Consumer Federation of America

April 9, 2003

The Honorable Mark B. McClellan
Commissioner of Food and Drugs
U.S. Food and Drug Administration
14-17 Parklawn Building
5600 Fishers Lane
Rockville, Maryland 20857

Dear Commissioner McClellan:

As prices for prescription drugs continue to rise, the Food and Drug Administration is increasingly considering whether to shift certain prescription drugs, or classes of drugs, to over-the-counter status. Assessing the impact of OTC conversions on consumers is complex. A host of safety and cost considerations must be examined and balanced. An OTC conversion could safely increase access to an important drug for tens of millions of consumers or force patients to pay far more out-of-pocket for drugs that could cause significant harm if misused. It depends on the drug.

Since the factors that must be evaluated are so complicated and variable, especially regarding safety considerations, the Consumer Federation of America[1] strongly urges the FDA to continue to consider the conversion of each drug on a case-by-case, not a class, basis.

Among the many factors that must be assessed when considering the safety implications of an OTC conversion are:

- The potential for harm if the patient over-uses the drug (a common practice with OTC medication)
- The length of time the drug has been on the market and amount of long-term data available about the drug's safety (requiring at least five years of market experience before considering OTC conversions generally makes sense)
- The potential for adverse drug reactions and interactions
- Whether the drug is used to treat chronic or self-limited conditions and the need for physician monitoring of the development of such conditions

[1] Consumer Federation of America is an association of approximately 300 pro-consumer groups organized in 1968 to advance the consumer interest through advocacy and education. CFA's positions are determined by its members, who vote on them in annual meetings, and by its elected board of directors.

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98P-0610

- The toxicity of the drug compared with other drugs in its class (For a more detailed description of the health factors that should be considered in OTC conversions, see the attached testimony before the FDA of Dr. Sidney M. Wolfe of the Public Citizen Health Research Group)

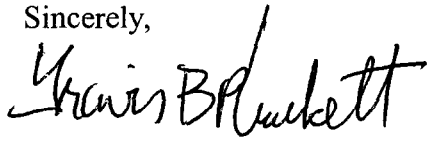
The cost implications of OTC conversions are also significant for consumers. One of the most pressing questions, of course, is what will be the "cost-shift" to consumers. Insured consumers are reimbursed for much of the cost of the drugs that are now being considered for OTC conversion. However, the answer to this simple question can vary dramatically from drug to drug, depending on a number of factors. These factors include:

- The price of the prescription drug and rate of reimbursement for the drug by most health plans
- Health plan policies regarding the drug's placement on a preferred-drug "formulary"
- Whether insurers have already dropped coverage or are planning to drop coverage for a particular drug as drugs in the same class become available over-the-counter
- Whether the drug come off-patent soon, and the potential for generic competition that would lower the prescription price
- Whether the drug will face meaningful price competition from other drugs in the same class that are already available over-the-counter.

In addition, any cost analysis would not be complete without considering whether an OTC conversion will lower prices enough to benefit the growing number of Americans who do not have prescription drug insurance. Once again, this will depend on many of the cost factors cited above.

Given these sometimes conflicting considerations, CFA strongly encourages the FDA to continue its longstanding practice of evaluating prescription-to-OTC changes thoroughly and on a case-by-case basis. We do not think it would be in the best interest of consumers to consider the wholesale conversion of entire classes of drugs, as some have requested.

Sincerely,



Travis Plunkett
Legislative Director

cc: FDA Docket Nos. 98P-0610, 02P-0163, 01P-0075

Comments at a Food and Drug Administration hearing on switching drugs from prescription to over-the-counter

Sidney M Wolfe, M.D
Director, Public Citizen's Health Research Group

FDA Hearing on Rx-to-OTC Switches
June 28, 2000

Before discussing the issue of new classes of diseases for which prescription to OTC switches might be considered, I will review some principles which, I believe, can be helpful when thinking about any Rx-to-OTC switch. Then, using these principles, I will discuss some of the reasons why the switch of cholesterol-lowering drugs should be opposed.

Seven Principles Which Need To Be Considered When Deciding on a Switch

1. Ease/possibility of self-diagnosis-- presence or absence of symptoms which can accurately make the diagnosis (eg. pain, itching, cold, allergy symptoms). Related to this is the question of self-diagnosis of other medical conditions which might counter-indicate the use of the drug.

2. Self-limited or chronic condition-- important for duration of treatment and the evolution of both a change in course of the disease and the occurrence of adverse reactions/interactions, which may require physician monitoring.

3. Benefit/risk ratio and its evaluation-- This is related to #2 because the continued evaluation of benefit and risk by the patient--arguably without any input from the physician--can significantly alter the ratio and hamper the need to keep it favorable for the patient.

4. "Low potential for harm which may result from abuse under conditions of widespread availability"-- This is a quote from the Federal Regulations which define the circumstances of OTC approval. Abuse, in this context, refers to the kind of abuse which occurs when a patient--generally believing that over-the-counter drugs are safer than prescription ones--may say "if one pill does so much good, two or three will be even better--so I will take more than one." Despite the introduction of most OTC versions of drugs at doses lower than the prescription form, this restriction can be easily overcome because of the history of patients increasing their dose. Related to this is the question of whether the potential for harm is such that the use of the drug without the involvement of a physician or other learned intermediary such as a pharmacist is not appropriate. The switch of drugs with a low margin of safety--ones where a doubling of dose may significantly increase the toxicity--should be generally opposed.

5. Number of adverse drug reactions or interactions and the ease of detecting them-- If there are numerous adverse reactions or interactions which may not be fully known to the patient or physician, there is even more cause for concern than the already-troublesome situation involving only prescription drugs. If the detection of the adverse reaction is hampered by the absence of signs which the patient can detect--such as abnormal laboratory tests which are an early signal of liver toxicity--the frequent absence of the physician's involvement because the drug is available OTC may be dangerous.

6. Long-term data from prescription use to assess likelihood of problems with OTC use. If there are problems which have arisen and been documented during use in prescription form, it is likely, if not certain, that the problem will be more common and/or more serious in the OTC version.

7. Toxicity compared with other drugs in the class-- If there are other drugs in the class how does the safety and benefit risk ratio compare to these?

Specific Concerns About Switching Cholesterol-lowering Drugs

Ease/ possibility of self-diagnosis: Given that the indications for these drugs in the OTC status would be a total cholesterol level of between 200 and 240 mg/dl, an LDL of over 130 mg/dl and the absence of established cardiovascular disease or diabetes, it is highly unlikely that this combination of evidence will be present before the OTC purchase of Mevacor or Pravachol. Since the indication for these drugs varies as a function of other risk

factors, the overly simplified indications by total and LDL cholesterol levels are, at the least, extremely misleading. The National Cholesterol Education Program guidelines state, for example, that those without established cardiovascular disease with only one other risk factor (such as smoking, hypertension or males over 45, females over 55) should start cholesterol lowering drugs only if their LDL cholesterol is 190 or over. Even with two other risk factors, the recommendation is 160 or over. This is in contrast to the companies' proposed recommendation of starting drugs for levels of over 130, as announced in the notice of the July FDA hearing. In addition to the problem of accurate ascertainment of cholesterol levels, the warning against use in people with established cardiovascular disease or diabetes belies the fact that many people with these diseases have not yet been diagnosed. Thus, self-diagnosis of these conditions is not a reality unless the patient has previously had a heart attack or angina or symptoms of diabetes that led to a diagnosis.

Self-limited or chronic condition: Because of the implications of an increased risk of cardiovascular disease associated with elevated cholesterol levels, the use of these drugs could well be on a chronic basis, forever. In addition to the need for a physician evaluation initially, medical follow-up is also necessary for the detection of either an evolution into cardiovascular disease and/or the occurrence of adverse reactions or interactions with other drugs, which may require physician monitoring.

Number of adverse drug reactions or interactions and the ease of detecting them: An additional problem with Mevacor and Pravachol concerns the impossibility of self-diagnosis of an early sign of liver toxicity, namely the presence of elevated liver enzymes in a blood test. At the earliest stages this is completely asymptomatic and can only be detected with regular monitoring under the supervision of a physician or other health professional such as a nurse practitioner. The current physician labeling for Mevacor (lovastatin) states: "Persistent increases (to more than 3 times the upper limit of normal) in serum transaminases [liver function tests] occurred in 1.9% of adult patients who received lovastatin for at least one year." Because of this, the labeling further states: It is recommended that liver function tests be performed before the initiation of treatment, at 6 and 12 weeks after initiation of therapy or elevation of dose, and periodically ." There is a similar warning in the labeling for Pravachol. The need for this kind of surveillance is not consistent with a switch to OTC status of these or any similar drugs.

Common to the concerns of switching cholesterol-lowering drugs, diabetes drugs and drugs for hypertension are many of the same concepts: All are used to treat lab values (cholesterol, blood sugar or elevated blood pressure) in diseases for which there are not necessarily any symptoms and which are chronic conditions for which therapy will likely have to continue for a very long time. There is no way of titrating the dose of the drug without repeat tests and evaluation of results. Medical checkups are needed periodically for determining if the drug is working and for assessing other aspects of the disease progression or the evolution of adverse reactions. For these reasons, we strongly oppose the switching of these drugs from prescription to over-the-counter status.