FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH (CDER)

Endocrinologic and Metabolic Drugs Advisory Committee
Meeting
July 9, 2003

Draft Questions to the Committee

Efficacy

1. Has the sponsor provided sufficient rationale for the addition of a new statin to the therapeutic armamentarium for the treatment of dyslipidemia to prevent or delay cardiovascular disease?

2. Do the efficacy data support a dose-response sufficient to justify use of the 40 mg dose?

Safety

Myotoxicity

1. Has the sponsor provided sufficient evidence that the myotoxic potential per LDL-lowering efficacy of rosuvastatin is similar to that of currently marketed statins?

2. Has the risk of muscle toxicity associated with rosuvastatin therapy been adequately evaluated in the clinical development program with respect to:

    a. number of patients studied and duration of trials
    b. special populations (e.g., elderly, drug-drug interactions, renal impairment, co-morbid medical conditions)

3. The sponsor does not propose clinical use of doses above 40 mg. Is there sufficient information on the safety and tolerability of the proposed doses (particularly 40 mg daily) to support clinical use?

Renal Toxicity

1. Has the sponsor adequately addressed the clinical safety finding of rosuvastatin-associated proteinuria? Has the risk of renal functional impairment been adequately investigated?

2. Is proteinuria a statin class effect? Is the potential for rosuvastatin to induce proteinuria similar to that of other statins? Is monitoring in clinical use recommended for this drug and possibly for all statins?

Dosing Recommendations

1. Are the data adequate to support the 5, 10, or 20 mg doses as safe start doses?

2. If yes, does the committee recommend a range of start doses (e.g., 5 to 20 mg) in which an individual may be initiated on therapy based on CHD risks, baseline LDL-C levels, and targeted goals OR should there be a fixed start dose of 10 mg recommended for the general population with 5 and 20 mg reserved for special circumstances, as proposed by the sponsor?