

July 4, 2011

## **Study Links Smoking Drug to Cardiovascular Problems**

By **DUFF WILSON**

Chantix, the best-selling prescription drug for smoking cessation, was linked to an increased risk of a heart attack, stroke or other serious cardiovascular event for smokers without a history of heart disease compared with smokers who did not use the drug, according to a Canadian medical journal report released on Monday.

The finding added to previous warnings about the pill's connection to psychiatric problems and cardiovascular risks for people with a history of heart disease.

It posed a new challenge to a product that has been prescribed to 13 million people and had \$755 million in sales last year.

Officials of Pfizer, the manufacturer of Chantix, and the Food and Drug Administration responded that they had been planning to conduct a joint analysis of clinical trials on whether Chantix posed heart risks, due next year.

"This would have raised a red flag for us if the flag hadn't already been flying," Dr. Celia Winchell, a team leader with the agency's Center for Drug Evaluation and Research, said in an interview.

Pfizer, in a statement, said the analysis in the Canadian Medical Association Journal was based on too few heart or cardiovascular events to draw conclusions about the risks. The company said Chantix brought "immediate and substantial" health benefits to smokers who quit.

The senior author of the new report, Dr. Curt D. Furberg, a Wake Forest medical professor, said there were better ways to quit and called for removal of the drug from the market.

"It piles up," he said. "I don't see how the F.D.A. can leave Chantix on the market."

The lead author, Dr. Sonal Singh, assistant professor of medicine at Johns Hopkins University, said the agency and Pfizer had failed to pursue signs of cardiovascular risk since Chantix was approved in 2006.

"The F.D.A. should have already put it on their warning label," Dr. Singh said. "The risk is substantial, the risk is present in smokers without heart disease, and Pfizer knew about this for five years."

Last month, the agency issued a safety notice about cardiovascular risk from Chantix use by people with a history of cardiovascular disease, based on a study of 700 people.

The new report is broader, analyzing 14 randomized clinical trials involving 8,200 patients, excluding those with cardiovascular disease so that it gives a better picture of which heart problems the drug could cause in otherwise healthy people trying to quit smoking.

The new study, known as a meta-analysis, compiled data from 14 random, blinded, placebo-controlled clinical trials that tracked cardiovascular outcomes. It found 52 out of 4,908 people taking Chantix had serious cardiovascular events, a rate of 1.06 percent, compared with 27 out of 3,308 people taking a placebo, a rate of 0.82 percent. While the absolute difference is only 0.24 percent, the weighted, relative difference is 72 percent.

“We have known for many years that Chantix is one of the most harmful prescription drugs on the U.S. market, based on the number of serious adverse effects reported to the F.D.A.,” Dr. Furberg said in a statement. “It causes loss of consciousness, visual disturbances, suicides, violence, depression and worsening of diabetes. To this list we now can add serious cardiovascular events.”

Dr. Furberg, who once directed clinical trials for the government and writes widely about drug safety, has been paid as an expert witness in cases against Pfizer. Dr. Singh and two other researchers said they had no conflicts of interest.

When combining studies of smokers with and without pre-existing disease, the study found that doctors could expect to get one extra cardiac event associated with Chantix for every 28 smokers they treated with the drug. The researchers also estimated one additional person would quit for every 10 treated with Chantix.

The benefit of Chantix was emphasized in a separate commentary in the journal by Dr. J. Taylor Hays of the Mayo Clinic in Rochester, Minn. He described the meta-analysis as “timely and important” but said it lacked overall size and standardization. Dr. Hays, who has been paid by Pfizer to study Chantix, said the benefits of quitting smoking outweighed the risks of the drug.

Chantix is selling well overseas. In Japan, for instance, some pharmacies ran out for a while recently, even as the drug failed to meet expectations in the United States because of health warnings and bad publicity.