

# Avandia Researchers Find Reason Behind Bone Fracture, Osteoporosis Side Effects

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Avandia places patients at a high risk of bone fractures and osteoporosis by affecting the way bone cells are replenished in the body. While bone fractures are a well known Avandia side effect, no one understood how the diabetes medication affected bone structure. Now, researchers at the Salk Institute for Biological Studies in La Jolla, California have discovered that Avandia affects the workings of two types of cells important to the process of replacing old bone. They surmise that Avandia's action on these cells, osteoblasts and osteoclasts, could account for the bone fracture risks faced by Avandia patients.

In the body, old bone cells are constantly being replaced by newer cells. This process helps to keep bones strong and resistant to fractures. But researchers studying the affects of Avandia on the bone structure of mice found that the medication interferes with this process in two important ways. While it was already known that Avandia inhibited the action of osteoblasts, cells in the body that build bone, the new research found that Avandia 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 Avandia, the public health impact from bone degradation could be substantial. Based on the California Avandia study, 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 Avandia. There are currently many diabetes drugs on the market that do not carry the bone fracture and osteoporosis risk that Avandia does.

Avandia has been a subject of debate since May 21, when an analysis of 42 clinical trails published by the Cleveland Clinic showed that patients taking the drug had a 43-percent higher risk of having a heart attack. In 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.