Consumers Union
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February 26, 2010

Commissioner Margaret Hamburg, MD
Food and Drug Administration

Dear Commissioner Hamburg,

Consumers Union is pleased that you are actively reviewing the research, evidence, data, and course of events surrounding the diabetes drug Avandia. We strongly urge acceleration of that review and a decision as soon as possible on whether the drug's sales and use should continue in the U.S. In light of the credible estimates of possible continuing harm to patients caused by this medicine and the fact that there are readily available alternative treatments, we recommend that the agency either (a) dispense with plans for a formal advisory committee meeting this summer and conduct an immediate internal review with input from external advisors, or (b) reschedule the advisory committee meeting on an urgent basis for not later than mid-April. Either way, we urge a decision not later than mid-May.

One possible outcome of that review is, or should be, a temporary suspension of sales and use (except in special circumstances for people currently taking the drug) until definitive evidence of safety becomes available. The weight of the evidence at this point argues powerfully against leaving Avandia on the market for months or even years while more evidence is gathered – for example, until the TIDE trial can be completed.

These recommendations are based on the FDA's internal (and newly released) 2008 evaluation of the research by Drs. Graham and Gelperin; the data and evidence contained in the comprehensive 2-year examination by the Senate Finance Committee of events surrounding the drug; a February 25, 2010 report from the Institute for Safe Medication Practices (ISMP) tallying more than 1,000 deaths attributed to or associated with Avandia between January and September 2009 based on FDA's MedWatch reporting system (www.ismp.org); and our own assessment of the evidence and comparison of oral diabetes drugs conducted in the context of the *Consumer Reports Best Buy Drugs* project (www.ConsumerReportsHealth.org/BestBuyDrugs).

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Consumers Union's evaluation was based on a meta-analysis of studies comparing the effectiveness of the oral diabetes drugs conducted by researchers at the Johns Hopkins University's Evidence-based Practice Center. The Johns Hopkins' analysis was conducted in 2006-2007 under contract with the Agency for Healthcare Research and Quality. Results were released in July 2007 in the *Annals of Internal Medicine*. Our initial 30-page report, *Treating Type 2 Diabetes: The Oral Diabetes Drugs – Comparing Effectiveness Safety, and Price*, was also released in July 2007 and was thoroughly reviewed before publication by the Johns Hopkins researchers who carried out the AHRQ-funded research. Our report was updated in February 2009.

In that updated report, we join many others in recommending first line treatment with metformin, with addition of a sulfonylurea drug if needed. We warn against use of Avandia or Actos as initial treatment and further question the use of these drugs in anyone with Type 2 diabetes. We base that conclusion on the lack of any proven added clinical benefit over other oral diabetes drugs and clear safety risks (heart failure for both drugs and, with Avandia, apparent added risk of heart attack) that, for the vast majority of patients, exceed risks associated with other oral diabetes drugs.

We know that you and Dr. Sharfstein are committed to changes at the FDA that put public health first and foremost in all the agency's deliberations. It strikes us that the events surrounding the review of Avandia from 2006 to the present (and perhaps pre-2006) offer important lessons on how the FDA can better assess the emergence of new evidence about a drug's risks, manage internal disagreements, become more transparent, and respond more rapidly to mitigate potential serious harm to the public.

Thank you for consideration of our views on this issue. If you have questions or follow up, please contact Mr. Findlay at 202-238-9248 or findst@consumer.org.

Sincerely,

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