July 14, 2000: Minutes of the Joint Meeting of Nonprescription Drugs Advisory Committee and the Endocrinological and Metabolic Drugs Advisory Committee

Pravachol® NDA 21-198, pravastatin sodium, 10mg, Bristol Myers Squibb

Proposed Indication: to treat individuals with total cholesterol levels of 200-240mg /dl and low density lipoprotein levels (LDL) over 130mg /dl. The proposed indication is for men over 40 years of age and postmenopausal women who do not have established cardiovascular disease or diabetes.

The meeting was held at the Holiday Inn, Bethesda, MD. Prior to the meeting, the members, consultants and guests had reviewed background material from the FDA and from BMS. In order for the public to be informed, the background material was also available on the Dockets page the day before the meeting. There were approximately 250 persons in attendance. The meeting started at 8 a.m. and ended at 4:30 p.m.

Attendance:
NDAC Members Present: Eric Brass, M.D., Ph.D., Chair, Richard Neill, M.D., Edward Krenzelok, Pharm.D., Edwin Gilliam, Ph.D., Julie Johnson, Pharm.D., Donald Uden, Pharm.D., Henry Williams, M.D. , George Blewitt, M.D.,(non voting)

NDAC Members Absent: Hari Sachs, M.D., Louis Cantilena, M.D., Ph.D., Francis Lam, Pharm.D.

E&M Members Present: Jaime Davidson, M.D., Barbara Luckert, M.D., Janet Silverstein, M.D., Marie Gelato, M.D., Ph.D., Deborah Grady, M.D., M.P.H., William Tamborlane, M.D.,

E&M Absent: Henry Bone, M.D., Thomas Aoki, M.D., Allan Sampson, Ph.D., Jules Hirsch, M.D.

Consultants: Janet Elashoff, M.D., Mark Molitch, M.D,

Non voting Guest: Luther T. Clark, M.D.

FDA Participants: Robert DeLap, M.D., Ph.D., Charley Ganley, M.D., Linda Katz, M.D., John Jenkins, M.D., David Orloff, M.D., Mary Parks, M.D., Daiva Shetty, M.D., Karen Lechter, J.D., Ph.D.

Overview of BMS Presentation:
Mark Kreston introduced the program. Jerome Cohen, M.D., gave an overview of cardiovascular risk factors and the OTC rationale. Rene Belder, M.D., reviewed pravachol safety followed by Carola Friedman, M.D., who

reviewed the clinical data. Patricia Kriger described the plans for education in post market studies.

Overview of FDA's Presentation:
David Orloff, M.D., gave an opening overview of the issues. Mary H. Parks, M.D. gave the medical review. Daiva Shetty, M. D., described the actual use trials. Karen Lechter, J.D., Ph.D critiqued the label comprehension study. Linda Katz. M.D., MPH, gave the charge to the committee.

Committee Discussion:

Efficacy and Safety in the Proposed Target Population

1. The sponsor proposes an indication, based upon an expectation of cardiovascular benefit, for the use of pravastatin 10 mg in individuals with TC 200-240 mg/dL and LDL-C > 130 mg/dL, regardless of HDL-C level, and without CHD or diabetes. Current guidelines for the treatment of hypercholesterolemia do not target such individuals for drug treatment.

   The committee altered the question and broke it into the following two:

   a. Based on the data submitted in the NDA, has the sponsor adequately demonstrated a clinical benefit, (defined as lowering of LDL) with pravastatin 10 mg in the target population?

   Yes=14 No=0

   b. Based on the data submitted in the NDA, has the sponsor adequately demonstrated a clinical benefit, (defined as reduction of cardiovascular events) with pravastatin

   Yes=1 No=13

1. Statins have been associated with myopathy, including rare cases of rhabdomyolysis, as well as with elevations in hepatic transaminases (although the association between use of these drugs and serious hepatic disease is less clear). Intercurrent illness, undefined individual susceptibility factors, and interactions with other drugs and/or foods may increase the risk for rhabdomyolysis with statins. Taking into account these and other safety issues, has the sponsor presented

adequate data to support the safety of pravastatin 10 mg in the target population?

Yes=13 No=0 Abstain=1

OTC Considerations

2. Assuming an indication for the use of pravastatin 10 mg in the proposed target population can be justified based upon an expectation of clinical benefit, has the sponsor adequately demonstrated that consumers can achieve such a clinical benefit in an OTC setting? In responding to this question, please consider the following:
   a. The ability of consumers to appropriately self-select (and de-select) based upon cholesterol levels and other risk factors.
   b. The ability of consumers to evaluate response to treatment and to monitor cholesterol levels (including understanding of how to undertake a fast and the frequency of re-testing).
   c. The ability of consumers to adhere to chronic therapy with pravastatin 10 mg.
   d. The need for the physician or other healthcare professional in the effective treatment and follow up of dyslipidemia.
   e. The capacity of the proposed label to direct consumers in the effective use of pravastatin 10 mg OTC.

Yes=8 No=6

1. Assuming that pravastatin 10 mg is deemed adequately safe when used for the proposed indication in the target population, has the sponsor presented adequate evidence that consumers will be able to use pravastatin 10 mg safely in an OTC setting? In responding to this question, please consider the following:
   a. The ability of the consumer to identify adverse reactions to pravastatin and to act appropriately.
   b. The ability of the consumer to monitor hepatic safety including the need for monitoring of hepatic transaminases and the ability of the consumer to perform such monitoring if needed.
   c. The need for and ability of the consumer to identify and avoid interacting drugs and other substances.
   d. The likelihood of use of pravastatin 10 mg at higher than recommended doses (1 tablet per day).
   e. The ability of women who are pregnant or likely to become so to appropriately avoid use of pravastatin 10 mg.
   f. The need for the physician or other healthcare professional in the safe treatment and follow up of dyslipidemia.

g. The capacity of the proposed label to direct consumers in the safe use of pravastatin 10 mg OTC.

Yes=11 No=3

Approvability

1. Has the sponsor provided sufficient evidence that pravastatin 10 mg can be used safely and effectively in an OTC setting?

Yes=2 No=12

A verbatim transcript of this meeting will be available on the FDA's Dockets Management Branch Website approximately 30 days after the meeting. The address is HTTP://www.fda.gov/ohrms/dockets/ac/acmenu.htm.

I certify that I attended the July 14, 2000 meeting of the Joint Meeting of the Nonprescription Drugs Advisory Committee and the Endocrinologic and Metabolic Advisory Committee and that these minutes accurately reflect what transpired.

S. Titus, PhD 7/17/00

Sandra Titus, Ph.D. Date
Executive Secretary, NDAC

Eric Brass, M.D., Ph.D. Dat
Chair, NDAC