Learn what your cholesterol levels actually mean, and how you may save money on your prescription each month with the LIPTOR Savings Program.

IMPORTANT SAFETY INFORMATION
LIPTOR® (atorvastatin calcium) tablets are not for everyone, including anyone who has previously had an allergic reaction to LIPTOR. 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 LIPTOR and call your doctor right away.

Please see additional Important Safety Information continued on the following pages and the full Prescribing and Patient Information for LIPTOR attached.
Understanding Cholesterol

Cholesterol is a waxy, fat-like substance produced by your body and found in your bloodstream. Your body makes all the cholesterol it needs, but it can also be found in the foods you eat. Foods high in saturated fats, trans fats, and cholesterol may raise your blood cholesterol level. Having too much cholesterol in your blood may lead to an increased risk for heart disease and stroke in certain people.

There are 2 main types of cholesterol:

- **High-density lipoprotein cholesterol (HDL-C):** known as the "good" cholesterol, HDL-C carries cholesterol from other parts of the body to the liver for removal. Unlike other cholesterol levels, the higher your HDL cholesterol, the better.

- **Low-density lipoprotein cholesterol (LDL-C):** known as the "bad" cholesterol, LDL-C in high levels can deposit in the walls of the arteries, which are blood vessels that carry blood from your heart to your body.

**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).

**IMPORTANT SAFETY INFORMATION (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.

*Please see additional Important Safety Information continued on the following pages and the full Prescribing and Patient Information for LIPITOR attached.*
Understanding Your Numbers*†

Knowing what your cholesterol levels mean may help play a role in keeping your heart healthy. Your test results will show your cholesterol levels in milligrams per deciliter of blood (mg/dL). Your doctor will assess these numbers along with other risk factors such as age, family history, smoking, and high blood pressure, as well as your clinical history.

### Total cholesterol levels

<table>
<thead>
<tr>
<th>Level</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;200 mg/dL</td>
<td>Desirable</td>
</tr>
<tr>
<td>200 to 239 mg/dL</td>
<td>Borderline high</td>
</tr>
<tr>
<td>≥240 mg/dL</td>
<td>High</td>
</tr>
</tbody>
</table>

### LDL-C levels

<table>
<thead>
<tr>
<th>Level</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;100 mg/dL</td>
<td>Optimal</td>
</tr>
<tr>
<td>100 to 129 mg/dL</td>
<td>Near or above optimal</td>
</tr>
<tr>
<td>130 to 159 mg/dL</td>
<td>Borderline high</td>
</tr>
<tr>
<td>160 to 189 mg/dL</td>
<td>High</td>
</tr>
<tr>
<td>≥190 mg/dL</td>
<td>Very high</td>
</tr>
</tbody>
</table>

### HDL-C levels

<table>
<thead>
<tr>
<th>Level</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;40 mg/dL</td>
<td>Low</td>
</tr>
<tr>
<td>≥60 mg/dL</td>
<td>High</td>
</tr>
</tbody>
</table>

### Triglycerides levels

<table>
<thead>
<tr>
<th>Level</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;150 mg/dL</td>
<td>Normal</td>
</tr>
<tr>
<td>150 to 199 mg/dL</td>
<td>Borderline high</td>
</tr>
<tr>
<td>200 to 499 mg/dL</td>
<td>High</td>
</tr>
<tr>
<td>≥500 mg/dL</td>
<td>Very high</td>
</tr>
</tbody>
</table>

**IMPORTANT SAFETY INFORMATION (continued)**

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.

*Please see additional Important Safety Information continued on the following pages and the full Prescribing and Patient Information for LIPITOR attached.*

*†Lipoprotein levels determined after a 9- to 12-hour fast.
 Levels according to the National Cholesterol Education Program: ATP III Guidelines At-A-Glance Quick Desk Reference.
How Does LIPITOR Work?
Lowers LDL-C and can raise HDL-C
LIPITOR® (atorvastatin calcium) blocks the enzyme that produces LDL-C so that less is made. As a result, the liver picks up more cholesterol from the bloodstream, and lower levels of cholesterol end up in the blood.

LIPITOR lowers the LDL-C and triglycerides levels in your blood.

LIPITOR can raise your HDL-C.

IMPORTANT SAFETY INFORMATION (continued)
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 additional Important Safety Information continued on the following pages and the full Prescribing and Patient Information for LIPITOR attached.

How Does LIPITOR Affect Cholesterol Levels for Those Diagnosed With High Cholesterol?
Along with a low-fat diet, LIPITOR has been shown to lower:

- Total cholesterol* 29% to 45%
- LDL-C* 39% to 60%
- Triglycerides* 19% to 37%

LIPITOR may start working within 2 weeks.
*Average effect depending on dose.

LIPITOR can also help reduce the risk of heart attack and stroke
In people who have heart disease or several risk factors for heart disease, LIPITOR, along with a low-fat diet, is clinically proven to reduce the risk of:
- Heart attack
- Stroke
- Certain kinds of heart surgeries
- Chest pain
If Eligible, Start Saving on LIPITOR Today

With the LIPITOR® Savings Card, you may pay as little as $4 a month with a maximum yearly savings of $1,800, depending on insurance*.

Ask your doctor or visit www.LIPITORDrugCardRequest.com for more information about this savings offer.

*LIPITOR SAVINGS CARD TERMS AND CONDITIONS

By participating in the LIPITOR® Savings Offer Program, you acknowledge that you currently meet the eligibility criteria and will comply with the Terms and Conditions described below:

- This Savings Offer is not valid for prescriptions that are eligible to be reimbursed, in whole or in part, by Medicaid, Medicare, Tricare, or other federal or state healthcare programs (including any state prescription drug assistance programs) and the Government Health Insurance Plan available in Puerto Rico (formerly known as “La Reforma de Salud”).
- Eligible patients will pay a minimum of $4 per monthly prescription fill. By using the Savings Offer, eligible patients will receive a savings of up to $150 per fill off their co-pay or out-of-pocket costs. The Savings Offer is good for a maximum savings of $1,800 per year ($150 per month x 12 months). The Savings Offer limits your prescription cost to $4, subject to a maximum $150 monthly benefit. Thus, if your co-pay or out-of-pocket cost is more than $150, you will save $150 off of your co-pay or total out-of-pocket costs. [Example: If your co-pay or out-of-pocket costs are $175, you will pay $25 ($175 – $150 = $25).] If your co-pay or out-of-pocket costs are no more than $150, you pay $4. For a mail-order 3-month prescription, your total maximum savings will be $450 ($150 x 3).
- This Savings Offer is not valid when the entire cost of your prescription drug is eligible to be reimbursed by your private insurance plans or other health or pharmacy benefit programs.
- The Savings Offer is not valid for Massachusetts residents whose prescriptions are covered, in whole or in part, by third-party insurance.
- This Savings Offer is not valid where prohibited by law.
- The Savings Offer cannot be combined with any other rebate/coupon, free trial, or similar offer for the specified prescription.
- The Savings Offer may not be redeemed more than once per month per patient.
- The Savings Offer will be accepted only at participating pharmacies.
- The Savings Offer is not health insurance.
- This Savings Offer is good only in the U.S. and Puerto Rico.
- The Savings Offer is limited to 1 per person during this offering period and is not transferable.
- Pfizer reserves the right to rescind, revoke, or amend the program without notice.
- No membership fees. The Savings Offer and Program expire on 12/31/2020.

*Terms and Conditions apply.
† You may pay less by receiving the generic.

IMPORTANT SAFETY INFORMATION (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.

Please see full Important Safety Information on the next page and the full Prescribing and Patient Information for LIPITOR® attached.
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.

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).

Please see the attached full Prescribing and Patient Information for LIPITOR.
Questions to Ask Your Doctor

You might have questions about your cholesterol levels and treatment with LIPITOR® (atorvastatin calcium). It may be helpful to review the questions below before speaking with your doctor to help frame your discussions during your next appointment.

What are my goals given my medical history?

How long does it take for LIPITOR to work?

How long should I take my medicine for?

What other factors (such as diet and exercise) affect my cholesterol levels?

What should I avoid while taking LIPITOR; specifically, what foods should I stay away from?

In order to get the brand

Be sure to ask your doctor to specify LIPITOR on your prescription with a note such as “No Substitutions,” “Brand Medically Necessary,” or “Dispense As Written (DAW)” to help ensure you receive brand-name LIPITOR.

IMPORTANT SAFETY INFORMATION (continued)

Tell your doctor if you have diabetes. Elevated blood sugar levels have been reported with statins, including LIPITOR.

Please see additional Important Safety Information on the previous pages and the full Prescribing and Patient Information for LIPITOR attached.
LIPITOR® (atorvastatin calcium) tablets, for oral use

Initial U.S. Approval: 1996

INDICATIONS AND USAGE

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 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 adult 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 (HoFH) after failing an adequate trial of diet therapy (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 Friedrickson Types I and V dyslipidemias (1.3).

DOSE 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 (>45%) 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).

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, HIV protease inhibitors). Predisposing factors include advanced age (>65), uncontrolled hypertension, 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 (5.1, 8.5).

• Liver enzyme abnormalities: Persistent elevations in hepatic transaminases may occur. Check liver enzyme tests before initiating therapy and as clinically indicated thereafter (5.3).

• 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

• 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 (7.8).

• Oral Contraceptives: Values for norethindrone and ethinyl estradiol may be increased (7.9).

• Rifampin or other Inducers of Cytochrome P450 3A4

FULL PRESCRIBING INFORMATION: CONTENTS*

1 INDICATIONS AND USAGE

1.1 Prevention of Cardiovascular Disease in Adults

1.2 Hyperlipidemia

1.3 Limitations of Use

2 DOSAGE AND ADMINISTRATION

2.1 Hyperlipidemia and Mixed Dyslipidemia

2.2 Heterozygous Familial Hypercholesterolemia in Pediatric Patients (10 Years to 17 Years of Age)

2.3 Homozygous Familial Hypercholesterolemia

2.4 Concomitant Lipid-Lowering Therapy

2.5 Dosage in Patients with Renal Impairment

2.6 Dosage in Patients Taking Cypскоррин, Clarithromycin, Itraconazole, or Certain Protease Inhibitors

3 DOSAGE FORMS AND STRENGTHS

4 CONTRAINDICATIONS

5 WARNINGS AND PRECAUTIONS

5.1 Skeletal Muscle

5.2 Liver Dysfunction

5.3 Endocrine Function

5.4 CNS Toxicity

5.5 Use in Patients with Recent Stroke or TIA

6 ADVERSE REACTIONS

6.1 Clinical Trials Experience

6.2 Postmarketing Experience

7 DRUG INTERACTIONS

7.1 Strong Inhibitors of CYP 3A4

7.2 Grapefruit Juice

7.3 Cyclosporine

7.4 Gemfibrozil

7.5 Other Fibrates

7.6 Nicotin

7.7 Rifampin or other Inducers of Cytochrome P450 3A4

7.8 Digoxin

7.9 Oral Contraceptives

7.10 Warfarin

7.11 Colchicine

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

8.2 Lactation

8.3 Females and Males of Reproductive Potential

8.4 Pediatric Use

8.5 Geriatric Use

8.6 Hepatic Impairment

10 OVERDOSAGE

11 DESCRIPTION

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

12.2 Pharmacodynamics

12.3 Pharmacokinetics

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

14 CLINICAL STUDIES

14.1 Prevention of Cardiovascular Disease

14.2 Hyperlipidemia and Mixed Dyslipidemia

14.3 Hypertriglyceridemia

14.4 Dysbetalipoproteinemia

14.5 Heterozygous Familial Hypercholesterolemia

14.6 Heterozygous Familial Hypercholesterolemia in Pediatric Patients

16 HOW SUPPLIED/STORAGE AND HANDLING

17 PATIENT COUNSELING INFORMATION

17.1 Muscle Pain

17.2 Liver Enzymes

17.3 Embryofetal Toxicity

17.4 Lactation

*Sections or subsections omitted from the full prescribing information are not listed.

Revised: 6/2017
In patients taking clarithromycin, itraconazole, 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 employed. In patients taking the HIV protease inhibitor nelfinavir or the hepatitis C protease inhibitor boceprevir, therapy with LIPITOR should be limited to 40 mg, and appropriate clinical assessment is recommended to ensure that the lowest dose necessary of LIPITOR is employed [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

- Active Liver 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 CYP3A4 inhibitors (e.g., clarithromycin, itraconazole, and HIV protease inhibitors) increases the risk of myopathy/rhabdomyolysis. There have been rare reports of immune-mediated necrotizing myopathy (IMM), an autoimmune myopathy, associated with statin use. IMM 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 cyclosporine, fibrin acid derivatives, erythromycin, clarithromycin, the hepatitis C protease inhibitor telaprevir, combinations of HIV protease inhibitors, including saquinavir plus ritonavir, lopinavir plus ritonavir, tipranavir plus ritonavir, darunavir plus ritonavir, fosamprenavir, and fosamprenavir plus ritonavir, niacin, or azole antifungals. Physicians considering combined therapy with LIPITOR and fibrin acid derivatives, erythromycin, clarithromycin, a combination of saquinavir plus ritonavir, lopinavir plus ritonavir, darunavir plus ritonavir, fosamprenavir, or fosamprenavir plus ritonavir, azole antifungals, or lipid-modifying doses of niacin 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, HIV protease inhibitors (tipranavir plus ritonavir), hepatitis C protease inhibitor (telaprevir)</td>
<td>Avoid atorvastatin</td>
</tr>
<tr>
<td>HIV protease inhibitor (lopinavir plus ritonavir)</td>
<td>Use with caution and lowest dose necessary</td>
</tr>
<tr>
<td>Clarithromycin, itraconazole, HIV protease inhibitors (saquinavir plus ritonavir), darunavir plus ritonavir, fosamprenavir, fosamprenavir plus ritonavir)</td>
<td>Do not exceed 20 mg atorvastatin daily</td>
</tr>
<tr>
<td>HIV protease inhibitor (nelfinavir)</td>
<td>Do not exceed 40 mg atorvastatin daily</td>
</tr>
</tbody>
</table>
| Hepatitis C protease inhibitor (boceprevir) | *Use with caution and with the lowest dose necessary (12.3) Cases of myopathy, including rhabdomyolysis, have been reported with atorvastatin co-administered with telocichine, and caution should be exercised when prescribing atorvastatin with colchicine [see Drug Interactions (7.11)]. 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 rhabdomyolysis (e.g., severe acute infection, hypotension, major surgery, trauma, severe metabolic, endocrine and electrolyte disorders, and uncontrolled seizures).
Table 3. 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).

<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>Naegloglycinuria</td>
<td>8.3</td>
<td>12.9</td>
<td>5.3</td>
<td>7.0</td>
<td>4.2</td>
<td>8.2</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>Diarrhea</td>
<td>6.8</td>
<td>7.3</td>
<td>6.4</td>
<td>14.1</td>
<td>5.2</td>
<td>6.3</td>
</tr>
<tr>
<td>Pain in extremity</td>
<td>6.0</td>
<td>8.5</td>
<td>3.7</td>
<td>9.3</td>
<td>3.1</td>
<td>5.9</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>5.7</td>
<td>6.9</td>
<td>6.4</td>
<td>8.0</td>
<td>4.1</td>
<td>5.6</td>
</tr>
<tr>
<td>Dyspepsia</td>
<td>4.7</td>
<td>5.9</td>
<td>3.2</td>
<td>6.0</td>
<td>3.3</td>
<td>4.3</td>
</tr>
<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>Musculoskeletal pain</td>
<td>3.8</td>
<td>5.2</td>
<td>3.2</td>
<td>5.1</td>
<td>2.3</td>
<td>3.6</td>
</tr>
<tr>
<td>Muscle Spasms</td>
<td>3.6</td>
<td>4.6</td>
<td>4.8</td>
<td>5.1</td>
<td>2.4</td>
<td>3.0</td>
</tr>
<tr>
<td>Myalgia</td>
<td>3.5</td>
<td>3.6</td>
<td>5.9</td>
<td>8.4</td>
<td>2.7</td>
<td>3.1</td>
</tr>
<tr>
<td>Insomnia</td>
<td>3.0</td>
<td>2.8</td>
<td>1.1</td>
<td>5.3</td>
<td>2.8</td>
<td>2.9</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>

*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, hepatic abnormalities
- Metabolic and nutritional system: transaminase increase, liver function test abnormal, abnormal alkaline phosphatase increase, creatine phosphokinase increase, hyperglycemia
- Nervous system: nightmare
- Respiratory system: epistaxis, Skin and appendages: urticaria
- Special senses: vision blurred, tinnitus
- Urinary system: white blood cells urine positive.

Other adverse reactions reported in placebo-controlled studies include:
- Body as a whole: malaise, pyrexia
- Digestive system: abdominal discomfort, eructation, flatulence, hepatic abnormalities
- Metabolic and nutritional system: transaminase increase, liver function test abnormal, abnormal alkaline phosphatase increase, creatine phosphokinase increase, hyperglycemia
- Nervous system: nightmare
- Respiratory system: epistaxis
- Special senses: vision blurred, tinnitus
- Urinary system: white blood cells urine positive.

Other adverse reactions reported in placebo-controlled studies include:
- Body as a whole: malaise, pyrexia
- Digestive system: abdominal discomfort, eructation, flatulence, hepatic abnormalities
- Metabolic and nutritional system: transaminase increase, liver function test abnormal, abnormal alkaline phosphatase increase, creatine phosphokinase increase, hyperglycemia
- Nervous system: nightmare
- Respiratory system: epistaxis
- Special senses: vision blurred, tinnitus
- Urinary system: white blood cells urine positive.

Other adverse reactions reported in placebo-controlled studies include:
- Body as a whole: malaise, pyrexia
- Digestive system: abdominal discomfort, eructation, flatulence, hepatic abnormalities
- Metabolic and nutritional system: transaminase increase, liver function test abnormal, abnormal alkaline phosphatase increase, creatine phosphokinase increase, hyperglycemia
- Nervous system: nightmare
- Respiratory system: epistaxis
- Special senses: vision blurred, tinnitus
- Urinary system: white blood cells urine positive.
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, bulbar 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 interstitial lung 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 nonserious, and reversible upon statin discontinuation, with variable times to symptom onset (1 day to 5 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 thiazide diuretics, lipid-modifying doses of niacin, cyclosporine, or strong CYP 3A4 inhibitors (e.g., clarithromycin, HIV protease inhibitors, and itraconazole) [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 HIV protease inhibitors, as well as with the hepatitis C protease inhibitor telaprevir, compared to that of LIPITOR alone [see Clinical Pharmacology (12.3)]. Therefore, in patients taking the HIV protease inhibitor tipranavir plus ritonavir, or the hepatitis C protease inhibitor telaprevir, concomitant use of LIPITOR should be avoided. In patients taking the HIV protease inhibitor lopinavir plus ritonavir, caution should be used when prescribing LIPITOR and the lowest dose necessary should be used. In patients taking the HIV protease inhibitors saquinavir plus ritonavir, darunavir plus ritonavir, fosamprenavir or saquinavir plus ritonavir, the dose of LIPITOR should not exceed 20 mg and should be used with caution [see Dosage and Administration (2.6) and Warnings and Precautions (5.1)].

Itraconazole

Atorvastatin AUC was significantly increased with concomitant administration of LIPITOR 40 mg and itraconazole 200 mg [see Clinical Pharmacology (12.3)]. Therefore, in patients taking itraconazole, caution should be used when the LIPITOR dose exceeds 20 mg [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 and atorvastatin-metabolites are substrates of the OATP1B1 transporter. Inhibitors of the OATP1B1 (e.g., cyclosporine) can increase the bioavailability of atorvastatin. Atorvastatin AUC was significantly increased with concomitant administration of LIPITOR 10 mg and cyclosporine 5.2 mg/kg/day compared to that of LIPITOR alone [see Clinical Pharmacology (12.3)]. The co-administration of LIPITOR with cyclosporine should be avoided [see Warnings and Precautions (5.1)].

7.4 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)].

7.5 Other FibrateS

Because it is known that the risk of myopathy during treatment with HMG-CoA reductase inhibitors is increased with concurrent administration of other fibrates, LIPITOR should be administered with caution when used concomitantly with other fibrates [see Warnings and Precautions (5.1)].

7.6 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)].

7.7 Rifampin or other Inducers of Cytochrome P450 3A4

Concomitant administration of LIPITOR with inducers of cytochrome P450 3A4 (e.g., rifampin, rifabutin) 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.

7.8 Digoxin

When multiple doses of LIPITOR and digoxin were co-administered, steady state plasma digoxin concentrations increased by approximately 20%. Patients taking digoxin should be monitored appropriately.

7.9 Oral Contraceptives

Co-administration of LIPITOR and an oral contraceptive increased AUC values for norethindrone and ethinyl estradiol [see Clinical Pharmacology (12.3)]. These increases should be considered when selecting an oral contraceptive for a woman taking LIPITOR.

7.10 Warfarin

LIPITOR had no clinically significant effect on prothrombin time when administered to patients receiving chronic warfarin treatment.

7.11 Colchicine

Cases of myopathy, including rhabdomyolysis, have been reported with atorvastatin co-administered with colchicine, and caution should be exercised when prescribing atorvastatin with colchicine.

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 embryo-fetal 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.

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 intravenous 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 small, and no definite or statistically significant risk could be established.

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 same class, simvastatin, 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)].

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 prepubertal 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.
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.

Atorvastatin 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; hydrogenpropyl 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.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action
ATORVASTATIN is a selective, competitive inhibitor of HMG-CoA reductase, the rate-limiting enzyme that converts 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) to mevalonate, an early and rate-limiting step in cholesterol biosynthesis. Atorvastatin calcium is [R-(R*, R*)]-2-(4-fluorophenyl)-ß,3-dihydroxy-5-(1-methylethyl)-3-phenyl-4-[(p-hydroxyphenyl)carbonyl]-1H-pyrrole-1-heptanonic acid, calcium salt (2:1) hydrate. The empirical formula of atorvastatin calcium is C21H15FN2O5·Ca·H2O and its molecular weight is 1209.42. Its structural formula is:

\[
\text{Atorvastatin calcium} = \text{C21H15FN2O5·Ca·H2O}
\]

Absorption: Atorvastatin 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 presystemic clearance in gastrointestinal mucosa and 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 administration compared with morning. However, LDL-C reduction is the same regardless of the time of day of drug administration [see Dosage and Administration (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 para-hydroxylated derivatives and various beta-oxidation products. In vitro inhibition of HMG-CoA reductase by ortho- and para-hydroxylated 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-hydroxy 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.

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</th>
<th>Dose (mg)</th>
<th>Change in Cmax (%)</th>
<th>Change in AUC (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>*Cyclosporine 5.2 mg/kg/day, stable dose</td>
<td>10 mg OD for 28 days</td>
<td>18.7 fold</td>
<td>110.7 fold</td>
<td></td>
</tr>
<tr>
<td>*Tipranavir 500 mg BID/ritonavir</td>
<td>200 mg BID, 7 days</td>
<td>19.4 fold</td>
<td>18.6 fold</td>
<td></td>
</tr>
<tr>
<td>*Telaprevir 750 mg qd, 10 days</td>
<td>20 mg, SD</td>
<td>17.8 fold</td>
<td>110.6 fold</td>
<td></td>
</tr>
<tr>
<td>*Saquinavir 400 mg BID/ritonavir</td>
<td>400mg BID, 15 days</td>
<td>13.9 fold</td>
<td>14.3 fold</td>
<td></td>
</tr>
<tr>
<td>*Clarithromycin 500 mg, 9 days</td>
<td>80 mg for 4 days</td>
<td>14.4 fold</td>
<td>15.4 fold</td>
<td></td>
</tr>
<tr>
<td>*Darunavir 300 mg BID/ritonavir</td>
<td>100 mg BID, 9 days</td>
<td>13.4 fold</td>
<td>12.5 fold</td>
<td></td>
</tr>
<tr>
<td>*Tricarboxylate 200 mg, 40 days</td>
<td>40 mg SD</td>
<td>13.3 fold</td>
<td>120%</td>
<td></td>
</tr>
<tr>
<td>*Fosamprenavir 700 mg BID/ritonavir</td>
<td>100 mg BID, 14 days</td>
<td>12.53 fold</td>
<td>12.84 fold</td>
<td></td>
</tr>
<tr>
<td>*Fosamprenavir 1400 mg BID, 14 days</td>
<td>10 mg for 4 days</td>
<td>12.3 fold</td>
<td>14.04 fold</td>
<td></td>
</tr>
<tr>
<td>*Telithromycin 1250 mg BID, 14 days</td>
<td>10 mg for 28 days</td>
<td>17%</td>
<td>12.2 fold</td>
<td></td>
</tr>
<tr>
<td>*Grapefruit Juice, 240 mL qd</td>
<td>40 mg, SD</td>
<td>137%</td>
<td>116%</td>
<td></td>
</tr>
<tr>
<td>*Diltiazem 240 mg, 28 days</td>
<td>40 mg, SD</td>
<td>151%</td>
<td>No change</td>
<td></td>
</tr>
<tr>
<td>*Erythromycin 500 mg, 7 days</td>
<td>10 mg, SD</td>
<td>133%</td>
<td>138%</td>
<td></td>
</tr>
<tr>
<td>*Amiodarone 10 mg, single dose</td>
<td>80 mg, SD</td>
<td>115%</td>
<td>12%</td>
<td></td>
</tr>
<tr>
<td>*Cimetidine 300 mg QD, 2 weeks</td>
<td>10 mg OD for 2 weeks</td>
<td>Less than 1%</td>
<td>11%</td>
<td></td>
</tr>
<tr>
<td>*Colestipol 10 mg BID, 28 weeks</td>
<td>40 mg OD for 28 weeks Not determined</td>
<td><strong>26%</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>*Maalox TC® 30 mL QD, 17 days</td>
<td>10 mg OD for 15 days</td>
<td>13%</td>
<td>34%</td>
<td></td>
</tr>
<tr>
<td>*Elavil 600 mg QD, 14 days</td>
<td>10 mg for 3 days</td>
<td>41%</td>
<td>1%</td>
<td></td>
</tr>
<tr>
<td>*Rifampin 600 mg, 7 days</td>
<td>40 mg SD</td>
<td>130%</td>
<td>12.7 fold</td>
<td></td>
</tr>
<tr>
<td>*Rifampin 600 mg OD, 5 days (doses separated)</td>
<td>40 mg SD</td>
<td>180%</td>
<td>40%</td>
<td></td>
</tr>
<tr>
<td>*Gemfibrozil 600mg BID, 7 days</td>
<td>40 mg SD</td>
<td>135%</td>
<td>Less than 1%</td>
<td></td>
</tr>
<tr>
<td>*Fenofibrate 160mg OD, 7 days</td>
<td>40 mg SD</td>
<td>13%</td>
<td>2%</td>
<td></td>
</tr>
<tr>
<td>*Becepruv 800 mg BID, 7 days</td>
<td>40 mg SD</td>
<td>12.3 fold</td>
<td>12.6 fold</td>
<td></td>
</tr>
</tbody>
</table>

* Data given as x-fold change represent a simple ratio between co-administration and atorvastatin alone (i.e., 1-fold = no change). Data given as % change represent % difference relative to atorvastatin alone (i.e., 0% = no change).
* See Sections 5 and 7 for clinical significance.
* Greater increases in AUC (up to 2.5 fold) and/or Cmax (up to 71%) have been reported with excessive grapefruit consumption (≥ 750 mL - 1.2 liters per day).
** 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.

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

<table>
<thead>
<tr>
<th>Atorvastatin</th>
<th>Co-administered drug and dosing regimen</th>
<th>Change in AUC</th>
<th>Change in Cmax</th>
</tr>
</thead>
<tbody>
<tr>
<td>80 mg OD for 15 days</td>
<td>Atorvastatin, 600 mg SD</td>
<td>13%</td>
<td>↓11%</td>
</tr>
<tr>
<td>80 mg OD for 14 days</td>
<td>Dextrodone 0.25 mg OD, 20 days</td>
<td>↓15%</td>
<td>↓120%</td>
</tr>
<tr>
<td>40 mg OD for 22 days</td>
<td>Oral contraceptive OD, 2 months</td>
<td>↓128%</td>
<td>↓123%</td>
</tr>
<tr>
<td></td>
<td>- norethindrone 1mg</td>
<td>↓119%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- ethinyl estradiol 35µg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10 mg, OD</td>
<td>Tipranavir 500 mg BID/ritonavir, 200 mg BID, 7 days</td>
<td>No change</td>
<td>No change</td>
</tr>
<tr>
<td>10 mg OD for 4 days</td>
<td>Fosamprenavir 1400 mg BID, 14 days</td>
<td>↓27%</td>
<td>↓18%</td>
</tr>
<tr>
<td>10 mg OD for 4 days</td>
<td>Fosamprenavir 700 mg BID/ritonavir 100 mg BID, 14 days</td>
<td>No change</td>
<td>No change</td>
</tr>
</tbody>
</table>

* See Section 7 for clinical significance.

#### 13 NONCLINICAL TOXICOLGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

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. This dose represents a plasma AUC (0-24) value of approximately 16 times the mean human plasma drug exposure after an 80 mg oral dose.

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. These findings occurred at plasma AUC (0-24) values of approximately 6 times the mean human plasma drug exposure after an 80 mg oral dose.

In vitro, atorvastatin was not mutagenic or clastogenic in the following tests with and without metabolic activation: the Ames test with Salmonella typhimurium and Escherichia coli, the HGPRT forward mutation assay in Chinese hamster lung cells, and the chromosomal aberration assay in Chinese hamster lung cells. Atorvastatin was negative in the in vivo micronucleus test.

In female rats, atorvastatin at doses up to 225 mg/kg (56 times the human exposure) did not cause adverse effects on fertility. Studies in male rats performed at doses up to 175 mg/kg (15 times the human exposure) produced no changes in fertility. There was aplasia and aspermia in the epididymis of 2 of 10 rats treated with 100 mg/kg/day of atorvastatin for 3 months (16 times the human AUC at the 80 mg dose); tests weights were significantly lower at 30 and 100 mg/kg and epididymal weight was lower at 100 mg/kg. Male rats given 100 mg/kg/day for 11 weeks prior to mating had decreased sperm motility, spermatid head concentration, and increased abnormal sperm. 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.

#### 14 CLINICAL STUDIES

14.1 Prevention of Cardiovascular Disease

In the Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT), the effect of LIPITOR on fatal and non-fatal coronary heart disease was assessed in 10,305 hypertensive patients 40–80 years of age (mean of 63 years), without a previous myocardial infarction and with TC levels ≤251 mg/dL (6.5 mmol/L). Additionally, all patients had at least 3 of the following cardiovascular risk factors: male gender (81.1%), age ≥55 years (84.5%), smoking (33.2%), diabetes (24.3%), history of CHD in a first-degree relative (21.6%), current smoking (33.2%), and prior myocardial infarction (14.7%). In this double-blind, placebo-controlled study, patients were treated with atorvastatin or placebo (mean dose 80 mg/day for 5 years). The primary endpoint was the occurrence of the following major cardiovascular events: death due to CHD, non-fatal myocardial infarction, acute myocardial infarction, unstable angina, coronary revascularization, or stroke. The primary analysis was the time to first occurrence of the primary endpoint. Baseline characteristics of subjects were: mean age of 62 years, mean LDL-C 120 mg/dL; mean TC:HDL >6 (14.3%); peripheral vascular disease (5.1%); left ventricular hypertrophy (14.4%); and prior myocardial infarction (14.7%). There was a significant difference between the treatment groups for an incidence of any major cardiovascular events: myoccardial infarction, acute CHD death, unstable angina, coronary revascularization, or stroke in the atorvastatin group vs. the placebo group.

In the Collaborative Atorvastatin Diabetes Study (CARDS), the effect of LIPITOR on cardiovascular disease (CVD) endpoints was assessed in 2838 subjects (94% white, 68% 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 ≤400 mg/dL. In addition to diabetes, subjects had 1 or more of the following risk factors: cigarette smoking (23%), hypertension (40%), retinopathy (30%), or microalbuminuria (9%) or macroalbuminuria (3%). Subjects were randomly assigned to either LIPITOR 10 mg daily (1429) or placebo (1411) in a 2:1 ratio and were followed for a median duration of 3.9 years. The primary endpoint was the occurrence of any of the major cardiovascular events: myocardial infarction, acute CHD death, unstable angina, coronary revascularization, or stroke. The primary analysis was the time to first occurrence of the primary endpoint. Baseline characteristics of subjects were: mean age of 62 years, mean HbA1c 7.7%, median LDL-C 120 mg/dL; median TC:HDL >6 (14.7%); peripheral vascular disease (5.1%); left ventricular hypertrophy (14.4%); and prior myocardial infarction (14.7%). There was a significant difference between the treatment groups for an incidence of any major cardiovascular event: myocardial infarction, acute CHD death, unstable angina, coronary revascularization, or stroke in the atorvastatin group vs. the placebo group.

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 2.5% for placebo). There was no significant difference between the treatment groups for death due to cardiovascular causes (p=0.01) 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, 68% 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 ≤400 mg/dL. In addition to diabetes, subjects had 1 or more of the following risk factors: cigarette smoking (23%), hypertension (40%), retinopathy (30%), or microalbuminuria (9%) or macroalbuminuria (3%). Subjects were randomly assigned to either LIPITOR 10 mg daily (1429) or placebo (1411) in a 2:1 ratio and were followed for a median duration of 3.9 years. The primary endpoint was the occurrence of any of the major cardiovascular events: myocardial infarction, acute CHD death, unstable angina, coronary revascularization, or stroke. The primary analysis was the time to first occurrence of the primary endpoint. Baseline characteristics of subjects were: mean age of 62 years, mean HbA1c 7.7%, median LDL-C 120 mg/dL; median TC:HDL >6 (14.7%); peripheral vascular disease (5.1%); left ventricular hypertrophy (14.4%); and prior myocardial infarction (14.7%). There was a significant difference between the treatment groups for an incidence of any major cardiovascular event: myocardial infarction, acute CHD death, unstable angina, coronary revascularization, or stroke in the atorvastatin group vs. the placebo group.

In the Collaborative Atorvastatin Diabetes Study (CARDS), the effect of LIPITOR on cardiovascular disease (CVD) endpoints was assessed in 2838 subjects (94% white, 68% 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 ≤400 mg/dL. In addition to diabetes, subjects had 1 or more of the following risk factors: cigarette smoking (23%), hypertension (40%), retinopathy (30%), or microalbuminuria (9%) or macroalbuminuria (3%). Subjects were randomly assigned to either LIPITOR 10 mg daily (1429) or placebo (1411) in a 2:1 ratio and were followed for a median duration of 3.9 years. The primary endpoint was the occurrence of any of the major cardiovascular events: myocardial infarction, acute CHD death, unstable angina, coronary revascularization, or stroke. The primary analysis was the time to first occurrence of the primary endpoint. Baseline characteristics of subjects were: mean age of 62 years, mean HbA1c 7.7%, median LDL-C 120 mg/dL; median TC:HDL >6 (14.7%); peripheral vascular disease (5.1%); left ventricular hypertrophy (14.4%); and prior myocardial infarction (14.7%). There was a significant difference between the treatment groups for an incidence of any major cardiovascular event: myocardial infarction, acute CHD death, unstable angina, coronary revascularization, or stroke in the atorvastatin group vs. the placebo group.
LIPITOR is effective in a wide variety of patient populations with hyperlipidemia, with and without hypertiglyceridemia, 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

<table>
<thead>
<tr>
<th>Treatment (Daily Dose)</th>
<th>Placebo</th>
<th>LIPITOR 10 mg</th>
<th>LIPITOR 20 mg</th>
<th>LIPITOR 40 mg</th>
<th>LIPITOR 80 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>349</td>
<td>348</td>
<td>348</td>
<td>348</td>
<td>348</td>
</tr>
<tr>
<td>Total-C</td>
<td></td>
<td>-21</td>
<td>-25</td>
<td>-26</td>
<td>-28</td>
</tr>
<tr>
<td>LDL-C</td>
<td></td>
<td>-37</td>
<td>-40</td>
<td>-42</td>
<td>-45</td>
</tr>
<tr>
<td>HDL-C</td>
<td></td>
<td>-17</td>
<td>-17</td>
<td>-17</td>
<td>-17</td>
</tr>
<tr>
<td>apo B</td>
<td></td>
<td>-19</td>
<td>-20</td>
<td>-20</td>
<td>-20</td>
</tr>
<tr>
<td>TG</td>
<td></td>
<td>-6</td>
<td>-7</td>
<td>-6</td>
<td>-7</td>
</tr>
<tr>
<td>Non-HDL-C/ HDL-C</td>
<td></td>
<td>-9</td>
<td>-11</td>
<td>-11</td>
<td>-11</td>
</tr>
</tbody>
</table>

### TABLE 8. Combined Patients With Isolated Elevated TG: Median (min, max)

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Placebo</th>
<th>LIPITOR 20 mg</th>
<th>LIPITOR 40 mg</th>
<th>LIPITOR 80 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular death</td>
<td>155</td>
<td>126</td>
<td>126</td>
<td>126</td>
</tr>
<tr>
<td>Non-cardiovascular death</td>
<td>127</td>
<td>158</td>
<td>158</td>
<td>158</td>
</tr>
<tr>
<td>Cancer death</td>
<td>75</td>
<td>85</td>
<td>85</td>
<td>85</td>
</tr>
<tr>
<td>Other non-CV death</td>
<td>43</td>
<td>58</td>
<td>58</td>
<td>58</td>
</tr>
<tr>
<td>Suicide, homicide, and other</td>
<td>9</td>
<td>15</td>
<td>15</td>
<td>15</td>
</tr>
<tr>
<td>traumatic non-CV death</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### 14.4 Dysbetalipoproteinemia

The results of an open-label crossover study of 16 patients (genotypes: 14 apo E2/E2 and 2 apo E3/E2) with dysbetalipoproteinemia (Fredrickson Type III) are shown in the table below (Table 10).
TABLE 10. Open-Label Crossover Study of 16 Patients With Dysbetalipoproteinemia (Fredrickson Type III)

<table>
<thead>
<tr>
<th>Baseline (mg/dL)</th>
<th>LIPITOR 10 mg</th>
<th>LIPITOR 80 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median (min, max)</td>
<td>Median % Change (min, max)</td>
<td></td>
</tr>
<tr>
<td>Total-C</td>
<td>442 (225, 1320)</td>
<td>-37 (-95, 17)</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>678 (273, 5990)</td>
<td>-39 (-95, -30)</td>
</tr>
<tr>
<td>IDL-C + VLDL-C</td>
<td>215 (111, 613)</td>
<td>-32 (-76, 9)</td>
</tr>
<tr>
<td>non-HDL-C</td>
<td>411 (218, 1272)</td>
<td>-43 (-87, -19)</td>
</tr>
</tbody>
</table>

14.5 Homozygous Familial Hypercholesterolemia

In a study without a concurrent control group, 29 patients ages 6 years to 37 years with HeFH received maximum daily doses of 20 to 80 mg of LIPITOR. The mean LDL-C reduction in this study was 18%. Twenty-five patients with a reduction in LDL-C had a mean response of 20% (range of 7% to 53%, median of 24%); the remaining 4 patients had 7% to 24% increases in LDL-C. Five of the 29 patients had absent LDL-receptor function. Of these, 2 patients also had a paracutaneous shunt and had no significant reduction in LDL-C. The remaining 3 receptor-negative patients had a mean LDL-C reduction of 22%.

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 $\geq$ 190 mg/dL or 2) a baseline LDL-C level $\geq$ 160 mg/dL and positive family history of FH or documented premature cardiovascular 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 uptitrated to 20 mg if the LDL-C level was > 130 mg/dL. The number of LIPITOR-treated patients who required uptitration to 20 mg after Week 4 during the double-blind phase was 75 (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).

TABLE 11. Lipid-altering Effects of LIPITOR in Adolescent Boys and Girls with Heterozygous Familial Hypercholesterolemia or Severe Hypercholesterolemia (Mean Percentage Change From Baseline at Endpoint in Intention-to-Treatment Population)

<table>
<thead>
<tr>
<th>DOSAGE</th>
<th>N</th>
<th>Total-C</th>
<th>LDL-C</th>
<th>HDL-C</th>
<th>TG</th>
<th>Apolipoprotein B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>47</td>
<td>-1.5</td>
<td>-0.4</td>
<td>-1.9</td>
<td>1.0</td>
<td>0.7</td>
</tr>
<tr>
<td>LIPITOR</td>
<td>140</td>
<td>-31.4</td>
<td>-39.6</td>
<td>2.8</td>
<td>-12.0</td>
<td>-34.0</td>
</tr>
</tbody>
</table>

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.

Atorvastatin was also studied in a three year open-label, uncontrolled trial that included 163 patients with HeFH who were 10 years to 15 years old (82 boys and 81 girls). All patients had a clinical diagnosis of HeFH confirmed by genetic analysis (if not already confirmed by family history). Approximately 86% were Caucasian, and less than 1% were Black or Asian. Mean LDL-C at baseline was 232 mg/dL. The starting atorvastatin dosage was 10 mg once daily and doses were adjusted to achieve a target of < 130 mg/dL LDL-C. The reductions in LDL-C from baseline were generally consistent across age groups within the trial as well as with previous clinical studies in both adult and pediatric placebo-controlled trials. 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 500
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 0071-0156-94 bottles of 5000
NDC 0071-0156-10 bottles of 1000

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 500
NDC 0071-0157-88 bottles of 2500
NDC 0071-0157-40 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 0071-0158-73 bottles of 500
NDC 0071-0158-88 bottles of 2500
NDC 0071-0158-92 8 x 8 unit dose blisters

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

17 PATIENT COUNSELING INFORMATION

Advising the patient to read the FDA-approved patient labeling (Patient Information). Patients taking LIPITOR 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 their healthcare professionals prescribing a new medication that they are taking LIPITOR.

17.1 Muscle Pain
All patients starting therapy with LIPITOR 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 LIPITOR. 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 LIPITOR and if signs or symptoms of liver injury occur. All patients treated with LIPITOR 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 LIPITOR [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.
PATIENT INFORMATION

LIPITOR
atorvastatin calcium

(LIP-i-tore)

Read the Patient Information that comes with LIPITOR before you start taking it and each time you get a refill. There may be new information. This leaflet does not take the place of talking with your doctor about your condition or treatment.

If you have any questions about LIPITOR, ask your doctor or pharmacist.

What is LIPITOR?
LIPITOR is a prescription medicine that lowers cholesterol in your 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, 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.

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.

LIPITOR dosing has 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

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

How Should I Take LIPITOR?
- Take LIPITOR exactly as prescribed by your doctor. 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. 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 Ingredients: atorvastatin calcium
Inactive Ingredients: calcium carbonate, USP; candelilla wax, FCC; croscarmellose sodium, NF; hydroxypropyl cellulose, NF; lactose monohydrate, NF; magnesium stearate, USP; microcrystalline cellulose, NF; Opadry White YS-1-7040 (hypromellose, polyethylene glycol, talc, titanium dioxide); polysorbate 80, NF; simethicone emulsion.

Distributed by
Parke-Davis
Division of Pfizer Inc., Kalamazoo, MI 49001

LAB-0348-9.0
June 2017