New Study Links Pfizer's Bextra, Similar to Vioxx, To Heart Attacks

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The incidence of heart attacks and strokes among patients given Pfizer's painkiller Bextra was more than double that of those given placebos, according to preliminary results of a study presented yesterday at the American Heart Association meeting in New Orleans.

The study, which pooled data from 5,930 patients taking part in 12 trials, found 2.19 times the number of heart attacks or strokes among patients given Bextra, compared with those given placebos. Merck recently withdrew Vioxx, a drug similar to Bextra, after a longer and better-controlled study showed that it doubled the risk of heart attack and stroke.

"The magnitude of the signal with Bextra is even higher than what we saw in Vioxx," Dr. Garret A. FitzGerald, a cardiologist and pharmacologist at the University of Pennsylvania, said in an interview after presenting the data. "This is a time bomb waiting to go off."

Susan Bro, a spokeswoman for Pfizer, said that a heart problem with Bextra appeared only in studies involving patients at very high risk for heart disease who were undergoing cardiac surgery -- a disclosure Pfizer made on Oct. 15. Other studies of Bextra involving 8,000 patients with arthritis who were followed for 6 to 52 weeks found no heart problems, she said.

Dr. FitzGerald is one of the world's leading experts in COX-2 drugs, a class of medicine that includes Vioxx, Bextra and Celebrex, which is also made by Pfizer. Vioxx had sales of $2.5 billion last year, while Celebrex had sales of $1.8 billion and Bextra $687 million. Celebrex and Bextra have been on their way to bigger sales this year.

In previous studies, Dr. FitzGerald was among the first to explain why COX-2 inhibitor drugs, which were developed to cure pain without causing ulcers, might create heart troubles.

Dr. Curt Furberg, professor of public health sciences at Wake Forest University School of Medicine, helped conduct the study that Dr. FitzGerald announced yesterday. "Basically, we showed that Bextra is no different than Vioxx, and Pfizer is trying to suppress that information," Dr. Furberg said.

The new study of Bextra, however, is not nearly as persuasive as the trial that led to Vioxx's withdrawal because it is backward-looking and simply reorganizes data presented in other settings. Ms. Bro, the Pfizer spokeswoman, said the new study grouped samples that were too disparate for conclusive results.

But Dr. FitzGerald said the latest findings added to growing worries that all COX-2 inhibitors, including Bextra and Celebrex, should be used with great caution.

There is no evidence that Celebrex causes heart problems, Pfizer said.

The FitzGerald study was not the only negative development regarding Bextra. News reports yesterday noted that Pfizer said in a Nov. 5 regulatory filing that the Food and Drug Administration had rejected an application to use

Bextra to treat migraines. The company said it was notified in August of the rejection.

Pfizer's stock slipped 25 cents yesterday to close at $25.99. It declined 38 cents on Monday, as investors digested the company's disclosure that it would probably add a "black box" warning -- the strongest kind -- to Bextra's label. The warning would note that, in rare instances, the drug could cause fatal skin rashes. In its Oct. 15 warning about Bextra's potential risks to patients after heart surgery, Pfizer acknowledged that it had known the results of this study for at least two months before announcing them. During that period, Pfizer representatives said publicly that the company had no evidence that either Celebrex or Bextra caused the kind of heart problems found in a large study of Vioxx.

Bextra is approved to treat arthritis pain. Unlike Vioxx, neither Bextra nor Celebrex has proved to be any safer on the stomach than older, cheaper medicines like ibuprofen or naproxen. Nor has Bextra or Celebrex been shown to alleviate pain any better than those older drugs.

As the COX-2 controversy has continued, the Food and Drug Administration has been criticized by some researchers and medical journal editors for failing to require Vioxx's withdrawal years ago. Yesterday, Health and Human Services Secretary Tommy G. Thompson defended the F.D.A.'s handling of the Vioxx withdrawal.

"You can always be a Monday morning quarterback and say, you know, this could have been done better," Mr. Thompson said. "I think the F.D.A. just does an outstanding job of protecting Americans' health."

Vioxx's maker, Merck, suffered a financial blow yesterday, as the rating on its $4.9 billion in long-term debt was cut two levels, to Aa2 from Aaa, by Moody's Investors Service. The company's share price has plummeted after the withdrawal of Vioxx, which accounted for 11 percent of the company's sales last year. Hundreds of lawsuits have been filed by lawyers for patients or their survivors claiming Vioxx caused injuries or deaths.

On Tuesday, Dr. FitzGerald also provided results of his further investigations into the mechanism by which COX-2 medicines may lead to heart troubles. Using mice, Dr. FitzGerald said, he found that inhibiting the COX-2 enzyme might reduce the heart protection of estrogen.