

Models for Payment Advised

Medical Homes from page 1

hensive care (Ann. Fam. Med. 2010; 8 [Suppl 1]:s57-67. doi:10.1370/afm.1121).

Patients may not have liked watching physicians work through the many changes, suggested Dr. Carlos Roberto Jaén, the principle investigator for the study's independent evaluation team. For example, a physician getting used to a new electronic medical record system may at first spend more time looking at the computer than at the patient, said Dr. Jaén, a professor of family and community medicine at the University of Texas Health Science Center at San Antonio.

The decline in patient satisfaction may also be due to the short evaluation period. "It's probably a combination of the rapid implementation and change, and no one likes change," he said.

But overall, the evaluation is good news for the feasibility of adopting the components of the patient-centered medical home, he added, especially in light of the fact that practices received no additional payments for the new services they were providing, such as increased access, e-visits, group visits, and coordination of care.

"The good news is that small practices can implement a large proportion of the components, and that's something we didn't know before," Dr. Jaén said.

Nevertheless, the evaluators recommended that the current medical-payment system be changed to accommodate the new model of care. Currently, the only way get paid is to see a patient, which means there is no financial incentive for a physician or nurse to e-mail or call a patient, even if those actions might negate the need for a hospitalization.

The current system puts physicians in a trap of seeing 30 to 40 patients a day, Dr. Jaén said, adding that payment reform might allow physicians to take care of 50 people but see only 10 face-to-face. The independent evaluation team recommended that payers consider new models for paying physicians such as

capitation and payment bundling (Ann. Fam. Med. 2010;8[Suppl 1]:s80-s90. doi:10.1370/afm.1107).

Dr. Robert Eidus, a solo family physician who participated in the facilitated arm of the study, said payment reform is essential to move the medical home model forward.

In his Cranford, N.J., practice, he and his staff were able to implement many of the medical home elements, such as team huddles and a disease registry, without additional funds, he said. But the practice didn't have the resources to make much progress in areas such as team care. He used existing staff as much as possible to create a care team, but without increased funding couldn't afford to hire other providers such as a pharmacist or a full-time care coordinator.

"We were operating with one hand tied behind our back," Dr. Eidus said. Both payers and physicians will have to be willing to move forward on the model, he said. Payers must identify what physicians need to do to qualify for payments, and practices must make whatever changes they can without additional reimbursement.

Payers are beginning to recognize the need to reimburse physicians for their role in providing medical homes, said Dr. Terry McGeeney, president and CEO of TransforMED, which ran the demonstration project. TransforMED, an AAFP subsidiary, helps primary care practices make the switch to a medical home model.

Since the demonstration project ended, many payers have launched projects to test alternative physician reimbursement schemes and patient incentives that could work with the medical home.

Dr. McGeeney said that these payers are looking closely at the medical home in ways they haven't done before. "Not just the practices are changing and not just the payment incentives are changing, but actually the payers are changing," he said.

One FP's Experience in the Demo

When Dr. Theresa Shupe became a part of the National Demonstration Project to test implementation strategies for the patient-centered medical home in 2006, she hadn't even opened the doors of her new family medicine practice.

Four years later, her staff has tripled, her practice is financially stable, and she's starting to outgrow her office space. It hasn't been an easy process, but Dr. Shupe said she's proud of the fact that she can offer her patients a medical home, complete with longer than average visits, same-day access, a patient portal, and a focus on chronic disease management.

"I'm kind of on a mission to prove this works," she said.

Around the time that the demonstration project was coming together, Dr. Shupe was preparing to leave the 12-provider group practice where she worked in Manassas, Va. She had signed a lease for a new office in Haymarket, Va., and was already planning to incorporate many aspects of the medical home model.

After being chosen for the demonstration project, she was randomized to the self-directed arm, so despite her involvement in the project, she was largely on her own to implement the new model (see story).

Some changes were easier to make than others. Early on, Dr. Shupe implemented an electronic health record and a patient portal. She also began open-access scheduling, with most patients getting appointments

within 24 hours. But other elements, such as group visits and extended hours, weren't a good fit for the practice. There just wasn't space in the office to do group visits, she said, and since all three of the physicians in the practice are working mothers, keeping the practice open for extra hours at night and on the weekends hasn't been feasible either. But Dr. Shupe tries to make up for that by not having an answering service so that patients can speak directly to their physician after hours. Patients can also send messages through the patient portal and have those messages returned over the weekend.

The biggest challenge hasn't been the medical home implementation, she said, but fighting with insurance companies over payments. As an employee in a larger practice, Dr. Shupe had never been involved in managing a practice's finances and working with insurance companies to resolve rejected claims. It took her about a year-and-a-half to learn what she needed to know to keep money flowing in.

Another frustration is the lack of payment for coordination of care. Dr. Shupe said that with payment for those services, she would be able to spend more time with patients. Additional funding for the medical home would also allow small practices to provide chronic disease management.

"It's just not financially viable to do everything that needs to be done to keep people healthy," she said.

—Mary Ellen Schneider

At the same time, health reform has advanced the concept of accountable care organizations, in which multiple providers join to treat patients and are paid based on the cost and quality of the care provided. Many health systems are looking closely at the concept of the medical home as a way to position them-

selves as accountable care organizations, Dr. McGeeney said.

"The [demonstration project] basically made the whole medical home concept credible," Dr. McGeeney said. "Now as we're getting outcome data and with health care reform, it has just absolutely exploded." ■

Specialist Frustrated By Lack of a Role in the Medical Home

BY MARY ELLEN SCHNEIDER

As implementation of health reform gains momentum, subspecialist physicians are concerned about their lack of a role in care coordination and the patient-centered medical home model.

"We're a little bit frustrated about where we fit in," said Dr. Karen Kolba, a rheumatologist in solo practice in Santa Maria, Calif., and chair of the American College of Rheumatology's Committee on Rheumatologic Care.

The ACR is one of a handful of medical specialty societies that has not signed on to the concept of the patient-centered medical home. It's not that the college doesn't support increased access for patients or coordinated care; rather, she said, they feel they have been excluded from the model.

In 2007, the American Academy of Family Physicians, the American Academy of Pediatrics, the American College of Physicians, and the American Osteopathic Association issued a paper outlining the principles of the patient-centered medical home, which seeks to pro-

vide comprehensive primary care to children and adults.

Under the model, each patient has a personal physician who directs a practice-based care team and is responsible for providing all of the patient's health care needs or coordinating that care with another provider. The model also emphasizes evidence-based medicine and clinical decision support, enhanced access for patients, and additional payment for the personal physician for providing care coordination and improving quality.

A voluntary recognition program created by the National Committee for Quality Assurance (NCQA) aims to operationalize the model; physicians who meet the program's standards can qualify for additional payment from certain health plans. The standards measure a practice on access and communication, patient tracking and registry functions, care management, referral tracking, and electronic prescribing, among others.

Although the medical home model doesn't specify that only a primary care physician can qualify, the criteria make it nearly impossible for specialists to act as a medical home, Dr. Kolba said. For example, rheuma-

tologists frequently are the main point of medical contact for patients with chronic rheumatologic diseases and they provide a significant amount of coordination of care, she said. However, few perform or coordinate nonrheumatologic care such as a patient's regular mammogram. And that's a sticking point in being able to qualify as a personal physician under the medical home, she said.

Dr. Kolba said she supports increasing payment for primary care, but not at the expense of other physicians. And she said primary care physicians ought to be entitled to additional pay for the work they do, without creating a new system to justify the increases.

AAFP leaders defend the medical home model and specialists' role in it. The patient-centered medical home was very purposefully defined to include a "personal physician"—not a primary care physician, said Dr. Terry McGeeney, the president and CEO of TransforMED, a subsidiary of the AAFP that helps primary care practices transition to the medical home model.

Although most practices using the medical home

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model will be led by primary care physicians, not all will be. The personal physician could be an infectious disease specialist, a neurologist, or an oncologist, he said.

But the key, Dr. McGeeney said, is that the physician must provide a medical home for the whole patient, and not focus on a certain disease or organ system. That means that a neurologist, for example, must keep track not only of the neurologic care, but also the patient's cholesterol levels and mammogram results. They don't have to perform these services themselves, but they have to coordinate and track them, he said. In the medical home, the personal physician is the "quarterback" for the patient's care and there's no "free pass" on those responsibilities for specialists, he said.

Specialists who do want to provide a medical home may even have an advantage, according to Dr. McGeeney, who pointed out that specialty practices tend to have more resources to invest in practice transformation. That said, specialists often have not been trained to provide the types and level of care required of medical homes.

Where specialists may fit in more easily, Dr. McGeeney said, is in the "medical home neighborhood," which includes all the physicians caring for a patient, as well as the emergency department, the hospital, and the pharmacy.

TransforMED is encouraging medical home practices to have letters of agreement with specialists regarding care coordination. As part of the agreement, the primary care physician promises to send all the patient's information to the specialist and to communicate with them about tests and results. These agreements aren't legally binding on either party, but they force everyone to have a conversation about coordination of care, he said.

Some specialists remain skeptical about their role in the medical home and the medical home neighborhood. Dr. Alfred Bove, past president of the American College of Cardiology and emeritus

professor of medicine at Temple University, Philadelphia, said cardiologists frequently act as a medical home for heart failure and transplantation patients, for example, and don't want to be left out. For years, many cardiologists have worked in multidisciplinary care teams, used electronic health records, and provided immunizations and screening, he said.

"We have all the ingredients needed to be a patient-centered medical home in an area of chronic disease that probably is better done by cardiologists that have a lot of experience in managing very sick

heart failure patients than in a primary care practice where there's a broad spectrum of different kinds of patients," Dr. Bove said.

The ACC has been advocating for specialty-based patient-centered medical homes in specific areas where the cardiologist's expertise is unique and they would be willing to assume responsibility for preventive care.

But another issue is what to do about specialty practices that act as a medical home for only a portion of their patients. In a recent article in the New England Journal of Medicine, researchers looked

at single-specialty practices in cardiology, endocrinology, and pulmonology to find out to what extent those specialty practices function as medical homes.

They found that a large percentage of the practices provided both primary care and specialty care, but generally for a subset of patients. For example, 81% of the 373 practices surveyed said they served as primary care physicians for 10% or fewer of their patients. Only 2.7% of the practices said they act as primary care physicians for more than 50% of their patients (N. Engl. J. Med. 2010;362:1555-8).

LIPITOR® (Atorvastatin Calcium) Tablets
Brief Summary of Prescribing Information

CONTRAINDICATIONS: Active liver disease, which may include unexplained persistent elevations in hepatic transaminase levels. Hypersensitivity to any component of this medication. **Pregnancy—**Women who are pregnant or may become pregnant. LIPITOR may cause fetal harm when administered to a pregnant woman. Serum cholesterol and triglycerides increase during normal pregnancy, and cholesterol or cholesterol derivatives are essential for fetal development. Atherosclerosis is a chronic process and discontinuation of lipid-lowering drugs during pregnancy should have little impact on the outcome of long-term therapy of primary hypercholesterolemia. There are no adequate and well-controlled studies of LIPITOR use during pregnancy; however in rare reports, congenital anomalies were observed following intrauterine exposure to statins. In rat and rabbit animal reproduction studies, atorvastatin revealed no evidence of teratogenicity. LIPITOR SHOULD BE ADMINISTERED TO WOMEN OF CHILDBEARING AGE ONLY WHEN SUCH PATIENTS ARE HIGHLY UNLIKELY TO CONCEIVE AND HAVE BEEN INFORMED OF THE POTENTIAL HAZARDS. If the patient becomes pregnant while taking this drug, LIPITOR should be discontinued immediately and the patient apprised of the potential hazard to the fetus [see Use in Specific Populations in full prescribing information]. **Nursing mothers—**It is not known whether atorvastatin is excreted into human milk; however a small amount of another drug in this class does pass into breast milk. Because statins have the potential for serious adverse reactions in nursing infants, women who require LIPITOR treatment should not breastfeed their infants [see Use in Specific Populations in full prescribing information].

WARNINGS AND PRECAUTIONS: 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. 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. 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, fibric acid derivatives, erythromycin, clarithromycin, combination of ritonavir plus saquinavir or lopinavir plus ritonavir, niacin, or azole antifungals. Physicians considering combined therapy with LIPITOR and fibric acid derivatives, erythromycin, clarithromycin, a combination of ritonavir plus saquinavir or lopinavir plus ritonavir, immunosuppressive drugs, azole antifungals, or lipid-modifying doses of niacin should carefully weigh the potential benefits and risks and should carefully monitor any signs or symptoms of myopathy, 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 1 [see also Dosage and Administration, Drug Interactions, Clinical Pharmacology in full prescribing information].

Table 1. Drug Interactions Associated with Increased Risk of Myopathy/Rhabdomyolysis

Interacting Agents	Prescribing Recommendations
Cyclosporine	Do not exceed 10 mg atorvastatin daily
Clarithromycin, itraconazole, HIV protease inhibitors (ritonavir plus saquinavir or lopinavir plus ritonavir)	Caution when exceeding doses > 20mg atorvastatin daily. The lowest dose necessary should be used.

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).

Liver Dysfunction—Statins, like some other lipid-lowering therapies, have been associated with biochemical abnormalities of liver function. Persistent elevations in ALT or AST (greater than 3 times the upper limit of normal) 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, transaminase levels returned to or near pretreatment levels without sequelae. Eighteen of 30 patients with persistent LFT elevations continued treatment with a reduced dose of LIPITOR. It is recommended that liver function tests be performed prior to and at 12 weeks following both the initiation of therapy and any elevation of dose, and periodically (e.g., semiannually) thereafter. Liver enzyme changes generally occur in the first 3 months of treatment with LIPITOR. Patients who develop increased transaminase levels should be monitored until the abnormalities resolve. Should an increase in ALT or AST of >3 times ULN persist, reduction of dose or withdrawal of LIPITOR is recommended. 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 in full prescribing information]. **Endocrine Function—**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, spiro lactone, and cimetidine. **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 received the same 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. **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 vs. placebo 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 (5.2, 2.3% atorvastatin vs. 3.3, 1.4% placebo; HR: 1.68, 95% CI: 1.09, 2.59; p=0.0168). The incidence of fatal hemorrhagic stroke was similar across treatment groups (17 vs. 18 for the atorvastatin and placebo groups, respectively). The incidence of nonfatal hemorrhagic stroke was significantly higher in the atorvastatin group (38, 1.6%) as compared to the placebo group (16, 0.7%). Some baseline characteristics, including hemorrhagic and lacunar stroke on study entry, were associated with a higher incidence of hemorrhagic stroke in the atorvastatin group [see Adverse Reactions in full prescribing information].

ADVERSE REACTIONS: The following serious adverse reactions are discussed in greater detail in other sections of the label: Rhabdomyolysis and myopathy [see Warnings and Precautions in full prescribing information], Liver enzyme abnormalities [see Warnings and Precautions in full prescribing information]. **Clinical Trial Adverse Experiences—**Because clinical trials are conducted under widely varying conditions, the adverse reaction rates observed in the clinical studies of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice. In the LIPITOR placebo-controlled clinical trial database of 16,066 patients (8755 LIPITOR vs. 7311 placebo; age range 10-93 years, 39% women, 91% Caucasians, 3% Blacks, 2% Asians, 4% other) with a median treatment duration of 53 weeks, 9.7% of patients on LIPITOR and 9.5% of the patients on placebo discontinued due to adverse reactions regardless of causality. The five most common adverse reactions in patients treated with LIPITOR that led to treatment discontinuation and occurred at a rate greater than placebo were: myalgia (0.7%), diarrhea (0.7%), nausea (0.4%), alanine aminotransferase increase (0.4%), and hepatic enzyme increase (0.4%). The most commonly reported adverse reactions (incidence ≥ 2% and greater than placebo) regardless of causality, in patients treated with LIPITOR in placebo controlled trials (n=8755) were: nasopharyngitis (8.3%), arthralgia (6.9%), diarrhea (6.8%), pain in extremity (6.0%), and urinary tract infection (5.7%). Table 2 summarizes the frequency of clinical adverse reactions, regardless of causality, reported in ≥ 2% and at a rate greater than placebo in patients treated with LIPITOR (n=8755), from seventeen placebo-controlled trials.

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

Adverse Reaction*	Any dose N=8755	10 mg N=3908	20 mg N=188	40 mg N=604	80 mg N=4055	Placebo N=7311
Nasopharyngitis	8.3	12.9	5.3	7.0	4.2	8.2
Arthralgia	6.9	8.9	11.7	10.6	4.3	6.5
Diarrhea	6.8	7.3	6.4	14.1	5.2	6.3
Pain in extremity	6.0	8.5	3.7	9.3	3.1	5.9
Urinary tract infection	5.7	6.9	6.4	8.0	4.1	5.6
Dyspepsia	4.7	5.9	3.2	6.0	3.3	4.3
Nausea	4.0	3.7	3.7	7.1	3.8	3.5
Musculoskeletal pain	3.8	5.2	3.2	5.1	2.3	3.6
Muscle Spasms	3.6	4.6	4.8	5.1	2.4	3.0
Myalgia	3.5	3.6	5.9	8.4	2.7	3.1
Insomnia	3.0	2.8	1.1	5.3	2.8	2.9
Pharyngolaryngeal	2.3	3.9	1.6	2.8	0.7	2.1

*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, cholelithiasis; *Musculoskeletal system:* musculoskeletal pain, muscle fatigue, neck pain, joint swelling; *Metabolic and nutritional system:* transaminases increase, liver function test abnormal, blood alkaline phosphatase increase, creatine phosphokinase increase, hyperglycemia; *Nervous system:* nightmare; *Respiratory system:* epistaxis; *Skin and appendages:* urticaria; *Special senses:* vision blurred, tinnitus; *Urogenital system:* white blood cells urine positive.

Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT)—In ASCOT [see Clinical Studies in full prescribing information] involving 10,305 participants (age range 40-80 years, 19% women; 94.5% Caucasians, 2.6% Africans, 1.5% South Asians, 1.3% mixed Blacks), 0.04% treated with LIPITOR 10 mg daily (n=5,188) or placebo (n=5,137), the safety and tolerability profile of the group treated with LIPITOR was comparable to that of the group treated with placebo during a median of 3.3 years of follow-up.

Collaborative Atorvastatin Diabetes Study (CARDS)—In CARDS [see Clinical Studies in full prescribing information] involving 2838 subjects (age range 39-77 years, 32% women; 94.3% Caucasians, 2.4% South Asians, 2.3% Afro-Caribbean, 1.0% other) with type 2 diabetes treated with LIPITOR 10 mg daily (n=1,428) or placebo (n=1,410), there was no difference in the overall frequency of adverse reactions or serious adverse reactions between the treatment groups during a median follow-up of 3.9 years. No cases of rhabdomyolysis were reported.

Treating to New Targets Study (TNT)—In TNT [see Clinical Studies in full prescribing information] involving 10,001 subjects (age range 29-78 years, 19% women; 94.1% Caucasians, 2.9% Blacks, 1.0% Asians, 2.0% other) with clinically evident CHD treated with LIPITOR 10 mg daily (n=5006) or LIPITOR 80 mg daily (n=4995), there were more serious adverse reactions and discontinuations due to adverse reactions in the high-dose atorvastatin group (92, 1.8%, 497, 9.9%, respectively) as compared to the low-dose group (69, 1.4%; 404, 8.1%, respectively) during a median follow-up of 4.3 years. Persistent transaminase elevations (≥3 x ULN twice within 4-10 days) occurred in 62 (1.3%) individuals with atorvastatin 80 mg and in nine (0.2%) individuals with atorvastatin 10 mg. Elevations of CK (≥ 10 x ULN) were low overall, but were higher in the high-dose atorvastatin treatment group (13, 0.3%) compared to the low-dose atorvastatin group (6, 0.1%).

Incremental Decrease in Endpoints through Aggressive Lipid Lowering Study (IDEAL)—In IDEAL [see Clinical Studies in full prescribing information] involving 8688 subjects (age range 26-80 years, 18% women; 93.3% Caucasians, 0.4% Blacks, 0.3% Asians, 0.04% other) treated with LIPITOR 80 mg daily (n=4439) or simvastatin 20-40 mg daily (n=4449), there was no difference in the overall frequency of adverse reactions or serious adverse reactions between the treatment groups during a median follow-up of 4.8 years.

Stroke Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL)—In SPARCL involving 4731 subjects (age range 21-92 years, 40% women; 93.3% Caucasians, 3.0% Blacks, 0.6% Asians, 3.1% other) without clinically evident CHD but with a stroke or transient ischemic attack (TIA) within the previous 6 months treated with LIPITOR 80 mg (n=2365) or placebo (n=2366) for a median follow-up of 4.9 years, there was a higher incidence of persistent hepatic transaminase elevations (≥ 3 x ULN twice within 4-10 days) in the atorvastatin group (0.9%) compared to placebo (0.1%). Elevations of CK (≥ 10 x ULN) were rare, but were higher in the atorvastatin group (0.1%) compared to placebo (0.0%). Diabetes was reported as an adverse reaction in 144 subjects (6.1%) in the atorvastatin group and 89 subjects (3.8%) in the placebo group [see Warnings and Precautions in full prescribing information].

In a post-hoc analysis, LIPITOR 80 mg reduced the incidence of ischemic stroke (218/2365, 9.2% vs. 274/2366, 11.6%) and increased the incidence of hemorrhagic stroke (55/2365, 2.3% vs. 33/2366, 1.4%) compared to placebo. The incidence of fatal hemorrhagic stroke was similar between groups (17 LIPITOR vs. 18 placebo). The incidence of non-fatal hemorrhagic strokes was significantly greater in the atorvastatin group (36 non-fatal hemorrhagic strokes) as compared to the placebo group (16 non-fatal hemorrhagic strokes). Subjects who entered the study with a hemorrhagic stroke appeared to be at increased risk for hemorrhagic stroke [7 (16%) LIPITOR vs. 2 (4%) placebo].

There were no significant differences between the treatment groups for all-cause mortality; 216 (9.1%) in the LIPITOR 80 mg 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 (8.3%) than in the placebo group (4.1%). The proportions of subjects who experienced noncardiovascular death were numerically larger in the LIPITOR 80 mg group (5.0%) than in the placebo group (4.0%).

Postmarketing Experience—The following adverse reactions have been identified during postapproval 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, fatigue, tendon rupture, hepatic failure, dizziness, memory impairment, depression, and peripheral neuropathy.

Pediatric Patients (ages 10-17 years)—In a 26-week controlled study in boys and postmenarcheal girls (n=140, 31% Caucasians, 1.0% Blacks, 1.0% Asians, 4.8% other), the safety and tolerability profile of LIPITOR 10 to 20 mg daily was generally similar to that of placebo [see Clinical Studies in full prescribing information and Use in Special Populations, Pediatric Use in full prescribing information].

OVERDOSAGE: There is no specific treatment for LIPITOR overdose. 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.

Please see full prescribing information for additional information about LIPITOR.

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