Senate report: Avandia maker knew of cardiac risks

February 22 2010, By BARBARA ORTUTAY , AP Business Writer

(AP) -- A Senate report said Saturday that drug maker GlaxoSmithKline knew of possible heart attack risks tied to Avandia, its diabetes medication, years before such evidence became public.

Sen. Max Baucus, chairman of the Senate Finance Committee, and Chuck Grassley, the committee's ranking Republican, released the report, which follows a two-year inquiry, on Saturday. They are also asking the U.S. Food and Drug Administration why it allowed a clinical trial of Avandia to continue even after the agency estimated that the drug caused 83,000 heart attacks between 1999 and 2007.

The agency ordered a warning to be included on Avandia's label in 2007, saying that it might increase the risk of heart attacks, though the data on those risk was inconclusive.

Soon afterwards Sen. Grassley, one of the FDA's toughest critics in Congress, disclosed that the agency's internal safety experts came within one vote of recommending a withdrawal of Avandia.

The Senate report suggests sharp disagreements remain at the FDA over how to handle Avandia's risks.

In a letter to FDA Commissioner Margaret Hamburg that was also released Saturday, the senators said the committee's report was based on researchers' studies of Avandia, internal GlaxoSmithKline documents and FDA documents. They said committee investigators had interviewed

GlaxoSmithKline and agency employees as well as what it called anonymous whistleblowers.

Based on its knowledge of the heart attack risks, GlaxoSmithKline "had a duty to sufficiently warn patients and the FDA of its concerns in a timely manner," the report said.

Instead, the company tried to downplay findings that the drug could increase cardiovascular risks while also working to downplay findings that a rival medication might reduce such risks, it said.

GlaxoSmithKline said in a statement the drug is safe. It said the committee report took data out of context from analyses of Avandia.

In May 2007, the New England Journal of Medicine published an analysis of dozens of studies on nearly 28,000 people who had taken Avandia. The journal said there was a 43 percent higher risk of heart attack for those taking Avandia compared to people taking other diabetes drugs or no diabetes medication. The findings raised concerns because two-thirds of the people with Type 2 diabetes, the most common form, die of heart problems.

"Contrary to the assertions in the report, and consistent with the FDA-approved labeling, the scientific evidence simply does not establish that Avandia increases cardiovascular ischemic risk or causes myocardial ischemic events," GlaxoSmithKline said.

In their letter to Hamburg, the senators said the documents the committee reviewed included an analysis conducted by two safety officials at the agency. The analysis compared Avandia to Takeda Pharmaceutical's diabetes drug Actos, and found that Avandia has an increased risk of heart attack and heart failure. Actos is co-promoted by Pfizer Inc.

At FDA's request, Glaxo agreed in 2007 to conduct a six-year study between its drug and Actos, to give a definitive picture of Avandia's safety. The study, which will involve 16,000 participants, is still enrolling patients.

But FDA researchers quoted in the report called the study "unethical and exploitative," since patients will continue taking Avandia, a drug with known risks, over Actos, which has not shown any links to heart prblems.

FDA spokesman George Strait said the FDA is reviewing new data on Avandia and will present those findings to an advisory committee this summer.

"Meanwhile, Commissioner Hamburg is reaching out to ensure that she has a complete understanding and awareness of all of the data and issues concerning this drug," Strait said.

Avandia was Glaxo's third best-selling drug in 2006 with revenue of $2.2 billion. But the safety concerns disclosed the following year slashed revenue to $1.2 billion by the end of 2008.

Avandia is intended to control blood sugar by increasing the body's sensitivity to insulin, a protein critical to digesting sugars.

Insulin-regulating treatments have long been presumed to lessen the heart risks already associated with diabetes, which is linked to obesity.

More information: Finance Committee letter and report: http://finance.senate.gov/press/Gpress/2010/prg022010b.pdf

GlaxoSmithKline: http://www.gsk.com

Food and Drug Administration: http://www.fda.gov