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Lipitor or Generic? Billion-Dollar Battle Looms

By [ALEX BERENSON](#)

The Lipitor war is about to begin.

Starting next June, insurers and government agencies will have the opportunity to save billions of dollars by moving patients from Lipitor, a [cholesterol](#)-lowering drug by [Pfizer](#) that is the world's top-selling medication, to an inexpensive generic version of Zocor, a similar but less potent drug now made by [Merck](#).

Some insurers are already planning ways to move patients from Lipitor to generic cholesterol drugs after Zocor loses its patent protection. But Pfizer, which plans to use marketing muscle and clinical data to fight that migration, says that Lipitor has unique benefits and is worth a premium price, especially for patients at high risk of heart attacks.

Both medicines belong to a class of drugs known as statins, which are the nation's best-selling medications, with almost 150 million prescriptions expected to be filled this year at a cost of \$16 billion. The insurers, and some cardiologists, say that switching patients from Lipitor to generic Zocor will be a safe way to cut costs in an era of skyrocketing pharmaceutical prices.

In many cases, they say, patients who now take the most commonly prescribed dosage of Lipitor - 10 milligrams daily - can reduce their cholesterol just as much with Zocor. Lipitor costs \$2 or more a day, while generic Zocor will probably cost 35 cents or less.

"If I was taking a statin, I'd want to take the cheapest one, as long as I get to the goal that I wanted to get to," said Dr. Scott Grundy, a researcher who has consulted for both Merck and Pfizer. Dr. Grundy led a federal panel that in 2001 wrote guidelines for treating people with high cholesterol.

But other doctors and epidemiologists say that Lipitor may be the best drug for many patients. "It would not be good medicine to go to a cheaper medicine that has less efficacy in our high-risk patients," said Dr. Robert Vogel, a cardiologist at the University of Maryland, who has been paid by Pfizer to help conduct a clinical trial of Lipitor.

Pfizer says it will fiercely defend Lipitor. "By taking any dose of Lipitor, you will reduce the risk of a cardiovascular event faster and to a greater degree than you will with any other medicine," said J. Patrick Kelly, Pfizer's president of United States [pharmaceuticals](#).

The fight over Lipitor involves a collision of fundamental forces in American health care. Spending on prescription drugs has jumped from \$40 billion in 1990 to almost \$250 billion this year, and continues to rise faster than overall inflation. But while many Americans say they believe that prescription drugs cost too much, they rarely want to accept generic medicines for themselves instead of more expensive drugs that may be only marginally better - especially since insurers or government agencies pay nearly 70 percent of all drug costs.

Dr. JoAnne Foody, a practicing cardiologist and a professor at Yale University School of Medicine, said she expected to continue prescribing Lipitor for her high-risk patients, who need the maximum possible reduction in cholesterol.

But she said she would be inclined to switch other patients off Lipitor onto generic Zocor, also called simvastatin, if the price difference was significant.

"There are a very large portion of patients where the data for simvastatin are equivalent and sometimes better than the data for Lipitor," Dr. Foody said.

But convincing American patients to give up a brand-name medicine and take a generic drug is not easy, said Albert Rauch, a drug industry analyst at A. G. Edwards, a regional brokerage firm based in St. Louis.

For example, even though the antacid Prilosec is available in an inexpensive over-the-counter form, people prefer three very similar but higher-priced prescription antacids - Prevacid, Nexium and Protonix. Those three will have \$10 billion in United States sales this year.

"Therapeutic substitution - substituting one product for another in the same class - just hasn't happened yet," Mr. Rauch said.

And Lipitor has more than Pfizer's marketing dollars working for it. Last month, an analysis of 14 clinical trials by Oxford University and the University of Sydney in Australia found that the more potent the statin and the greater the cholesterol reduction, the lower the risk of [heart disease](#).

Dr. Colin Baigent, who oversaw the analysis, did not directly endorse Lipitor but said he believed that statins were not interchangeable.

"The aim should be to get their LDL cholesterol as low as possible," Dr. Baigent said, referring to low-density lipoprotein, or LDL, cholesterol - commonly called bad cholesterol. "There is potential for many patients benefiting more."

Statins work by interfering with the liver's ability to synthesize LDL cholesterol. All statins are chemically similar, although Lipitor, whose active ingredient is called atorvastatin, is more potent than Zocor, or simvastatin.

The highest dosage of Lipitor (80 milligrams) can reduce cholesterol as much as 57 percent in an average patient, while the highest dosage of simvastatin lowers cholesterol 47 percent. But because most patients are not placed on the highest dosages, the two drugs can achieve comparable cholesterol-lowering results in many cases.

Several large clinical trials have shown that statins reduce the risk of heart attacks and strokes. And statins appear to be safe for most patients, although they can cause muscle weakness in some people and occasionally lead to severe muscle damage.

As a result, statins have become among the most commonly prescribed drugs. This year's forecast of 150 million statin prescriptions in this country is up from 82 million in 1999, according to [IMS Health](#), a Pennsylvania company that compiles data about drug usage.

About half of those prescriptions will be for Lipitor, which is taken by 12 million Americans a year, at a cost of about \$8 billion. Worldwide, Lipitor sales are forecast to top \$12 billion this year, making the drug by far the best-selling prescription medicine.

Prescription drugs are protected by patents that give their inventors the exclusive right to sell them for up to 20 years, though they usually must spend part of that time gaining federal approval. The patent protection enables the drug maker that discovered the drug to earn back its development costs and make a profit. Otherwise, other companies could make and sell identical versions of the medicine, undercutting the company that invented it.

But when a patent expires, the legal protection disappears. At that point any company can make the drug, as long as it proves to the Food and Drug Administration that its version is identical to the original. The patent on Lipitor is to expire in 2011, but that patent has been challenged.

Zocor will lose its patent protection next June 23, and be opened to competition. [Ivax](#), a generic drug company, has already said it will produce a generic version of the drug, and other companies plan to follow. As more generics enter the market, the price of generic simvastatin could fall to 35 cents a pill or less, compared with \$3 or more now, according to Richard T. Evans, a drug industry analyst at Sanford C. Bernstein & Company.

Merck will lose billions of dollars in annual sales and profits when Zocor loses its patent protection. To recoup its profits, Merck has introduced another anticholesterol drug, Vytorin, which combines Zocor with Zetia, a medicine from [Schering-Plough](#) that is not a statin but also reduces cholesterol.

Vytorin is about as effective as Lipitor at lowering cholesterol, so both Merck and Pfizer have a stake in convincing doctors and insurers that they should pay extra for the increased potency their drugs offer over generic Zocor. But because Lipitor is so much more popular than Vytorin, Pfizer has more to lose than Merck and Schering-Plough if generic simvastatin becomes a standard treatment.

Last week, Express Scripts, a Missouri company that helps companies design drug benefit plans, said it would drop Lipitor from its list of preferred drugs. Instead, Express Scripts has devised a plan that will offer patients taking generic simvastatin a much lower co-payment on their prescriptions.

Steve Littlejohn, a spokesman for Express Scripts, said simvastatin was a viable alternative to Lipitor for most patients.

At its minimum 10-milligram dose, Lipitor reduces bad cholesterol an average of 39 percent. In contrast, a 40-milligram dose of simvastatin cuts cholesterol by as much as 41 percent. For patients who need a higher-potency statin, Vytorin will be available, Mr. Littlejohn said. "Consumers and physicians and employers have seen the steady, almost inexorable rise in pharmacy costs, and said nothing can be done," Mr. Littlejohn said. "We're saying something can be done."

Other insurers also say the Zocor patent expiration is an opportunity to reduce drug spending. Robert Seidman, the chief pharmacy officer for WellPoint, the nation's largest publicly traded health insurer, estimated that wide use of simvastatin could reduce the nation's drug costs by \$2 billion or more a year. To encourage patients to switch from Lipitor, WellPoint plans to offer members four to six months of free simvastatin as soon as generic versions are available, he said.

But Pfizer is fighting back. To demonstrate Lipitor's benefits in different kinds of patients, Pfizer has conducted 400 clinical trials on Lipitor, covering 80,000 people. Lipitor's edge over other statins goes beyond its superior ability to lower cholesterol, said Mr. Kelly.

The data from those clinical trials has enabled Pfizer to repeatedly broaden Lipitor's label of approved uses, changes that must be approved by the F.D.A. Last month, the F.D.A. said Pfizer could begin to market Lipitor for the prevention of heart attacks and strokes in [diabetics](#). To build brand loyalty, Pfizer also has thousands of sales representatives discussing Lipitor with doctors and spends at least \$60 million annually to advertise Lipitor to consumers, according to Brandweek magazine. Pfizer declined to discuss how much it spends to market Lipitor.

Dr. David Hyman, professor of medicine at Baylor College of Medicine in Houston, said he did not expect many patients to be switched off Lipitor. He pointed to drugs that lower [blood pressure](#), where expensive branded medicines dominate cheaper generics despite extensive research showing the generics work as well. "So much of the market is really not price-responsive."

But other experts on drug benefits said they believed that generic simvastatin might put a dent in Lipitor's sales, because companies, government agencies and patients had become so concerned about drug costs.

"It's very likely that a large portion of the market, especially those covered by managed care organizations, will switch to generic Zocor," said Albert Wertheimer, a professor of pharmacy at Temple University. "It seems like a reasonable thing to try."