

Jeffrey L. Anderson, MD  
June 29, 2000  
Statement Before The FDA Public Hearing on OTC Products  
OTC Lipid-lowering Therapy

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**Jeffrey Anderson, M.D.**  
**Presentation at Food and Drug Administration**  
**Public Hearing on OTC Drug Products**  
**June 29, 2000**

Members of FDA, Ladies And Gentlemen. Good morning, I am Dr. Jeffrey Anderson, Professor of Internal Medicine and Chief of the Division of Cardiology at the University of Utah. I thank the FDA for the opportunity to address the potential for OTC availability of cholesterol-lowering medication. I wish to address the committee as an advocate. I do so as a physician with a long history of interest and broad research and clinical experience in pharmaceutical therapies. I also have been exposed to industry's important role in drug development and respect the value of ethical pharmaceuticals. I understand the special responsibilities of regulatory agencies, having served on the FDA's cardiorenal advisory committee.

I wish to disclose that my participation today was suggested by Merck & Co., and they are sponsoring my trip. However, the views I share are my own.

Cardiovascular disease is our leading cause of death and disability. Almost 1 million Americans die of it each year. Perhaps surprisingly, slightly *more* women than men are affected, although women develop disease 10 years later. Coronary heart disease is the single *most* important cause of cardiovascular death, claiming almost 1/2 million lives annually. Over 1 million suffer a myocardial infarction, or heart attack each year. 12 million are alive with a history of a heart attack or angina pectoris, and perhaps an equal number have undiagnosed disease. Heart disease also is the leading cause of disability. Medicare spends \$11 billion dollars annually for

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High blood cholesterol is a major and well-established risk factor for coronary heart disease. Even "average" levels of cholesterol and its low density or "bad" lipoprotein fraction are associated with increased risk when accompanied by low levels of high density, or "good", lipoprotein cholesterol.

Almost 60% of the U.S. population has undesirable levels of total, LDL, or HDL cholesterol or clinical heart disease. Half, about 30%, have cholesterol levels of 200-240 mg/dl, a range that is average or only slightly elevated. I count myself in this category. Further, the Framingham Study indicates that 1/3 of all coronary events occur in patients in this range, who are not eligible for drug treatment under current guidelines.

Full recognition of the importance of lowering serum cholesterol for risk reduction has been long in coming. I recall my excitement as a first year Harvard medical student reading a landmark study in the *New England Journal Of Medicine* published in 1967 by Drs. Federickson, Levy, and Lees describing how fats are transported in lipoproteins and classifying the hyperlipoproteinemias into 5 distinct types. I pursued my interests with an NIH student fellowship in their laboratories and clinics as a third year student in 1971 and shared in the excitement of those years.

However, the early experience with lipid lowering was *not* particularly promising. Available drugs were only modestly effective and poorly tolerated, and some *actually* increased adverse outcomes (for example, D-Thyroxin and estrogen therapy in men).

Diet also fell short. Adherence was difficult and inherited metabolic factors were found to be more important than diet in determining cholesterol levels. I recall a particularly cynical article in the NEJM in 1977, entitled "Diet-Heart: End of an Era". Cholesterol-lowering had hit rock bottom.

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Then, in the 1980's, a new approach emerged: blockade of cholesterol synthesis at the level of the key enzyme HMG-COA-Reductase. Drugs that inhibited this synthetic enzyme were designated "statins."

I was an investigator in EXCEL, a major study, published in 1991, of the first marketed statin, Lovastatin, in 8,000 patients. The excellent tolerance, safety, and cholesterol-lowering ability of Lovastatin were impressive. What remained was to show that cholesterol-lowering with statins would reduce adverse outcomes, such as myocardial infarction, and save lives.

This beneficial potential of statins has now been well demonstrated in a series of singularly successful and self-reinforcing studies published within the last 6 years. These began with populations at highest *secondary* risk and concluded with those at average to slightly elevated *primary* risk.

The first of these, The Scandinavian Simvastatin Survival Study, published in 1994, tested Simvastatin in patients after an MI who had high cholesterol levels. 4S demonstrated substantial survival benefits: deaths were reduced by 30%; coronary deaths, 42%, and any coronary event, 34%.

The care and lipid trials with Pravastatin extended benefits to the majority of patients after MI, many with "average" cholesterol levels.

The West Of Scotland Study, WOSCOPS, next showed that statin therapy could prevent a *first* heart attack in subjects with very high levels of cholesterol.

Most recently, in 1998, The AIR FORCE/TEXAS CORONARY ATHEROSCLEROSIS PREVENTION STUDY, extended the demonstration of primary prevention benefit to those with average cholesterol levels and *no* evident heart disease. Among 6,600 participants, Lovastatin reduced fatal and nonfatal heart attacks, unstable angina, and sudden cardiac death by 37%.

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AFCAPS/TexCAPS also indicated beneficial potential and safety in subjects resembling those who would be candidates for OTC statin therapy.

What is the next step in primary risk reduction through cholesterol-lowering? I believe the next logical step is review and approval of statins for appropriate OTC use. Today, the public is better informed and more interested than ever in personal risk factor reduction. At the same time, and sadly, funding for programs within our traditional health care system is diminishing. There is a growing gap between primary preventive efforts and public concern about risk factors.

The consumer already has moved to fill this gap, even if ill-advised, through self-medication with so-called "nutraceuticals". 65 million people, one quarter of all adults, are concerned about their cholesterol levels. Of these, one-half use a nutraceutical such as vitamin E, garlic, niacin, or an herbal preparation. Though often relatively ineffective in cholesterol-lowering and largely unsupported by randomized trials, these products form the fastest growing segment of the health product market, with \$12 billion dollars spent last year. Patients in my own practice regularly list self-selected "health supplements" in their medical history.

One of these, red yeast rice, contains Lovastatin in doses that approximate the proposed OTC dose, is available to the public, and has generated substantial interest.

We in the healthcare community should recognize this entrenched and growing public movement toward self-medication for risk reduction, and we should respond constructively.

The availability of low-dose OTC statins is one solution to the primary prevention dilemma, but should this be done, and, if so, how? Four questions come to mind:

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First: What is the advantage of OTC statins? These products derive from good manufacturing processes, ensuring reliable dosing and purity, are backed by clinical trials, are marketed in a regulated, educational environment, and are safe. The adverse event rate with a dose of 20 mg of Lovastatin, twice the proposed OTC dose, is no greater than placebo. A further public health advantage of expanded statin use is that each individual who lowers his or her risk contributes to the general health of our nation.

Second: Why should we move ahead now? Now is the appropriate time because of the convergence of evidence, feasibility, and interest. Evidence for benefit and safety of long-term statins in the "average-to-slightly elevated" cholesterol primary prevention population now is available from AFCAPS/TexCAPS. Easy, reliable, automated approaches to cholesterol testing to guide therapy also are now available directly to the public. Finally, the public already has shown substantial interest in pursuing OTC approaches to coronary risk reduction, as mentioned.

Third: What should be the target population? The greatest unmet need and demand lies in the population with average to mildly elevated cholesterol levels. These levels of 200-240 generally do not meet guidelines for drug therapy, yet over 1/3 of total events occur in this range. There is now evidence for benefit and safety of statins in this cohort. Why limit choice and access of interested, responsible individuals within this group to unproven, relatively unregulated nutraceuticals?

Fourth: How will this affect the physician/patient relationship? The answer is, I believe, that it should enhance it. The patient encounter with an ethically formulated and marketed product can educate and triage. Patients whose cholesterol levels place them at high risk and those with concomitant diseases or interacting medications, would be instructed *not* to self-medicate but to see their physicians.

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A proper OTC initiative would increase awareness of the use of drug therapy as an adjunct to diet and exercise in primary prevention and open a new dialogue among physicians, other healthcare providers, and the public. This population targeted for OTC use otherwise is unlikely to be treated by physicians or covered by current insurance plans. Finally, the educational encounter could reassure those at low risk, who should continue with healthy lifestyles.

In summary, I believe that OTC cholesterol-lowering with low-dose statins is a rational treatment option that healthcare consumers should have the reasonable right to choose. I urge the FDA to consider and carefully review applications for OTC statin use by subjects at moderate coronary risk who choose to practice improved primary prevention.

Thank you for your attention.

Reference:

- 1) Smith SC. Expanding the Impact of Statin Therapy. *Am J Cardiol*, June 22, 2000, Suppl to Vol. 85 (12)
- 2) AHA, Heart Facts 2000 (web site)