CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-366/S-016

CLINICAL PHARMACOLOGY AND BIOPHARMACEUTICS REVIEW(S)

Memo to File

NDA 21-366 Crestor (Rosuvastatin calcium) Tablets
SE1 (016) Dated 4/8/09

CRESTOR® (rosuvastatin calcium) is a selective, potent and competitive inhibitor of HMGCoA reductase and a member of the statin drug class of lipid lowering agents. HMG-CoA is the rate-limiting enzyme that converts 3-hydroxy-3-methlyglytaryl coenzyme A to mevalonate, a precursor of cholesterol.

AstraZeneca conducted a large, placebo-controlled, double-blind study called the "Justification for the Use of Satins in Primary Prevention: an Intervention Trial Evaluating Rosuvastatin," which is referred to as the JUPITER study, to assess the long-term safety and cardiovascular risk reducing efficacy of CRESTOR™. AstraZeneca is submitting this marketing application, and seeks approval of an indication for rosuvastatin to reduce total mortality and the risk of major cardiovascular events in adult patients with an increased risk of cardiovascular disease.

The JUPITER study was a Phase III study conducted in 17802 adult subjects, who were considered to have an increased risk of cardiovascular disease based on their age (≥ 50 years for men, ≥60 years for women) and the presence of a hsCRP level ≥2.0 mg/L at an initial screening visit. Although these study participants frequently had multiple risk factors for cardiovascular disease, they did not require cholesterol-lowering treatment based on guidelines that were in place when the study was initiated. The study treatment intervention utilized the 20 mg dose of rosuvastatin, with no up- or down-titration for the duration of the study. According to sponsor the principle results of the JUPITER study were that subjects who received 20 mg once daily rosuvastatin compared to placebo had:

- A 44% reduction in the risk of sustaining a major cardiovascular event (cardiovascular death, nonfatal stroke, nonfatal myocardial infarction, unstable angina, or arterial revascularization), which was the primary endpoint of the study
- A 20% reduction in total mortality
- A 48% reduction in the risk of fatal or nonfatal stroke
- A 54% reduction in the risk of fatal or nonfatal myocardial infarction
- A 46% reduction in the risk of undergoing an arterial revascularization procedure

No new clinical pharmacology and Biopharmaceutics data has been submitted in this supplement.

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/s/

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7/14/2009 03:06:14 PM
BIOPHARMACEUTICS

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