January 13-14, 2005
Joint Meeting of the Nonprescription Drugs Advisory Committee and the Endocrinologic & Metabolic Drugs Advisory Committee
Hilda F. Scharen

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This is the final report of the Joint Meeting of the Nonprescription Drugs Advisory Committee and the Endocrinologic & Metabolic Drugs Advisory Committee held on January 13-14, 2005. A verbatim transcript will be available in about 2 weeks, sent to the Division and posted on the FDA website at http://www.fda.gov/ohrms/dockets/ac/cder05.html#NonprescriptionDrugs

All external requests should be submitted to the Freedom of Information office.

The Nonprescription Drugs Advisory Committee and the Endocrinologic & Metabolic Drugs Advisory Committee of the Food and Drug Administration, Center for Drug Evaluation and Research, met jointly on January 13-14, 2005, at the Versailles Ballrooms, Holiday Inn, Bethesda, Maryland.
Alastair Wood, M.D. chaired the meeting.

Nonprescription Drugs Advisory Committee (voting):
Alastair Wood, M.D. (Chair), Neal Benowitz, M.D. , Terrence F. Blaschke, M.D., Leslie Clapp, M.D., Ernest B. Clyburn, M.D., Frank F. Davidoff, M.D., Jack E. Fincham, Ph.D., Ruth M. Parker, M.D., Sonia Patten, Ph.D. [CR], Wayne R. Snodgrass, M.D., Ph.D., Robert E. Taylor, M.D., Ph.D., F.A.C.P., F.C.P., Mary E. Tinetti, M.D.

Endocrinologic & Metabolic Drugs Advisory Committee (voting):
Sonia Caprio, Thomas O. Carpenter, M.D., Dean A. Follmann, Ph.D., Michael R. McClung, M.D., David S. Schade, M.D., Morris Schambelan, M.D., Nelson B. Watts, M.D., Margaret E. Wierman, M.D., Paul D. Woolf, M.D.

Special Government Employee (SGE) Consultants (voting):
Richard A. Neill, M.D., James Schultz (patient representative)

Government Employee (voting):
Susan Makris, Ph.D.

Industry Representative (non-voting):
Steven W. Ryder, M.D.

FDA Speakers:
Karen Davis-Bruno, Ph.D., Charles Ganley, M.D., Michael Koenig, Ph.D., Mary Parks, M.D., Laura Shay, RN, M.S., C-ANP, Daiva Shetty, M.D.

FDA Participants:
Jonca Bull, M.D., Charles Ganley, M.D., John Jenkins, M.D., Robert Meyer, M.D., David Orloff, M.D., Mary Parks, M.D., Curtis Rosebraugh, M.D.

Open Public Hearing Speakers (January 14, 2004):
James McKenney, PharmD - National Lipid Association
Suzanne Hughes MSN RN - Preventive Cardiovascular Nurses Association
Stewart S. Levy, R. Ph. - Impact Health
Robin Edison, M.D., MPH
Dr. Boisey Barnes - Association of Black Cardiologists, Inc.
Sidney M. Wolfe, M.D. - Public Citizen's Health Research Group
Alice Rein, M.S. - National Consumer League
Penny M. Kris-Etherton, Ph.D., R.D. - Penn State University
William L. Greene, Pharm.D., BCPS, FASHP - American Society of Health-System Pharmacists
Tracy Hankin - WebMD
Bob Dufour - Walmart
Jan Engle, - American Pharmacists Association
Laurie Tansman - Mt Sinai NYU Health
Christopher Maus - Lifestreams Technologies, Inc.

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These summary minutes for the January 13 and 14, 2005 of the Joint Meeting of the Nonprescription Drugs Advisory Committee and the Endocrinologic & Metabolic Drugs Advisory Committee of the Food and Drug Administration were approved on February 3, 2005.

I certify that I attended the January 13 and 14, 2005, Joint Meeting of the Nonprescription Drugs Advisory Committee and the Endocrinologic & Metabolic Drugs Advisory Committee of the Food and Drug Administration meeting and that these minutes accurately reflect what transpired.

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Hilda F. Scharen, M.S.
Executive Secretary

_____//S//_____
Alastair Wood, M.D.
Chair

On both days, the committees considered the safety and efficacy of new drug application (NDA) 21-213, proposing over-the-counter (OTC) use of Mevacor 20 mg a day, (lovastatin), Merck & Co., Inc., to help lower LDL "bad" cholesterol, which may prevent a first heart attack.

Alastair Wood, M.D. (Committee Chair), called the meeting to order at 8:00 a.m. on January 13, 2005. The Committee members, consultants, and FDA participants introduced themselves. The conflict of interest statement was read into the record by Hilda Scharen, M.S. The agenda proceeded as follows:

Introduction Regulatory History and Overview of Current Proposed OTC Program	Mary Parks, M.D., Deputy Director Division of Metabolic and Endocrinologic Drug Products Office of Drug Evaluation II
Sponsor Presentations:	
Introduction	Edwin Hemwall, Ph.D., Vice President Worldwide Regulatory and Scientific Affairs Johnson & Johnson / Merck Consumer Pharmaceuticals
Rationale for OTC Lovastatin	Richard Pasternak, M.D. – VP, Clinical Research Merck Research Labs
Mevacor OTC Self Management System	Jerry Hansen, RPh - Vice President Business Development and Consumer Research, Johnson & Johnson / Merck Consumer Pharmaceuticals
Actual Use Study Results	Robert Tipping, M.S. Director, Biostatistics Merck Research Labs
Medical Perspective and Conclusion	Jerome D. Cohen, M.D., FACC, FACP Professor of Internal Medicine/Cardiology Director, Preventive Cardiology Programs St. Louis University Health Sciences Center
FDA Presentations:	
Reproductive and Fetal Toxicity	Karen Davis-Bruno, Ph.D. Division of Metabolic and Endocrinologic Drug Products Office of Drug Evaluation II

Label Comprehension Study	Laura Shay, RN, M.S., C-ANP Division of Over-the-Counter (OTC) Drug Products Office of Drug Evaluation V
CUSTOM – Actual Use Study	Daiva Shetty, M.D. Division of Over-the-Counter (OTC) Drug Products Office of Drug Evaluation V
Nonprescription Simvastatin in the United Kingdom	Michael Koenig, Ph.D. Division of Over-the-Counter (OTC) Drug Products Office of Drug Evaluation V

The meeting was adjourned at approximately 5:20 p.m. on January 13, 2005.

Alastair Wood, M.D. (Committee Chair), called the meeting to order at 8:04 a.m. on January 14, 2005. The conflict of interest statement was read into the record by Hilda Scharen, M.S. The agenda proceeded as follows:

Open Public Hearing Presentations

***Questions to the Committee**:*

1. Taking into consideration the efficacy data from the AFCAPS/TexCAPS and EXCEL studies, plus any additional information provided by the sponsor, please respond to the following questions:

a. Does the proposed target population merit treatment with a statin to lower cholesterol and thereby reduce heart disease risk?

Yes: 24
No: 0
Abstain: 0

Discussion: The subcommittee agreed the proposed target population would benefit from treatment with a statin to lower cholesterol and reduce heart disease, along with improved diet and exercise.

b. Has the sponsor provided adequate rationale for the use of a fixed dose of lovastatin 20 mg to lower cholesterol and heart disease risk in this population? Is this an effective dose to reduce cholesterol in this population?

Yes: 24
No: 0
Abstain: 0

Discussion: The subcommittee discussed that this study assumes adherence to the label. In addition, the members emphasized that there is not enough data, especially for Over-The-Counter use, of the efficacy of a 20mg dose versus usual care.

2. Lovastatin and other statins cause elevation in hepatic transaminase serum levels of unknown clinical significance in individuals with normal baseline hepatic function.

a. Does the Committee think that pretreatment baseline liver function tests are required prior to starting lovastatin therapy?

Yes: 0
No: 24
Abstain: 0

b. Are the liver function tests necessary during administration?

Yes: 0
No: 24
Abstain: 0

Discussion: Some members underlined that baseline liver function tests (LFT) should be required before administration of lovastatin 20 mg. Other committee members also felt that LFT should be required during therapy, for continued safe use of the drug.
The committee members generally found that the risk of liver toxicity with statins seems to be similarly low and were not excessively concerned about patients with undiagnosed liver problems taking Mevacor Daily.

3. Statins have been associated with the development of serious muscle toxicity. Furthermore, drug-drug interactions with lovastatin may increase the risk of muscle toxicity. Is the risk of muscle toxicity with lovastatin 20 mg acceptable for an OTC drug; as applied to the population indicated in the label?

Yes: 24
No: 0
Abstain: 0

Discussion: The subcommittee argued that the study indicated problems in the self-selection of patients for use of lovastatin, which may cause some safety concerns.

4. Lovastatin and other statins are currently labeled as Pregnancy Category X (the drug should not be used during pregnancy). Have you heard data that suggests to you that the drug is not so potentially toxic to the fetus to prevent its marketing OTC under any circumstance?

Yes: 18
No: 5
Abstain: 0

Is the label adequate for this group?

Yes: 0
No: 24
Abstain: 0

Discussion: The subcommittee discussed that the CUSTOM study is not a good representation of the general population, especially for women of child-bearing age who might take Mevacor. Some members indicated that the drug comparison study included drugs not comparable to Mevacor. The members added that some of the drugs used in this study are not Over-The-Counter and are used only under Physician's care, such as Epinephrine.

The members highlighted that the label advising against use of the drug during pregnancy or while trying to become pregnant, should include consequences, such as how significant the risk of damage may be to the fetus. In addition, the members were concerned that women who were unaware that they were pregnant would take Mevacor and possibly damage the developing fetus.

The Committee recognized it is difficult to estimate the risks of birth defects, as well as be able to correlate animal drug studies to humans. The members concluded that the data presented is not conclusive enough to extrapolate risk versus benefit to an OTC situation.

Taking into consideration the results from the CUSTOM actual use study:

5. Does the frequency of appropriate self-diagnosis and self selection support the conclusion that lovastatin 20 mg can be used safely and effectively in the OTC setting? Please describe which analysis influenced your decision.

Yes: 5
No: 18
Abstain: 0

Discussion: The members felt they did not have insight into the population that self-selected and used inappropriately; this information would be critical as product understanding comes from the users. Thus, the committee added that the label comprehension study should be made a part of the actual use study.

Some members emphasized that the information needed to self-manage, while taking Mevacor, is too complex to reduce to an understandable level for the general population. In addition, the members discussed that the CUSTOM study literacy level was higher than that of the general population.

The committee indicated that there is a need for more organized tests to test what is critical information and reduce confusion. The members concluded that the self-diagnosis results of the CUSTOM study did not support that lovastatin 20 mg can be used safely and effectively in the OTC setting.

6. A high percentage of study subjects in the CUSTOM actual use study relied upon a physician for correct self-selection and/or self-diagnosis.

a. Do you expect the general population will have this degree of health care provider interaction?

Yes: 2
No: 16
Abstain: 5 (Those who abstained from voting felt that there was not enough information available to answer this questions.)

b. Do the CUSTOM actual use study results support a conclusion that individuals can use lovastatin 20 mg safely and effectively in the OTC setting without the guidance of a physician?

Yes: 3
No: 20
Abstain: 0

Discussion: The committee members pointed to the fact that close to two-thirds of the patients were not among the intended population for treatment with the statin and that a high percentage of patients relied upon a physician for correct self-selection and/or self-diagnosis to start treatment with lovastatin.

Some members abstained from voting because they did not feel they had enough information to extrapolate the degree of interaction of subjects with their health care provider to the general population.

Although the committee members criticized the CUSTOM study, they praised Merck for its efforts to bring the statin to Over-The-Counter and encouraged the company to continue its efforts, as a means to address the enormous and growing cardiovascular public health problem in the country.

The committee concluded that based on patients' inability to self-select for treatment and to comply with long-term use and testing, individuals could not safely and effectively use lovastatin in the OTC setting.

7. Do the results regarding self management (i.e. user behavior after the initiation of treatment) raise any concerns about the safe and effective use lovastatin 20 mg in the OTC setting? If yes, what are the concerns? Please consider in your discussion: monitoring LDL-C, physician interaction, new risk factors or medication after initiation of therapy.

Yes: 23
No: 0
Abstain: 0

Discussion: The subcommittee expressed some concerns of potential drug interactions with the use of lovastatin. In addition, the members the study presented was not conclusive enough to indicate adequate self-monitoring of individuals taking 20 mg lovastatin. Some members added that patients with low income and no insurance would be unlikely to get LDL tests, which would make it difficult to recognize any new conditions these individuals may have.

Based on all the information provided:

8. Should Mevacor OTC be marketed OTC for the proposed target population?

a. If no, why not?
b. If yes, why?
c. If yes, do you think Mevacor OTC is safe and effective for use in the OTC setting without the "self-management system"?

Hilda F. Scharen

Yes: 3
No: 20
Abstain: 0

Discussion: The members argued that making Mevacor more easily available would help get needed treatment to millions of Americans at moderate risk of heart disease that needed to lower cholesterol levels.

The committee felt that the safety and benefits of Mevacor are well-established, but was concerned that the wrong people might take it if available in an OTC setting, especially after an aggressive advertising campaign.

The members expressed worry that patients will skip necessary doctor visits or inaccurately determine the drug is for them, while forgoing important advice about changing diet and exercise in order to control their elevated level of cholesterol.

The committee concluded that the Health Care System is currently not designed for such OTC use of statins and individuals could not operate in this system effectively. The concerns expressed by the members stemmed that this may set precedence for approval for other “silent” diseases drugs, such as anti-diabetic or high blood pressure drugs, to go OTC while the infrastructure is not adequate to support this.

Some committee members expressed interest in seeing an in-between option in an OTC setting, where patients could buy the drug without a prescription but only after speaking with a pharmacist; such an option is available in Britain, where a similar drug is being sold "behind-the-counter”.

Finally, the committee praised Merck in the efforts to address the needs of individuals without health insurance, who should also have the right to have treatment with statins. In addition, the members felt that FDA and Merck need to work together to bring more effective and cost effective drugs to an OTC setting.

The meeting was adjourned at approximately 3:00 p.m. on January 14, 2005.