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US FDA approves AstraZeneca's Crestor for broader patient population

09 February 2010
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The US FDA has expanded the approval of AstraZeneca's Crestor (rosuvastatin) such that it can now be used to prevent heart disease in individuals with normal low-density lipoprotein (LDL) levels and no clinically relevant heart disease, so long as they have other risk factors.

As expected, following a positive panel review meeting in December (scripnews .com, December 16th, 2009.com), the cholesterol-lowering drug has now been approved to reduce the risk of stroke, heart attack and arterial revascularisation procedures in patients who have no clinically evident heart disease but are at an increased risk of heart disease due to the combined effect of three risk factors: age (>50 years in men; >60 years in women); elevated high-sensitivity C-reactive protein (hsCRP) levels (>2 mg/l); and presence of at least one additional cardiovascular risk factor (high blood pressure, low HDL-Cholesterol levels, smoking or a family history of premature heart disease).

This approval makes Crestor the first HMG-CoA reductase inhibitor (statin) to take hsCRP levels into account during prescribing, said the company.

Crestor was previously approved to lower cholesterol and triglycerides in combination with diet and exercise in patients with high cholesterol and/or triglycerides, and to slow the progression of atherosclerosis.

Jefferies analysts write in a research note that while the approval is good news, and expands the potential patient base, the "initial impact on prescribing practice may be more muted than expected by many commentators". They argue this in part because CRP levels are not routinely screened for by primary care physicians, but also believe that data supporting the expanded label are already incorporated into current prescribing trends.

They continue to forecast peak sales of $8.2 billion in 2014, but note that the consensus forecast is $7 billion.

Panel Review Of Trial Data

A panel of 17 experts met to discuss the results from the JUPITER trial, which were filed to support the expanded indication. In JUPITER, 17,000 middle-aged and older men and women with LDL-C levels <130mg/dl and hsCRP values of 2mg/l or greater were treated with 20mg/day of Crestor or placebo (scripnews.com, November 11th, 2008). Treatment reduced the risk of experiencing a cardiovascular event – a composite primary endpoint of cardiovascular death, non-fatal stroke, non-fatal myocardial infarction, hospitalisation for unstable angina or arterial revascularisation – by 44% compared with placebo after a mean follow-up of nearly two years.

On the basis of these findings, the panel voted 12–4 (with one abstention) in favour of the now approved indication. However, the panel voted against approving the drug for a broader indication: use in all patients with elevated hsCRP levels.

In addition to known statin safety concerns – including muscle-related adverse events and increases in liver transaminases – the JUPITER study also showed that patients treated with Crestor had a higher risk of developing diabetes (2.8% versus 2.3%). Previous meta-analysis studies have suggested that this effect is not unique to Crestor, but rather is a class effect.

There were also 13 deaths due to gastrointestinal disorders in the Crestor group, compared with one in the placebo group. And, 18 patients in the Crestor group reported experiencing confusion, compared with four in the placebo group.