Anzitor®

Atorvastatin

COMPOSITION

Anzitor® 10 : Each film coated tablet contains Atorvastatin 10 mg as Atorvastatin Calcium INN.
Anzitor® 20 : Each film coated tablet contains Atorvastatin 20 mg as Atorvastatin Calcium INN.
Anzitor® 40 : Each film coated tablet contains Atorvastatin 40 mg as Atorvastatin Calcium INN.

PHARMACOLOGY

Anzitor® is a selective, competitive inhibitor of HMG-CoA reductase, the rate-limiting enzyme responsible for the conversion of 3- hydroxy- 3- methyl- glutaryl- coenzyme A to mevalonate, a precursor of sterols, including cholesterol. Triglycerides (TG) and cholesterol in the liver are incorporated into VLDL and released into the plasma for delivery to peripheral tissues. Low-density lipoprotein (LDL) is formed from VLDL and is catabolised primarily through the high affinity LDL receptor.

Anzitor® lowers plasma cholesterol and lipoprotein levels by inhibiting HMG-CoA reductase and cholesterol synthesis in the liver and increases the number of hepatic LDL receptors on the cell surface for enhanced uptake and catabolism of LDL. **Anzitor®** reduces LDL production and the number of LDL particles. **Anzitor®** produces a profound and sustained increase in LDL receptor activity coupled with a beneficial change in the quality of circulating LDL particles.

PHARMACODYNAMIC PROPERTIES

Anzitor® 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.

PHARMACOKINETIC PROPERTIES

Absorption:

Anzitor® is rapidly absorbed after oral administration; maximum plasma concentrations occur within 1 to 2 hours. Extent of absorption increases in proportion of Atorvastatin dose. The absolute bioavailability of **Anzitor®** is approximately 14% and the systemic availability of HMG-CoA reductase inhibitory activity is approximately 30%.

Distribution:

Mean volume of distribution of **Anzitor®** is approximately 381 L. Atorvastatin is > 98% bound to plasma proteins.

Metabolism:

Anzitor® is extensively metabolized to ortho- and parahydroxylated derivatives and various beta-oxidation products.

Excretion:

Anzitor® is eliminated primarily in bile following hepatic and/or extrahepatic metabolism. However, the drug does not appear to undergo significant enterohepatic recirculation. Mean plasma elimination half-life of **Anzitor®** in human is approximately 14 hours. The half-life of inhibitory activity of HMG-CoA reductase is approximately 20-30 hours due to the contribution of active metabolites.

THERAPEUTIC INDICATIONS

Anzitor® is indicated as an adjunct to diet for reduction of elevated total cholesterol, LDL-cholesterol, apolipoprotein B, and triglycerides in patients with-

1. Primary hypercholesterolemia (heterozygous familial and non-familial hypercholesterolemia and mixed dyslipidemia (Fredrickson types IIa and IIb))
2. Elevated serum TG levels (Fredrickson type IV)
3. Primary dysbetalipoproteinemia (Fredrickson type III) who do not respond adequately to diet.
4. Homozygous familial hypercholesterolemia as an adjunct to other lipid-lowering treatments (eg, LDL apheresis) or if such treatments are unavailable.

DOSAGE & ADMINISTRATION

Patients should be placed on a standard cholesterol-lowering diet before receiving **Anzitor®** and should continue on this diet during treatment with **Anzitor®**. The usual starting dose for all the indications is 10 mg once daily. The doses range is 10 to 80 mg once daily. Doses should be individualised according to baseline LDL-C levels, the goal of therapy, and patient response. Adjustment of dosage should be made at intervals of 4 weeks or more. Doses may be given at anytime of day with or without food.

Children:

Treatment experience in a paediatric population with dose of **Anzitor®** up to 80 mg/day is limited.

Geriatric (>70 years) use:

The safety and efficacy of **Anzitor®** in this population is as similar as < 70 years of age patients with the dose upto 80 mg/day.

In patients with Renal Insufficiency:

No dosage adjustment is required.

ADVERSE EFFECTS

Atorvastatin is generally well tolerated. Adverse reactions have usually been mild and transient. Reversible myositis is rare but significant side effect of the statins. The statins also cause headache, altered liver-function tests and gastro-intestinal effects including abdominal pain, flatulence, diarrhoea, nausea and vomiting. Thrombocytopenia, rash and hypersensitivity reactions have been reported rarely. Other side effects are reported with Atorvastatin therapy includes insomnia, angioedema, anorexia, asthenia, paraesthesia, peripheral neuropathy, alopecia, pruritus, rash, impotence, chest pain, hypoglycemia and hyperglycemia.

SPECIAL WARNINGS AND SPECIAL PRECAUTIONS FOR USE

Liver effects:

Liver function tests should be performed before the initiation of treatment and periodically thereafter. Should an increase in ALT or AST of greater than 3 times the upper limit of normal 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.

Skeletal muscle effects:

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. Should significant increases in CPK persist, reduction of dose or withdrawal of Atorvastatin is recommended. Rare cases of rhabdomyolysis with acute renal failure secondary to myoglobinuria have been reported with Atorvastatin and with other drugs in this class.

INTERACTIONS WITH OTHER MEDICAMENTS AND OTHER FORMS OF INTERACTIONS

The risk of myopathy during treatment with other drugs in this class is increased with concurrent administration of cyclosporin, fibric acid derivatives, erythromycin, azole antifungals, or niacin (nicotinic acid). These risks may also occur when combining these drugs with Atorvastatin. No clinically significant interactions were seen when Atorvastatin was administered with antihypertensives and or hypoglycemic agents. Caution should also be exercised when Atorvastatin is administered with inhibitors of P450 3A4 (macrolide antibiotics and azole antifungals). The effect of inducers of cytochrome P450 3A4 (rifampicin or phenytoin) on Atorvastatin is unknown. Patients should be closely monitored if Atorvastatin is added to digoxin, erythromycin, oral contraceptives, colestipol, antacid and warfarin. No interaction was found with cimetidine.

CONTRAINDICATIONS

Atorvastatin is contraindicated in patients with hypersensitivity to any component of this medication, active liver disease or unexplained persistent elevations of serum transaminases, during pregnancy, while breast-feeding, and in women of child-bearing potential not using appropriate contraceptive measures.

USE IN PREGNANCY AND LACTATION

Atorvastatin is contraindicated in pregnancy and while breast-feeding. Women of child bearing potential should use appropriate contraceptive measures. If the woman become pregnant while taking Atorvastatin, it should be discontinued.

OVERDOSAGE

Specific treatment is not available for Atorvastatin overdosage. If an overdose occur, the patient should be treated symptomatically and supportive measures instituted, 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.

PHARMACEUTICAL PRECAUTION

Store below 25^{0} C. Protect from light and moisture. Keep all medicines out of the reach of children.

HOW SUPPLIED

Anzitor® 10: Each box contains 50 film coated tablets in Alu-Alu blister pack.
Anzitor® 20: Each box contains 30 film coated tablets in Alu-Alu blister pack.
Anzitor® 40: Each box contains 10 film coated tablets in Alu-Alu blister pack.

Manufactured by :

SQUARE
PHARMACEUTICALS LTD.
BANGLADESH