FDA approves Zetia -- first new class to treat cholesterol since statins introduced

WHITEHOUSE STATION & KENILWORTH, N.J., October 28, 2002 -- Following a 10-month review, the FDA has approved Zetia (ezetimibe), the first in a new class of cholesterol-lowering agents that inhibit the intestinal absorption of cholesterol.

Merck/Schering-Plough Pharmaceuticals announced that the once-daily tablet of Zetia 10 mg was approved for use either by itself or together with statins in patients with high cholesterol, to reduce both LDL ("bad") cholesterol and total cholesterol.

Cholesterol-lowering medicines are recommended for use, in addition to an appropriate diet, when the response to diet and exercise has been inadequate.

In clinical trials, Zetia was generally well tolerated with an overall side effect profile similar to placebo.

"Sixty percent of the estimated 13 million patients taking statins continue to have LDL cholesterol higher than recommended levels," said H. Bryan Brewer, M.D., chief of the molecular disease branch, National Heart, Lung and Blood Institute, National Institutes of Health (NIH).

"As the first breakthrough to treat cholesterol since statins were introduced 15 years ago, Zetia provides physicians with a new option to get more of these patients to goal. This is particularly important in view of last year's changes to the NIH's cholesterol guidelines, which substantially expand the number of Americans eligible for drug therapy and call for lower cholesterol goals for many patients," he said.

"Discovered by Schering-Plough scientists and developed in partnership with Merck, Zetia offers patients an important therapeutic advance in the treatment of high cholesterol," said Richard Jay Kogan, Chairman and CEO of Schering-Plough.

Zetia has a unique, complementary mechanism of action. Cholesterol in the blood is controlled primarily by two organs: the liver, which produces cholesterol and bile acids (which are used in digestion); and the intestine, which absorbs cholesterol both from food and from the bile (made by the liver). Zetia lowers cholesterol through a unique mechanism of action by inhibiting cholesterol absorption in the intestine.

This mechanism of action makes Zetia complementary to statins, which work in the liver. Therefore, patients who take Zetia with a statin can achieve additional reductions in LDL and total cholesterol. The mechanism of Zetia is also quite different from a currently available class of drugs known as "bile acid sequestrants," which lower cholesterol by physically binding to bile acids in the small intestine.

In a pivotal, multi-center study known as the "Add-On" study, patients who had not reached their LDL cholesterol goal on a stable dose of a statin alone had Zetia or placebo added to their statin regimen. The statin dose remained constant. The study showed that adding Zetia to ongoing statin treatment provided a 25 percent (36 mg/dL) additional reduction in LDL cholesterol versus 4 percent (6 mg/dL) with the addition of placebo. Mean LDL cholesterol levels of patients on statin therapy dropped from 138 mg/dL to 102 mg/dL when Zetia was added versus a drop from 139 mg/dL to 133 mg/dL when placebo was added.

Most of the response in LDL cholesterol reduction was seen within two weeks of adding Zetia and the additive reduction provided by Zetia was generally consistent across all statins tested.

Cholesterol Education Program (NCEP) II target LDL cholesterol goal when either Zetia or placebo was added to their ongoing statin therapy. The study showed that 72 percent of the patients who were not at goal on their statin dose at baseline reached goal when Zetia was added, compared to 19 percent of patients with the addition of placebo.

Zetia delivered significant reductions in LDL cholesterol when co-administered with all statins tested, including Lipitor and Zocor.

The U.S. approval of Zetia was also based on four placebo-controlled co-administration studies, in which Zetia and either Lipitor (atorvastatin), Zocor (simvastatin), Pravachol (pravastatin) or Mevacor (lovastatin) were started together in previously untreated patients with high cholesterol levels.

Zetia co-administered with Lipitor and Zocor further improved triglycerides and HDL ("good") cholesterol.

The FDA also approved Zetia for use in two rare genetic disorders: homozygous familial hypercholesterolemia and homozygous sitosterolemia. In homozygous familial hypercholesterolemia, Zetia, administered with Lipitor or Zocor, is indicated for the reduction of elevated total cholesterol and LDL cholesterol as an adjunct to other lipid-lowering treatments.

In sitosterolemia, Zetia is indicated as adjunctive therapy for the reduction of elevated sitosterol and campesterol levels in addition to diet. Zetia is the only medicine approved for this serious condition.

Source: Merck/Schering-Plough Pharmaceuticals

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