

The Endocrine Society
Statement in Response to the Senate Finance Committee Report on Avandia

February 22, 2010

On February 20, 2010, the Senate Finance Committee released a letter to the Food and Drug Administration (FDA), along with an accompanying report, which detailed its concerns about the safety of the drug rosiglitazone (Avandia). The letter suggests that the FDA has inappropriately permitted continued marketing of rosiglitazone and ongoing studies of its use despite evidence that the drug poses severe cardiovascular safety problems for patients.

In 2007, the FDA conducted a detailed analysis of the safety and efficacy of rosiglitazone, including an extensive review by a panel of outside experts, and concluded that rosiglitazone should remain available to patients but with additional warnings. In addition, the FDA asked the maker of rosiglitazone to perform a cardiovascular safety trial, called TIDE (Thiazolidinedione Intervention With Vitamin D Evaluation), to compare Avandia to other diabetes treatments such as pioglitazone. This study is currently recruiting patients.

In light of the Senate Finance Committee's letter, and in view of the substantial amount of new information about rosiglitazone's safety that has been released since 2007, The Endocrine Society (Society) urges the FDA to formally reconsider this issue by re-convening the Endocrinologic and Metabolic Drugs Advisory Committee to reassess the drug's safety prior to the completion of the TIDE study. This established process will permit both outside experts, the specialists within the FDA, and the general public to participate in an open and objective deliberation ensuring that scientifically valid conclusions will be generated which can garner the trust of the medical community and our patients.

As this reevaluation process proceeds, two points should be kept in mind. First, there is a well-recognized hierarchy of scientific validity among different types of studies, and the greatest weight should be given to prospective, randomized-controlled trials of adequate power having pre-specified and adjudicated endpoints (e.g., the RECORD study -- which did not show a statistically significant increase in the risk of cardiovascular events associated with rosiglitazone).

Second, virtually all drugs used to treat diabetes have adverse effects, some of which are quite serious. Moreover, placebo (i.e., no treatment) is not an acceptable alternative to rosiglitazone in actual clinical practice. Consequently, results of placebo-controlled studies have limited usefulness to the clinician; of greater utility are clinical trials which compare the safety of rosiglitazone to the safety of an alternative active treatment.

The FDA is the federal agency with the responsibility for determining the safety and efficacy of drugs. The Society maintains that the FDA should remain the arbiter of controversies over drug safety and the final decision maker, particularly when data are conflicting or inadequate. The Society encourages the FDA to re-examine the safety of rosiglitazone and the appropriate criteria used to define such safety, with the shared aim of providing evidence-based information for practitioners and diabetic patients to use in their joint goal of improving health.

As it stated in 2007, when rosiglitazone safety was also at issue, the Society recommends that providers should react in a measured way to the ongoing controversy until more information can be gathered from the re-convened FDA panel; switching patients from rosiglitazone to another drug in the same or another class can be associated with its own difficulties. The Society also recommends that providers discuss with each diabetic patient taking rosiglitazone both the safety issues that have been raised with this drug's use and the risk/benefit ratio of continuing rosiglitazone versus changing therapy; the recent safety criticisms should be considered as well as the more reassuring findings of the RECORD study.

The Society continues to emphasize cardiovascular risk reduction by aggressive treatment of hyperlipidemia and hypertension in all diabetic patients.