

Statins and Over-the-Counter Availability

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Approximately 1000 active ingredients are currently in use in more than 100,000 over-the-counter medications in the United States, with combined annual sales exceeding \$17 billion. Many drugs have recently been switched from prescription to over-the-counter status; other such switches have been proposed and rejected, in decisions that have sometimes been controversial. Drugs that have been approved by the Food and Drug Administration (FDA) for shifts to over-the-counter status include some nonsteroidal antiinflammatory drugs (such as ibuprofen, naproxen, and ketoprofen), histamine₂-receptor blockers (such as cimetidine, ranitidine, and famotidine), topical antifungal agents, and nicotine-based smoking-cessation products. Recent controversial decisions include those regarding nonsedating antihistamines (switched by the FDA despite objections by the manufacturers), hormonal postcoital pregnancy-prevention drugs (i.e., the “morning-after pill,” which was denied over-the-counter status), and statins, for which a proposed status change was rejected.

Over-the-counter status offers some clear potential advantages over prescription status. The medication becomes easier to obtain, and access to it broadens. The price of the drug often drops, and patients avoid both the cost and the delay of a visit to a prescribing physician. Patients’ ability to choose their own medications increases their autonomy, and patients benefit from educating themselves about their options. There are also benefits for the manufacturer, which gains a new opportunity for profits after its patent has expired and competitors have entered the market, since patent protection is frequently extended when such a switch is made.

Of course, there are a number of potential disadvantages as well, including risks related to self-

treatment by patients — risks of misdiagnosis, delays in obtaining a correct diagnosis, adverse interactions with other medications, reduced opportunities to receive counseling about possible lifestyle therapies (such as exercise and diet), poorer compliance (by patients who view over-the-counter drugs as different from “real” medications), use by patients who are unlikely to benefit from the drug but will nevertheless be exposed to its risks, and patterns of taking medications inappropriately (e.g., “if one is good, two are better”). In addition, patients with insurance that covers medications face the paradox of increased, rather than reduced, costs for their medications, because insurers ordinarily do not cover over-the-counter drugs, prices of which may exceed the amount of patients’ copayments for the prescription versions. Finally, over-the-counter use renders it more difficult to study a drug’s effects, since prescription databases can no longer be used for that purpose.

Generally, drugs are eligible for over-the-counter status if they can be used safely and effectively and have a label that is easily understood by the average person in order to permit self-treatment. Although determining whether a drug meets this standard is ultimately a matter of judgment, there are some generally accepted criteria that may be useful in guiding that judgment. Typically, the condition treated by the medication can be self-diagnosed by consumers, the success of the therapy monitored by patients, and the condition expected to be short-lived, so that consumers can be directed to visit a physician if it continues or worsens. Furthermore, the condition and its other treatments need to be sufficiently understandable to consumers that they can choose whether to initiate treatment, as well as which drug to use and at what dose and frequency to take it. It is also useful if the condition being treated is sufficiently innocuous that symptomatic treatment will not prove counterproductive by delaying definitive treatment.

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Selected Drugs Switched by the Food and Drug Administration from Prescription to Over-the-Counter Status, 1995 to 2003.*				
Drug	Adult Dose	Type of Product	Date Switch Approved	Brand Name
Famotidine	10 mg, up to 20 mg/day	Acid reducer	April 28, 1995	Pepcid AC
Ibuprofen suspension (100 mg/5 ml) for pediatric use†	7.5 mg/kg of body weight, up to 4 times/day	Internal analgesic–antipyretic	June 16, 1995	Children's Motrin
Cimetidine	200 mg up to twice a day	Acid reducer	June 19, 1995	Tagamet HB
Ketoprofen	12.5 mg every 4–6 hr	Internal analgesic	Oct. 16, 1995	Orudis KT, Actron
Ranitidine	75 mg up to twice a day	Acid reducer	Dec. 19, 1995	Zantac 75
Butoconazole nitrate	2.0% cream and applicators (3 days)	Anticandidal	Dec. 26, 1995	Femstat 3
Minoxidil	2.0% topical solution	Hair-growth stimulant	Feb. 9, 1996	Rogaine
Nicotine polacrilex	2-mg and 4-mg gum	Smoking cessation	Feb. 9, 1996	Nicorette
Nizatidine	75 mg up to twice a day	Acid reducer	May 9, 1996	Axid AR
Miconazole nitrate	2.0% cream and 200-mg inserts	Anticandidal	April 16, 1996	Monistat 3
Nicotine transdermal system	15-mg patch	Smoking cessation	July 3, 1996	Nicotrol
Nicotine transdermal system	21-mg, 14-mg, and 7-mg patches	Smoking cessation	August 2, 1996	NicoDerm CQ, Habitrol
Cromolyn sodium	4% nasal solution	Allergy prevention and treatment	Jan. 6, 1997	Nasal crom
Tioconazole	6.5% vaginal ointment	Anticandidal	Feb. 11, 1997	Vagistat-1, Monistat 1
Ketoconazole	1% shampoo	Antidandruff shampoo	Oct. 10, 1997	Nizoral
Terbinafine hydrochloride	1.0% cream	Antifungal	March 9, 1999	Lamisil AT
Butenafine hydrochloride	1.0% cream	Antifungal	Dec. 7, 2001	Lotrimin Ultra
Loratadine	10 mg/day	Antihistamine	Nov. 27, 2002	Claritin
Loratadine–pseudoephedrine sulfate	10 mg loratadine plus 240 mg pseudoephedrine sulfate daily	Antihistamine–decongestant	Nov. 27, 2002	Claritin D
Omeprazole magnesium	20 mg/day	Acid reducer	June 20, 2003	Prilosec OTC

* Data are from the Web site of the Consumer Healthcare Products Association, at www.chpa-info.org/web/advocacy/general_issues/switch/switch_list.pdf.

† Because the ingredients are formulated for pediatric use, the dose shown is for children.

In addition, the drug might be assessed according to certain criteria. Generally, it would have established efficacy for the treatment of a self-diagnosed condition, consumers would be able to determine whether they had any contraindications to its use, and any complications would be self-diagnosable and self-treatable. Furthermore, the drug should have a large safety margin, at high doses, that has been proved in large numbers of patients, and it should be established enough that doctors and patients are aware of its serious adverse effects. It should have a low potential for misuse and abuse and should have no or few adverse interactions with other drugs. Treatment with it should not have the capacity to mask serious illness. Its efficacy and safety should not depend critically on the precise dose or frequency of administration, and it should be possible to label it in lay terminology for proper use. Finally, it should be safe even when

used by consumers other than those for whom it is recommended on the label — pregnant women, for instance, and people outside the recommended age range.

Given these considerations, it is relatively easy to see why an FDA advisory committee, faced with a second proposal to grant over-the-counter status to statins, recently recommended against doing so. Proponents of over-the-counter access for this class of drugs cite their dramatic efficacy, relative safety, and underuse, stating that many people in the United States would benefit from more aggressive efforts to lower levels of cholesterol. Moreover, serious illness is unlikely to be masked by this therapy, and there is precedent in the United Kingdom, where some statins are no longer restricted to prescription access.

The experience in the United Kingdom, however, is largely irrelevant, since the drugs there are

available not over the counter but, rather, “behind the counter” (a third option that is not used in the United States), meaning that an intervention by a pharmacist is still required. More important, statins fail to meet many of the other criteria for a switch to over-the-counter status.

Hypercholesterolemia, the indication for statin use, is not self-diagnosable. Treatment is long-term. The efficacy of statins is dose-related, and monitoring is required for titration. Over-the-counter drugs are typically formulated at a lower dose than are prescription drugs, to address concerns about the safety margin, but access to lower-dose statin therapy may delay or prevent patients from receiving higher-dose (albeit not curative) therapy under a physician’s direction. Furthermore, patients might conflate hypercholesterolemia with its complications (e.g., coronary artery disease) and might purchase statins rather than visit their physician when they have angina. Other consumers, despite having normal cholesterol levels, might treat themselves for peace of mind — which would significantly affect the therapy’s risk–benefit balance.

Statins have not been proved effective for a self-diagnosed condition, and their contraindications and complications, such as liver disease, are unlikely to be self-diagnosed. It is true that statins have a large safety margin and have been used in many patients, but whereas the potential for abuse is clearly low, the potential for misuse is not. For example, some patients may self-medicate irrationally (“I ate a hamburger, so I’ll take an extra pill”), increasing the risk of dose-related adverse effects (such as rhabdomyolysis), and the risk of serious toxic effects increases when these drugs interact with other medications.

The label on prescription statins recommends monitoring of liver function at baseline, at 12 weeks, after any increase in dose, and periodically thereafter. Some physicians also monitor patients for toxic effects on muscle. The efficacy of these agents is sensitive to the proper choice of dose, frequency, and with some statins, whether the medication is taken with meals.

Compliance is known to be woefully inadequate among many recipients of prescription statins. Studies show that patients need one to two years of continuous therapy for benefit to be achieved; even with a physician’s supervision, such a course of treatment is not completed by a large proportion of patients. Would patients follow directions better with over-the-counter statins? Furthermore, given that insured patients would need to pay for the drugs out of their own pockets, it is unclear that their use would increase.

Finally, safety in special populations, especially pregnant women, is uncertain. Indeed, on the basis of studies in animals, statins have been classified as category X drugs, which are contraindicated during pregnancy.

The motivation for making statins available over the counter is understandable: to increase access to an effective and underused therapy. But it is unclear that such a switch would help to achieve that goal. Although statins are great prescription drugs, these considerations suggest that they would make poor over-the-counter drugs.

Dr. Strom reports having received consulting fees or funding from AstraZeneca, Bayer, Bristol-Myers Squibb, Merck, Novartis, and Pfizer and having provided legal testimony in cases involving Bayer, Bristol-Myers Squibb, and Pfizer.

The Uncertain Future of Specialty Hospitals

John K. Iglehart

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In November 2003, Congress enacted legislation that imposed an 18-month moratorium on the development of new specialty hospitals that are partly owned by physicians who refer their patients to them.¹ President George W. Bush signed the mea-

sure into law December 8 as part of the Medicare Prescription Drug, Improvement, and Modernization Act of 2003. Very soon, Congress must decide whether to extend the moratorium, as recommended by one of the two federal agencies that legislators directed to study the matter, or adopt policies that enable physician-owners to build new

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