Ezetimibe

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As trial evidence accumulates, target goals for lowering levels of total and low density lipoprotein-cholesterol (LDL-C) in secondary and primary prevention of atherosclerosis continue to fall. This places increasing demands on lipid-lowering therapies to deliver reductions in LDL-C of 50% or more.

Ezetimibe is a novel inhibitor of cholesterol absorption. It is the first of a new generation of drugs that inhibit cholesterol uptake without disrupting bile acid metabolism and, hence, without consequent effects on the absorption of fat-soluble vitamins or other lipid-soluble drugs.

As monotherapy and in combination with statins, ezetimibe delivers a 12–18% reduction in LDL-C, a moderate reduction in

triglycerides and a modest increase in high density lipoprotein-cholesterol. In patients with homozygous familial hypercholesterolemia and minimal LDL-receptor function, ezetimibe therapy results in an impressive 20% fall in LDL-C.

No significant excess of gastrointestinal adverse effects is seen with ezetimibe, in contrast to bile acid sequestrants. It has no adverse pharmacokinetic or pharmacodynamic interactions with statins. As high doses of statins predispose to an increased risk of adverse effects, the use of well-tolerated combination therapy with ezetimibe allows statins in 10–20mg doses to deliver LDL-C lowering efficacy usually associated with 40–80mg doses. Ezetimibe coadministered with statins considerably increases the number of patients achieving LDL-C goals.

Ezetimibe is approved in the US. The drug looks to be an extremely promising agent, either as monotherapy or coadministered with statins, for lowering LDL-C. ▲