For the use of a Registered Medical Practitioner only

1. GENERIC NAME AND BRAND NAME

Atorvastatin Tablets I.P.
CAAT™ 10, CAAT™ 20, CAAT™ 40, CAAT™ 80

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

CAAT™ 10
Each film coated tablet contains:
Atorvastatin Calcium I.P.
equivalent to Atorvastatin 10mg
Excipients q.s.
Colour: Titanium Dioxide I.P.

CAAT™ 20
Each film coated tablet contains:
Atorvastatin Calcium I.P.
equivalent to Atorvastatin 20mg
Excipients q.s.
Colour: Titanium Dioxide I.P.

CAAT™ 40
Each film coated tablet contains:
Atorvastatin Calcium I.P.
equivalent to Atorvastatin 40mg
Excipients q.s.
Colour: Titanium Dioxide I.P.

CAAT™ 80
Each film coated tablet contains:
Atorvastatin Calcium I.P.
equivalent to Atorvastatin 80mg
Excipients q.s.
Colour: Titanium Dioxide I.P.

3. DOSAGE FORM AND STRENGTH

Kindly refer section 1 and 2

4. CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATION

- As an Adjunct to Diet to Reduce Elevated Total Cholesterol and Triglyceride Levels in Patients with Primary Hypercholesterolemia and Mixed Dyslipidemia (Type IIa and IIIb).
- In adult patients with type II diabetes and without clinically evident coronary heart disease to reduce the risk of myocardial infarction and stroke.
- To reduce the risk of stroke in adult patients without clinically evident coronary heart disease but multiple risk factors for coronary heart disease.

4.2 POSOLOGY AND METHOD OF ADMINISTRATION

Atorvastatin calcium should be administered within the dosage range of 10–80 mg/day as a single daily dose. Atorvastatin calcium can be taken with or without food, at any time of the day. According to the target lipid levels therapy should be individualized, the recommended goal of therapy and the patient's response. Lipid levels should be re-analyzed within 4 weeks after initiation and/or upon titration of atorvastatin calcium and dosage adjusted according to the patient's response.

Primary Hypercholesterolaemia and Mixed Dyslipidemia

With 10 mg atorvastatin calcium once a day the majority of patients are controlled. The maximum response is usually achieved within four weeks, and a therapeutic response is evident within two weeks. During chronic therapy the response is maintained.

4.3 CONTRAINDICATIONS

- Active liver disease or unexplained persistent elevations of serum transaminases
- Hypersensitivity to any component of this medication
- Pregnancy and lactation - Women of childbearing potential, unless on an effective contraceptive and highly unlikely to conceive
- Concomitant use with fusidic acid

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Keep out of reach of children.

Before instituting therapy, 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.

Skeletal muscle effects (e.g., rhabdomyolysis and myopathy):

When higher doses are used concomitantly with cyclosporine and strong CYP3A4 inhibitors (e.g., clarithromycin, itraconazole, HIV protease inhibitors), risk increases. Predisposing factors include advanced age (> 65), renal impairment and uncontrolled hypothyroidism. Rare cases of rhabdomyolysis with acute renal failure secondary to myoglobinuria have been reported. In cases of rhabdomyolysis or myopathy, therapy should be temporarily withheld or discontinued. Liver enzyme abnormalities: Persistent elevations in hepatic transaminases can occur. Before initiating therapy check liver enzyme tests and as clinically indicated thereafter. In patients without CHD, a higher incidence of hemorrhagic stroke was seen but with stroke or TIA within the previous 6 months in the Atorvastatin Calcium 80 mg group vs. placebo.

Liver Dysfunction

Elevations of serum transaminases have been reported following therapy with atorvastatin, as with other lipid-lowering agents of the same class, moderate (>3 x upper limit of normal [ULN]).

In 0.7% of patients who received atorvastatin in clinical trials persistent increases in serum transaminases >3 x ULN occurred. The incidence of these abnormalities was 0.2, 0.2, 0.6 and 2.3% for 10, 20, 40 and 80 mg respectively. Increases were generally not associated with jaundice or other clinical symptoms or signs. Transaminase levels returned to pre-treatment levels when the dosage of atorvastatin was reduced, or drug treatment interrupted or

discontinued. Most patients continued treatment on a reduced dose of Atorvastatin Calcium without sequelae.
It is recommended that liver enzyme tests be obtained prior to initiating therapy with atorvastatin and repeated as clinically indicated.
In patients who consume substantial quantities of alcohol and/or have a history of liver disease, Atorvastatin Calcium should be used with caution. Active liver disease or unexplained persistent transaminase elevations are contraindications to the use of atorvastatin
Patient should be advised to notify if they have following symptoms of liver problems, unusual fatigue, or weakness; loss of appetite upper belly pain; dark colored urine; yellowing of skin or whites of the eyes.

Skeletal Muscle
In atorvastatin-treated patients uncomplicated myalgia has been reported. Myopathy, defined as muscle aching or muscle weakness in conjunction with increases in creatine kinase (CK) values >10 x ULN, should be considered in any patient with diffuse myalgias, muscle tenderness or weakness and/or marked elevation of CK. Patients should be advised to report promptly tenderness or weakness, unexplained muscle pain, particularly if accompanied by fever or malaise. If markedly elevated CK levels occur or myopathy is diagnosed or suspected, Atorvastatin Calcium therapy should be discontinued.
During treatment with other drugs in this class the risk of myopathy is increased with concurrent administration of fibric acid derivatives, cyclosporin, erythromycin, azole antifungals, niacin, colchicine, hepatitis C protease inhibitors (e.g. telaprevir, † boceprevir) or the combination of tipranavir/ritonavir.
Physicians considering combined therapy with Atorvastatin Calcium and fibric acid derivatives, immunosuppressive drugs, erythromycin, azole antifungals, or lipid-lowering doses of niacin should carefully weigh the potential benefits and risks and should carefully monitor patients for any signs and symptoms of tenderness, muscle pain, or weakness, particularly during the initial months of therapy and during any periods of upward dosage titration of either drug. Therefore, lower starting and maintenance doses of atorvastatin should also be considered when taken concomitantly with the aforementioned drugs.

Endocrine Function
Atorvastatin interferes with cholesterol synthesis and theoretically might blunt adrenal and/or gonadal steroid production. Caution should be exercised if an HMG-CoA reductase inhibitor is administered concomitantly with drugs that may decrease the levels or activity of endogenous steroid hormones, such as ketoconazole, spironolactone, and cimetidine. Increases in HbA1c and fasting serum glucose levels have been reported with statin use.

Haemorrhagic Stroke
The increased risk of haemorrhagic stroke was observed in patients who entered the study with prior haemorrhagic stroke or prior lacunar infarct. All cause mortality was also increased in these patients with prior haemorrhagic stroke or prior lacunar infarct. The potential risk of haemorrhagic stroke should be carefully considered before initiating treatment with atorvastatin in patients with recent stroke or TIA.
A post-hoc analysis of a clinical study in patients without known coronary heart disease who had a recent stroke or TIA, showed a higher incidence of haemorrhagic stroke in patients on atorvastatin 80 mg compared to placebo. Throughout the study, all cause mortality was

numerically higher in the atorvastatin arm than the placebo arm. At study end all cause mortality was 9.1% on atorvastatin vs. 8.9% on placebo.

Cognitive effects:

Certain cognitive effects have been reported with statin use; generally, these are not been serious and reversible after stopping statin therapy. However, patient should be advised if the experience memory loss and confusion.

Information for Patients

Due to the risk of myopathy with drugs of the HMG-CoA reductase class, patients should be advised to report promptly unexplained muscle pain, tenderness, or weakness, particularly if accompanied by malaise or fever. Fenofibrate when given in combination with statins in resistant hyperlipidemias, the incidence of muscle problems and rhabdomyolysis is increased, and care must be exercised.

Patients should alert the doctor if they have symptoms such as memory loss and confusion.

Patients should notify to the doctor if they have symptoms of liver problems, unusual fatigue or weakness; loss of appetite upper belly pain; dark colored urine; yellowing of skin or whites of the eyes.

Special Populations

Geriatric

Atorvastatin: Plasma concentrations of atorvastatin are higher (approximately 40% for Cmax and 30% for AUC) in healthy elderly subjects (age >65 years) than in young adults. Clinical data suggest a greater degree of LDL-lowering at any dose of atorvastatin in the elderly population compared to younger adults. Dosage should be reduced if there is any evidence of renal impairment.

Pediatric

Atorvastatin: Pharmacokinetic data in the pediatric population are not available.

Gender

Plasma concentrations of atorvastatin in women differ from those in men (approximately 20% higher for Cmax and 10% lower for AUC); however, there is no clinically significant difference in LDL-C reduction with atorvastatin between men and women.

Renal Insufficiency

Atorvastatin: Renal disease has no influence on the plasma concentrations or LDL-C reduction of atorvastatin; thus, dose adjustment of atorvastatin in patients with renal dysfunction is not necessary.

Hemodialysis

Hemodialysis is not expected to significantly enhance clearance of atorvastatin since the drug is extensively bound to plasma proteins.

Hepatic Insufficiency

Atorvastatin: In patients with chronic alcoholic liver disease, plasma concentrations of atorvastatin are markedly increased. Cmax and AUC are each 4-fold greater in patients with Childs-Pugh A disease. Cmax and AUC of atorvastatin are approximately 16-fold and 11-fold increased, respectively, in patients with Childs-Pugh B disease.

Carcinogenesis, mutagenesis, impairment of fertility

Atorvastatin: In a 2-year carcinogenicity study in rats at dose levels of 10, 30, and 100 mg/kg/day. 2 rare tumors were found in muscle in high-dose females: in one, there was a rhabdomyosarcoma and, in another, there was a fibrosarcoma. A 2-year carcinogenicity study in mice given 100, 200, or 400 mg/kg/day resulted in a significant increase in liver adenomas in high-dose males and liver carcinomas in high dose females. Atorvastatin was not mutagenic or clastogenic in mutagenicity tests. Studies in rats performed at doses up to 175 mg/kg (15 times the human exposure) produced no changes in fertility. Atorvastatin caused no adverse effects on semen parameters, or reproductive organ histopathology in dogs given doses of 10, 40 or 120 mg/kg for two years.

Pregnancy:

Pregnancy Category D

The definition of Pregnancy Category D is drugs which have caused, are suspected to have caused or may be expected to cause, an increased incidence of human foetal malformations or irreversible damage. These drugs may also have adverse pharmacological effects. Atorvastatin is contraindicated in pregnancy.

Nursing Mothers

Women taking this combination should not breast-feed.

Geriatric Use

The safety and efficacy of atorvastatin in this population were similar to those of patients <65 years of age.

4.5 DRUG INTERACTIONS

No	Drug	Drug interaction	Remark
1	Inhibitors of cytochrome P450 3A4 Atorvastatin is metabolised by cytochrome P450 3A4.	Concomitant administration of atorvastatin with inhibitors of cytochrome P450 3A4 can lead to increases in plasma concentrations of atorvastatin. The extent of interaction and potentiation of effects depends on the variability of effect on cytochrome P450 3A4. † Pharmacokinetic drug interactions that result in increased systemic concentration of atorvastatin have been noted with HIV protease inhibitors	Based on experience with other HMG-coa reductase inhibitors, caution should be exercised when Atorvastatin Calcium is administered with inhibitors of cytochrome P450 3A4 (e.g. Cyclosporin, macrolide antibiotics including erythromycin and azole antifungals including itraconazole).

		(fosamprenavir and combinations of lopinavir/ritonavir, saquinavir/ritonavir, darunavir/ritonavir, fosamprenavir/ritonavir), hepatitis C protease inhibitors (boceprevir), clarithromycin and itraconazole.	
2.	Other HMG-coa reductase inhibitors	The risk of myopathy during treatment with other HMG-coa reductase inhibitors is increased with concurrent administration of cyclosporin, fibric acid derivatives, erythromycin, azole antifungals, or niacin.	
3.	Inducers of cytochrome P450 3A4 E.g. Efavirenz, rifampicin, phenytoin	Concomitant administration of atorvastatin with inducers of cytochrome P450 3A4 (e.g. Efavirenz, rifampicin, phenytoin) can lead to variable reductions in plasma concentrations of atorvastatin.	Due to the dual interaction mechanism of rifampicin (cytochrome P450 3A4 induction and inhibition of hepatocyte uptake transporter (OATP1B1)), simultaneous co-administration of atorvastatin with rifampicin is recommended, as delayed administration of atorvastatin after administration of rifampicin has been associated with a significant reduction in atorvastatin plasma concentrations.
4.	Fusidic Acid	The risk of myopathy including rhabdomyolysis may be increased by the concomitant administration of systemic fusidic acid with statins. Co-administration of this combination may cause increased plasma concentrations of both agents.	The mechanism of this interaction (whether it is pharmacodynamics or pharmacokinetic, or both) is yet unknown.

5.	Colchicine	Although interaction studies with atorvastatin and colchicine have not been conducted, cases of myopathy have been reported with atorvastatin co-administered with colchicines	Caution should be exercised when prescribing atorvastatin with colchicines
6.	Antacid	Co-administration of an oral antacid suspension containing magnesium and aluminium hydroxides with atorvastatin decreased atorvastatin plasma concentrations approximately 35%, however, LDL-C reduction was not altered.	
7.	Colestipol	Plasma concentrations of atorvastatin were lower (approximately 25%) when colestipol and atorvastatin were co-administered. However, LDL-C reduction was greater when atorvastatin and colestipol were co-administered than when either drug was given alone.	
8.	Transporter Inhibitors	Atorvastatin and atorvastatin metabolites are substrates of the OATP1B1 transporter. Inhibitors of the OATP1B1 (e.g. Cyclosporin) can increase the bioavailability of atorvastatin. Concomitant administration of atorvastatin 10 mg and cyclosporin 5.2 mg/kg/day resulted in an increase in exposure to atorvastatin	
9.	Erythromycin/Clarithromycin	In healthy individuals, co-administration of atorvastatin (10 mg once daily) and erythromycin (500 mg four times a day), or clarithromycin (500 mg	

		twice daily), known inhibitors of cytochrome P450 3A4, was associated with higher plasma concentrations of atorvastatin	
10.	Protease Inhibitors	Co-administration of atorvastatin and protease inhibitors, known inhibitors of cytochrome P450 3A4, was associated with increased plasma concentrations of atorvastatin	
11.	Diltiazem Hydrochloride	Co-administration of atorvastatin (40 mg) with diltiazem (240 mg) was associated with higher plasma concentrations of atorvastatin.	
12.	Itraconazole	Concomitant administration of atorvastatin (20 to 40 mg) and itraconazole (200 mg) was associated with an increase in atorvastatin AUC.	
13.	Grapefruit Juice	Contains one or more components that inhibit cytochrome P450 3A4 and can increase plasma concentrations of atorvastatin, especially with excessive grapefruit juice consumption (>1.2 L per day).	

4.6 USE IN SPECIAL POPULATIONS (SUCH AS PREGNANT WOMEN, LACTATING WOMEN, PAEDIATRIC PATIENTS, GERIATRIC PATIENTS ETC.)

Paediatric population

No clinically significant effect on growth and sexual maturation was observed with atorvastatin in a 3-year study based on the assessment of overall maturation and development, assessment of Tanner Stage, and measurement of height and weight.

Pregnancy

Atorvastatin is contraindicated during pregnancy. Safety in pregnant women has not been established. No controlled clinical trials with atorvastatin have been conducted in pregnant

women. Treatment with Atorvastatin should be suspended for the duration of pregnancy or until it has been determined that the woman is not pregnant.

Lactation
Because of the potential for serious adverse reactions, women taking Atorvastatin should not breast-feed their infants. Atorvastatin is contraindicated during breast-feeding.
Refer Section 4.4

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Atorvastatin has negligible influence on the ability to drive and use machines

4.8 UNDESIRABLE EFFECTS

Atorvastatin Calcium is generally well tolerated. Adverse events have usually been mild and transient.

Clinical Adverse Events

The most frequent (≥1%) adverse events that may be associated with Atorvastatin Calcium therapy, reported in patients participating in placebo-controlled clinical studies include:
Infections and infestations: nasopharyngitis.
Gastrointestinal disorders: dyspepsia, flatulence, nausea, diarrhoea.
Investigations: liver function test abnormal, blood creatine phosphokinase increased.
Musculoskeletal and connective tissue disorders: myalgia, pain in extremity, musculoskeletal pain, arthralgia, muscle spasms, joint swelling.
Metabolism and nutrition disorders: hyperglycaemia.
Respiratory, thoracic and mediastinal disorders: pharyngolaryngeal pain, epistaxis

Additional Adverse Events

The following have been reported in clinical trials of atorvastatin, however, not all the events listed have been causally associated with atorvastatin therapy

Common
Infections and infestations: urinary tract infection
Gastrointestinal disorders: constipation.
Nervous system disorders: headache.

Uncommon
Eye disorders: vision blurred.
Ear and labyrinth disorders: deafness.
Gastrointestinal disorders: abdominal discomfort, abdominal pain, vomiting.
Infections and infestations: infection, influenza.
Metabolism and nutrition disorders: anorexia
General disorders and administration site conditions: asthenia, malaise.
Musculoskeletal and connective tissue disorders: back pain, neck pain.
Nervous system disorders: paraesthesia.
Psychiatric disorders: insomnia, nightmare.
Respiratory, thoracic and mediastinal disorders: asthma
Reproductive system and breast disorders: erectile dysfunction.
Skin and subcutaneous tissue disorders: rash, urticaria, pruritus.

4.9 OVERDOSE

There is no specific treatment for Atorvastatin Calcium overdosage. Should an overdose occur, the patient should be treated symptomatically, and supportive measures instituted as required. In symptomatic patients, BUN, monitor serum creatinine, creatinine phosphokinase and urine myoglobin for indications of renal impairment secondary to rhabdomyolysis. Liver function tests should be performed in symptomatic patients.
Consider administration of activated charcoal, if there has been significant ingestion. Activated charcoal is most effective when administered within 1 hour of ingestion. In patients who are not fully conscious or have impaired gag reflex, consideration should be given to administering activated charcoal via nasogastric tube once the airway is protected. For rhabdomyolysis, administer sufficient 0.9% saline to maintain urine output of 2 to 3 mL/kg/hr. Diuretics may be necessary to maintain urine output. Urinary alkalinisation is not routinely recommended. Haemodialysis is not expected to significantly enhance atorvastatin clearance due to extensive drug binding to plasma proteins.

5. PHARMACOLOGICAL PROPERTIES

5.1 MECHANISM OF ACTION

Refer Section 5.2

5.2 PHARMACODYNAMIC PROPERTIES

Atorvastatin is a synthetic lipid-lowering agent. Atorvastatin is an inhibitor of HMG-CoA reductase, the rate-limiting enzyme that converts 3-hydroxy-3-methyl-glutaryl-coenzyme A to mevalonate, a precursor of sterols, including cholesterol.

Atorvastatin and its metabolites are responsible for pharmacological activity in humans. The liver is its primary site of action and the principal site of cholesterol synthesis and LDL clearance. Drug dose rather than systemic drug concentration correlates better with LDL-C reduction. Individualization of drug dose should be based on therapeutic response.

5.3 PHARMACOKINETIC PROPERTIES

	Atorvastatin Calcium
Absorption	Atorvastatin is rapidly absorbed after oral administration; maximum plasma concentrations occur within 1 to 2 hours. A constant proportion of atorvastatin is absorbed intact. The absolute bioavailability is 14%. The low systemic availability is attributed to pre-systemic clearance in gastrointestinal mucosa and/or hepatic first-pass metabolism.
Distribution	The mean volume of distribution of atorvastatin is about 400 litres. Atorvastatin is ≥98% bound to plasma proteins. A RBC/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.
Metabolism	In humans, atorvastatin is extensively metabolised to ortho- and para-hydroxylated derivatives. In vitro inhibition of HMG-CoA reductase by ortho- and para-hydroxylated 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 co-administration with erythromycin, a known inhibitor of this isozyme.
Excretion	Atorvastatin is eliminated primarily in bile following hepatic and/or extrahepatic metabolism; however, the drug does not appear to undergo enterohepatic recirculation. Less than 2% of a dose of atorvastatin is recovered in urine following oral administration.
Half life	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.

6. NONCLINICAL PROPERTIES

6.1 ANIMAL TOXICOLOGY OR PHARMACOLOGY

Atorvastatin was negative for mutagenic and clastogenic potential in a battery of 4 in vitro tests and 1 in vivo assay. Atorvastatin was not found to be carcinogenic in rats, but high doses in mice (resulting in 6-11fold the AUC0-24h reached in humans at the highest recommended dose) showed hepatocellular adenomas in males and hepatocellular carcinomas in females.

There is evidence from animal experimental studies that HMG-CoA reductase inhibitors may affect the development of embryos or fetuses. In rats, rabbits and dogs atorvastatin had no effect on fertility and was not teratogenic, however, at maternally toxic doses fetal toxicity was observed in rats and rabbits. The development of the rat offspring was delayed and post-natal survival reduced during exposure of the dams to high doses of atorvastatin. In rats, there is evidence of placental transfer.

7. DESCRIPTION

CAAT is supplied for oral administration, as a film-coated tablet. Each film coated tablet of CAAT contains Atorvastatin Calcium equivalent to Atorvastatin 10mg, 20mg, 40mg, 80mg.

8. PHARMACEUTICAL PARTICULARS

8.1 INCOMPATIBILITIES

Not applicable

8.2 SHELF-LIFE

Refer Pack

8.3 PACKAGING INFORMATION

Refer Pack

8.4 STORAGE AND HANDLING INSTRUCTIONS

Refer Pack

9. PATIENT COUNSELLING INFORMATION

Atorvastatin belongs to a group of medicines known as statins, which are lipid (fat) regulating medicines. Refer Section 4.3, 4.4 and 4.6. for contraindications, special warnings and precautions for use and use in special populations.

10. DETAILS OF MANUFACTURER
Refer Pack for manufacturer details.

MARKETED BY
Abbott Healthcare Private Limited
Angel Space, Bldg. D-4, Gala No. 1 to 3 & 11 to 13
Ground Floor, 101 to 106 & 111 to 116 First Floor, 201 to 206 &
211 to 216 2nd Floor, Pimplas, Dist. Thane, Bhiwandi - 421 302,
Maharashtra, India.

11. DETAILS OF PERMISSION OR LICENCE NUMBER
Refer Pack for Permission/Licence details

12. DATE OF REVISION
Version 5.0, dated 24-Nov-25

For Product Complaints/Adverse events or Queries please write to
webmasterindia@abbott.com