Diabetes drug risks reported ahead of FDA hearing

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(AP) -- A new study led by a federal drug safety expert ties the controversial diabetes drug Avandia to a higher risk of heart problems, strokes and deaths in older adults, and says it is more dangerous than a rival drug, Actos.

The study, a huge review of Medicare records, comes two weeks ahead of a Food and Drug Administration hearing on Avandia's safety. The lead author, Dr. David Graham, is an FDA scientist who wants the pill banned.

As many as 100,000 heart attacks, strokes, deaths and cases of heart failure may be due to Avandia since it came on the market in 1999, Graham said in an interview with The Associated Press.

Harms from Avandia are great enough to "put you in a hospital or in a cemetery," he said.

Editors at the Journal of the American Medical Association rushed to release the study online on Monday, so the information would be available before the July 13-14 hearing, a spokeswoman said.

Avandia is a once-blockbuster drug for Type 2 diabetes, the most common form of the disease and the kind often tied to obesity. Avandia and Actos are pills that help the body make better use of insulin, a key digestive hormone.

The American Heart Association issued a statement reminding patients not to stop taking any medicine without talking with their doctors first. The new study is not definitive enough to prove harm but "deserves serious consideration" and should be discussed between patients and their doctors, the statement says.

Avandia has been under a cloud since May 2007, when a review of dozens of studies suggested it may raise the risk of heart attacks and heart-related deaths. Warnings were added to its label, and the American Diabetes Association told patients to avoid using it until safety questions were resolved.

The FDA and Congress have held meetings on the drug but it has remained on the market, still used by hundreds of thousands of Americans.

Avandia's maker, the British company GlaxoSmithKline PLC, maintains that its drug is safe. A spokeswoman said the new study has limitations, and that the company looks forward to a full discussion of evidence at the FDA hearing.

The study involved 227,571 Medicare patients, average age 74, who started on Actos or Avandia from July 2006 through June 2009 and were followed for three years on average.

Avandia patients were 27 percent more likely to suffer strokes, 25 percent more likely to develop heart failure and 14 percent more likely to die than those on Actos, researchers found.

There were 2,593 heart attacks, heart failure cases, strokes and deaths among the 67,593 Avandia users, and 5,386 of those problems among the 159,978 people taking Actos. Just dividing these numbers to compare side effect rates can't be done, though, because people were on

the drugs for differing lengths of time.

Unlike studies in younger patients that implicated Avandia, heart attack risks were similar in both groups in the Medicare study. Sudden cardiac deaths are much more common in older adults, and whether Avandia affects heart risks differently in older versus younger patients is unknown, the researchers note.

The findings suggest that if 60 people were treated with Avandia for one year, one extra case of heart failure, stroke or death would occur that could have been avoided if they'd taken Actos instead, Graham said.

"The evidence is overwhelming," he said. "There is not a single study where those two drugs are compared where Avandia doesn't look worse than Actos. How many studies do you have to do before you come to your senses?"

The study was observational, with the researchers examining data on patients whose doctors had prescribed Avandia or Actos. That's less rigorous than studies that randomly assign patients to take different drugs, and therefore cannot prove that the drug is riskier.

But Dr. Alvin Powers, a diabetes specialist at Vanderbilt University, called it "important information that's consistent with prior studies," even if it is not definitive. He said he doesn't prescribe Avandia because of uncertainty over its safety.

Another AMA journal, Archives of Internal Medicine, on Monday released online an expanded analysis by the same authors who did the original one in 2007; both suggest higher heart risks for Avandia.

At its hearing next month, the FDA plans to examine the latest safety data and air internal disagreement among its scientists over what should

be done.

At the FDA's request, Glaxo began a big study last year comparing heart and stroke risks in patients on Avandia or Actos, made by Japan's Takeda Pharmaceuticals. It aims to enroll thousands of patients, but an editorial in JAMA about the Medicare study says it would be unethical to let the study continue.

The editorial, by Dr. David Juurlink of the University of Toronto, says it is hard to understand why patients and doctors would choose Avandia when a safer alternative exists. He led a previous study of elderly diabetics in Ontario that also found higher risks with Avandia versus Actos.

More information: JAMA: http://jama.ama-assn.org
Archives: http://www.archinternmed.com
Drug comparisons:
http://www.effectivehealthcare.ahrq.gov/reports/final.cfm
Diabetes information: http://www.diabetes.org
and http://diabetes.niddk.nih.gov/