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FDA panel wants heart failure risk on AstraZeneca drugs

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Federal health advisers say AstraZeneca's Onglyza and a related diabetes drug should carry new information about a possible association with heart failure and death.

The Food and Drug Administration's panel of diabetes experts voiced concern about data suggesting Onglyza and Kombiglyze can increase hospitalization due to heart failure and overall mortality. The panel voted 14-1 that that information should appear on the drugs' prescribing labeling. Yet the panelists also said complicating factors make it difficult to tell whether the risk is real or a statistical fluke.

Considering the drug's overall benefits for treating diabetes, the panel voted 13-1, with one abstention, that the drugs' heart safety profile was acceptable.

The FDA convened Tuesday's meeting to review data from a 16,000-patient study looking at Onglyza and Kombiglyze's heart safety. The agency began requiring such studies in 2008 after several high-profile safety controversies involving diabetes medications and links to heart attack. But pinpointing the heart impacts of diabetes drugs is difficult, because people with the disease are already predisposed to heart problems and other risks.

AstraZeneca's study did not show links to heart attack, but did show a higher rate of heart failure, in which the heart doesn't pump enough blood to maintain blood flow. Six percent of patients taking

AstraZeneca's drugs were hospitalized for heart failure or died of heart-related complications, compared with 5.3 percent of patients taking a placebo. And when FDA scientists analyzed the company data, they found patients taking the drugs had a slightly higher overall chance of dying during the study.

However, panelists had difficulty interpreting the seriousness of the findings. AstraZeneca's study was not especially designed to measure heart failure, instead focusing on heart attack and stroke. And patients enrolled in the study were already predisposed to have heart problems, raising questions about the applicability of the findings to all patients taking AstraZeneca's diabetes drugs.

Some panelists said further studies are needed.

"I don't feel we have resolved concerns about cardiovascular risk," said Dr. Robert Smith, a professor at Brown University, who chaired the FDA panel.

The FDA is not required to follow the guidance of its panelists, though it often does.

Onglyza and Kombiglyze are part of a recently-developed class of diabetes drugs called DPP-4 inhibitors, which also includes Merck & Co.'s Januvia and Tradjenta, made by Eli Lilly & Co. and Boehringer Ingelheim.

The drugs work by making the body produce more insulin after meals, to reduce levels of glucose in the blood, and by limiting the amount of glucose made by the liver.

Merck is expected to release results from its own large study of Januvia's heart risks in coming months.

Leerink Swann analyst Seamus Fernandez said in a recent investment note that if Merck's drug is clear of heart risks it could cut sales of AstraZeneca's diabetes drugs by 50 percent. Fernandez estimates peak sales for Onglyza and Kombiglyze of $1.8 billion.

Those drugs had U.S. sales of $265 million in 2013, according to London-based AstraZeneca's most recent annual report.