Keep the Cholesterol Conversation Going

Make the most of your treatment with LIPITOR by filling out and taking this Doctor Discussion Guide to your next appointment. That way, you can get your questions answered and understand how your treatment is working for you. It’s easy to forget what you wanted to ask in the middle of an appointment. Review the below questions beforehand to see which matter most to you. There is space to add your own questions on the next page.

How long does it take for LIPITOR to start working?

What are my latest test results? Does this mean LIPITOR is working for me?

How long should I continue taking my medicine?

What are my cholesterol treatment goals?

How often should I come see you and have my cholesterol levels checked?

What kind of diet can help me manage my cholesterol?

How much exercise is recommended to help me manage my cholesterol?

What other lifestyle changes can I make to help me manage my cholesterol?

What foods and medications should I avoid while taking LIPITOR?

Tell your doctor about all your medical conditions and all the medicines you take, including prescription, non-prescription, vitamins, and herbal supplements. Especially tell your doctor if you take medicines for your immune system, cholesterol, infections, birth control, heart failure, HIV or AIDS. My current medications:

What are possible side effects of LIPITOR, and when should I call my doctor? (ie, muscle pain, tenderness, weakness, etc)

IMPORTANT SAFETY INFORMATION

LIPITOR® (atorvastatin calcium) tablets are not for everyone, including anyone who has previously had an allergic reaction to LIPITOR. It is not for those with liver problems. And it is not for women who are nursing, pregnant, or may become pregnant. If you get pregnant, stop taking LIPITOR and call your doctor right away.

Please see accompanying Important Safety Information and Indication continued on following page. Please see accompanying full Prescribing and Patient Information for LIPITOR.
IMPORTANT SAFETY INFORMATION AND INDICATION (continued)

If you take LIPITOR® (atorvastatin calcium) tablets, tell your doctor if you feel any new muscle pain or weakness. This could be a sign of rare but serious muscle problems that can lead to kidney problems, including kidney failure. Tell your doctor about all your medical conditions and all medications you take. This may help avoid serious drug interactions. Your doctor should do blood tests to check your liver function before starting LIPITOR and during your treatment if you have symptoms of liver problems. Call your doctor right away if you have the following symptoms of liver problems - feel tired or weak or have a loss of appetite, upper belly pain, dark amber colored urine or yellowing of your skin or the whites of your eyes.

Tell your doctor if you have diabetes. Elevated blood sugar levels have been reported with statins, including LIPITOR. Common side effects are diarrhea, upset stomach, muscle and joint pain, and changes in some blood tests. Talk to your healthcare provider if you have side effects that bother you or that will not go away.

INDICATIONS

LIPITOR® (atorvastatin calcium) is a prescription medicine that lowers cholesterol in the blood. It lowers the LDL-C (“bad” cholesterol) and triglycerides in your blood. It can raise your HDL-C (“good” cholesterol) as well. LIPITOR is for adults and children over 10 whose cholesterol does not come down enough with exercise and a low-fat diet alone. LIPITOR can lower the risk for heart attack, stroke, certain types of heart surgery, and chest pain in patients who have heart disease or risk factors for heart disease such as age, smoking, high blood pressure, low HDL-C, or heart disease in the family. LIPITOR can lower the risk for heart attack or stroke in patients with diabetes and risk factors such as eye problems, kidney problems, smoking, or high blood pressure.

Limitations of Use: LIPITOR has not been studied in people who have an increase of chylomicrons (Fredrickson Types I and V).

*Eligibility required. Terms and conditions apply. Full terms and conditions can be found at LIPITOR.com/terms-conditions. Card will be accepted only at participating pharmacies. Card is not health insurance. No membership fees. Maximum savings of $2,500 per calendar year. This offer is not valid for prescriptions that are reimbursed, in whole or in part, by Medicaid or other federal or state health programs, and cannot be used in conjunction with use of Medicare Part D prescription benefit for LIPITOR. For further information, call 1-800-314-7957, or write: LIPITOR Savings Card, 2250 Perimeter Park Drive, Suite 300, Morrisville, NC 27560.

Please see accompanying full Prescribing and Patient Information for LIPITOR.
LIPITOR is an HMG-CoA reductase inhibitor indicated as an adjunct therapy to diet to:

- Reduce the risk of MI, stroke, revascularization procedures, and angina in adult patients with CHD, but with multiple risk factors (1.1).
- Reduce the risk of MI and stroke in adult patients with type 2 diabetes without CHD, but with multiple risk factors (1.1).
- Reduce the risk of non-fatal MI, fatal and non-fatal stroke, revascularization procedures, hospitalization for CHF, and angina in adult patients with CHD (1.1).
- Reduce elevated total-C, LDL-C, apo B, and TG levels and increase HDL-C in patients with primary hyperlipidemia (heterozygous familial and nonfamilial) and mixed dyslipidemia (1.2).
- Reduce elevated TG in adult patients with hypertriglyceridemia and primary dysbetalipoproteinemia (1.2).
- Reduce total-C and LDL-C in patients with homozygous familial hypercholesterolemia (HeFH) (1.2).
- Reduce elevated total-C, LDL-C, and apo B levels in pediatric patients, 10 years to 17 years of age, with heterozygous familial hypercholesterolemia (HeFH) after failing an adequate trial of diet therapy (1.2).

Limitations of Use:

- LIPITOR has not been studied in Fredrickson Types I and V dyslipidemias (1.3).

---

## DOSAGE AND ADMINISTRATION

**Dose range:** 10 to 80 mg once daily (2.1).

**Recommended start dose:** 10 or 20 mg once daily (2.1).

**Patients requiring large LDL-C reduction (>40%)** may start at 40 mg once daily (2.1).

**Pediatric patients with HeFH starting dose:** 10 mg once daily; dose range: 10 to 20 mg/day for patients 10 years to 17 years of age (2.2).

---

**DOSE FORMS AND STRENGTHS**

Tablets: 10, 20, 40, and 80 mg of atorvastatin (3.3).

**CONTRAINDICATIONS**

- Active liver disease, which may include unexplained persistent elevations in hepatic transaminase levels (4).
- Hypersensitivity to any component of this medication (4).
- Pregnancy (4, 8.1, 8.3).
- Lactation (4, 8.2).

---

## WARNINGS AND PRECAUTIONS

- Skeletal muscle effects (e.g., myopathy and rhabdomyolysis): Risks increase when higher doses are used concomitantly with cyclosporine and strong CYP3A4 inhibitors (e.g., clarithromycin, itraconazole, human immunodeficiency virus [HIV] or hepatitis C virus [HCV] protease inhibitors). Predispelling factors include advanced age (> 65), uncontrolled hypothyroidism, and renal impairment. Rare cases of rhabdomyolysis with acute renal failure secondary to myoglobinuria have been reported. Advise patients to promptly report to their physician unexplained and/or persistent muscle pain, tenderness, or weakness. LIPITOR therapy should be discontinued if myopathy is diagnosed or suspected (2.6, 8.1, 8.3).

- Liver enzyme abnormalities: Persistent elevations in hepatic transaminases may occur. Check liver enzyme tests before initiating therapy and as clinically indicated thereafter (5.2).
- A higher incidence of hemorrhagic stroke was seen in patients without CHD but with stroke or TIA within the previous 6 months in the LIPITOR 80 mg group vs. placebo (5.5).

## ADVERSE REACTIONS

The most commonly reported adverse reactions (incidence > 2%) in patients treated with LIPITOR in placebo-controlled trials regardless of causality were: nasopharyngitis, arthralgia, diarrhea, pain in extremity, and urinary tract infection (6.1).

To report SUSPECTED ADVERSE REACTIONS, contact Pfizer at (1-800-438-1985 and www.pfizer.com) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

---

## DRUG INTERACTIONS

Drug Interactions Associated with Increased Risk of Myopathy/Rhabdomyolysis (2.6, 5.1, 7, 12.3)

- Other Lipid-Lowering Medications: Use with fibrate products or lipid-modifying doses (≥ 1 g/day) of niacin increases the risk of adverse skeletal muscle effects. Caution should be used when prescribing with LIPITOR (7).
- Digoxin: Patients should be monitored appropriately (7.9).
- Oral Contraceptives: Values for norethindrone and ethinyl estradiol may be increased (7.10).
- Rifampin should be simultaneously co-administered with LIPITOR (7.8).

---

## USE IN SPECIFIC POPULATIONS

- Hepatic impairment: Plasma concentrations markedly increased in patients with chronic alcoholic liver disease (8.6, 12.3).
- Females of reproductive potential: Advise females of reproductive potential to use effective contraception during treatment with LIPITOR (8.3).

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.
2.6 Dosage in Patients Taking Cyclosporine, Clarithromycin, Itraconazole, or Certain Protease Inhibitors

In patients taking cyclosporine or the HIV protease inhibitor tipranavir plus ritonavir or the hepatitis C virus (HCV) protease inhibitor glecaprevir plus pibrentasvir, therapy with LIPITOR should be avoided. In patients with HIV taking lopinavir plus ritonavir, use the lowest dose necessary of LIPITOR. In patients taking clarithromycin, itraconazole, elbasvir plus grazoprevir, or in patients with HIV taking a combination of saquinavir plus ritonavir, darunavir plus ritonavir, fosamprenavir, or fosamprenavir plus ritonavir, therapy with LIPITOR should be limited to 20 mg, and appropriate clinical assessment is recommended to ensure that the lowest dose necessary of LIPITOR is used. In patients taking the HIV protease inhibitor neflunavir therapy with LIPITOR should be limited to 40 mg. When co-prescribing atorvastatin with other protease inhibitors, appropriate clinical assessment is recommended to ensure that the lowest dose necessary of LIPITOR is used (see Warnings and Precautions (5.1) and Drug Interactions (7)).

3 DOSAGE FORMS AND STRENGTHS

LIPITOR tablets are white elliptical, film-coated, and are available in four strengths (see Table 1).

Table 1: LIPITOR Tablet Strengths and Identifying Features

<table>
<thead>
<tr>
<th>Tablet Strength</th>
<th>Identifying Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 mg of atorvastatin</td>
<td>“PD 155” on one side and “10” on the other</td>
</tr>
<tr>
<td>20 mg of atorvastatin</td>
<td>“PD 156” on one side and “20” on the other</td>
</tr>
<tr>
<td>40 mg of atorvastatin</td>
<td>“PD 157” on one side and “40” on the other</td>
</tr>
<tr>
<td>80 mg of atorvastatin</td>
<td>“PD 158” on one side and “80” on the other</td>
</tr>
</tbody>
</table>

4 CONTRAINDICATIONS

- ActiveLiver Disease, Which May Include Unexplained Persistent Elevations in Hepatic Transaminase Levels
- Hypersensitivity to Any Component of This Medication
- Pregnancy [see Use in Specific Populations (8.1)]
- Lactation [see Use in Specific Populations (8.2)]

5 WARNINGS AND PRECAUTIONS

5.1 Skeletal Muscle

Rare cases of rhabdomyolysis with acute renal failure secondary to myoglobinuria have been reported with LIPITOR 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.

Atorvastatin, like other statins, occasionally causes myopathy, defined as muscle aches or muscle weakness in conjunction with increases in creatine phosphokinase (CPK) values >10 times ULN. The concomitant use of higher doses of atorvastatin with certain drugs such as cyclosporine and strong cytochrome P450 3A4 (CYP3A4) inhibitors (e.g., clarithromycin, itraconazole, and HIV and HCV protease inhibitors) increases the risk of myopathy/rhabdomyolysis.

There have been rare reports of immune-mediated necrotizing myopathy (IMNM), an autoimmune myopathy, associated with statin use. IMNM is characterized by: proximal muscle weakness and elevated serum creatine kinase, which persist despite discontinuation of statin treatment; muscle biopsy showing necrotizing myopathy without significant inflammation; improvement with immunosuppressive agents. Myopathy should be considered in any patient with diffuse myalgias, muscle tenderness or weakness, and/or marked elevation of CPK. Patients should be advised to report promptly unexplained muscle pain, tenderness, or weakness, particularly if accompanied by malaise or fever or if muscle signs and symptoms persist after discontinuing LIPITOR. LIPITOR therapy should be discontinued if markedly elevated CPK levels occur or myopathy is diagnosed or suspected.

The risk of myopathy during treatment with drugs in this class is increased with concurrent administration of the drugs listed in Table 2. Physicians considering combined therapy of LIPITOR with any of these drugs should carefully weigh the potential benefits and risks and should carefully monitor patients for any signs or symptoms of muscle pain, tenderness, or weakness, particularly during the initial months of therapy and during any periods of upward dosage titration of either drug. Lower starting and maintenance doses of atorvastatin should be considered when taken concomitantly with the aforementioned drugs [see Drug Interactions (7)]. Periodic creatine phosphokinase (CPK) determinations may be considered in such situations, but there is no assurance that such monitoring will prevent the occurrence of severe myopathy.

Prescribing recommendations for interacting agents are summarized in Table 2 [see Dosage and Administration (2.6), Drug Interactions (7), and Clinical Pharmacology (12.3)].

Table 2. Drug Interactions Associated with Increased Risk of Myopathy/Rhabdomyolysis

<table>
<thead>
<tr>
<th>Interacting Agents</th>
<th>Prescribing Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyclosporine, tipranavir plus ritonavir, glecaprevir plus pibrentasvir</td>
<td>Avoid atorvastatin</td>
</tr>
<tr>
<td>Clarithromycin, itraconazole, saquinavir plus ritonavir*, darunavir plus ritonavir, fosamprenavir plus ritonavir, elbasvir plus grazoprevir</td>
<td>Do not exceed 20 mg atorvastatin daily</td>
</tr>
<tr>
<td>Nelfinavir</td>
<td>Do not exceed 40 mg atorvastatin daily</td>
</tr>
<tr>
<td>锟斤拷</td>
<td>Loc</td>
</tr>
</tbody>
</table>

*Use the lowest dose necessary (12.3)

LIPITOR 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 myoglobinuria (e.g., severe acute infection, hypotension, major surgery, trauma, severe metabolic, endocrine and electrolyte disorders, and uncontrolled seizures).
5.2 Liver Dysfunction

Statin, like some other lipid-lowering therapies, have been associated with biochemical abnormalities of liver function. Persistent elevations (>3 times the upper limit of normal [ULN] occurring on 2 or more occasions) in serum transaminases occurred in 0.7% of patients who received LIPITOR in clinical trials. The incidence of these abnormalities was 0.2%, 0.2%, 0.6%, and 2.3% for 10, 20, 40, and 80 mg, respectively.

One patient in clinical trials developed jaundice. Increases in liver function tests (LFT) in other patients were not associated with jaundice or other clinical signs or symptoms. Upon dose reduction, drug interruption, or discontinuation, transaminases returned to or near pretreatment levels. On sequential elevations of 30 patients with persistent LFT elevations, 10 patients had a reduced dose of LIPITOR.

It is recommended that liver enzyme tests be obtained prior to initiating therapy with LIPITOR and repeated as clinically indicated. There have been rare postmarketing reports of fatal and non-fatal hepatic failure in patients taking statins, including atorvastatin. If serious liver injury with symptoms and/or hyperbilirubinemia or jaundice occurs during treatment with LIPITOR, promptly interrupt therapy. An alternate etiology is not found, do not restart LIPITOR.

LIPITOR should be used with caution in patients who consume substantial quantities of alcohol and/or have a history of liver disease. Active liver disease or unexplained persistent transaminase elevations are contraindications to the use of LIPITOR [see Contraindications (4)].

5.3 Endocrine Function

Increases in hHDL and fasting serum glucose levels have been reported with HMG-CoA reductase inhibitors, including LIPITOR.

Statins interfere with cholesterol synthesis and theoretically might blunt adrenal and/or gonadal steroid production. Clinical studies have shown that LIPITOR does not reduce basal plasma cortisol concentration or impair adrenal reserve. The effects of statins on male fertility have not been studied in adequate numbers of patients. The effects, if any, on the pituitary-gonadal axis in premenopausal women are unknown. Caution should be exercised if a statin is administered concomitantly with drugs that may decrease the levels or activity of endogenous steroid hormones, such as ketoconazole, spironolactone, and cimetidine.

5.4 CNS Toxicity

Brain hemorrhage was seen in a female dog treated for 3 months at 120 mg/kg/day. Brain hemorrhage and optic nerve vacuolation were seen in another female dog that was sacrificed in moribund condition after 11 weeks of escalating doses up to 280 mg/kg/day. The 120 mg/kg dose resulted in a systemic exposure approximately 16 times the human plasma area-under-the-curve (AUC; 0-24 hours) based on the maximum human dose of 80 mg/day. A single tonic convulsion was seen in each of 2 male dogs (one treated at 10 mg/kg/day and one at 120 mg/kg/day) in a 2-year study. No CNS lesions have been observed in mice after chronic treatment for up to 2 years at doses up to 400 mg/kg/day or in rats at doses up to 100 mg/kg/day. These doses were 6 to 11 times (mouse) and 8 to 16 times (rat) the human AUC (0-24) based on the maximum recommended human dose of 80 mg/day.

CNS vascular lesions, characterized by perivascular hemorrhages, edema, and mononuclear cell infiltration of perivascular spaces, have been observed in dogs treated with other members of this class. A chemically similar drug in this class produced optic nerve degeneration (Wallerian degeneration of retinogeniculate fibers) in clinically normal dogs in a dose-dependent fashion at a dose that produced plasma drug levels about 30 times higher than the mean drug level in humans taking the highest recommended dose.

5.5 Use in Patients with Recent Stroke or TIA

In a post-hoc analysis of the Stroke Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL) study where LIPITOR 80 mg dose was administered in 4,731 subjects without CHD who had a stroke or TIA within the preceding 6 months, a higher incidence of hemorrhagic stroke was seen in the LIPITOR 80 mg group compared to placebo (5.5% vs. 3.8% placebo; age range 55–74 years, 34% women, 94.3% Caucasians, 2.9% Asians, 1.6% other) with a higher incidence of hemorrhagic stroke in the LIPITOR 80 mg/day group vs. 211 (8.9%) in the placebo group. The proportions of subjects who experienced cardiovascular death were numerically smaller in the LIPITOR 80 mg group (3.3%) than in the placebo group (4.1%). The proportions of subjects who experienced non-cardiovascular death were numerically larger in the LIPITOR 80 mg group (5.0%) than in the placebo group (4.0%).

5.6 Adverse Reactions

The following serious adverse reactions are discussed in greater detail in other sections of the label:

- Adverse Reaction ≥2% in any dose greater than placebo

Other adverse reactions reported in placebo-controlled studies include:

- **Body as a whole:** malaise, pyrexia
- **Digestive system:** abdominal discomfort, eructation, flatulence, hepatitis, cholestasis
- **Musculoskeletal system:** musculoskeletal pain, muscle fatigue, neck pain, joint swelling
- **Mucocutaneous and sensory disorders:** increased sweat, thirst, xerostomia, odynophagia
- **Nervous system:** nervousness, dizziness, paresthesia, depression, akathisia
- **Special senses:** blurred vision, tinnitus
- **Taste perversion:** anorexia

5.7 Use in Special Populations

5.7.1 Geriatric Patients

5.7.2 Pediatric Patients

5.7.3 Pediatric Use

5.8 Labor and Delivery

5.8.1 Pregnancy

5.8.2 Lactation

5.8.3 Nursing Mothers

5.9 Incompatibilities

5.10 Carcinogenesis, Mutagenesis, Impairment of Fertility

5.11 Postmarketing Experience

5.11.1 Other adverse reactions reported in placebo-controlled trials include:

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>Any dose</th>
<th>10 mg</th>
<th>20 mg</th>
<th>40 mg</th>
<th>80 mg</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>4.0</td>
<td>3.7</td>
<td>3.7</td>
<td>7.1</td>
<td>3.8</td>
<td>3.5</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>6.9</td>
<td>8.9</td>
<td>11.7</td>
<td>10.6</td>
<td>4.3</td>
<td>6.5</td>
</tr>
<tr>
<td>Pharyngolaryngeal pain</td>
<td>2.3</td>
<td>3.9</td>
<td>1.6</td>
<td>2.8</td>
<td>0.7</td>
<td>2.1</td>
</tr>
</tbody>
</table>

Table 3. Clinical adverse reactions occurring in ≥2% in patients treated with any dose of LIPITOR and at an incidence greater than placebo regardless of causality (% of patients).

Other adverse reactions reported in placebo-controlled studies include:

- Other reactions reported in placebo-controlled studies include:

  - **Body as a whole:** malaise, pyrexia
  - **Digestive system:** abdominal discomfort, eructation, flatulence, hepatitis, cholestasis
  - **Musculoskeletal system:** musculoskeletal pain, muscle fatigue, neck pain, joint swelling
  - **Mucocutaneous and sensory disorders:** increased sweat, thirst, xerostomia, odynophagia
  - **Nervous system:** nervousness, dizziness, paresthesia, depression, akathisia
  - **Special senses:** blurred vision, tinnitus
  - **Taste perversion:** anorexia

5.12 Other Information

5.12.1 Other information includes:

- **Body as a whole:** malaise, pyrexia
- **Digestive system:** abdominal discomfort, eructation, flatulence, hepatitis, cholestasis
- **Musculoskeletal system:** musculoskeletal pain, muscle fatigue, neck pain, joint swelling
- **Mucocutaneous and sensory disorders:** increased sweat, thirst, xerostomia, odynophagia
- **Nervous system:** nervousness, dizziness, paresthesia, depression, akathisia
- **Special senses:** blurred vision, tinnitus
- **Taste perversion:** anorexia

5.13 Description

5.13.1 Description includes:

- White to light tan, round, film-coated tablets, marked “L” on one side and “80” on the other side

5.14 Warnings and Precautions

5.14.1 Warnings and Precautions include:

- Use in Patients with Recent Stroke or TIA

5.15 Use in Patients with Recent Stroke or TIA

5.15.1 Use in Patients with Recent Stroke or TIA includes:

- In the IDEAL study involving 10,305 participants (age range 40–80 years, 19% women; 94.6% Caucasians, 2.6% Africans, 1.5% South Asians, 1.3% mixed/other) treated with LIPITOR 10 mg daily (n=5,056), the most common adverse reactions of the group treated with LIPITOR compared to the placebo group were:

  - **Body as a whole:** malaise, pyrexia
  - **Digestive system:** abdominal discomfort, eructation, flatulence, hepatitis, cholestasis
  - **Musculoskeletal system:** musculoskeletal pain, muscle fatigue, neck pain, joint swelling
  - **Mucocutaneous and sensory disorders:** increased sweat, thirst, xerostomia, odynophagia
  - **Nervous system:** nervousness, dizziness, paresthesia, depression, akathisia
  - **Special senses:** blurred vision, tinnitus
  - **Taste perversion:** anorexia

5.16 Adverse Reactions

5.16.1 Adverse Reactions include:

- Other adverse reactions reported in placebo-controlled studies include:

  - **Body as a whole:** malaise, pyrexia
  - **Digestive system:** abdominal discomfort, eructation, flatulence, hepatitis, cholestasis
  - **Musculoskeletal system:** musculoskeletal pain, muscle fatigue, neck pain, joint swelling
  - **Mucocutaneous and sensory disorders:** increased sweat, thirst, xerostomia, odynophagia
  - **Nervous system:** nervousness, dizziness, paresthesia, depression, akathisia
  - **Special senses:** blurred vision, tinnitus
  - **Taste perversion:** anorexia
6.2 Postmarketing Experience

The following adverse reactions have been identified during post-approval use of LIPITOR. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure. Adverse reactions associated with LIPITOR therapy reported since market introduction, that are not listed above, regardless of causality assessment, include the following: anaphylaxis, angioneurotic edema, bullous rashes (including erythema multiforme, Stevens-Johnson syndrome, and toxic epidermal necrolysis), rhabdomyolysis, myositis, fatigue, tendon rupture, fatal and non-fatal hepatic failure, dizziness, depression, peripheral neuropathy, pancreatitis, and intestinal lymph disease. There have been rare reports of immune-mediated necrotizing myopathy associated with statin use [see Warnings and Precautions (5.1)]. There have been rare postmarketing reports of cognitive impairment (e.g., memory loss, forgetfulness, amnesia, memory impairment, confusion) associated with statin use. These cognitive issues have been reported for all statins. The reports are generally non-serious, and reversible upon statin discontinuation, with variable times to symptom onset (1 day to years) and symptom resolution (median of 3 weeks).

7 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 and HIV protease inhibitors, and tetracaine) [see Warnings and Precautions (5.1) and Clinical Pharmacology (12.3)].

7.1 Strong Inhibitors of CYP 3A4

LIPITOR is metabolized by cytochrome P450 3A4. Concomitant administration of LIPITOR with strong inhibitors of CYP 3A4 can lead to increases in plasma concentrations of atorvastatin. The extent of interaction and potentiation of effects depend on the variability of effect on CYP 3A4.

Clarithromycin
Atorvastatin AUC was significantly increased with concomitant administration of LIPITOR 80 mg with clarithromycin (500 mg twice daily) compared to that of LIPITOR alone [see Clinical Pharmacology (12.3)]. Therefore, in patients taking clarithromycin, caution should be used when the LIPITOR dose exceeds 20 mg [see Dosage and Administration (2.6) and Warnings and Precautions (5.1)].

Combination of Protease Inhibitors
Atorvastatin AUC was significantly increased with concomitant administration of LIPITOR with several combinations of protease inhibitors [see Clinical Pharmacology (12.3)]. In patients taking tipranavir plus ritonavir or glecaprevir plus pibrentasvir, concomitant use of LIPITOR should be avoided. In patients taking lopinavir plus ritonavir, or simeprevir, use the lowest necessary LIPITOR dose. In patients taking saquinavir plus ritonavir, darunavir plus ritonavir, fosamprenavir, fosamprenavir plus ritonavir, or elbasvir plus grazoprevir, the dose of LIPITOR should not exceed 20 mg. In patients taking nefavir the dose of LIPITOR should not exceed 40 mg and close clinical monitoring is recommended [see Dosage and Administration (2.6) and Warnings and Precautions (5.1)].

7.2 Grapefruit Juice

Contains one or more components that inhibit CYP 3A4 and can increase plasma concentrations of atorvastatin, especially with excessive grapefruit juice consumption (>1.2 liters per day).

7.3 Cyclosporine

Atorvastatin is a substrate of the hepatic transporters. 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 LIPITOR 10 mg and cyclosporine 5.2 mg/kg/day compared to that of LIPITOR alone [see Clinical Pharmacology (12.3)]. Therefore, in patients taking cyclosporine, caution should be used when the LIPITOR dose exceeds 20 mg [see Dosage and Administration (2.6) and Warnings and Precautions (5.1)].

7.4 Glecaprevir and Pibrentasvir; Elbasvir and Grazoprevir

Concomitant administration of glecaprevir and pibrentasvir or elbasvir and grazoprevir may lead to increased plasma concentrations of atorvastatin and an increased risk of myopathy. Coadministration of glecaprevir and pibrentasvir with atorvastatin increase plasma concentrations of atorvastatin by 8.3-fold in dose comparisons of 180 mg and 300 mg, respectively, the human exposure at the maximum recommended human dose (MRHD) of 80 mg, based on body surface area (mg/m²). When multiple doses of LIPITOR and digoxin were co-administered, steady state plasma digoxin concentrations increased [see Clinical Pharmacology (12.3)]. Patients taking digoxin should be monitored appropriately.

7.5 Gemfibrozil

Due to an increased risk of myopathy/rhabdomyolysis when HMG-CoA reductase inhibitors are co-administered with gemfibrozil, concomitant administration of LIPITOR with gemfibrozil should be avoided [see Warnings and Precautions (5.1)].

7.6 Other Fibrate

Because it is known that the risk of skeletal muscle effects may be enhanced when LIPITOR is used in combination with niacin; a reduction in LIPITOR dosage should be considered in this setting [see Warnings and Precautions (5.1)].

7.7 Niacin

The risk of skeletal muscle effects may be enhanced when LIPITOR is used in combination with niacin; a reduction in LIPITOR dosage should be considered in this setting [see Warnings and Precautions (5.1)].

7.8 Rifampin or other Inducers of Cytochrome P450 3A4

Concomitant administration of LIPITOR with inducers of cytochrome P450 3A4 (e.g., efavirenz, rifampin) can lead to variable reductions in plasma concentrations of atorvastatin. Due to the dual interaction mechanism of rifampin, simultaneous co-administration of LIPITOR with rifampin is recommended, as delayed administration of LIPITOR after administration of rifampin has been associated with a significant reduction in atorvastatin plasma concentrations.

7.9 Digoxin

When multiple doses of LIPITOR and digoxin were co-administered, steady state plasma digoxin concentrations increased [see Clinical Pharmacology (12.3)]. Patients taking digoxin should be monitored appropriately.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

LIPITOR is contraindicated for use in pregnant women since safety in pregnant women has not been established and there is no apparent benefit of lipid lowering drugs during pregnancy. Because HMG-CoA reductase inhibitors decrease cholesterol synthesis and possibly the synthesis of other biologically active substances derived from cholesterol, LIPITOR may cause fetal harm when administered to a pregnant woman. LIPITOR should be discontinued as soon as pregnancy is recognized [see Contraindications (4)]. Limited published data on the use of atorvastatin is insufficient to determine a drug-associated risk of major congenital malformations or miscarriage. In animal reproduction studies in rats and rabbits there was no evidence of embryofetal toxicity or congenital malformations at doses up to 30 and 20 times, respectively, the human exposure at the maximum recommended human dose (MRHD) of 80 mg, based on body surface area (mg/m²). In rats administered atorvastatin during gestation and lactation, decreased postnatal growth and development was observed at doses ≥ 6 times the MRHD (see Data). The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively.

Data

Human Data

Limited published data on atorvastatin calcium from observational studies, meta-analyses and case reports have not shown an increased risk of major congenital malformations or miscarriage. Rare reports of congenital anomalies have been received following intrauterine exposure to other HMG-CoA reductase inhibitors. In a review of approximately 100 prospectively followed pregnancies in women exposed to simvastatin or lovastatin, the incidences of congenital anomalies, spontaneous abortions, and fetal deaths/stillbirths did not exceed what would be expected in the general population. The number of cases is too small to exclude a theoretical risk of other than minor birth defects. In 3017 women treated with atorvastatin, no congenital anomalies were reported. In a subsequent report of 3001 pregnancies, including 2079 exposed to atorvastatin in the first trimester, no congenital anomalies were reported.

Animal Data

Atorvastatin crosses the rat placenta and reaches a level in fetal liver equivalent to that of maternal plasma. Atorvastatin was administered to pregnant rats and rabbits during organogenesis at oral doses up to 300 mg/kg/day and 100 mg/kg/day, respectively. Atorvastatin was not teratogenic in rats at doses up to 300 mg/kg/day or in rabbits at doses up to 100 mg/kg/day. These doses resulted in multiples of about 30 times (rat) or 20 times (rabbit) the human exposure at the MRHD based on surface area (mg/m²). In rats, the maternally toxic dose of 300 mg/kg resulted in increased post-implantation loss and decreased fetal body weight. At the maternally toxic doses of 50 and 100 mg/kg/day in rabbits, there was increased post-implantation loss, and at 100 mg/kg/day fetal body weights were decreased. In a study in pregnant rats administered 20, 100, or 225 mg/kg/day from gestation day 7 through to lactation day 20 (weaning), there was decreased survival at birth, postnatal day 4, weaning, and post-weaning in pups of mothers dosed with 225 mg/kg/day; a dose at which maternal toxicity was observed. Atorvastatin body weight was decreased through postnatal day 21 at 100 mg/kg/day and through postnatal day 91 at 225 mg/kg/day; pinnae detachment and eye opening at 225 mg/kg/day. These doses correspond to 6 times (100 mg/kg) and 22 times (225 mg/kg) the human exposure at the MRHD, based on AUC.

8.2 Lactation

Risk Summary

LIPITOR use is contraindicated during breastfeeding [see Contraindications (4)]. There is no available information on the effects of the drug on the breastfed infant or the effects of the drug on milk production. It is not known whether atorvastatin is present in human milk, but it has been shown that another drug in the class passes into human milk and atorvastatin is present in rat milk. Because of the potential for serious adverse reactions in a breastfed infant, advise women that breastfeeding is not recommended during treatment with LIPITOR.

8.3 Females and Males of Reproductive Potential

Contraception

LIPITOR may cause fetal harm when administered to a pregnant woman. Advise females of reproductive potential to use effective contraception during treatment with LIPITOR [see Use in Specific Populations (8.1)].
8.4 Pediatric Use

Heterozygous Familial Hypercholesterolemia (HeFH)

The safety and effectiveness of LIPITOR have been established in pediatric patients, 10 years to 17 years of age, with HeFH as an adjunct to diet to reduce total cholesterol, LDL-C, and apo B levels when, after an adequate trial of diet therapy, the following are present:

- LDL-C ≥ 190 mg/dL, or
- LDL-C ≥ 160 mg/dL and
  - a positive family history of FH, or premature CVD in a first, or second-degree relative, or
  - two or more other CVD risk factors are present.

Use of LIPITOR for this indication is supported by evidence from [see Dosage and Administration (2.2), Adverse Reactions (6.1), Clinical Pharmacology (12.3), and Clinical Studies (14.6)].

A placebo-controlled clinical trial of 6 months duration in 187 boys and postmenarchial girls, 10 years to 17 years of age. Patients treated with 10 mg or 20 mg daily LIPITOR had an adverse reaction profile generally similar to that of patients treated with placebo. In this limited controlled study, there was no significant effect on growth or sexual maturation in boys or on menstrual cycle length in girls.

A three year open-label uncontrolled trial that included 163 pediatric patients 10 to 15 years of age with HeFH who were titrated to achieve a target LDL-C ˂ 130 mg/dL. The safety and efficacy of LIPITOR in lowering LDL-C appeared generally consistent with that observed for adult patients, despite limitations of the uncontrolled study design

Advise postmenarchal girls of contraception recommendations, if appropriate for the patient [see Use in Specific Populations (8.1), (8.3)].

The long-term efficacy of LIPITOR therapy initiated in childhood to reduce morbidity and mortality in adulthood has not been established.

The safety and efficacy of LIPITOR have not been established in pediatric patients younger than 10 years of age with HeFH.

Homozygous Familial Hypercholesterolemia (HoFH)

Clinical efficacy of LIPITOR with dosages up to 80 mg/day for 1 year was evaluated in an uncontrolled study of patients with HoFH including 8 pediatric patients [see Clinical Studies (14.5)].

8.5 Geriatric Use

Of the 39,828 patients who received LIPITOR in clinical studies, 15,813 (40%) were ≥65 years old and 2,800 (7%) were ≥75 years old. No overall differences in safety or effectiveness were observed between these subjects and younger subjects, and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older adults cannot be ruled out. Since advanced age (≥65 years) is a predisposing factor for myopathy, LIPITOR should be used with caution in the elderly.

8.6 Hepatic Impairment

Lipitor is contraindicated in patients with active liver disease which may include unexplained persistent elevations in hepatic transaminase levels [see Contraindications (4) and Clinical Pharmacology (12.3)].

10 OVERDOSAGE

There is no specific treatment for LIPITOR 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 LIPITOR clearance.

11 DESCRIPTION

LIPITOR is a synthetic lipid-lowering agent. Atorvastatin is an inhibitor of 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase. This enzyme catalyzes the conversion of HMG-CoA to mevalonate, a precursor of sterols, including cholesterol.

Atorvastatin calcium is a white to off-white crystalline powder that is insoluble in aqueous solutions of pH 4 and below. Atorvastatin calcium is very slightly soluble in distilled water, pH 7.4 phosphate buffer, and acetonitrile; slightly soluble in ethanol; and freely soluble in methanol.

LIPITOR Tablets for oral administration contain 10, 20, 40, or 80 mg of atorvastatin and the following inactive ingredients: calcium carbonate, USP; candelilla wax, FCC; croscarmellose sodium, NF; hydroxypropyl cellulose, NF; lactose monohydrate, NF; magnesium stearate, NF; microcrystalline cellulose, NF; Opadry White YS-1-7040 (hypromellose, polyethylene glycol, lac, titanium dioxide); polysorbate 80, NF; simethicone emulsion.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

LIPITOR 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 sterol, including cholesterol. In animal models, LIPITOR 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; LIPITOR also reduces LDL production and the number of LDL particles.

12.2 Pharmacodynamics

LIPITOR, 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. Drug dosage, rather than systemic drug concentration, correlates better with LDL-C reduction. Individualization of drug dosage should be based on therapeutic response [see Dosage and Administration (2)].

12.3 Pharmacokinetics

Absorption: LIPITOR is rapidly absorbed after oral administration; maximum plasma concentrations occur within 1 to 2 hours. Extent of absorption increases in proportion to LIPITOR 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 pre-systemic clearance in gastrointestinal mucosal mas 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 LIPITOR is given with or without food. Plasma LIPITOR 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 [see Use in Specific Populations (8.2)].

Distribution: Mean volume of distribution of LIPITOR is approximately 381 liters. LIPITOR 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, LIPITOR is likely to be secreted in human milk [see Contraindications (4) and Use in Specific Populations (8.2)].

Metabolism: LIPITOR 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 LIPITOR. Approximately 70% of circulating inhibitory activity for HMG-CoA reductase is attributed to active metabolites. In vitro studies suggest the importance of LIPITOR metabolism by cytochrome P450 3A4, consistent with increased plasma concentrations of LIPITOR in humans following co-administration with erythromycin, a known inhibitor of this isozyme [see Drug Interactions (7.1)]. In animals, the ortho-hydroxyl metabolite undergoes further glucuronidation.

Excretion: LIPITOR 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 LIPITOR 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 LIPITOR is recovered in urine following oral administration.

Specific Populations

Geriatric: Plasma concentrations of LIPITOR 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 drug in the elderly patient population compared to younger adults [see Use in Specific Populations (8.5)].

Pediatric: Apparent oral clearance of atorvastatin in pediatric subjects appeared similar to that of adults when scaled aometrically by body weight as the body weight was the only significant covariate in atorvastatin population PK model with data including pediatric HeFH patients (ages 10 years to 17 years of age with HeFH who were titrated to achieve a target LDL-C < 130 mg/dL. The safety and efficacy of LIPITOR in lowering LDL-C appeared generally consistent with that observed for adult patients, despite limitations of the uncontrolled study design

Advise postmenarchal girls of contraception recommendations, if appropriate for the patient [see Use in Specific Populations (8.1), (8.3)].

The long-term efficacy of LIPITOR therapy initiated in childhood to reduce morbidity and mortality in adulthood has not been established.

The safety and efficacy of LIPITOR have not been established in pediatric patients younger than 10 years of age with HeFH.
### TABLE 4. Effect of Co-administered Drugs on the Pharmacokinetics of Atorvastatin

<table>
<thead>
<tr>
<th>Co-administered drug and dosing regimen</th>
<th>Atorvastatin Dose (mg)</th>
<th>Ratio of AUC</th>
<th>Ratio of Cmax</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clopipramine 5.2 mg/kg/day,</strong> stable dose</td>
<td>10 mg OD* for 28 days</td>
<td>8.69</td>
<td>10.66</td>
</tr>
<tr>
<td><em><em>Tipranavir 500 mg BID</em>/ritonavir 200 mg BID</em>*, 7 days</td>
<td>10 mg, SD†</td>
<td>9.36</td>
<td>8.58</td>
</tr>
<tr>
<td><strong>Gliclazide 400 mg QD/pantoprazol 120 mg QD</strong>, 7 days</td>
<td>10 mg OD* for 7 days</td>
<td>8.28</td>
<td>22.00</td>
</tr>
<tr>
<td><strong>Telaprevir 750 mg q8h, 10 days</strong></td>
<td>20 mg, SD†</td>
<td>7.88</td>
<td>10.60</td>
</tr>
<tr>
<td><strong>Sorafenib 400 mg BID</strong>, 15 days</td>
<td>40 mg QD* for 4 days</td>
<td>3.93</td>
<td>4.31</td>
</tr>
<tr>
<td><strong>Ebsapvir 50 mg OD/graftoprevir 200 QD</strong>, 13 days</td>
<td>10 mg SD*</td>
<td>1.94</td>
<td>4.34</td>
</tr>
<tr>
<td><strong>Simprevir 150 mg QD</strong>, 10 days</td>
<td>40 mg SD†</td>
<td>2.12</td>
<td>1.70</td>
</tr>
<tr>
<td><strong>Clobertomycin 500 mg QD</strong>, 9 days</td>
<td>80 mg QD* for 8 days</td>
<td>4.54</td>
<td>5.38</td>
</tr>
<tr>
<td><strong>Darunavir 500 mg BID/ritonavir 100 mg BID</strong>, 9 days</td>
<td>10 mg OD* for 4 days</td>
<td>3.45</td>
<td>2.25</td>
</tr>
<tr>
<td><strong>Itraconazole 200 mg QD</strong>, 4 days</td>
<td>40 mg SD†</td>
<td>3.32</td>
<td>1.20</td>
</tr>
<tr>
<td><strong>Fosamprenavir 700 mg BID/ritonavir 100 mg BID</strong>, 14 days</td>
<td>10 mg OD* for 4 days</td>
<td>2.53</td>
<td>2.84</td>
</tr>
<tr>
<td><strong>Fosamprenavir 1400 mg BID</strong>, 14 days</td>
<td>10 mg OD* for 4 days</td>
<td>2.30</td>
<td>4.04</td>
</tr>
<tr>
<td><strong>Nelfinavir 1250 mg BID</strong>, 14 days</td>
<td>10 mg OD* for 28 days</td>
<td>1.74</td>
<td>2.22</td>
</tr>
<tr>
<td><strong>Grapefruit Juice, 240 mL QDa</strong></td>
<td>40 mg, SD‡</td>
<td>1.37</td>
<td>1.16</td>
</tr>
<tr>
<td><strong>Diltiazem 240 mg QD</strong>, 28 days</td>
<td>40 mg, SD†</td>
<td>1.51</td>
<td>1.00</td>
</tr>
<tr>
<td><strong>Erythromycin 500 mg QD</strong>, 7 days</td>
<td>10 mg, SD§</td>
<td>1.33</td>
<td>1.38</td>
</tr>
<tr>
<td><strong>Amlodipine 10 mg, single dose</strong></td>
<td>0 mg, SD†</td>
<td>1.18</td>
<td>0.91</td>
</tr>
<tr>
<td><strong>Clarithromycin 500 mg QDa, 2 weeks</strong></td>
<td>10 mg OD* for 2 weeks</td>
<td>1.00</td>
<td>0.89</td>
</tr>
<tr>
<td><strong>Colestipol 10 g BID</strong>, 24 weeks</td>
<td>40 mg QD* for 8 weeks</td>
<td>NA</td>
<td>0.74**</td>
</tr>
<tr>
<td><strong>Maluix TCI® 30 mL QID</strong>, 17 days</td>
<td>10 mg OD* for 15 days</td>
<td>0.68</td>
<td>0.67</td>
</tr>
<tr>
<td><strong>Etilizav 600 mg QD</strong>, 14 days</td>
<td>10 mg OD* for 3 days</td>
<td>0.59</td>
<td>1.01</td>
</tr>
<tr>
<td><strong>Rifaxam 600 mg QD</strong>, 7 days (co-administered)</td>
<td>40 mg SD†</td>
<td>1.12</td>
<td>2.90</td>
</tr>
<tr>
<td><strong>Rifaxam 600 mg QD</strong>, 5 days (doses separated)</td>
<td>40 mg SD†</td>
<td>0.20</td>
<td>0.60</td>
</tr>
<tr>
<td><strong>Gemfibrozil 600 mg BID</strong>, 7 days</td>
<td>40 mg SD†</td>
<td>1.35</td>
<td>1.00</td>
</tr>
<tr>
<td><strong>Fenofibrate 160 mg QD</strong>, 7 days</td>
<td>40 mg SD†</td>
<td>1.03</td>
<td>1.02</td>
</tr>
<tr>
<td><strong>Bocrepavir 600 mg TID</strong>, 7 days</td>
<td>40 mg SD†</td>
<td>2.32</td>
<td>2.66</td>
</tr>
</tbody>
</table>

* Represents ratio of treatments (co-administered drug plus atorvastatin vs. atorvastatin alone).
† See Sections 5.1 and 7 for clinical significance.
‡ Greater increases in AUC (ratio of AUC up to 2.5) and/or Cmax (ratio of Cmax up to 1.71) have been reported with excessive grapefruit consumption (> 750 mL - 1.2 liters per day).
§ Ratio based on a single sample taken 8-16 h post dose.
* Due to the dual interaction mechanism of rifampin, simultaneous co-administration of atorvastatin with rifampin is recommended, as delayed administration of atorvastatin after administration of rifampin has been associated with a significant reduction in atorvastatin plasma concentrations.
† The dose of saquinavir plus ritonavir in this study is not the clinically used dose. The increase in atorvastatin exposure when used clinically is likely to be higher than what was observed in this study. Therefore, caution should be applied and the lowest dose necessary should be used.
‡ Once daily
§ Twice daily
§ Single dose
* Three times daily
§ Four times daily
§ Every 8 hours

### TABLE 5. Effect of Atorvastatin on the Pharmacokinetics of Co-administered Drugs

<table>
<thead>
<tr>
<th>Atorvastatin Drug/Dose (mg)</th>
<th>Co-administered drug and dosing regimen</th>
<th>Ratio of AUC</th>
<th>Ratio of Cmax</th>
</tr>
</thead>
<tbody>
<tr>
<td>80 mg OD* for 15 days</td>
<td>Antipyrine, 600 mg SD†</td>
<td>1.03</td>
<td>0.89</td>
</tr>
<tr>
<td>80 mg OD* for 10 days</td>
<td>* Digoxin 0.25 mg OD; 20 days</td>
<td>1.15</td>
<td>1.20</td>
</tr>
<tr>
<td>40 mg OD* for 22 days</td>
<td>Oral contraceptive OD; 2 months - norethindrone 1 mg - ethinyl estradiol 35 μg</td>
<td>1.28</td>
<td>1.23</td>
</tr>
<tr>
<td>10 mg, SD†</td>
<td>Tipranavir 500 mg BID/ritonavir 200 mg BID**, 7 days</td>
<td>1.08</td>
<td>0.96</td>
</tr>
<tr>
<td>10 mg OD* for 4 days</td>
<td>Fosamprenavir 1400 mg BID**, 14 days</td>
<td>0.73</td>
<td>0.82</td>
</tr>
<tr>
<td>10 mg OD* for 4 days</td>
<td>Fosamprenavir 700 mg BID/ritonavir 100 mg BID**, 14 days</td>
<td>0.99</td>
<td>0.94</td>
</tr>
</tbody>
</table>

* See Section 7 for clinical significance.
† Once daily
§ Twice daily
§ Single dose

### Figure 1: Effect of LIPITOR 10 mg/day on Cumulative Incidence of Non-Fatal Myocardial Infarction or Coronary Heart Disease Death (in ASCOT-LLA)

LIPITOR also significantly decreased the relative risk for revascularization procedures by 42% (incidences of 1.4% for LIPITOR and 2.5% for placebo). Although the reduction of fatal and non-fatal strokes did not reach a pre-defined significance level (p=0.01), a favorable trend was observed with a 26% relative risk reduction (incidences of 1.7% for LIPITOR and 2.3% for placebo). There was no significant difference between the treatment groups for death due to cardiovascular causes (p=0.51) or noncardiovascular causes (p=0.17).

In the Collaborative Atorvastatin Diabetes Study (CARDS), the effect of LIPITOR on cardiovascular disease (CVD) endpoints was assessed in 2838 subjects (94% white, 66% male), ages 40-75 with type 2 diabetes based on WHO criteria, without prior history of cardiovascular disease and with LDL ≤ 160 mg/dL and TG ≤ 160 mg/dL. In addition to diabetes, subjects had 1 or more of the following risk factors: current smoking (23%), hypertension (80%), retinopathy (30%), or microalbuminuria (9%) or macroalbuminuria (3%). No subjects on hemodialysis were enrolled in the study. In this multicenter, placebo-controlled, double-blind clinical trial, subjects were randomly allocated to either LIPITOR 10 mg daily (n=5168) or placebo (n=5137), using a covariate adaptive method which took into account the distribution of nine baseline characteristics of patients already enrolled and minimized the imbalance of those characteristics across the groups. Patients were followed for a median duration of 3.3 years.

The effect of 10 mg/day of LIPITOR on lipid levels was similar to that seen in previous clinical trials.

LIPITOR significantly reduced the rate of coronary events [either fatal coronary heart disease (46 events in the placebo group vs. 40 events in the LIPITOR group) or non-fatal MI (108 events in the placebo group vs. 60 events in the LIPITOR group) with a relative risk reduction of 36% [based on incidences of 1.9% for LIPITOR vs. 3.0% for placebo], p=0.0005 (see Figure 1)]. The risk reduction was consistent regardless of age, smoking status, obesity, or presence of renal dysfunction. The effect of LIPITOR was seen regardless of baseline LDL levels. Due to the small number of events, results for women were inconclusive.
Baseline characteristics of subjects were: mean age of 62 years, mean HbA1c 7.7%, median LDL-C 120 mg/dL; median TC 207 mg/dL; median TG 151 mg/dL; median HDL-C 52 mg/dL.

The effect of LIPITOR 10 mg/day on lipid levels was similar to that seen in previous clinical trials. LIPITOR significantly reduced the rate of major cardiovascular events (primary endpoint events) (83 events in the LIPITOR group vs. 127 events in the placebo group) with a relative risk reduction of 37%, HR 0.63, 95% CI (0.53, 0.74) (p=0.001) (see Figure 2). An effect of LIPITOR was seen regardless of age, sex, or baseline lipid levels.

LIPITOR significantly reduced the risk of death by 48% (21 events in the LIPITOR group vs. 39 events in the placebo group), HR 0.58, 95% CI (0.39, 0.86) (p=0.007). There was no significant difference between the treatment groups for angina, revascularization procedures, and acute CHD death.

There were 61 deaths in the LIPITOR group vs. 82 deaths in the placebo group (HR 0.73, p=0.059).

**Components of the Primary Endpoint**

- CHD death
- Non-fatal, non-procedure related MI
- Non-fatal, non-procedure related MI
- Non-cardiac death
- Stroke (fatal and non-fatal)

**SECONDARY ENDPOINTS**

- First MI with hospitalization
- First MI with angiography
- First MI with CABG or other coronary revascularization procedure
- All-cause mortality

**Components of All-Cause Mortality**

- Cardiovascular death
- Noncardiovascular death
- Cancer death
- Other non-cardiac death
- Suicide, homicide, and other traumatic or non-traumatic non-CV death

**Secondary endpoints not included in primary endpoint**

- CHF=congestive heart failure; CI=myocardial infarction; MI=myocardial infarction; CABG=coronary artery bypass graft

**Confidence intervals for the Secondary Endpoints were not adjusted for multiple comparisons**

Of the events that comprised the primary efficacy endpoint, treatment with LIPITOR 80 mg/day significantly reduced the rate of non-fatal, non-procedure related MI and fatal and non-fatal stroke, but not CHD death or resuscitated cardiac arrest (Table 6). Of the predefined secondary endpoints, treatment with LIPITOR 80 mg/day significantly reduced the rate of coronary revascularization, angina, and hospitalization for heart failure, but not peripheral vascular disease. The reduction in the rate of CHF with hospitalization was only observed in the 8% of patients with a prior history of CHF.

There was no significant difference between the treatment groups for all-cause mortality (Table 6). The proportions of subjects who experienced cardiovascular death, including the components of CHD death and fatal stroke, were numerically smaller in the LIPITOR 80 mg group than in the LIPITOR 10 mg treatment group. The proportions of subjects who experienced noncardiovascular death were numerically larger in the LIPITOR 80 mg group than in the LIPITOR 10 mg treatment group.

In the Incremental Decrease in Endpoints Through Aggressive Lipid Lowering Study (IDEAL), treatment with LIPITOR 80 mg/day was compared to treatment with simvastatin 20–40 mg/day in 8,888 subjects up to 80 years of age with a history of CHD to assess whether reduction in CV risk could be achieved. Patients were mainly male (81%), white (99%) with an average age of 61.7 years, and an average LDL-C of 121.5 mg/dL at randomization; 76% were on statin therapy. In this prospective, randomized, open-label, blinded endpoint (PROBE) trial with no run-in period, subjects were followed for a median duration of 4.8 years. The mean LDL-C, TC, TG, and HDL cholesterol levels at 12 weeks were 73, 145, 128, 98, and 47 mg/dL during treatment with 80 mg of LIPITOR and 99, 177, 152, 129, and 48 mg/dL during treatment with 10 mg of LIPITOR.

Treatment with LIPITOR 80 mg/day significantly reduced the rate of MACE (434 events in the 80 mg/day group vs. 548 events in the 10 mg/day group) with a relative risk reduction of 22%, HR 0.78, 95% CI (0.69, 0.89), p=0.0002 (see Figure 3 and Table 6). The overall risk reduction was consistent regardless of age (≥65 years) or gender.

**TABLE 6. Overview of Efficacy Results in TNT**

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Atorvastatin 10 mg (N=5006)</th>
<th>Atorvastatin 80 mg (N=4995)</th>
<th>HR* (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PRIMARY ENDPOINT</td>
<td>n (%)</td>
<td>n (%)</td>
<td>0.78 (0.69, 0.89)</td>
</tr>
<tr>
<td>First major cardiovascular event</td>
<td>548 (10.9)</td>
<td>434 (8.7)</td>
<td>0.78 (0.69, 0.89)</td>
</tr>
<tr>
<td>Components of the Primary Endpoint</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CHD death</td>
<td>127 (2.5)</td>
<td>101 (2.0)</td>
<td>0.80 (0.61, 1.03)</td>
</tr>
<tr>
<td>Non-fatal, non-procedure related MI</td>
<td>308 (6.2)</td>
<td>243 (4.9)</td>
<td>0.78 (0.66, 0.93)</td>
</tr>
<tr>
<td>Resuscitated cardiac arrest</td>
<td>26 (0.5)</td>
<td>25 (0.5)</td>
<td>0.96 (0.56, 1.67)</td>
</tr>
<tr>
<td>Stroke (fatal and non-fatal)</td>
<td>155 (3.1)</td>
<td>117 (2.3)</td>
<td>0.75 (0.59, 0.96)</td>
</tr>
</tbody>
</table>

**SECONDARY ENDPOINTS**

- First MI with hospitalization
- First MI with angiography
- First MI with CABG or other coronary revascularization procedure
- All-cause mortality

**Components of All-Cause Mortality**

- Cardiovascular death
- Noncardiovascular death
- Cancer death
- Other non-cardiac death
- Suicide, homicide, and other traumatic or non-traumatic non-CV death

**Secondary endpoints not included in primary endpoint**

- CHF=congestive heart failure; CI=myocardial infarction; MI=myocardial infarction; CABG=coronary artery bypass graft

**Confidence intervals for the Secondary Endpoints were not adjusted for multiple comparisons**

LIPITOR is effective in a wide variety of patient populations with hyperlipidemia, with and without hypertriglyceridemia, in men and women, and in the elderly.
In two multicenter, placebo-controlled, dose-response studies in patients with hyperlipidemia, LIPITOR given as a single dose over 6 weeks, significantly reduced total-C, LDL-C, apo B, and TG. (Pooled results are provided in Table 7.)

### Table 7. Dose Response in Patients With Primary Hyperlipidemia (Adjusted Mean % Change From Baseline)*

<table>
<thead>
<tr>
<th>Dose</th>
<th>N</th>
<th>TC</th>
<th>LDL-C</th>
<th>Apo B</th>
<th>TG</th>
<th>HDL-C</th>
<th>Non-HDL-C/ HDL-C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>21</td>
<td>4</td>
<td>4</td>
<td>3</td>
<td>10</td>
<td>3</td>
<td>-7</td>
</tr>
<tr>
<td>10</td>
<td>22</td>
<td>-29</td>
<td>-39</td>
<td>-32</td>
<td>-19</td>
<td>6</td>
<td>-34</td>
</tr>
<tr>
<td>20</td>
<td>20</td>
<td>-33</td>
<td>-43</td>
<td>-35</td>
<td>-26</td>
<td>9</td>
<td>-41</td>
</tr>
<tr>
<td>40</td>
<td>21</td>
<td>-37</td>
<td>-50</td>
<td>-42</td>
<td>-29</td>
<td>6</td>
<td>-45</td>
</tr>
<tr>
<td>80</td>
<td>23</td>
<td>-43</td>
<td>-60</td>
<td>-50</td>
<td>-37</td>
<td>5</td>
<td>-53</td>
</tr>
</tbody>
</table>

*Results are pooled from 2 dose-response studies.

In patients with Fredrickson Types IIa and IIb hyperlipoproteinemia pooled from 24 controlled trials, the median (25th and 75th percentile) percent changes from baseline in HDL-C for LIPITOR 10, 20, 40, and 80 mg were 6.4 (-1.4, 14), 8.7 (0, 17), 7.8 (0, 16), and 5.1 (-2.7, 15), respectively. Additionally, analysis of the pooled data demonstrated consistent and significant decreases in total-C, LDL-C, TG, total-C/HDL-C, and LDL-C/HDL-C.

In three multicenter, double-blind studies in patients with hyperlipidemia, LIPITOR was compared to other statins. After randomization, patients were treated for 16 weeks with either LIPITOR 10 mg per day or a fixed dose of the comparator agent (Table 8).

### Table 8. Mean Percentage Change From Baseline at Endpoint (Double-Blind, Randomized, Active-Controlled Trials)

<table>
<thead>
<tr>
<th>Treatment (Daily Dose)</th>
<th>N</th>
<th>Total-C</th>
<th>LDL-C</th>
<th>Apo B</th>
<th>TG</th>
<th>HDL-C</th>
<th>Non-HDL-C/ HDL-C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo 21 mg</td>
<td>47</td>
<td>-1.5</td>
<td>-0.4</td>
<td>-1.9</td>
<td>1.0</td>
<td>0.7</td>
<td>-34.0</td>
</tr>
<tr>
<td>LIPITOR 10 mg</td>
<td>47</td>
<td>-1.5</td>
<td>-0.4</td>
<td>-1.9</td>
<td>1.0</td>
<td>0.7</td>
<td>-34.0</td>
</tr>
</tbody>
</table>

1. A negative value for the 95% CI for the difference between treatments favors LIPITOR for all except HDL-C, for which a positive value favors LIPITOR. If the range does not include 0, this indicates a statistically significant difference.

2. Significantly different from lovastatin, ANCOVA, p < 0.05
3. Significantly different from pravastatin, ANCOVA, p < 0.05
4. Significantly different from simvastatin, ANCOVA, p < 0.05

The impact on clinical outcomes of the differences in lipid-altering effects between treatments shown in Table 8 is shown in the table below (Table 9). For the LIPITOR-treated patients, median (min, max) baseline TG level was 209 (50–1502). The mean achieved LDL-C value was 130.7 mg/dL (range: 70.0–242.0 mg/dL) in the LIPITOR group compared to 228.5 mg/dL (range: 152.0–385.0 mg/dL) in the placebo group during the 26-week double-blind phase.

### Table 9. Combined Patients With Elevated TG: Median (min, max) Percentage Change From Baseline

<table>
<thead>
<tr>
<th></th>
<th>Placebo (N = 12)</th>
<th>LIPITOR 10 mg (N = 37)</th>
<th>LIPITOR 20 mg (N = 15)</th>
<th>LIPITOR 80 mg (N = 14)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Triglycerides</td>
<td>-1.24 (-36.6, 82.7)</td>
<td>-41.0 (-76.2, 49.4)</td>
<td>-38.7 (-62.7, 23.5)</td>
<td>-51.8 (-82.8, 41.3)</td>
</tr>
<tr>
<td>Total-C</td>
<td>-2.3 (-15.5, 24.4)</td>
<td>-28.2 (-44.9, 4.8)</td>
<td>-34.9 (-49.6, -15.2)</td>
<td>-44.4 (-63.5, -3.8)</td>
</tr>
<tr>
<td>LDL-C</td>
<td>3.6 (-31.3, 31.6)</td>
<td>-26.5 (-57.7, 9.8)</td>
<td>-30.4 (-53.9, 0.3)</td>
<td>-40.5 (-60.6, -13.0)</td>
</tr>
<tr>
<td>HDL-C</td>
<td>3.8 (-18.6, 13.4)</td>
<td>13.8 (-9.7, 61.5)</td>
<td>11.0 (-3.2, 25.2)</td>
<td>7.5 (10.8, 37.2)</td>
</tr>
<tr>
<td>VLDL-C</td>
<td>-1.0 (-31.9, 53.2)</td>
<td>-48.8 (-85.8, 57.3)</td>
<td>-44.6 (-62.2, -10.8)</td>
<td>-62.0 (-88.2, 37.6)</td>
</tr>
<tr>
<td>non-HDL-C</td>
<td>-2.8 (-17.6, 30.0)</td>
<td>-33.0 (-52.1, -13.3)</td>
<td>-42.7 (-53.7, -17.4)</td>
<td>-51.5 (-72.9, -4.3)</td>
</tr>
</tbody>
</table>

14.4 Homozygous Familial Hypercholesterolemia

In a study without a concurrent control group, 29 patients ages 6 years to 37 years with HeFH received maximum daily doeses of 20 to 80 mg of LIPITOR. The mean LDL-C reduction in this study was 18%. Twenty-five patients had a reduction in LDL-C of 40% or more; 21 patients were 63–80% LDL-C responders. The mean LDL-C reduction was 21.8 mg/dL (range: 135.8–365.0 mg/dL) in the LIPITOR group compared to 230.0 mg/dL (range: 160.0–324.5 mg/dL) in the placebo group. The dosage of LIPITOR (once daily) was 10 mg for the first 4 weeks and up titrated to 20 mg if the LDL-C level was > 130 mg/dL. The number of LIPITOR-treated patients who required up titration to 20 mg after Week 4 during the double-blind phase was 78 (55.7%).

LIPITOR significantly decreased plasma levels of total-C, LDL-C, triglycerides, and apolipoprotein B during the 26-week double-blind phase (see Table 11).

14.6 Heterozygous Familial Hypercholesterolemia in Pediatric Patients

In a double-blind, placebo-controlled study followed by an open-label phase, 187 boys and post-menarchal girls 10 years to 17 years of age (mean age 14.1 years) with heterozygous familial hypercholesterolemia (HeFH) or severe hypercholesterolemia, were randomized to LIPITOR (n=140) or placebo (n=47) for 26 weeks and then all received LIPITOR for 26 weeks. Inclusion in the study required 1) a baseline LDL-C level > 190 mg/dL or 2) a baseline LDL-C level > 160 mg/dL and positive family history of FH or documented premature coronary disease in a first or second-degree relative. The mean baseline LDL-C value was 218.6 mg/dL (range: 138.5–385.0 mg/dL) in the LIPITOR group compared to 230.0 mg/dL (range: 160.0–324.5 mg/dL) in the placebo group. The dosage of LIPITOR (once daily) was 10 mg for the first 4 weeks and up titrated to 20 mg if the LDL-C level was > 130 mg/dL. The number of LIPITOR-treated patients who required up titration to 20 mg after Week 4 during the double-blind phase was 78 (55.7%).

The long-term efficacy of LIPITOR therapy in childhood to reduce morbidity and mortality in adulthood has not been established.

16 HOW SUPPLIED/STORAGE AND HANDLING

10 mg tablets (10 mg of atorvastatin): coded “PD 155” on one side and “10” on the other.

NDC 0071-0155-23 bottles of 90
NDC 0071-0155-34 bottles of 5000
NDC 0071-0155-40 10 x 10 unit dose blisters
NDC 0071-0155-10 bottles of 1000

20 mg tablets (20 mg of atorvastatin): coded “PD 156” on one side and “20” on the other.

NDC 0071-0156-23 bottles of 90
NDC 0071-0156-40 10 x 10 unit dose blisters
NDC 0071-0156-50 bottles of 2000
NDC 0071-0156-100 10 x 10 unit dose blisters

40 mg tablets (40 mg of atorvastatin): coded “PD 157” on one side and “40” on the other.

NDC 0071-0157-23 bottles of 90
NDC 0071-0157-34 bottles of 5000
NDC 0071-0157-40 10 x 10 unit dose blisters
NDC 0071-0157-50 bottles of 2000
NDC 0071-0157-100 10 x 10 unit dose blisters

80 mg tablets (80 mg of atorvastatin): coded “PD 158” on one side and “80” on the other.

NDC 0071-0158-23 bottles of 90
NDC 0071-0158-34 bottles of 5000
NDC 0071-0158-40 10 x 10 unit dose blisters
NDC 0071-0158-50 bottles of 2000
NDC 0071-0158-100 10 x 8 unit dose blisters

Storage

Store at controlled room temperature 20 - 25°C (68 - 77°F) [see USP].
17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Patient Information).

Patients taking LIPTOR should be advised that cholesterol is a chronic condition and they should adhere to their medication along with their National Cholesterol Education Program (NCEP)-recommended diet, a regular exercise program as appropriate, and periodic testing of a fasting lipid panel to determine goal attainment.

Patients should be advised about substances they should not take concomitantly with atorvastatin [see Warnings and Precautions (5.1)]. Patients should also be advised to inform other healthcare professionals prescribing a new medication that they are taking LIPTOR.

17.1 Muscle Pain

All patients starting therapy with LIPTOR should be advised of the risk of myopathy and told to report promptly any unexplained muscle pain, tenderness, or weakness particularly if accompanied by malaise or fever or if these muscle signs or symptoms persist after discontinuing LIPTOR. The risk of this occurring is increased when taking certain types of medication or consuming larger quantities (>1 liter) of grapefruit juice. They should discuss all medication, both prescription and over the counter, with their healthcare professional.

17.2 Liver Enzymes

It is recommended that liver enzyme tests be performed before the initiation of LIPTOR and if signs or symptoms of liver injury occur. All patients treated with LIPTOR should be advised to report promptly any symptoms that may indicate liver injury, including fatigue, anorexia, right upper abdominal discomfort, dark urine, or jaundice.

17.3 Embryofetal Toxicity

Advise females of reproductive potential of the risk to a fetus, to use effective contraception during treatment and to inform their healthcare provider of a known or suspected pregnancy [see Contraindications (4) and Use in Specific Populations (8.1, 8.3)].

17.4 Lactation

Advise women not to breastfeed during treatment with LIPTOR [see Contraindications (4) and Use in Specific Populations (8.2)].

This product's label may have been updated. For current full prescribing information, please visit www.pfizer.com.
Tell your doctor if you:
- age, smoking, high blood pressure, low HDL-C, heart disease in the family.
- eye problems, kidney problems, smoking, or high blood pressure.
- diet changes and exercise. LIPITOR starts to work in about 2 weeks.

What is Cholesterol?
Cholesterol and triglycerides are fats that are made in your body. They are also found in foods. You need some cholesterol for good health, but too much is not good for you. Cholesterol and triglycerides can clog your blood vessels. It is especially important to lower your cholesterol if you have heart disease, smoke, have diabetes or high blood pressure, are older, or if heart disease starts early in your family.

Who Should Not Take LIPITOR?
Do not take LIPITOR if you:
- are pregnant or think you may be pregnant, or are planning to become pregnant. LIPITOR may harm your unborn baby. If you get pregnant, stop taking LIPITOR and call your doctor right away.
- are breast feeding. LIPITOR can pass into your breast milk and may harm your baby.
- have liver problems.
- are allergic to LIPITOR or any of its ingredients. The active ingredient is atorvastatin. See the end of this leaflet for a complete list of ingredients in LIPITOR.
- have not been established in children under 10 years of age.

Before You Start LIPITOR
Tell your doctor if you:
- have muscle aches or weakness
- drink more than 2 glasses of alcohol daily
- have diabetes
- have a thyroid problem
- have kidney problems

Some medicines should not be taken with LIPITOR. Tell your doctor about all the medicines you take, including prescription and non-prescription medicines, vitamins, and herbal supplements. LIPITOR and certain other medicines can interact causing serious side effects. Especially tell your doctor if you take medicines for:
- your immune system
- cholesterol
- infections
- birth control
- heart failure
- HIV or AIDS
- hepatitis C virus

Know all the medicines you take. Keep a list of them with you to show your doctor and pharmacist.

How Should I Take LIPITOR?
Do not change your dose or stop LIPITOR without talking to your doctor. Your doctor may do blood tests to check your cholesterol levels during your treatment with LIPITOR. Your dose of LIPITOR may be changed based on these blood test results.

Take LIPITOR each day at any time of day at about the same time each day. LIPITOR can be taken with or without food.

Don’t break LIPITOR tablets before taking.

Your doctor should start you on a low-fat diet before giving you LIPITOR. Stay on this low-fat diet when you take LIPITOR.

If you miss a dose of LIPITOR, take it as soon as you remember. Do not take LIPITOR if it has been more than 12 hours since you missed your last dose. Wait and take the next dose at your regular time. Do not take 2 doses of LIPITOR at the same time.

If you take too much LIPITOR or overdose, call your doctor or Poison Control Center right away. Or go to the nearest emergency room.

What Should I Avoid While Taking LIPITOR?
Talk to your doctor before you start any new medicines. This includes prescription and non-prescription medicines, vitamins, and herbal supplements. LIPITOR and certain other medicines can interact causing serious side effects.

Do not get pregnant. If you get pregnant, stop taking LIPITOR right away and call your doctor.

What are the Possible Side Effects of LIPITOR?
LIPITOR can cause serious side effects. These side effects have happened only to a small number of people. Your doctor can monitor you for them. These side effects usually go away if your dose is lowered or LIPITOR is stopped. These serious side effects include:
- Muscle problems. LIPITOR can cause serious muscle problems that can lead to kidney problems, including kidney failure. You have a higher chance for muscle problems if you are taking certain other medicines with LIPITOR.
- Liver problems. Your doctor should do blood tests to check your liver before you start taking LIPITOR and if you have symptoms of liver problems while you take LIPITOR. Call your doctor right away if you have the following symptoms of liver problems:
  - feel tired or weak
  - loss of appetite
  - upper belly pain
  - dark amber colored urine
  - yellowing of your skin or the whites of your eyes

Call your doctor right away if you have:
- muscle problems like weakness, tenderness, or pain that happen without a good reason, especially if you also have a fever or feel more tired than usual. This may be an early sign of a rare muscle problem.
- muscle problems that do not go away even after your doctor has advised you to stop taking LIPITOR. Your doctor may do further tests to diagnose the cause of your muscle problems.
- allergic reactions including swelling of the face, lips, tongue, and/or throat that may cause difficulty in breathing or swallowing which may require treatment right away.
- nausea and vomiting.
- passing brown or dark-colored urine.
- you feel more tired than usual.
- your skin and whites of your eyes get yellow.
- stomach pain.
- allergic skin reactions.

In clinical studies, patients reported the following common side effects while taking LIPITOR: diarrhea, upset stomach, muscle and joint pain, and alterations in some laboratory blood tests.

The following additional side effects have been reported with LIPITOR: tiredness, tendon problems, memory loss, and confusion.

Talk to your doctor or pharmacist if you have side effects that bother you or that will not go away. These are not all the side effects of LIPITOR.

Ask your doctor or pharmacist for a complete list.

How do I store LIPITOR?
- Store LIPITOR at room temperature, 68 to 77°F (20 to 25°C).
- Do not keep medicine that is out of date or that you no longer need.
- Keep LIPITOR and all medicines out of the reach of children. Be sure that if you throw medicine away, it is out of the reach of children.

General Information About LIPITOR
Medicines are sometimes prescribed for conditions that are not mentioned in patient information leaflets. Do not use LIPITOR for a condition for which it was not prescribed. Do not give LIPITOR to other people, even if they have the same problem you have. It may harm them.

This leaflet summarizes the most important information about LIPITOR. If you would like more information, talk with your doctor. You can ask your doctor or pharmacist for information about LIPITOR that is written for health professionals. Or you can go to the LIPITOR website at www.lipitor.com.

What are the Ingredients in LIPITOR?
Active Ingredient: atorvastatin calcium
Inactive Ingredients: calcium carbonate, USP; candellila wax, FCC; croscarmellose sodium, NF; hydroxypropyl cellulose, NF; lactose monohydrate, NF; magnesium stearate, NF; microcrystalline cellulose, NF; Opadry White YS-1–7040 (hypromellose, polyethylene glycol, talc, titanium dioxide); polysorbate 80, NF; simethicone emulsion.