



## FDA Warns of Bladder Cancer Risk With Actos

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June 16, 2011

Patients taking the diabetes drug [Actos](#) for more than a year may have an increased risk of [bladder cancer](#), according to an FDA interim review of an ongoing epidemiological study. The warning comes just days after two European countries banned use of the drug. The European Medicines Agency (EMA) has yet to release any guidance on use of Actos. Five-year data show that although there's no overall increased risk of bladder cancer, patients with the longest exposure to and the highest cumulative dose of the drug were at greater risk, the agency said.

Actos is now the second medication in the thiazolidinedione (TZD) class to be associated with serious side effects within the past year. Last fall, the use of [Avandia](#) was severely restricted in the U.S. because of concerns about an increased risk of heart attack. Some researchers suspect that this may prompt physicians to back away from prescribing the class at all, moving toward newer therapies, particularly the incretins, when metformin alone is no longer working for type 2 diabetes patients. "I will ask my patients on Actos to consider dropping it and give them an alternative," Dr. Albert Levy of Mount Sinai School of Medicine in N.Y., said in an email to [MedPage Today](#). Under the FDA's restrictions last fall, Avandia is to be used only in patients who have failed therapy with Actos. Researchers say the latest warning probably won't change that process, but there doesn't appear to be much interest in choosing between what some see as the lesser of two evils with the drug class. Dr. Lee Green of the University of Michigan said Avandia has a "solidly established association with heart disease. I wouldn't switch someone from a drug that might turn out to be a problem [Actos] to one that we know is a problem." Dr. David Nathan of Massachusetts General Hospital, said he doubts that Avandia, "a potentially dangerous drug, will replace [Actos] -- another potentially harmful drug, if the bladder cancer risk proves to be real -- given the numerous other choices to treat type 2 diabetes." Instead, many clinicians may move directly to incretin therapy if metformin no longer does the trick. Levy said he would jump to a GLP-1 agonist like liraglutide (Victoza) or exenatide (Byetta) or DPP-4 inhibitors like

sitagliptin (Januvia) for patients who aren't well controlled on metformin. Those drugs may pose problems, too. For example, on Tuesday, the FDA issued a warning about the risks of thyroid cancer and pancreatitis associated with liraglutide. Sue Kirkman, MD, vice president of medical affairs for the American Diabetes Association, said just prior to the FDA's recent decision that the evidence of bladder cancer risk with pioglitazone has been "conflicting, and it's hard to know whether this is real problem or not." She said her organization's main concern is that patients might stop taking their medication after hearing the news about the increased risk rather than talking to their doctors first. Still, Kirkman acknowledges that some of the clinicians her organization represents have made the decision not to use the class, or have at least given it serious consideration before prescribing. "We already knew there were other issues with the class, aside from those seen with rosiglitazone," she said. "There are concerns about fractures, fluid retention, and congestive heart failure." **FDA Warns of Bladder Cancer Risk With Actos** But not all clinicians were quick to decry use of Actos or the TZD class. Dr. Joel Zonszein of Albert Einstein College of Medicine in New York City called the earlier European decision "precipitous and premature" because it was based on a retrospective study and found only a minor increase in cancer risk. He added that triple therapy -- with



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metformin, a TZD, and incretins -- is an "excellent combination, particularly in the more aggressive type 2 diabetes we see nowadays." "During the last three decades, studies have shown that treating diabetes early and aggressively results in much better outcomes," Zonszein said. "There is a need for medications such as Actos that can slow down the devastating results of the diabetes epidemic." Green said that while the recent decisions in the U.S., France, and Germany have made his "antennae go up," they won't yet change his prescribing. He said he also hears a greater public health message within the controversy. "I think the larger message is not about which drugs for diabetes, but about the ultimate foolishness of trying to fix the problem with drugs," Green said. "As long as we keep supersizing ourselves, eating too much and moving too little, we'll have this problem." The FDA began its review of Actos and the potential risk of bladder cancer last September, and said it will continue to monitor data until the full 10-year study is complete.



PHOTO: ABC NEWS