Rosuvastatin: A Highly Effective New HMG-CoA Reductase Inhibitor

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ABSTRACT

Rosuvastatin, a new statin, has been shown to possess a number of advantageous pharmacological properties, including enhanced HMG-CoA reductase binding characteristics, relative hydrophilicity, and selective uptake into/activity in hepatic cells. Cytochrome P450 (CYP) metabolism of rosuvastatin appears to be minimal and is principally mediated by the 2C9 enzyme, with little involvement of 3A4; this finding is consistent with the absence of clinically significant pharmacokinetic drug-drug interactions between rosuvastatin and other drugs known to inhibit CYP enzymes. Dose-ranging studies in hypercholesterolemic patients demonstrated dose-dependent effects in reducing low-density lipoprotein cholesterol (LDL-C) (up to 63%), total cholesterol, and apolipoprotein (apo) B across a 1- to 40-mg dose range and a significant 8.4% additional reduction in LDL-C, compared with atorvastatin, across the dose ranges of the two agents. Rosuvastatin has also been shown to be highly effective in reducing LDL-C, increasing high-density lipoprotein cholesterol (HDL-C), and producing favorable modifications of other elements of the atherogenic lipid profile in a wide range of dyslipidemic patients. In patients with mild to moderate hypercholesterolemia, rosuvastatin has been shown to produce large decreases in LDL-C at starting doses, thus reducing the need for subsequent dose titration, and to allow greater percentages of patients to attain lipid goals, compared with available statins. The substantial LDL-C reductions and improvements in other lipid measures with rosuvastatin treatment should facilitate achievement of lipid goals and reduce the requirement for combination therapy in patients with severe hypercholesterolemia. In addition, rosuvastatin’s effects in reducing triglycerides, triglyceride-containing lipoproteins, non–HDL-C, and LDL-C and increasing HDL-C in patients with mixed dyslipidemia or elevated triglycerides should be of considerable value in enabling achievement of LDL-C and non–HDL-C goals in the numerous patients with combined dyslipidemias or metabolic syndrome who require lipid-lowering therapy. Rosuvastatin is well tolerated alone, and in combination with fenofibrate, extended-release niacin, and cholestyramine, and has a safety profile similar to that of currently marketed statins. A large, long-term clinical trials program is under way to investigate the effects of rosuvastatin on atherosclerosis and cardiovascular morbidity and mortality.