Endocrinologic and Metabolic Drugs Advisory Committee #73
Food and Drug Administration
Center for Drug Evaluation and Research
Bethesda Marriott, 5151 Pook's Hill Road, Bethesda MD

April 22, 1999
NDA 21-071, Avandia (rosiglitazone maleate) SmithKline Beecham

Agenda

8:00 Call to Order, Introductions, Opening Comments:
Henry G. Bone III, M.D., Chair
Endocrinologic and Metabolic Drugs Advisory Committee
Meeting Statement: Kathleen Reedy, Executive Secretary
Endocrinologic and Metabolic Drugs Advisory Committee

8:30 SmithKline Beecham Presentation
Introduction and Preclinical Highlights: David E. Wheadon, MD, VP & Director
North American Regulatory Affairs
Efficacy Profile: Anthony S. Rebuck, MD, VP & Director
Pulmonary and Diabetes Therapeutic Unit
Safety Profile: Elizabeth B. Rappaport, MD, Group Director,
Diabetes and Metabolism
Risk/Benefit Assessment: Douglas A. Greene, MD, Professor, Internal Medicine
Director, Michigan Diabetes Research Center, University of Michigan
Summary: Tadataka Yamada, MD, Chairman, Research and Development
SmithKline Beecham Pharmaceuticals

10:00 Break

10:15 FDA Presentation
Pharmacology/Toxicology: Ronald W. Steigerwalt, Ph.D.
Division of Metabolic and Endocrine Drugs
Statistical Review: Joy Mele, M.S.
Division of Biometrics II
Medical Review: Robert Misbin, M.D.
Division of Metabolic and Endocrine Drugs

11:15 Open Public Hearing
Sidney Wolfe, MD, Public Citizens Health Research Group

11:45 Lunch

1:00 Discussion and Questions
Break
5:00 Adjourn

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Questions

1. Do the data demonstrate that rosiglitazone is effective for the treatment of hyperglycemia in type 2 diabetes mellitis:
   a) as monotherapy?

   b) in combination with metformin?

2. What comments do you have from the safety standpoint about the effects of rosiglitazone on:
   a) liver?

   b) lipids?

   c) hemoglobin?

   d) heart?

3. Based on the available information, do the benefits outweigh the risks for the use of rosiglitazone in the treatment of hyperglycemia in type 2 diabetes mellitis:
   a) as monotherapy?

   b) in combination with metformin?

4. Do you have any recommendations for the labeling of rosiglitazone (other than for possible effects on the liver, which will be discussed later)?

5. If rosiglitazone were to be approved for marketing, do you have any recommendations for phase 4 (post-marketing) studies?

NOTE: Class Labeling and patient monitoring for all drugs in this class will also be discussed tomorrow after the product-specific discussion is completed.

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Class Labeling Questions

1. Should the labeling for other members of the thiazolidinedione class of drugs address the subject of hepatotoxicity observed with troglitazone and, if so, how?

2. Should the labeling for other members of the class specify that liver testing should be performed at periodic intervals and, if so, how frequently?