July 13, 2000: Minutes of the Joint Meeting of Nonprescription Drugs Advisory Committeee and the Endocrinological and Metabolic Drugs Advisory Committee

Mevacor® NDA 21-213, lovastatin, 10mg, Merck and Company

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 Merck. 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 275 persons in attendance. The meeting started at 8 a.m. and ended at 5:30 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., Marie Gelato, M.D., Ph.D., Deborah Grady, M.D., M.P.H., William Tamborlane, M.D.

E&M Members Absent: Henry Bone, M.D., Thomas Aoki, M.D., Allan Sampson, Ph.D., Janet Silverstein, M.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 Temple, M.D., 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., Andrea Leonard Segal, M.D., Karen Lechter, J.D., Ph.D.

Open Public Hearing:
The following individuals made statements:

1. Rene F. Rodriguez, M.D., Inter-American College of Physicians and Surgeons

2. Waine Kong, Ph.D., J.D., CEO, Association of Black Cardiologists

3. Debra Judelson, M.D., American Medical Women's Association

4. Sidney Wolfe, M.D., Director, Public Citizen Health Research Group

5. Thomas Pearson, M.D., Ph.D., Chair, Department of Community and Preventive Medicine, University of Rochester, N.Y.

6. Suzanne Hughes, RN, Preventive Cardiovascular Nurses Association, Cleveland, Ohio.

7. Penny Kris Etherton, Ph.D., R.D., Distinguished Professor of Nutrition, Penn State University, Pennyslvania

8. John A. Gans, Pharm.D., Vice President, American Pharmaceutical Association (AphA)

9. Brett Kay, Program Associate, National Consumers League, Washington D.C.

10. Bernhard Kaston, M.D., Quest Diagnostics Incorporated

11. Warren Pinckert, CEO, Cholestech Corporation

Overview of Merck's Presentation:
Eve Slater, M.D., presented the introduction. Polly Beere, M.D., Ph. D. discussed the benefit of lovastatin in an OTC Population. Scott Korn, M.D. presented on the safety of lovastatin. Edwin Hemwall, PhD concluded with a presentation on Label Development and Consumer Behavior .

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. Andrea Leonard Segal, 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 lovastatin 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 lovastatin 10 mg in the target population?

Yes=13 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 lovastatin 10 mg in the target population?

Yes=1 No=12

2. 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 lovastatin 10 mg in the target population?

Yes=13 No=0

OTC Considerations

3. Assuming an indication for the use of lovastatin 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 lovastatin 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 lovastatin 10 mg OTC.

Yes=0 No=13

4. Assuming that lovastatin 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 lovastatin 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 lovastatin 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 lovastatin 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 lovastatin 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 lovastatin 10 mg OTC.

Yes=7 No=6

Approvability

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

Yes=1 No=11 Abstain=1

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 13, 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.

Sandra Titus July 15, 2000 — July 21, 2000

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

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