



November 29, 2007

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

**Re: Joint Meeting of the Nonprescription Drugs Advisory Committee and the Endocrinologic and Metabolic Drugs Advisory Committee concerning the proposed over-the-counter use of Mevacor (lovastatin)**

Dear Sir/Madam:

The American Society of Health-System Pharmacists (ASHP) is pleased to submit written comments pertaining to the proposed over-the-counter (OTC) use of lovastatin 20 milligrams a day. ASHP represents pharmacists who practice in hospitals and health systems. The Society's more than 30,000 members include pharmacists and pharmacy technicians who practice in a variety of health-system settings, including inpatient, outpatient, home care, and long-term-care settings.

The effectiveness of statins in reducing low-density lipoprotein cholesterol (LDL-C) has prompted calls for more widespread use, including suggestions for a reclassification of statins as an OTC medication. ASHP does not support reclassification to OTC status as that status is currently constructed, although the Society does believe that alternative nonprescription models for dispensing these valuable medications should be explored.

ASHP believes that existing models of OTC dispensing do not provide the safeguards required to ensure the safe and effective use of 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitors ("statins") as part of a multimodal approach to preventing coronary heart disease (CHD).<sup>1</sup> However, ASHP supports the goal of more widespread use of CHD-preventive therapies, including statin therapy, and encourages FDA to consider behind-the-counter (BTC) availability of statins to advance CHD prevention.

On November 14, 2007, FDA held a public meeting relating to BTC availability of certain drugs. ASHP testified at this meeting, and also plans to submit written comments to the agency. ASHP strongly supports BTC availability of certain drug products. BTC availability of statins in particular would provide a significant health benefit to consumers, who would be able to draw on the education, training, and experience of pharmacists to help them assess their need for the medication, and its appropriate use.

ASHP would support the implementation of a BTC system that would require an initial laboratory assessment of LDL-C levels and ongoing monitoring of response to statin therapy, thereby alleviating concerns that patients in the highest risk groups for cardiovascular disease might receive BTC therapy at suboptimal dosing. Pharmacist consultation would prevent inappropriate use of statins, and result in increased physician referrals for those patients who need more complex care.

ASHP supports the use of statins to lower cholesterol and reduce morbidity and mortality in patients at risk for cardiovascular events. Elevated cholesterol, specifically LDL-C, is an important risk factor for the development of CHD. ASHP has recommended that evaluation and management of lipid disorders be guided by the recommendations of the National Cholesterol Education Program (NCEP), the latest of which are contained in the Adult Treatment Panel III (ATP III) guidelines.<sup>2,3</sup> Statins are considered the drug of choice for most patients with dyslipidemia who require lipid-lowering therapy. They are effective in lowering elevated LDL-C, and studies have demonstrated that statins reduce the risk of cardiovascular events in patients without known CHD (primary prevention). In addition, statins have been shown to reduce cardiovascular events and mortality in patients with CHD (secondary prevention). Individuals with multiple cardiovascular risk factors and a low LDL-C derive an absolute benefit in reducing risk of CHD for a given milligram-per-deciliters lowering of LDL-C. However, for individuals with lower LDL-C levels and fewer risk factors for CHD, the benefits of lowering LDL-C level are less dramatic.<sup>4</sup>

Interest in enhancing consumer access to these therapies is not without merit. Cardiovascular disease is the leading cause of death for both men and women in the United States.<sup>5</sup> In 1999, the risk of developing CHD after 40 years of age was estimated at 49 percent for men and 32 percent for women.<sup>6</sup> If the current epidemic of obesity in this country continues, these rates will likely increase in the coming years.

### **OTC Status Not Appropriate**

To approve reclassification to OTC status, FDA must find that 1) a drug is safe and effective in its proposed use(s), 2) the benefits of the drug outweigh its risks, and 3) that consumers will be able to use the drug's labeling (e.g., its package insert) to safely use the medication in an OTC setting.<sup>7</sup> ASHP believes that a decision to approve nonprescription status for statins should be based on evidence that, under the proposed model, the target population would receive a clinical benefit in primary prevention of CHD from the medication and that patients can safely use the medications to achieve that clinical benefit. To achieve the goal of safe and effective use, any nonprescription dispensing model for statins should:

- identify candidates for appropriate therapeutic interventions, including statin therapy, based on cholesterol levels, other risk factors for CHD events, and the patient's medical and family history;

- allow patients and health care providers to monitor response to treatment, including adverse drug events; and
- maximize the effectiveness of treatment through appropriate consultation with health care professionals that encourage adherence to therapy.

ASHP believes that before a patient begins statin therapy, a cardiac risk assessment should be performed by a competent health care professional in order to:

- determine the patient's LDL-C value, which can be used to determine whether the patient is a candidate for statin treatment and, if statin therapy is appropriate, as a baseline value to assess response to treatment;
- assess the individual for other cardiovascular risk factors such as smoking, diabetes, hypertension, and family history of cardiovascular disease and lifestyle factors such as diet, weight, and extent of exercise; and
- develop the optimal treatment plan based on ATP III guidelines and the patient assessment described here.

Individuals with 2 or more risk factors or a family history of cardiovascular disease who have never been evaluated should be triaged for a complete medical assessment and intervention by a physician. If statins are an appropriate therapeutic option, they should be part of a multimodal approach to reducing the overall CHD risk that would include managing and treating modifiable risk factors such as hypertension, smoking, obesity, improper diet, and sedentary lifestyle. Diet and exercise therapy should be a fundamental part of all cholesterol-lowering treatment regimens.

Statins are not suitable for OTC status as that class is currently regulated and under the real-use conditions that would be anticipated for this drug. One study has examined the use of statins in a simulated OTC setting. The CUSTOM study was a small-scale, open-label study designed to observe consumers' initial and continued use of a statin to lower LDL-C.<sup>8</sup> While the study found that many individuals were able to use an OTC statin as directed, the study was not specifically designed to evaluate clinical outcomes and therefore could not demonstrate effectiveness. While patients with recorded baseline and concluding LDL-C levels did show improvement, this monitoring was not routinely performed. Patient self-report of improved dietary and exercise habits, as assessed in this study, is not sufficient to demonstrate that the existing OTC model provides the level of counseling required to reduce cardiovascular risk factors other than LDL-C levels.

While some results of the CUSTOM study might seem encouraging, caution should be exercised when extrapolating such information to a larger population, especially information regarding safety. It is imperative that any medication that is reclassified to nonprescription status have a wide margin of safety. After statin therapy starts, ongoing evaluations are needed to assess the patient's response, reassess risk factors, and monitor for and report adverse drug events. The existing model for OTC medications would place the entire burden for performing these functions on the patient. Although adverse events from prescription statins are rare, particularly at lower doses, they may occur

months or years after therapy is initiated. The wider use encouraged by OTC status may also include use of statins by individuals with multiple disease states or those taking potentially interacting medications (e.g., cyclosporin, diltiazem, verapamil, macrolide antibiotics, azole antifungals, or protease inhibitors).

Because statins are a chronic therapy, new risks may develop as the patient's health status changes. For this reason, current prescription only use of statins requires ongoing vigilance on the part of the patient as well as health care providers. Transferring this responsibility to the patient would likely result in increased therapeutic failures and adverse drug events. A system that relies on patients' voluntary reporting of adverse drug events may be inadequate to protect the public or detect subtle signals. In addition, most patients are likely to be unfamiliar with the system used to report an adverse event, if the adverse event is even recognized.

Finally, ASHP urges the FDA consider that, like all therapies in this class, lovastatin is a pregnancy category X drug. As such, the package labeling for this product indicates that the drug should be administered to women of childbearing age only when such patients are highly unlikely to conceive.<sup>9</sup> ASHP believes that appropriate caution in the use of this drug in women of childbearing age is unlikely under current models for nonprescription product availability.

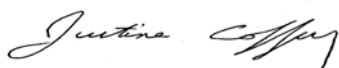
ASHP believes that, for these reasons, reclassification of statins to OTC status as currently constructed is not advisable, but that alternative nonprescription models for dispensing these valuable medications, including a BTC category, should be explored.

## **Conclusion**

ASHP supports nonprescription dispensing models for statins that ensure their safe and effective use as part of a multimodal approach to prevent CHD. Given the complexities of therapies to prevent CHD, ASHP encourages consideration of alternatives, including a BTC category, to the current models of OTC distribution for statins.

The Society appreciates this opportunity to present its written comments on the proposed OTC use of lovastatin 20 milligrams a day. Feel free to contact me if you have any questions regarding our comments. I can be reached by telephone at 301-664-8702, or by e-mail at [jcoffey@ashp.org](mailto:jcoffey@ashp.org).

Sincerely,



Justine Coffey, JD, LLM  
Director, Federal Regulatory Affairs

## References

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