Drug Has No Benefit in Trial, Makers Say

By ALEX BERENSON

A clinical trial of Zetia, a cholesterol-lowering drug prescribed to about 1 million people a week, failed to show that the drug has any medical benefits, Merck and Schering-Plough said on Monday.

The results will add to the growing concern over Zetia and Vytorin, a drug that combines Zetia with another cholesterol medicine in a single pill. About 60 percent of patients who take Zetia do so in the form of Vytorin, which combines Zetia with the cholesterol drug Zocor.

While Zetia lowers cholesterol by 15 percent to 20 percent in most patients, no trial has ever shown that it can reduce heart attacks and strokes — or even that it reduces the growth of the fatty plaques in arteries that can cause heart problems.

This trial was designed to show that Zetia could reduce the growth of those plaques. Instead, the plaques actually grew almost twice as fast in patients taking Zetia along with Zocor than in those taking Zocor alone.

Patients in the trial who took the combination of Zetia and Zocor were receiving it in the form of Vytorin pills. The trial, called Enhance, lasted two years and covered about 720 patients with extremely high cholesterol, mostly in the Netherlands.

Dr. Steven Nissen, the chairman of cardiology at the Cleveland Clinic, said the results were "shocking." Patients should not be prescribed Zetia unless all other cholesterol drugs have failed, he said.

"This is as bad a result for the drug as anybody could have feared," Dr. Nissen said. Millions of patients may be taking a drug that has no benefits for them, raising their risk of heart attacks and exposing them to potential side effects, he said.

Still, patients who are taking Vytorin or Zetia should talk to their doctors if they are concerned and not discontinue taking the medicines on their own, Dr. Nissen said.

Dr. Howard Hodis, a cardiologist at the University of Southern California, also said he was concerned by the trial's results. Growth in fatty plaques — called atherosclerosis — is highly correlated with heart attacks and strokes, Dr. Hodis said.

"Clearly, progression of atherosclerosis is the only way you get events," Dr. Hodis said. "If you don’t treat progression, then you get events."

The results of the trial "necessitate further investigation — that just can’t be ignored," Dr. Hodis said.

Both companies' stocks fell on Monday, with Merck's share price down a bit more than 1 percent. Shares of Schering-Plough, whose profits are much more dependent on the drugs, were down nearly 8 percent.