FDA Issues Warnings About Statin Dosing to Reduce Muscle Injury Risk

In early June, the Food and Drug Administration sent out a warning to health care providers about the maximum dose of a common generic statin because of concerns of risk of muscle injury in patients exposed to the previously allowed highest dose. Although this notice may have been missed by most of the public, it is important to keep all of these recommendations in context in case your doctors comment on this new guideline if you are on this commonly used and proven effective cholesterol lowering medication.

First, all statins have been shown to reduce major cardiovascular events in patients at risk for the development or progression of heart and vascular disease.

Second, the side effects (and benefits) of all statins are generally dose-dependent, i.e., the higher dose one can tolerate, the greater the clinical benefit. But the risk of an adverse or side effect also increases commensurately with the dose. The benefits of statins include increased survival, fewer heart attacks, strokes and less heart failure if you are a high-risk patient or have already experienced a cardiac event. The adverse effect of primary concern in this FDA recommendation is the known issue of muscle discomfort that can range of just achiness and weakness (myopathy), to an inflammatory response that may cause some actual muscle injury (myositis), to an uncommon, but potentially fatal, destruction of large amounts of muscle that may lead to kidney failure (rhabdomyolysis). The incidence of myopathy is in the low single digit percentage points, but has been (over)estimated to be as high as 10%. The risk is increased if one is taking certain medications that may cross-react metabolically, or if one is of certain ethnic backgrounds. Simply cutting the dose or trying another statin can usually ameliorate these bothersome symptoms. The more serious adverse effects are each orders of magnitude less common.

The focus of the FDA recommendation is the 80 mg per day dose of the generic statin simvastatin that was sold under the brand name of Zocor™ in the U.S. This maximal dose was prescribed to about 2 million patients in 2010 (although an unknown number may actually be using lower doses by splitting the pill to save money) and had been the highest dose approved in the U.S. since simvastatin was first marketed almost twenty years ago. In a large clinical trial called SEARCH, this highest dose of simvastatin was associated with a statistically increased risk of all muscle complications described above compared to other agents. The FDA decided to issue a statement instructing physicians not to use the 80 mg/d dose in patients who have not been on that dose, and to continue it only if patients have been on the that dose for 12 months without complications. The FDA further reduced the approved doses if one is taking medications that may interact with simvastatin due to shared metabolic pathways. These may be certain antifungal agents, antibiotics, anti-HIV, fibrates, some calcium channel blockers and antiarrhythmic agents. Talk to your doctor if you have any concerns that you may be at risk, or if you have had any symptoms that may be muscle related complications.

Since its release in generic form a few years ago, simvastatin has been an extremely popular medication with the health care plans due to its favorable pricing compared to more potent, but also more expensive, statins such as Lipitor™ (which becomes generic at the end of 2011) and Crestor™ or higher dose combination agents like Vytorin™. It remains an extremely effective and valuable agent in the primary and secondary prevention of cardiovascular disease. Like many medications, closer and careful scrutiny, often through randomized clinical trials, yields important and more targeted recommendations to optimize the use and safety of drugs even after their original release.

The Ventura Heart Institute and its research partner, Westlake Medical Research, have new lipid agents in clinical trials that have the promise of favorably modifying blood fats without muscle aches or other common adverse effects of the agents currently available. Through such development of innovative therapies and continued surveillance of existing therapies, the health care profession will make further progress in the reduction in the mortality and morbidity of heart and vascular disease.

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