

## Labeling Changes to Statins Address Adverse Health Effects

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On February 28, the Food and Drug Administration announced safety changes to the labeling of statins (Lipitor, Lescol, Mevacor, Altoprev, Livalo, Pravachol, Crestor, Zocor, Advicor, Simcor, and Vytorin) based on recent information about increases in blood sugar levels, cognitive effects, and the potential for rare but serious liver injury. These changes were made to provide the public with more information for the safe and effective use of statins and are based on FDA's comprehensive review of the statin class of drugs.

### *Increases in Blood Sugar Levels*

Increases in glycosylated hemoglobin (HbA1c) and fasting serum glucose levels have been reported with statin use. Based on clinical trial meta-analyses and epidemiological data from the published literature, information concerning an effect of statins on incident diabetes and increases in HbA1c and/or fasting plasma glucose will be added to statin labels.

The FDA has reviewed the results from the Justification for the Use of Statins in Primary Prevention: an Intervention Trial Evaluating Rosuvastatin (JUPITER) which found a 27% increase in investigator-reported diabetes mellitus in rosuvastatin-treated patients compared to placebo-treated patients. High-dose atorvastatin had also been associated with worsening glycemic control in the Pravastatin or Atorvastatin Evaluation and Infection Therapy- Thrombolysis In Myocardial Infarction 22 (PROVE-IT TIMI 22) sub-study. In their review of several meta-analyses, the FDA noted that there was a 9-13% increased risk for incident diabetes. Retrospective data analysis from the Women's Health Initiative also showed that there was a class-effect of statin use conveying a 48% increased risk of new-onset diabetes in postmenopausal women.

### *Cognitive Effects*

The label changes will also include information on cognitive effects. There have been rare post-marketing reports of cognitive impairment (e.g., memory loss, forgetfulness, amnesia, memory impairment, confusion) associated with statin use. These reported symptoms are generally not serious and reversible upon statin discontinuation, with variable times to symptom onset (1 day to years) and symptom resolution (median of 3 weeks). However, data from the observational studies and clinical trials did not suggest that cognitive changes associated with statin use are common or lead to clinically significant cognitive decline.

### *Liver Injury*

Based on a review of clinical studies, the FDA has concluded that serious liver injury with statins is rare and unpredictable in individual patients, and that routine periodic monitoring of liver enzymes does not appear to be effective in detecting or preventing serious liver injury. The labels have been revised to remove the need for routine periodic monitoring of liver enzymes in patients taking statins and, instead, will recommend that liver enzyme tests be performed before starting statin therapy and as clinically indicated thereafter.

Although the FDA has added these safety warnings to the labels of statins, physicians should be aware that these decisions were based on the findings from short-term studies and anecdotal reports. Because

there is ample evidence in prospective trials that statins reduce cardiovascular events and mortality in patients with and without diabetes, The Endocrine Society recommends that physicians discuss these new warnings with their patients and individualize their advice of continuing the medication based on an analysis of the benefit vs. risk in that person.

Additional information and a summary of the data can be found on the FDA's [website](#).