



Selling Statins Over-the-Counter

*FDA Weighs Whether to Let Patients Buy
Cholesterol Drugs Without a Prescription*

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SHOULD cholesterol-lowering statins, the biggest selling drugs in the world, be available to consumers as easily as aspirin—on drugstore shelves without a prescription?

A joint venture between Merck & Co. and Johnson & Johnson is asking for permission to sell a 20-milligram dose of Merck's Mevacor over the counter, arguing that the step would extend the benefits of the drugs to potentially millions of patients who currently aren't taking them. Statins are a major weapon against heart attacks, strokes and death from cardiovascular disease. A Food and Drug Administration advisory panel will discuss the issue today, with its vote expected to foreshadow the agency's ultimate decision.

The FDA, which is under scrutiny from Congress for its handling of safety matters on painkillers and other drugs, so far is taking a skeptical tone. An agency analysis sent to the panel concluded that Merck's own study showed "the majority of consumers cannot correctly self-select" to use Mevacor without assistance from a health-care provider. Some of the study participants chose to take the drug even though they didn't actually know their cholesterol levels.

The outcome will be important in a far larger debate that has grown as Internet-educated con-

Statin Targets

A proposed over-the-counter 20 milligram dose of Mevacor would be aimed at:

- **Men 45 and older and women 55 and older**
- **With LDL between 130 and 170**
- **And at least one of these heart-disease risks: a smoker; HDL (good cholesterol) of 39 or under; high blood pressure; heart disease in a father or brother before age 55 or in a mother or sister before 65**

Source: Merck & Co.

sumers seek to take more control of their health-care choices. The key question is which decisions patients can make on their own—and which should be left to a doctor. Whatever happens with Mevacor, the issue will come up again: Bristol-Myers Squibb Co. has said it plans a new attempt to switch its own statin, Pravachol, to over the counter.

The statins are a landmark test of the FDA's thinking on over-the-counter medicines. Traditionally, drugstores carry remedies for short-term problems, like headaches. But statins have to be taken for a long period of time to tame chronically high cholesterol, which doesn't have symptoms. Patients would have to decide for themselves whether they need the drug, and monitor their own progress.

In the United Kingdom, regulators allow consumers to buy a different statin, Zocor, over the counter. But that program included a big role for pharmacists in advising patients, a structure that may not be easy to duplicate in the U.S., where consumers are used to grabbing their own medicines off the shelf.

In the U.S., where an FDA advisory panel in 2000 turned down over-the-counter requests for Mevacor and Pravachol, many doctors remain skeptical that consumers can manage their own risks for something as serious as heart disease. "Statins are strong medicines for a condition that

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is potentially life-threatening," says Steven Nissen, a cardiologist at the Cleveland Clinic. They "should be prescribed by physicians with the training and experience...to choose the right thing for the right patient at the right time."

The goal with an over-the-counter statin would be to get treatment to millions of Americans who under current guidelines should be taking the drugs but aren't. The joint venture, Johnson & Johnson/Merck, says 15 million to 20 million Americans are at risk of a first heart attack or stroke—with moderately elevated LDL, or bad cholesterol, between 130 and 170. National guidelines advise getting LDL below 130. Yet only three million to five million of them are getting treatment because, among other reasons, they aren't seeing a doctor regularly, they lack insurance or their doctors aren't effectively monitoring their risks.

Switching to over the counter would ease access and potentially reduce costs, the drug makers say. And at 20 milligrams, the companies say the Mevacor drug would be effective enough to reduce LDL in this moderate-risk population while still having a low risk of side effects.

Merck and Johnson & Johnson say that their program can ensure that the right patients take Mevacor. The plan entails a "self management system" that includes, among other things, detailed criteria noted in the packaging to help consumers decide whether their LDL cholesterol, age and other risk factors make them candidates for Mevacor. The packaging also directs consumers to a Web site and a toll-free call center for information and a cholesterol-testing referral service. Consumers are encouraged to contact their doctors.

As a test of how well consumers can choose, the companies mounted an unusual study intended to mimic real-world practice. They set up 14 mock storefront drugstores in seven regions of the U.S., with products lined up on shelves and a nurse to represent a pharmacist. They recruited customers to come in and consider Mevacor as an over-the-counter drug. All told, 3,316 people showed up, of whom 1,061 decided to purchase the medicine. These people were then tracked for six months.

The companies' researchers concluded that 84% of the participants made an "appropriate" initial decision on whether to purchase the drug, based on whether they met criteria listed in the packaging label. But that number included

everyone who decided against making a purchase: The companies viewed those consumers as having made a correct decision, though there was no follow-up.

Of the consumers who did choose to take the drug, 66% met or came close to meeting the criteria, according to the analysis. During the study, 23 participants, or 2%, either took Mevacor with drugs that could cause adverse reactions or otherwise used the medicine in a fashion that raised risks, though no serious consequences resulted.

The study, which was published in November in the American Journal of Cardiology, found that of 878 participants who had their cholesterol measured after six months, 548, or 62%, got their LDL to a target below 130. And the study prompted many participants to contact their doctors—a result company officials regard as an indication the program works.

But the FDA said the study didn't reflect real-world conditions. According to the FDA's own analysis, just 55% of participants made the right decision about

whether to take Mevacor, and only 41% correctly continued to use the drug by the sixth week. The biggest problem was that consumers didn't know their cholesterol levels. Among people who said they did know, only half accurately identified their LDL. Some who didn't know their total cholesterol profiles, including both good and bad forms, still chose to take the drug.

The FDA also raised questions about whether consumers would use a statin safely without oversight from a doctor. The FDA reviewer cautioned that because the study limited the amount of Mevacor consumers could buy, it didn't truly reflect the risk of overdosing. The agency also questioned whether consumers should take the drug without a requirement for a doctor to test periodically for liver problems, a possible side effect of statins, and whether patients would be cautious enough about interactions with other drugs and substances.

Statins have built up an impressive record on both safety and effectiveness

over more than 15 years on the market. But the class has blemishes too: Bayer AG pulled its statin Baycol from the market in 2001 because of a heightened risk of a very rare but potentially lethal muscle-wasting side effect called rhabdomyolysis, and AstraZeneca PLC's Crestor has been hobbled by worries about similar side effects, especially at high doses.

Another concern is that patients at high risk of heart attack or stroke might not get all the treatment they need. "We would not want people who had heart disease that required very aggressive treatment to think that all they need to do is take a low-dose statin," says Sidney Smith, a cardiologist at the University of North Carolina at Chapel Hill.

Still, even skeptics acknowledge that new strategies are needed. "I don't think we're ready to sell statins over the counter tomorrow," says Edgar Lichstein, a cardiologist and chairman of medicine at Maimonides Medical Center, New York. But "It's an idea that should be explored."