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ASHP Statement on the Over-the-Counter Availability of Statins

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Position

The American Society of Health-System Pharmacists (ASHP) believes that existing models for over-the-counter (OTC) dispensing do not provide the safeguards required to ensure the appropriate 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). ASHP supports the goal of more widespread use of CHD-preventive therapies, including statin therapy, and encourages consideration of alternative nonprescription dispensing models for statins that would advance CHD prevention.

Since 1985, ASHP has called for changes in federal statutes and regulations to establish an intermediate category of drug products that do not require a prescription but are available only from pharmacists and other licensed health care professionals authorized to prescribe medications.⁽¹⁾ ASHP believes that consideration of OTC reclassification for statins presents an opportunity to explore the creation of such a category of drugs. ASHP has suggested that the regulatory system for such an intermediate category of drug products would allow pharmacists to provide drugs in this intermediate category directly to patients without a prescription, on the basis of appropriate assessment and professional consultation, while ensuring that licensed health professionals who currently have prescribing authority would continue to have the ability to prescribe such medications. ASHP believes that under such a regulatory system, data from postmarketing surveillance, epidemiologic studies, and adverse-drug-reaction reporting should be collected to help determine a drug product's eventual movement to nonprescription status, return to prescription-only status, or continuation in the intermediate category.⁽¹⁾ ASHP believes that statins are an ideal candidate for dispensing under such a model.

Background

ASHP supports the use of statins to lower cholesterol and reduce morbidity and mortality in patients at risk for cardiovascular events⁽²⁾. Elevated cholesterol, specifically low-density lipoprotein cholesterol (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.(3,4) 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). Cardiovascular disease is the leading cause of death for both men and women in the US, and CHD is responsible for nearly 75 percent of all deaths from cardiovascular disease.(5) 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-decilitr 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.(6)

Nonprescription Dispensing Models

The efficacy of statins in reducing LDL-C has prompted calls for more widespread use, including suggestions for a reclassification of statins as an OTC medication. Although ASHP does not support reclassification to OTC status as that status is currently constructed, alternative nonprescription models for dispensing these valuable medications should be explored.

To approve a reclassification to OTC status, FDA reviewers 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.(7) ASHP believes that a decision to approve nonprescription dispensing models 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 reactions; and
- maximize the effectiveness of treatment by encouraging adherence to therapy and appropriate interactions with health care professionals.

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 as a baseline value if the patient is a candidate for treatment;
- assess the individual for other cardiovascular risk factors such as smoking, diabetes, hypertension, diet, weight, amount of exercise, and family history of cardiovascular disease; and

- develop the optimal treatment plan based on ATP III guidelines and the assessment above.

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

Current OTC Model. Statins are not suitable for OTC status as that class is currently regulated. One study has examined the use of statins in a simulated OTC setting. The CUSTOM study (8) was an open-label study designed to observe consumers' initial and continued use of a statin to lower LDL-C. Although the study may indicate that some individuals in its sample were able to use an OTC statin as directed, the study was by its own admission not designed to evaluate clinical outcomes and therefore could not determine if the study certainly did not prove that the existing OTC model would provide the level of counseling required to reduce cardiovascular risk factors other than LDL-C levels.

However encouraging these results might seem, caution should be exercised when extrapolating such information to a larger population, especially information regarding safety. Adverse drug effects should always be assessed, especially if the medications that cause them are easily available to the public. A system that relies on the voluntary reporting of adverse drug effects by patients may be inadequate to protect the public or detect subtle signals. It is imperative that the decision to reclassify a statin to a nonprescription status include a wide margin of safety. After statin therapy starts, ongoing evaluations should assess the patient's response, reassess risk factors, and monitor for and report adverse events. The existing model for OTC medications would place the entire burden for performing this evaluation and reassessment on the patient. Most patients are likely to be unfamiliar with the system used to report an adverse event, if the adverse event is even recognized. 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 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 be introduced as the patient's health varies, requiring vigilance on the part of the patient as well as health care providers.

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 should be explored.

Alternative Nonprescription Models

ASHP believes that there are alternatives to prescription-only status that would allow expanded use of statins to reduce cardiovascular events in primary prevention patients. Since 1985, ASHP has advocated a policy that urges changes in federal statutes and regulations that would create an intermediate category of drug products that do not require a prescription but are available only from pharmacists and other licensed health care professionals.(1) ASHP believes that the regulatory system for this intermediate category of drug products should contain the following features:

1. Drug products appropriate for this intermediate category would be identified through the advice of pharmacists, physicians, and other licensed health professionals who are authorized to prescribe medications, on the basis of the medical conditions to be treated and potential adverse effects (as indicated in FDA-approved labeling);
2. Pharmacists would be able to provide drugs in this intermediate category directly to patients without a prescription, on the basis of appropriate assessment and professional consultation;
3. Licensed health professionals who currently have prescribing authority would continue to have the ability to prescribe medications in this intermediate category; and
4. Data from postmarketing surveillance, epidemiologic studies, and adverse-drug-reaction reporting would be collected to help determine a drug product's eventual movement to nonprescription status, return to prescription-only status, or continuation in the intermediate category.(1)

Drugs that present concerns about their safe and efficacious use as nonprescription products could be better controlled, monitored, and evaluated by making them available only from pharmacists and licensed health care professionals who are authorized to prescribe medications. Pharmacists have the education, training, and expertise to help patients make appropriate therapeutic decisions associated with the use of such products. ASHP believes that statins are a good candidate for dispensing under such a model, much as is done in Great Britain, where simvastatin was approved for "counterprescribing" in May 2004.(9)

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 to the current models of OTC distribution for statins.

References

1. Policy Position 0220: Intermediate Category of Drugs. In: Best practices for hospital and health-system pharmacy 2004-2005. Positions and practice documents of ASHP. Bethesda, MD: American Society of Health-System Pharmacists; 2004. p. 89.

2. ASHP Therapeutic Position Statement on the Use of Statins in the Prevention of Atherosclerotic Disease in Adults. *Am J Health Syst Pharm.* 2003; 60:593-8.
3. Expert panel on detection, evaluation, and treatment of high blood cholesterol in adults. Executive summary of the third report of the national cholesterol education program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (adult treatment panel III). *JAMA* 2001;285:2486-2497.
4. National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). Third report of the national cholesterol education program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (adult treatment panel III) final report. *Circulation* 2002; 106: 3134-3421.
5. American Heart Association. 2002 heart and stroke statistical update. www.americanheart.org/presenter (accessed 2002 May 14).
6. Grundy SM et al. Implications of recent clinical trials for the national cholesterol education program adult treatment panel III guidelines. *Circulation* 2004; 110:227-239.
7. Berardi RR, ed. Handbook of nonprescription drugs: an interactive approach to self-care. 14th ed. Washington, DC: American Pharmacists Association; 2004. pp. 62-64.
8. Melin JM, Struble WE, Tipping RW, et al. A consumer use study of over-the-counter lovastatin (CUSTOM). *Am J Cardiol* 2004;94:1243-1248.
9. Royal Pharmaceutical Society of Great Britain. Concise version of practice guidance on the sale of OTC simvastatin. July 2004. Available at: <http://www.rpsgb.org.uk/pdfs/otcsimvastatincardguid.pdf>. Accessed January 4, 2005.

