

## Avandia Heart Attack Cases are Now Settling

A red poster with white and green text. At the top, the title "Avandia Dangers!" is written in a large, bold, white serif font. Below the title, on the left, is the text "Breaking News July 2010" in bold white, followed by "FDA Committee meets to determine if they will withdraw popular diabetes drug Avandia from the market." in white. On the right, under the heading "SIDE EFFECTS & INJURIES" in white, is a list of six side effects, each preceded by a white right-pointing arrow: "Heart Failure", "Heart Attack", "Liver failure or damage", "Pulmonary edema (fluid in the lungs)", "Macular edema (swelling of the eye)", and "Cardiac Related Death". In the center of the poster is a photograph of a white box of Avandia 8mg Rosiglitazone Maleate Tablets. At the bottom left, the text "Have you taken Avandia?" is written in white. At the bottom right is the Avandia logo, which consists of the word "Avandia" in green with a red triangle above the 'v', followed by "rosiglitazone maleate" and "2 mg, 4 mg, 8 mg tablets" in smaller green text.

# Avandia Dangers!

**Breaking News July 2010**  
FDA Committee meets to determine if they will withdraw popular diabetes drug Avandia from the market.

**SIDE EFFECTS & INJURIES**

- ▶ Heart Failure
- ▶ Heart Attack
- ▶ Liver failure or damage
- ▶ Pulmonary edema (fluid in the lungs)
- ▶ Macular edema (swelling of the eye)
- ▶ Cardiac Related Death

**Have you taken Avandia?**

**Avandia**  
rosiglitazone maleate  
2 mg, 4 mg, 8 mg tablets

## FDA Committees Critical of Avandia

### Plurality of Agency's Expert Panel Members Votes to Pull Product From Market

July 20, 2010 02:25 pm News Staff – A plurality of members of two committees that advise the FDA on medications has voted to recommend that the agency remove rosiglitazone, which is marketed as Avandia, from the market because the diabetes drug has been linked to an increased risk for cardiovascular events.

The medication, which is manufactured by GlaxoSmithKline, or GSK, has been under FDA scrutiny since 2007, and recent studies in JAMA: The Journal of the American Medical Association and the Archives of Internal Medicine concluded that use of the drug significantly increases patients' heart attack risk.

During a July 13-14 joint meeting ([www.fda.gov](http://www.fda.gov)) of the FDA's Endocrinologic and Metabolic Drugs Advisory Committee and the agency's Drug Safety and Risk Management Advisory Committee, 18 of 33 committee members indicated that available data on rosiglitazone, which is a member of the thiazolidinedione class of drugs, are sufficient to raise significant safety concerns for ischemic cardiovascular events in patients with type 2 diabetes in relation to nonthiazolidinediones, such as metformin and the sulfonylureas. Six committee members disagreed.

Twenty-one of the members of the two committees, however, indicated that data are sufficient to raise significant safety concerns about ischemic cardiovascular events in patients with type 2 diabetes who take rosiglitazone compared with use of a second thiazolidinedione, pioglitazone, which is marketed as Actos.

Nine panelists said they were not able to make a finding regarding either question.

When asked what regulatory action the FDA should pursue in regard to rosiglitazone, 12 committee members recommended that the drug be removed from the market. Ten members, however, recommended allowing continued marketing of the medication on the condition that the current package label is revised to include additional warnings and additional restrictions put in place. According to the FDA, such restrictions could include limiting prescribing to physicians who have enrolled in a program and completed required training.

In addition, seven members of the committees recommended allowing continued marketing of rosiglitazone with only the addition of further label warnings, three voted for continued marketing with no label changes, and one member abstained.

Members of the two committees also were asked whether the multicenter Thiazolidinedione Intervention with Vitamin D Evaluation, or TIDE, trial should continue if rosiglitazone remains on the market. Nineteen members recommended that the trial continue in that scenario. Eleven opposed that option.

TIDE is testing the cardiovascular effects of long-term treatment with either rosiglitazone or pioglitazone when used as part of standard of care compared to a similar standard of care without use of either drug in patients with type 2 diabetes who have a history of, or are at risk for, cardiovascular disease. The trial also is evaluating the effects of long-term vitamin D supplementation on mortality and cancer.

It's worth noting that CBS News reported July 14 ([www.cbsnews.com](http://www.cbsnews.com)) that all TIDE arms being conducted in India have been suspended, although the trial continues in hundreds of other sites worldwide. The NIH's [ClinicalTrials.gov](http://ClinicalTrials.gov) website confirms this action.

According to the NIH, TIDE is not expected to be completed until 2015.

Joshua Sharfstein, M.D., the FDA's principal deputy commissioner, said in a July 8 media briefing before the joint meeting of the two committees that there was no set timeline for the FDA to act on the recommendations of its expert panels.

"Obviously, we're going to have to look at a lot of information and really understand the advice that we're getting," Sharfstein said, "and we're going to try to make a decision as quickly as we can under those circumstances."

Meanwhile, GSK said in a July 15 news release that it will record a \$2.36 billion legal charge in the second quarter of fiscal year 2010 for settlements related to rosiglitazone; a U.S. Department of Justice investigation into the manufacturer's Cidra, Puerto Rico, facility; and product liability and antitrust litigation related to GSK's antidepressant drug paroxetine, which is marketed as Paxil.

GSK said it would pay \$750 million to settle a Department of Justice investigation of its now shuttered Puerto Rico facility, which once produced Avandia and the combination rosiglitazone/metformin drug Avandamet.

The manufacturer did not disclose the amount of the rosiglitazone settlements, but Bloomberg L.P. reported July 13 ([www.bloomberg.com](http://www.bloomberg.com)) that GSK had settled about 10,000 liability cases for \$460 million.

Elsewhere, the Committee for Medicinal Products for Human Use was scheduled to review the benefit/risk profile of rosiglitazone on behalf of the European Medicines Agency -- the European Union's FDA counterpart -- during a July 19-22 meeting ([www.ema.europa.eu](http://www.ema.europa.eu)).

Rosiglitazone also is the subject of an ongoing inquiry by the U.S. Senate Committee on Finance ([finance.senate.gov](http://finance.senate.gov)).