-Cholesterol mg/dL, (mmol/L) | |
|--------------------------|----------------------------------|---------------------------------|------------------|
| | | Initiation Level | Minimum Goal |
| No | No | ≥ 190 (≥ 4.9) | < 160 (< 4.1) |
| No | Yes | ≥ 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 (≤ 0.91 mmol/L); and diabetes mellitus. Subtract 1 risk factor if HDL-C is ≥ 60 mg/dL (≥ 1.6 mmol/L).

Dosage and Administration

Hypercholesterolemia (Heterozygous Familial and Nonfamilial) and Mixed Dyslipidemia (Fredrickson Types IIa and IIb)

The recommended starting dose of atorvastatin is 10 mg daily. The dosage range is 10 to 80 mg once daily. Atorvastatin can be administered as a single dose at any time of the day with or without food. Therapy should be individualized according to goal of therapy and response. After initiation and/or upon titration of atorvastatin, lipid levels should be analysed within 2 to 4 weeks and dosage adjusted accordingly.

Homozygous Familial Hypercholesterolemia

The dosage of atorvastatin in these patients is 10 to 80 mg daily. Atorvastatin should be used as an adjunct to other lipid-lowering treatments (eg LDL apheresis) in these patients or if such treatments are unavailable.

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.

Warnings and Precautions

DRUG INTERACTIONS

Erythromycin: Concurrent administration with erythromycin may result in higher plasma concentrations of atorvastatin.

Oral contraceptives: Administration of atorvastatin with an oral contraceptive containing norethindrone and ethinyl oestradiol produces increased plasma concentrations of norethindrone and ethinyl oestradiol.

Colestipol: Although plasma concentrations of atorvastatin are lower when colestipol is administered with atorvastatin the lipid effects are greater than when either drug is given alone.

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 antacid 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 by coadministration of cimetidine.

LIVER FUNCTION ABNORMALITIES

HMG-CoA reductase inhibitors, like some other lipid lowering therapies, have been associated with biochemical abnormalities of liver function. Liver function tests should be performed before treatment starts, at 6 weeks and 12 weeks after initiation of therapy or elevation in dose, and periodically thereafter. Liver enzyme changes generally occur in the first three 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 the upper limit of normal persist, reduction of dose or withdrawal of atorvastatin is recommended. The drug should be used with caution in patients who consume substantial quantities of alcohol and/or have a past history of liver disease

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 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 and electrolyte disorders, and uncontrolled seizures).

Rhabdomyolysis with acute renal failure secondary to myoglobinuria has been reported with other drugs in this class. Atorvastatin may cause an elevation in serum creatine phosphokinase levels. This should be considered in the differential diagnosis of chest pain in patients on therapy with atorvastatin.

Uncomplicated myalgia has been reported in atorvastatin-treated patients. Atorvastatin therapy should be discontinued if markedly elevated CPK levels occur or myopathy is diagnosed or suspected.

The risk of myopathy during treatment with other drugs in this class is increased with concurrent administration of cyclosporine, fibric acid derivatives, erythromycin, niacin or azole anti-fungals. Patients should be advised to report promptly any unexplained muscle pain, tenderness or weakness, particularly if accompanied by malaise or fever.

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 have not been established in children.

HEPATIC IMPAIRMENT

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.

RENAL IMPAIRMENT

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 of 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, diarrhea, asthenia and insomnia.

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 only rarely have patients had concurrent muscle pain, tenderness or weakness.

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.

Presentation

LIPOREST-10 (Blister pack of 10 tablets)