

Over-the-counter statins: a new controversy

Jonathan Abrams

J Abrams is Professor of Medicine in the Division of Cardiology, Department of Internal Medicine, at The University of New Mexico Health Sciences Center.

The UK recently became the first country to provide nonprescription statins, when its National Health Service approved the pharmaceutical company Merck Sharp & Dohme's application to sell 10 mg simvastatin over the counter (OTC).¹ This decision was supported by the Department of Health and the Committee on Safety of Medicines. By contrast, in January of this year an FDA advisory panel overwhelmingly rejected Merck Sharp & Dohme's request to make 20 mg lovastatin available OTC in the US, because of concerns over safety, but not efficacy. This issue, however, is not over and this viewpoint highlights some of the arguments for and against the sale of OTC statin therapy.^{2,3}

The results of the Heart Protection Study⁴ suggested that statin therapy should be provided to individuals with vascular disease or those at increased cardiovascular risk, irrespective of cholesterol level. In participants older than 55 years of age who had diabetes and raised cardiovascular risk but no current cardiovascular disease, statin therapy reduced risk by 24%. This reduction was similar to that in participants with established vascular disease overall. Interestingly, marked variance in baseline LDL-cholesterol levels did not affect the proportionate risk reduction provided by 40 mg simvastatin daily. These findings, along with others, helped convince the American Diabetes Association and the National Cholesterol Education Program (NCEP) to establish diabetes as a coronary artery disease equivalent. In addition, the lipid-lowering arm of the Anglo-Scandinavian Cardiac Outcomes Trial⁵ showed that 10 mg atorvastatin decreased cardiovascular morbidity and mortality compared with placebo in hypertensive individuals with mild hypercholesterolemia. Thus, in patients with diabetes or hypertension, with no or mild hyperlipidemia and no vascular disease, low-dose statin therapy can substantially decrease cardiovascular morbidity and mortality.^{4,5}

In the Consumer Use Study of OTC Mevacor⁶ survey of outcomes among 3,316 consumers in a simulated OTC setting, individuals with LDL cholesterol between 3.37 and 4.40 mM/l

(130–170 mg/dl) and one or more risk factors could buy a cholesterol test 6 weeks after initiation of therapy, with a free test provided at 26 weeks. Just over a third of participants bought OTC 20 mg lovastatin, of whom 1,061 took at least one dose. Overall, a 20% decrease in LDL cholesterol was seen. Participants reported that they would have found more information on drug interactions useful, and responses in general were not reassuring. Approximately 25% of participants did not undergo lipid testing before buying OTC statins, however, 62% had discussed their cholesterol levels with their physician the year before study entry and many consulted their physicians during the study. The researchers concluded that OTC statins can safely achieve desirable LDL-cholesterol responses in a large number of consumers not currently taking lipid-lowering therapy.

The UK's decision to sell OTC statins has provoked various comments, many of which have been negative. The publicity surrounding the decision, however, did not emphasize that the drug can be sold only to moderate-risk consumers (i.e. 10–15% risk of myocardial infarction over 10 years, and only bought directly from a pharmacist.⁷ Higher-risk patients still need a prescription for statins.

Even modest reductions in total and LDL cholesterol in an adult population would lower overall cardiovascular morbidity and mortality. Thus, an estimated 25–30% decrease in LDL cholesterol with 20 mg lovastatin or 10 mg simvastatin⁸ would bring many healthy individuals with mild hypercholesterolemia within recommended NCEP Adult Treatment Panel III targets. Many individuals do not visit their physician regularly, others choose not to see a doctor on a regular basis and millions cannot afford medical care. If such people are found to have dyslipidemia, particularly elevated LDL cholesterol, OTC availability would result in an expansion of statin use. Patients could benefit from low-dose statins, despite not having a health plan.

A 2004 update of the NCEP guidelines,⁹ however, recommends an LDL-cholesterol

Correspondence

Division of Cardiology
Department of Internal
Medicine
The University of New
Mexico Health Sciences
Center
1 University of New Mexico
ACC 5
Albuquerque
NM 87131-0001
USA
jabrams@salud.unm.edu

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goal of 1.81 mM/l (70 mg/dl) for very high-risk patients. Although OTC 20 mg lovastatin was rejected by the FDA, one obvious issue is the disconnect between its modest efficacy and the aggressive LDL-cholesterol targets for high-risk patients. Target LDL-cholesterol levels would be achievable with OTC products only if baseline lipids were slightly elevated. Clearly, the modest potency of 20 mg lovastatin would reduce population risk, but in many individuals the decrease would not bring total-cholesterol and LDL-cholesterol levels within the desirable range. Conversely, others would not need this dose to achieve their ideal LDL-cholesterol levels.

Importantly, some individuals might disregard heart-healthy behaviors, such as diet and exercise, because of an enhanced sense of health, antipathy to pharmacologic agents, or even a sense of invulnerability caused by the cholesterol medication. Notably, self-monitoring of LDL-cholesterol levels will be difficult and too expensive for some individuals. The degree of physician involvement in follow-up lipid testing is questionable, so pharmacy-based cholesterol testing might be an important adjunct to OTC statin use. Without a physician, important information might not be available and appropriate dose monitoring would not occur. Other issues, such as genetic polymorphisms that are associated with altered drug efficacy,¹⁰ complicate matters further.

Adverse effects are a concern. Statin therapy in combination with certain drugs increases the risk of myopathy and rhabdomyolysis.¹⁰ Although these risks are quite small with low-dose statins, a substantial increase in the number of people taking statins will increase the frequency of complications. Information on potential adverse effects and drug interactions must be made available to all statin users, but how to provide it is a challenge.

In the UK, the sale of statin over the counter should shift much of the cost burden from the National Health Service to the consumer. This is an important rationale for direct consumer acquisition. OTC pricing might, however, make statins unavailable to non-insured or indigent patients.

Is the benefit worth the risk? How can OTC statin availability be made as safe as possible? Careful, continuing monitoring of OTC use in the UK and accumulated experience in the US must be performed to provide accurate assessment of drug acceptance, use and adverse effects, as well as unforeseen problems and issues. It seems reasonable that knowledgeable pharmacy staff,

well-educated as to the rationale for OTC statin use, could effectively control drug dispensation in the US, readily screening individuals with a short, on-the-spot questionnaire. As mentioned by the FDA advisory panel, however, a change in congressional legislation would probably be required to establish UK pharmacists-based OTC control in the US. Clear guidelines must be established to define the individuals who would benefit from low-dose OTC statins. For people already receiving statins, careful attention must be given to assure that the desired degree of lipid lowering is achieved with low-dose OTC statins. If care and thought are taken in designing an OTC program that is educational and emphasizes the adverse effects and potential drug–drug interactions, with the admonition that concerns should be directed to knowledgeable health-care professionals, a truly effective consortium consisting of industry, pharmacists and the consumer could be achieved.

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Competing interests

The author declared he has no competing interests.