Ezetimibe: A First-in-Class, Novel Cholesterol Absorption Inhibitor

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ABSTRACT

Significant numbers of patients at risk for coronary heart disease (CHD) fail to reach National Cholesterol Education Program (NCEP)-designated low density lipoprotein cholesterol (LDL-C) goals in spite of the wide range of currently available treatments, including combination therapies. Ezetimibe, the first in a class of novel cholesterol absorption inhibitors, demonstrated lipid-lowering and antiatherosclerotic activity in experimental and clinical hypercholesterolemia. Studies in hypercholesterolemic dogs showed that ezetimibe coadministered with statins caused greater lipid-lowering effects compared to either drug alone. These effects were confirmed in clinical studies of patients with primary hypercholesterolemia where initiation of treatment with ezetimibe plus a statin, or addition of ezetimibe to ongoing statin therapy, produced significant incremental reductions in LDL-C, as well as incremental increases in high-density lipoprotein cholesterol (HDL-C) and reductions in triglyceride levels. Combination therapy also significantly increased the number of patients attaining LDL-C goal at the end of treatment, compared to statin monotherapy. In studies using simvastatin, atorvastatin, pravastatin, and lovastatin, addition of ezetimibe to low dose statin was as effective as a 2- to 3-fold upward titration of the corresponding statin dose. Ezetimibe-statin combination therapy provided similar improvements in patients with primary hypercholesterolemia, as well as with heterozygous and homozygous familial hypercholesterolemia. Ezetimibe monotherapy effectively reduced plasma campesterol and sitosterol in patients with homozygous sitosterolemia. Clinical studies showed that ezetimibe was well tolerated, with a safety profile comparable to placebo when administered as monotherapy and comparable to statin alone when coadministered with a statin. These data provide strong evidence that, through their complementary lipid-lowering mechanisms, ezetimibe coadministered with a statin offers an

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effective combination treatment option for patients with hypercholesterolemia, including those with genetically inherited disease.