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American Association of Clinical Endocrinologists
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January 6, 2005

Cathy A. Groupe
Center for Drug Evaluation and Research (HFD-21)
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

Dear Ms. Groupe:

On behalf of the American Association of Clinical Endocrinologists (AACE), I would like to offer our comments regarding the proposed over-the-counter use of Mevacor (lovastatin). AACE is a professional medical organization with over 5,000 members in the United States and 70 other countries. Founded in 1991, AACE is dedicated to the optimal care of patients with endocrine problems. AACE initiatives inform the public about endocrine disorders. AACE also conducts continuing education programs for clinical endocrinologists, physicians whose advanced, specialized training enables them to be experts in the care of endocrine disease, such as diabetes, thyroid disorders, growth hormone deficiency, osteoporosis, cholesterol disorders, hypertension and obesity.

AACE strongly supports the concerns expressed to you by Dr. Michael D. Maves, Executive Vice President and CEO of the American Medical Association, in his letter of December 22, 2004, a copy of which is attached. We feel that the legal, patient safety and health welfare, and ethical issues inherent in this proposal are paramount, and that authorizing the over-the-counter dispensing of statin pharmaceuticals of any kind should not be allowed. We, therefore, urge the FDA's disapproval of this proposal.

Your favorable consideration of these comments and recommendations for disapproval will be greatly appreciated.

Sincerely,

Carlos R. Hamilton, Jr., MD, FACE
President

CRH/bd
cc: Michael D. Maves, MD, MBA, EVP & CEO, AMA

Via Betty Daly
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American Medical Association

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December 22, 2004

Cathy A. Groupe
Center for Drug Evaluation and Research (HFD-21)
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

RE: NDA 21-213, Proposing Over-the-Counter (OTC) Use of MEVACOR [Lovastatin]

Dear Ms. Groupe:

The American Medical Association (AMA), our nation's largest professional association representing physicians and physicians-in-training, appreciates the opportunity to comment on NDA 21-213, which proposes over-the-counter (OTC) MEVACOR [lovastatin], 20 milligrams a day, to help lower LDL "bad" cholesterol, which may prevent a first heart attack. This would represent the first prescription (Rx) to OTC switch of a HMG-CoA reductase inhibitor, commonly known as "statins," in the United States.

The AMA strongly opposes the Rx-to-OTC switch of MEVACOR [lovastatin] as a cholesterol-lowering agent. While the AMA recognizes there is an underutilization of statins to treat hypercholesterolemia in this country, we do not believe that moving a statin to OTC status is the solution. To potentially lose the benefits of physician supervision by switching statins to OTC status would, in the AMA's view, be detrimental to the health of many individuals and to the public. The AMA also opposes the sale of OTC drug products only by pharmacies, i.e. the establishment of a "third class" of drugs in the United States. The following comments support these positions.

The use of statins (e.g., MEVACOR) to treat hypercholesterolemia should be managed by physicians.

Hypercholesterolemia is an asymptomatic disease that is not easily recognized, and it requires a fasting lipid profile blood test to confirm the diagnosis. In addition to elevated LDL cholesterol, high total cholesterol, abnormally low HDL cholesterol, hypertriglyceridemia, or any combination of the above are among the problems that may be identified from this test. Also, many individuals with elevated LDL cholesterol may have other risk factors for coronary heart disease (CHD), such as diabetes, hypertension, obesity, smoking history, or parents or siblings with premature CHD. Furthermore, individuals may have other co-morbidities that could affect their prognosis.

The AMA believes that only physicians have the training and capability to do a thorough history and physical examination of an individual, in addition to the lipid profile and other necessary laboratory tests, to make the correct differential diagnosis and to recommend the best treatment strategy. The use of a statin to lower LDL cholesterol may be only one part of a more complex patient management strategy, and the physician should decide which statin and at what dosage. While consumers may be able to determine if their LDL cholesterol is between 130 and 170 mg/dl, they are not capable of considering all of the other important factors that must be considered in reaching the correct diagnosis. Allowing the OTC availability of MEVACOR likely will result in some, if not many, individuals being inappropriately treated.

The management of hypercholesterolemia is more than just drug therapy with a statin. Lifestyle changes, such as dietary modifications, increased exercise, and smoking cessation, are very important. Similarly, effective treatment of other diseases, such as hypertension and diabetes, is essential. The AMA believes that the value of physician counseling to encourage patients to institute lifestyle changes and to take their medications properly is a necessary part of a successful patient management program. However, many consumers would not receive this valuable counseling if all they had to do was purchase OTC MEVACOR.

Statin therapy for hypercholesterolemia also is chronic and must be taken for the life of the individual. During the course of treatment, the condition of the individual may change. For example, statin dosage may need adjustment based on periodic laboratory testing of lipid profiles, new diseases may occur that require treatment or that alter the desired endpoints of statin therapy, or adverse events due to the statin, another drug, a drug interaction, or disease progression could occur. For long-term clinical outcomes to be successful, appropriate and continuous monitoring of the patient by a physician for medication adherence, disease status and outcomes, and adverse events is necessary.

The current product labeling for MEVACOR recommends that liver function tests be performed before the initiation of treatment, at 6 and 12 weeks after initiation of therapy, and periodically thereafter (e.g., semiannually). Such monitoring will not occur, or be haphazard at best, if a consumer is self-medicating with OTC MEVACOR in the absence of ongoing physician interaction. Additionally, although infrequent, lovastatin may cause myopathy/rhabdomyolysis. The risk of this complication increases in the presence of drugs that inhibit CYP3A4, including commonly administered drugs like itraconazole, erythromycin, clarithromycin, as well as grapefruit juice. Finally, MEVACOR carries an FDA Pregnancy Rating of "X," indicating a drug with a high potential to cause fetal damage. Thus, the AMA believes that there are sufficient concerns about the safety of MEVACOR (or any other statin) to require continued physician oversight of its use by patients and to deny its OTC availability.

A "third class" of (pharmacist-only) drugs in the United States is contrary to current federal law and is unnecessary.

In its proposal to make MEVACOR an OTC drug, the sponsor indicates that the drug will only be available for sale in retail outlets where there is a pharmacist. However, this is inconsistent with current federal law (Section 503 of the Food, Drug and Cosmetic Act) that codifies only two classes of drugs in the United States. Prescription drugs can only be dispensed pursuant to an order from a licensed practitioner (usually a physician) and OTC drugs can be purchased directly by a consumer without oversight. There is no provision in current law for a third class of drugs that must be purchased from a pharmacist.

The AMA continues to strongly advocate for two classes of drug products, prescription and OTC, in the United States. The AMA believes there is no evidence to support the addition of a third (pharmacist-controlled) class of drugs in this country. When a drug product is not safe for use by consumers without supervision - whether due to its toxicity, its method of use, or the collateral measures necessary for its use – a physician who is adequately trained to evaluate and diagnose disease and is licensed to prescribe drugs should be responsible for supervising the use of that drug product. In addition to current federal law, the AMA's position is supported by numerous government and nongovernmental bodies. In particular, the U.S. General Accounting Office (GAO) did a thorough analysis of this issue and concluded:

> "Little evidence supports the establishment of a pharmacy or pharmacist class of drugs in the United States at this time, as either a fixed or a transitional class. The evidence that is available tends to undermine the contention that major benefits are being obtained in the countries that have such a class." (Nonprescription drugs: Value of a pharmacist-controlled class has yet to be demonstrated [GAO/PEMD-95-12, Aug. 1995])

In conclusion, the AMA urges the FDA to reject NDA 21-213 and not allow the OTC use of MEVACOR or any other statin to treat elevated LDL cholesterol. The benefits of physician diagnosis (including other pre-existing conditions), prescription of the right drug at the right dosage, counseling, and monitoring for compliance, therapeutic response and adverse effects for patients with hypercholesterolemia, or other chronic and asymptomatic diseases, are very important. To potentially lose these benefits of physician supervision by switching drug products, like MEVACOR or another statin, to OTC status would be detrimental to the health of many individuals and to the public.

Sincerely,

Michael D. Maves, MD, MBA