

# Another Study Confirms Avandia, Actos Bone Fracture Risk

Apr 29, 2008

Avandia, a diabetes drug already mired in controversy, may double the risk of bone fractures, according to a new study. The study, conducted by Swiss researchers, found a similar risk with the diabetes drug Actos. Previous studies have found that these drugs increase the risk of bone fractures, but the Swiss study sheds light on how serious this problem might be.

Avandia has been a subject of debate since last May, when an analysis of 42 clinical trials published by the Cleveland Clinic showed that patients taking the drug had a 43-percent higher risk of having a heart attack. Last July, the Food & Drug Administration (FDA) convened a panel to discuss the issues surrounding Avandia's heart attack risk. The panel voted 20-3 that the drug did in fact raise the chance of heart attacks, yet the panel still voted 22-1 to allow it to remain on the market. In November, the FDA announced the addition of a long-awaited black box warning for Avandia's increased risk of heart attacks. However, many patient advocates and FDA critics thought the black box warning was a weak response to Avandia's safety issues. These critics continue to call on both GlaxoSmithKline, the maker of Avandia, and the FDA to pull the drug from the market. One diabetes expert, Dr. John Buse, has said that inaction on Avandia might be responsible for as many as 83,000 preventable heart attacks.

According to the Swiss bone fracture study, those on Avandia or Actos had double or triple the odds of non-spine fractures. The odds for fracture were increased among patients who took the drugs for approximately 12 to 18 months and the risk was highest for those with two or more years of therapy. The researchers came to their conclusions by comparing the records of 1,020 diabetic patients with fractures diagnosed by British doctors between 1994 and 2005 against a control group of diabetics who did not have fractures.

Avandia and Actos belong to a class of medicines called thiazolidinediones. Last December, researchers in California published a study that explained the possible reasons for the drugs' effects on bone health. In the body, old bone cells are constantly being replaced by newer cells. This process helps to keep bones strong and resistant to fractures. While it was already known that thiazolidinediones inhibited the action of osteoblasts, cells in the body that build bone, the new research found that thiazolidinediones also appears to affect a key cellular protein called the peroxisome proliferator-activated receptor (PPAR-gamma). In their study, the California team discovered that activating this receptor in mice also stimulates the production of osteoclasts, cells whose key function is to degrade bone. Proper bone health is maintained by a balance between osteoclasts and osteoblasts. When this balance is upset, a patient becomes more susceptible to bone fractures, and stands a much higher chance of developing osteoporosis.

With an estimated 3.5 million or more U.S. patients taking thiazolidinediones, the public health impact from bone degradation could be substantial. Based on both the Swiss and California studies, diabetes patients already at a high risk for bone fractures and

osteoporosis - for example, post-menopausal women - might want to ask their doctors about alternatives to thiazolidinediones. There are currently many diabetes drugs on the market that do not carry a similar bone fracture and osteoporosis risk.