

House Panel Scrutinizes Trial of Drug

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A Congressional committee is investigating Merck and Schering-Plough for their handling of a critical clinical trial of Zetia, their blockbuster cholesterol-lowering drug.

On Tuesday, the House Committee on Energy and Commerce demanded more information about delays in the trial, which was completed in April 2006 but whose results have not yet been released.

In a letter to Merck and Schering, the committee's top two members asked officials at both companies to agree to talk to investigators and said both companies should retain important documents about the trial, called Enhance.

Independent scientists have viewed Enhance as crucial because it is the first trial that would answer whether Zetia's ability to lower cholesterol has real biological benefits for patients. The results might also help answer nagging questions about Zetia's safety.

Zetia and Vytorin, a companion drug, are among the most popular of all prescription medicines. One million prescriptions are filled worldwide each week, at a cost of \$5 billion annually. But compared with other cholesterol drugs there is far less evidence of their safety and effectiveness.

"We are concerned with the delay in releasing the results of the study," said the letter, which was signed by two Michigan Democrats, John D. Dingell, the committee's chairman, and Bart Stupak, the chairman of the committee's subcommittee on oversight and investigations.

The letter asked the companies to provide their records to the committee by Dec. 25.

Lee Davies, a Schering spokesman, said the companies had not yet officially received the letter as of Tuesday night and could not comment on it. Schering and Merck jointly market Zetia and Vytorin and split their profits about equally.

The Enhance trial covered 720 patients with very high cholesterol and was intended to prove that the combination of Zetia and an older cholesterol medicine would reduce the growth of plaque in the arteries more than the older medicine alone.

Cardiologists view the growth of plaque as a good marker for the risk of heart attack and strokes. If the trial revealed that patients taking Zetia did not have a reduction in plaque growth, the results would add to questions about Zetia's effectiveness.

Schering and Merck were originally expected to release the results of the trial at a conference in the spring of 2007, then in the fall. Last month, after being criticized by cardiologists, they said they would release the results next March. The companies say

the results are still blinded, meaning that they do not know whether the drug succeeded or failed.

Zetia, whose generic name is ezetimibe, is a relatively new cholesterol medicine that works differently from cholesterol drugs like Lipitor. Medicines like Lipitor, called statins, slow the liver's ability to produce cholesterol, while Zetia limits the body's absorption of cholesterol.

Doctors often prescribe Zetia with low-dose statins, as an alternative to increasing the statin dose. Some patients dislike high-dose statins because they can cause muscle pain.

Some prominent cardiologists, including Dr. Steven Nissen, the chairman of cardiovascular medicine at the Cleveland Clinic, are concerned that Zetia may not work as well as statins, which have added benefits, he said.

Other doctors are not as concerned. Zetia has been proved to lower LDL, or bad, cholesterol by 15 to 20 percent. Every other medicine that lowers LDL also reduces heart attacks, and there is no reason to believe Zetia to be an exception, said Dr. Michael Crawford, the interim chief of cardiology at the University of California, San Francisco.