

Analysis of the Movement of Prescription Drugs to Over-the-Counter Status

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ABSTRACT

BACKGROUND: The transition of prescription drugs (Rx) to over-the-counter (OTC) status is a very complex and multifaceted process involving many parties and many issues. This article examines the regulatory history and process and presents a review of the issues involved, using recent Rx-to-OTC conversions as examples.

FINDINGS: Data are presented on the growth of the OTC market and the impact recently switched products have had on this market growth. Drug product characteristics that make drug products amenable to OTC conversion are described. Reasons are presented for why more and more prescription drug products are being reviewed as candidates for OTC conversion. A list of high-profile Rx-to-OTC products is provided, along with a discussion of new proposals for OTC conversions and those products that have not been approved for OTC conversion.

CONCLUSION: Conversion of prescription products to over-the-counter availability can have an impact on prescription-drug-benefit costs and on total health care costs. There are opportunities and limitations for managed care organizations in the coverage and promotion of OTC products as therapeutic alternatives to prescription-only drugs.

KEYWORDS: Prescription-to-OTC switches, OTC medications, FDA regulations on OTC switches, Prescription-to-nonprescription drug switches

J Managed Care Pharm. 2002(8)6:499-508

The planned introduction of over-the-counter (OTC) loratadine (Claritin, marketed by Schering-Plough) at year-end 2002 and the proposed OTC status for omeprazole (Prilosec, marketed by AstraZeneca) brought renewed attention to the subject of prescription drug to OTC "switches." These 2 developments alone are significant.

Total retail community pharmacy sales of loratadine were \$2.25 billion in 2001.¹ It ranked number 11, representing approximately 1.2% of total community pharmacy prescription drug sales. The total prescription antihistamine market was approximately \$4.69 billion for that year, with loratadine accounting for nearly 50%. Two other second-generation antihistamines, fexofenadine (Allegra) and cetirizine (Zyrtec), accounted for 24.8% and 20.8%, respectively, of this market.¹ Omeprazole ranked number 2 in terms of community pharmacy expenditures on prescription drugs in the United States in 2001.¹ It had retail sales of \$3.99 billion, accounting for 2.6% of the total community pharmacy prescription drug market.¹ The combined antiulcer therapeutic category accounted for nearly \$10.81 billion in prescription drug sales in 2001, or about 7% of all such sales in the United States.

This paper will focus on the regulatory background governing the change in status of drugs from prescription to OTC availability. It will also examine the mechanism of the switch process; proposed, permitted, and rejected switches; and also a number of therapeutic categories in which the switch process has, or is likely to have, a significant effect. Finally, it will review the impact of prescription-to-OTC changes on health care costs and the perspectives of managed care and the pharmaceutical industry on the switch process.

The Pharmaceutical Market

Expenditures on prescription drugs in the United States continue to rise faster than any other medical service sector.¹ Over the past several years, prescription drug spending has risen by more than 15% per annum.¹ These rising costs have attracted considerable attention, politically, from consumer protection groups and the health care industry. The rise in costs has not been limited to that of the prescription market. In 2000, U.S. consumers were estimated to spend \$19.1 billion on OTC drugs.² The OTC market has expanded significantly in the last 10 years, from an estimated \$10.2 billion in 1991² (Figure 1).

Reasons cited for this increase in OTC sales include

- a growing emphasis on individual autonomy in health care,
- a trend toward prescription drug deregulation in the United States,
- cost-containment efforts by health care organizations,
- profit interests of the pharmaceutical industry, and

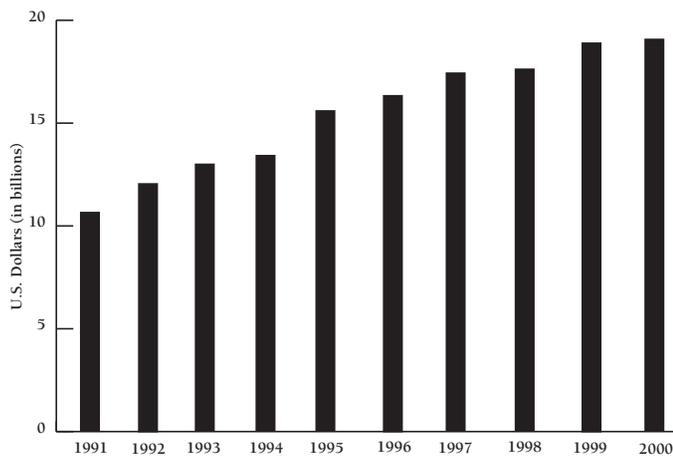
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FIGURE 1 The Growth of U.S. OTC Retail Drug Sales Over a 10-Year Period



Source: Consumer Healthcare Products Association (CHPA)

- a steady increase in the number of OTC products.

Consumer choice within the OTC market has also increased. Approximately 600 of the currently available OTC products use ingredients and dosages only available by prescription 20 years ago.³ U.S. consumers have embraced this concept of self-care. In January 2001, the Consumer Healthcare Products Association, the trade organization that represents manufacturers and distributors of OTC medicines and dietary supplements, commissioned a survey on OTC product usage by Roper Starch Worldwide.⁴ This survey of 1,505 adults revealed a more empowered American public. Findings included the following:

- 59% reported that they would be more likely to treat their own health conditions now than they were a year ago,
- Consumers used OTC medications to treat 38% of all their health care problems, and
- 77% of consumers used an OTC medication in the past year (compared to 43% who consulted a physician and 38% who took a prescription medication).⁴

Despite these trends, OTC drugs account for less than 2 cents of every dollar spent annually on health care in the United States.²

Depending on the perspective of the study, there are conflicting arguments as to the cost savings associated with the switch-process of prescription to OTC drugs. In a study by Kline and Company, it was estimated that American consumers saved almost \$13 billion a year by using medications switched from prescription-only availability to OTC status.⁵ Furthermore, they reported that 63% of total U.S. OTC sales in 1996 (approximately \$10.2 billion) were from prescription-to-OTC-switched products and products formulated with switched ingredients. Others argue that the trend merely transfers the burden of costs from third parties to consumers.

Regulatory Background

The Food, Drug and Cosmetic Act of 1938 established a number of basic requirements before a drug could be marketed. It required that new drugs must be proven to be safe and be properly labeled. The legislation stated that drug labeling must contain “adequate directions for use” and that these directions are to appear on the package with “conspicuousness and in the terms such as to render it likely to be read and understood by the ordinary individual under customary conditions of purchase and use.”⁶ These requirements appear to pertain to labeling for OTC drugs more than prescription drugs. The 1938 regulations did not distinguish between prescription and OTC drugs, with the result that regulatory intervention was inconsistent.⁶

In 1951, the Durham-Humphrey Amendment provided a statutory basis to differentiate between prescription-only and OTC drugs.⁷ Specifically, a prescription is required for the following categories of drugs:

- habit-forming drugs;
- drugs that can only be used safely under the supervision of a licensed medical practitioner, or, in other words, it must be demonstrated that consumers can take an OTC medication without professional oversight, using the information available on the product label; and
- new drugs if they have been approved as a result of new-drug applications for use under professional supervision.⁸

The Durham-Humphrey Amendment eliminated the 1938 labeling requirements for prescription drugs. Labeling needed to be directed only to the physician and pharmacist and no longer needed to meet the criteria of being understood by the ordinary individual under customary conditions of purchase and use.⁹ An important component of this amendment is that the same drug, at the same dose, and for the same indication, cannot be simultaneously available on a prescription and nonprescription basis. However, drugs switched to OTC status may continue to have prescription-only status for certain doses and treatment indications.⁹

The 1962 Kefauver-Harris Amendment further expanded regulatory requirements for drug approval.¹⁰ The primary component of this amendment is that the FDA must assess that new drugs are proven to be both safe and efficacious for their stated therapeutic claims before they can be marketed.⁸ It also mandated a review of existing prescription and OTC drugs. Specifically, it requires proof that an OTC product is effective when used without supervision by a health care practitioner. These amendments established the OTC Drug Review panels, which evaluated more than 700 ingredients contained in OTC products for safety and efficacy.⁸

The Drug Price Competition and Patent Restoration Act of 1984 (Waxman-Hatch) provides for a patent extension of 3 years for drugs switched from prescription to OTC status if the company has been required to provide additional clinical trials for the switch to be evaluated.¹¹ The period of exclusivity begins at product approval and is limited to changes in the product license supported by the new clinical study.¹⁰

Analysis of the Movement of Prescription Drugs to Over-the-Counter Status

TABLE 1 Some Recent Popular Prescription-to-OTC (Switch) Products

OTC Product	Active Ingredient	Manufacturer	Switch Year
Actron	Ketoprofen	Bayer	1995
Aleve	Naproxen	Bayer	1994
Axid AR	Nizatidine	Whitehall Robins	1996
Children's Advil	Ibuprofen	Whitehall Robins	1996
Children's Motrin	Ibuprofen	McNeil Consumer	1995
Femstat 3	Butoconazole nitrate	Bayer Consumer	1995
Gyne-Lotrimin	Clotrimazole	Schering-Plough	1990
Lamisil AT	Terbinafine	Novartis	1999
Monistat 3 Combination Pack	Miconazole nitrate	Advanced Care Products	1996
Motrin-Migraine Pain	Ibuprofen	McNeil Consumer	2000
Mycelex-7	Clotrimazole	Bayer	1991
Nasal crom	Cromolyn sodium	Pharmacia & Upjohn	1997
Nicorette	Nicotine polacrilex	SmithKline Beecham	1996
Nicotrol	Nicotine transdermal	Pharmacia & Upjohn	1996
Orudis KT	Ketoprofen	Whitehall Robins	1995
Pepcid AC	Famotidine	Merck	1995
Rogaine	Minoxidil	Pharmacia & Upjohn	1996
Tagamet HB	Cimetidine	SmithKline Beecham	1995
Tavist-1	Clemastine fumarate	Novartis Consumer	1992
Vagistat-1	Tioconazole	Bristol-Myers Squibb	1997
Zantac-75	Ranitidine	Warner Lambert	1995

Sources: Kalarma Information, LLC. *The Market for RX to OTC Switches, June 2000*; and Consumer Healthcare Products Association. Available at: www.chpa.org. Accessed July 29, 2002.

■ Mechanism of Switch

Under current regulations, there are 2 modalities by which either a new drug or a drug already approved for prescription-only sale can be exempted from prescription-only status:

- Food and Drug Administration (FDA) approval of a new-drug application supporting the use of a drug on an OTC basis. This requires submission of additional information showing that a drug is appropriate for self-administration. This information is usually submitted by a manufacturer as an addendum to the original new-drug application. However, there are no regulations to specify who may petition the FDA, so long as the petitioner provides the FDA with sufficient information demonstrating the drug's safety and effectiveness.¹²
- A product is exempt if the ingredients of a product are included in previously published regulations defining the requirements for OTC sale and if the labeling of the product complies with these regulations. Panels of nongovernment experts are involved in ongoing OTC drug reviews assessing the effectiveness of drugs approved prior to 1962 (before a proof of efficacy was a requirement). These panels also review current

prescription ingredients to assess appropriateness for OTC marketing. This process has approved approximately 40 former prescription-only drugs.¹²

Typically, a manufacturer submits results of clinical trials with issues specifically related to OTC availability. These include studies of label comprehension to assess ability to read and understand important information on the proposed label and package insert, or actual-use studies, that is, trials conducted in a manner to simulate the use of a drug without professional supervision.

Demonstration of safety and efficacy for an OTC drug includes a number of requirements that are distinct from those for a prescription drug:

- Is the condition self-diagnosable?
- In reading a product label, can the patient extract the key information necessary to use the drug properly?
- Is the OTC drug effective when used as recommended?
- Is the OTC drug safe when used as instructed? This places a substantial onus on the patient to understand the label and determine whether or not contraindications or drug interactions apply.¹²

The extent to which a product line is switched varies. For example,

- there is a complete switch in which all of the doses and all of the indications, which are currently marketed as prescription products, are taken OTC, eliminating the need for a prescription product;
- There is a partial switch in which some of the doses and some of the indications are taken OTC and some remain unchanged in the prescription form; and
- a new lower dose of a prescription product or a product with a new indication is marketed that would not require a learned intermediary's (e.g., a pharmacist's) intervention.¹³

■ Previous Prescription-to-OTC Switches

As noted earlier, more than 600 currently available OTC products include ingredients or doses only available by prescription 20 years ago.³ Table 1 illustrates a list of recent popular switched products. A review of a number of switched products is included here to illustrate some of the issues pertaining to this matter. In addition, the literature documenting cost savings for the products is presented.

■ Vaginal Antifungal Agents

In June 1990, following petitions by several sponsors, the FDA conducted an advisory committee meeting to examine the feasibility of switching a number of vaginal antifungal agents to OTC status.¹⁴ This committee approved the OTC use of 7-day treatment courses of clotrimazole and miconazole for candidal vaginitis. Subsequently, several other prescription antifungal medications were switched to OTC status. A number of studies have investigated the impact of these switches. Gurwitz et al. examined switch-related changes to the use of prescription drugs, professional services, and laboratory services for a one-year period after clotrimazole was switched from prescription to OTC status.¹⁵ They examined the database records of 50,000 Health Maintenance Organization (HMO) enrollees, and they noted a significant decrease in the number of prescriptions dispensed for vaginal antifungal agents (6.42 per 100 female members age 11 years or older). A decline in the number of physician visits (0.66 per 100 members) and laboratory charges were also noted for female enrollees. On the basis of these changes, it was estimated that, in one year, the HMO saved approximately \$42,000 in medication costs. Depending on the assumptions made about foregone laboratory tests and physician visits, the HMO saved an additional \$13,000 to \$26,000. This study concluded that the prescription-to-OTC switch of vaginal antifungal treatments reduced health care costs to the insurer in the managed care setting. However, the authors also noted that these favorable effects on costs should be weighed against shifts in medication cost to consumers and potential adverse consequences to the patient relating to errors in self-diagnosis.

In 1999, Lipsky et al. corroborated the findings of Gurwitz's study.¹⁶ Using National Ambulatory Medical Care Survey data,

they documented a 15% decline in the number of visits to practitioners for vaginitis from 1991 to 1994. This, they theorized, could be potentially attributed to the availability of OTC antifungal preparations. Using a rough estimate of \$61 per physician office visit, this decrease amounted to more than \$45 million in direct cost savings per year. An additional saving of \$18.75 million could be attributed to savings in indirect costs associated with time lost from work when visiting a physician.

In a study published in 2000, Ferris et al. concluded that women who self-diagnose and use an OTC product for the treatment of presumed vulvovaginal candidiasis frequently do not have that condition.¹⁷ Neither a history of a previous clinical-based diagnosis of vulvovaginal candidiasis nor reading the package label helped women to accurately self-diagnose vulvovaginal candidiasis. They concluded that ready access to these products is associated with wasted financial expenditures and a delay in a correct diagnosis for a substantial number of patients. The authors noted that the sale of antifungal preparations almost doubled since being approved for OTC status. This occurred despite little evidence of a concomitant increase in the incidence of candidal vaginitis. This they believed strengthened the position that these products may be overused, particularly in those patients for whom the initial diagnosis of a candidal infection was not established.

■ Histamine₂ Receptor Antagonists (H₂RAs)

Famotidine (Pepcid AC) was the first of the H₂RAs to be switched to an OTC status, in April 1995. Three other agents from this class—cimetidine, ranitidine, and nizatidine—were also switched within the ensuing year.² In each case, the manufacturers pursued a dual marketing strategy for their products, that is, continued prescription availability of the product for the existing doses and indications and a new OTC status at a lower dose for the symptomatic relief of heartburn, acid indigestion, and "sour stomach."

The switching of agents within this product class provoked significant debate. Of primary concern was the potential for increased patient morbidity and mortality due to widespread indiscriminate use of these agents. Specifically, there was the potential for these agents to mask symptoms of severe disease such as cancer, thereby delaying patient presentation to physicians. However, a link between the use of H₂RAs and gastric or esophageal cancer has not been established.¹⁸

The economic savings to managed care organizations (MCOs) and patients have been investigated in a number of studies. Kunz et al. estimated that the OTC availability of H₂RAs would result in \$6 million savings over a 5-year period for a 260,000-member managed care organization, that is, a 25% reduction in the overall cost of treatment of nonsevere heartburn and nonulcer dyspepsia.¹⁹ Estimated savings were based on the avoidance of unnecessary physician visits, laboratory tests, and prescriptions. Similar savings were noted in a study investigating the impact of OTC availability of H₂RAs on medication and health care utiliza-

tion patterns among chronic users of H₂RAs in a health maintenance organization.²⁰ Kalish et al. assessed the societal costs associated with the treatment of initial dyspepsia prior to and subsequent to the OTC availability of the H₂RAs.²¹ Costs to both the patient and the MCO were identical, regardless of the status of the product (\$204/\$203 and \$149/\$149, respectively). This finding was based on 2 assumptions: that the efficacy of the H₂RAs in the treatment of initial dyspepsia is similar to that of the antacids and that there would be an increase in physician-ordered diagnostic tests following symptom-relief failure on OTC H₂RAs.²¹

■ Nicotine Replacement Therapy

The switching of nicotine replacement products to OTC status was particularly controversial. An OTC indication appeared to be precluded on the basis that nicotine is an addictive substance. There was concern in relation to how access to these products could be controlled in the OTC environment in order to prevent inappropriate use, particularly by minors.²² There was also a question of whether the efficacy of nicotine replacement therapy demonstrated in the prescription environment would translate to the OTC setting.²² In February 1996, Nicorette gum was the first nicotine replacement therapy to be switched to an OTC status following collaboration between the manufacturer, SmithKline Beecham, and the FDA.² As part of the approval process, the company conducted extensive clinical studies and label-comprehension studies to demonstrate safety and efficacy in the OTC setting.²²

Equivocal evidence has been presented in relation to the societal benefits from the OTC availability of nicotine replacement therapy. Keeler et al. estimated net annual societal benefits of \$1.8 to \$2 billion based on an increase in smoking cessation and the value of quality-adjusted-life years added from reduced smoking.²³ These estimates were based on assumed quit rates following a 78% to 92% increase in the consumption of nicotine patches and a 180% increase in consumption of nicotine gum subsequent to their OTC availability. In contrast, in a study based on Massachusetts Tobacco Surveys, Thorndike et al. noted no change in the use of nicotine replacement therapy at a quit attempt prior to or subsequent to the OTC availability of these agents.²⁴ In addition, they found no significant change in the proportion of smokers who made a quit attempt or who quit smoking associated with the change in product status.

■ Proposed Switches

1. Proton Pump Inhibitors

In June 2002, the joint Nonprescription Drugs Advisory Committee (NDAC) and the Gastrointestinal Drugs Advisory Committee reversed an earlier October 2000 decision by voting 16 to 2 in favor of an OTC status for Prilosec.²⁵ This OTC status was approved for a dose of 20 mg daily for 14 days for the prevention of symptoms of frequent heartburn and was conditional, based on certain OTC label revisions and the completion of a patient-label-comprehension study. Continued concern was

voiced in relation to the suitability of the proton pump inhibitor agents for OTC use, and, in particular, the potential link between proton pump inhibitor therapy and the proliferation of preexisting esophageal adenocarcinoma. Prilosec 10 mg, 20 mg, and 40 mg capsules would continue to be marketed as prescription products for their existing indications.²⁶ Prilosec, with 2001 sales of approximately \$4 billion ranked number 2 in U.S. retail sales.¹ The Prilosec patent expired in October 2001,²⁷ but its availability as a generic drug was held up by litigation.²⁸

2. Emergency Contraception

Considerable attention was given to the issue of emergency oral contraception (EC) in 2001. Currently, there are 2 FDA prescription-approved products (Preven and Plan B) for emergency contraception. Medical and legal commentators argued that under long-standing federal legislation, the FDA is authorized and should be required to switch EC to OTC status without delay.²⁹ Experts predicted that widespread access to EC could prevent up to half of the 3 million unintended pregnancies in the United States each year. They argued that the designated EC products meet all the criteria for OTC use: low toxicity, no potential for overdose or addiction, no risk of causing birth defects, no need for medical screening, self-identification of need, uniform dosing, and no important drug interactions; that is, that there is no medical reason for the prescription status of EC. In February 2001, the Planned Parenthood Federation of America and 56 other organizations filed a citizen's petition to the FDA to request a switch from prescription to OTC status for Preven and Plan B and any new drug eligible for filing an abbreviated NDA because of equivalence to these products.³⁰

3. Second-Generation Antihistamines

The prescription antihistamine market is lucrative and growing. In 2001, sales of these agents totaled \$4.69 billion, an increase of 22.4% (\$3.74 billion) from 2000.¹ Three of the nonsedating antihistamine class agents, loratadine (Claritin), fexofenadine (Allegra), and cetirizine (Zyrtec), accounted for more than 96% of this market and ranked at numbers 11, 22, and 31, respectively, in terms of year-2001 total retail community pharmacy sales.¹ In a landmark case, WellPoint Healthcare, Inc., the parent company of Blue Cross of California, petitioned the FDA in July 1998, to exempt a number of second-generation antihistamines, notably cetirizine, fexofenadine, and loratadine, from prescription requirements.³¹ WellPoint proposed the following arguments in favor of its petition:

- The second-generation antihistamines have favorable adverse-event profiles over the traditional OTC antihistamines and decongestants in terms of sedation and anticholinergic profiles.
- Patients are being deprived of access to quality pharmaceutical care.
- Patients are currently being exposed to more dangerous and less tolerable OTC antihistamine products.

- It places undue time and financial constraints on patients by requiring them to schedule an office visit to obtain a safe medication.
- It trivializes the patient-physician relationship.

They cited that, based on recent historic precedent, the cost of the OTC version of the drugs would be 50% of the prescription drug cost. WellPoint has also stated that it would save \$45 million a year if the drugs were available OTC.³¹

The petition by WellPoint was initially opposed by a number of parties, including Schering-Plough, the maker of Claritin. The company stated that it believed that there was not an adequate basis to support the OTC use of the drugs being considered. This is in spite of the fact that Claritin and Zyrtec were, at that time, approved in 80 countries as nonprescription allergy drugs. Schering-Plough made the following allegations:

- The WellPoint petition lacked the data to support an OTC switch.
- Self-care and self-treatment are often inappropriate.
- Further labeling was required to ensure safe and effective OTC use, and this could not be developed without further study.
- While safety was generally established, there was a need for further study to establish safety in the OTC setting without physician supervision and in at-risk groups of patients.
- The switch would cause cost shifting to patients that would reduce access to care.
- The physician role is critical to optimal patient care.
- Allergies may be a complex disease.³²

The Pharmaceutical Research and Manufacturers of America (PhRMA) supported this position, asserting that

- the FDA did not have the statutory authority to switch a drug over the objection of the NDA holder and without following the adjudicatory hearing processes set forth in section 505(e) of the Food Drug and Cosmetic Act,
- a forced switch would violate the NDA holder's proprietary rights to its safety and effectiveness data, and
- forced switches would represent poor public health policy.³³

The switch of the second-generation antihistamines to OTC status was also strongly opposed by the American Academy of Allergy, Asthma and Immunology.³⁴ Its position regarding the proposed switch was based on the following arguments:

- It would result in reduced availability of these medications to patients who currently receive them through insurance-covered formularies.
- It would eliminate the role of the physician, with the potential for overuse of these agents in conditions for which there is no proven efficacy and underutilization in appropriate allergic disorders. This would be associated with increased health care costs.
- Allergies are not necessarily self-diagnosable. Whereas public surveys indicate that up to 75% of U.S. consumers feel that they have allergies, the actual prevalence in the United States is 20% to 30%.

- It trivializes allergies, possibly leading to a delay in the diagnosis of other conditions.³⁴

The Academy argued that it was clear that the real motive is the fiscal bottom-line of the insurance companies. Countering this, it was alleged that the reason for physician opposition to the switch was in part financial, with some physicians expected to experience significant losses due to loss of revenue from office visits.³⁵

On May 11, 2001, the NDAC and the Pulmonary and Allergy Drugs Association of the FDA voted to recommend that the agency switch Claritin, Allegra, and Zyrtec to OTC status.³⁶ This prompted a swift response from the pharmaceutical industry. Robert J. Spiegel, chief medical officer of Schering-Plough, stated that they "strongly believed that Claritin should remain a prescription product," and that "the prescription status of these medications is necessary to protect and optimize public health." They also asserted that significant legal and public policy issues would be raised if the FDA were to require such a switch without drug sponsor's support.³⁷

By March 2002, with the imminent patent expiration of Claritin in December, Schering-Plough had rethought its policy in relation to OTC Claritin. In a company newsletter, Richard W. Zahn, president of Schering Labs, the U.S. prescription pharmaceutical marketing arm of Schering-Plough, announced that "with the market introduction of Clarinex"... "moving Claritin" to OTC status would give Schering-Plough an opportunity to establish brand leadership in both the prescription and OTC categories."³⁸ He stated that "rapid market acceptance of Clarinex and the proposed conversion of Claritin to OTC status represents a strategic business and medical decision designed to address potential changes in the regulatory, health, and legal environment," that it allowed the "introduction of a safe second-generation antihistamine in the OTC marketplace," and that it would "position these products as the premier brands in the prescription and OTC categories" and would serve to "maximize the combined value of the Claritin and Clarinex brands." Consistent with previous arguments of the company, he noted that "it is the continued medical position of the company that allergies are a complex disease often requiring physician management and oversight," a niche it is presumed that Clarinex will conveniently fill.

WellPoint announced that it planned to steer allergy patients from prescription medications to OTC drugs, causing a major dilemma for Aventis and Pfizer, the manufacturers of Allegra and Zyrtec.³⁹ It announced that it would raise copayments on Allegra and Zyrtec to \$30 to \$40 per month, up from \$17. Besides increasing the copayment, WellPoint signaled its intent to not cover Allegra or Zyrtec unless Claritin does not work for a patient. Coverage of Clarinex was uncertain. Other insurers were expected to follow suit. Faced with higher copays, patients may choose to switch to the cheaper, OTC Claritin. There is an expectation that the companies may be required to launch OTC versions of their drugs long before their patents expire in 2013 and 2007, respectively.

At the time of preparation of this manuscript, Schering-Plough had not announced the price it intended to charge for OTC Claritin, but it was expected that uninsured consumers would benefit substantially because the price is expected to drop significantly from the current prescription price of \$80 to \$90 per month. It was predicted that the price of Allegra, Claritin, and Zyrtec would drop by as much as 80% when switched to OTC status. This would make them comparable in price to other existing OTC antihistamine products.³⁵ As a final complication to the picture, 2 other drug companies, units of Johnson & Johnson, Inc., and American Home Products Corp., had filed applications with the FDA to market generic OTC versions of Claritin. Schering filed a lawsuit arguing that the generics violate a separate patent that does not expire until 2004.

The switch of the second-generation antihistamines is expected to have a significant impact on the U.S. market for OTC cough and cold remedies. This market had contracted, falling by 2.7% in 2000 following strong sales in 1999, to a value of \$3.9 billion.⁴⁰ Reasons cited for this decline included a mild winter and the growing popularity of prescription medications on which substantial sums had been spent on direct-to-consumer advertising. Led by the prescription-to-OTC switch of Claritin, the market is now expected to grow 14.5% to a value of \$4.5 billion by 2005, with the expansion of the antihistamine component of the sector by 36.6%, for a projected market size of \$734.4 million.⁴⁰

■ Unapproved OTC Switches

OTC status has been rejected for a number of products. For example, in 1994, OTC status for oral acyclovir for the treatment and suppression of genital herpes was rejected at a joint meeting of the FDA and the Antiviral NDAC.⁴¹ Although the committees appreciated that concerns existed in relation to self-diagnosis, misdiagnosis, misuse, and safety, the switch was rejected on the grounds that it would give precedence for the OTC use of other anti-infective agents, hastening the development of viral and accelerated microbial resistance.

In July 2000, the FDA's NDAC, together with the Endocrinologic and Metabolic Drugs Advisory Committee, rejected requests by Merck for its agent lovastatin (Mevacor) and by Bristol-Myers Squibb for pravastatin (Pravachol) to be sold OTC.⁴² In issuing the rejection, the panel said that it had not been demonstrated that these products could be used safely and effectively in the consumer setting. Pravachol, with 2001 sales of \$1.42 billion, ranked number 17 in terms of U.S. 2001 retail sales.¹ Its patent is scheduled to expire in January 2003.⁴³

■ Effect of Prescription-to-OTC Switches on Health Care Costs

In addition to the studies mentioned on cost savings estimated from switching products from prescription to OTC status, the following study published in 2002 by Gianfrancesco et al. illustrates economic implications of the switch process.⁴³ The authors examined out-of-pocket health care costs and medical service use for 4 products newly switched from prescription to OTC status:

cromolyn sodium (Nasalcrom), tioconazole (Vagistat), ketoconazole (Nizoral), and terbinafine (Lamisil) and for 3 different insurance scenarios: indemnity/managed care plan, Kaiser Permanente HMO, and Maryland Medicaid.⁴³ They noted that prescription charges for all 4 products were much higher than OTC retail prices. However, for persons who had prescription drug coverage, out-of-pocket payments for the prescription products were far less than the OTC prices. For all 4 products and all 3 insurance plans, consumer drug costs at point of purchase were higher when products were obtained OTC. Costs ranged from 2% to 113% below consumer OTC costs for the indemnity/managed care plan and 54% to 233% below for the HMO. The greatest difference obviously was for Medicaid, for which copayments were miniscule. The effect on medical service use varied by product. However, it appeared that OTC approval was associated with elevated rather than reduced medical service use. They suggested that users of cromolyn and tioconazole experienced more-costly visits after OTC approval. This, they postulated, would be consistent with complications resulting from self-care or due to more-costly visits resulting from non-self-treatment by patients because of increased out-of-pocket expenses.

The combined effect of increased out-of-pocket medical expenses and out-of-pocket drug costs contributed to higher out-of-pocket health care costs for all categories of consumers. From the perspective of the third-party payer, savings were noted for all insurance plans for these products despite the increase in medical services utilization.

■ The Perspective of Managed Care on Prescription-to-OTC Switches

Approximately 75% of Americans have prescription drug coverage. As noted earlier, Americans without prescription drug coverage generally benefit from the switch process since OTC prices of the switched products are generally lower than the previous prescription prices. The American Medical Association has stated that while it is in favor of drugs that are appropriately switched from prescription status, there is a concern that the effect of out-of-pocket expenditures may reduce the availability of these products to patients.⁴⁴ For this reason, it actively advocates for the provision of drugs for medically indigent populations, including the payment by Medicaid for OTC drugs when they are the drugs of choice.

In recent years, MCOs have investigated the possibility of extending coverage to OTC products. It is thought that in doing so, they would encourage the use of these medications in preference to their higher-cost prescription counterparts. Results of MCO pharmacy director surveys for the year 2000 suggested that, among MCOs, Medicaid had the most liberal OTC policy, with 11.5% of plans covering all OTC products and nearly 81% covering selected products.⁴⁵ Some OTC coverage was reported for 80.6% of commercial/group plans and for 87.9% of Medicare plans. According to a 1999 Novartis Pharmacy Benefit Report, only 32.4% of plans covered selected OTC products.⁴⁶ Similarly, only 31.5% reported continued coverage of products switched

from prescription to OTC status. And, among the HMOs that covered OTC drugs, coverage was limited in 62% of the plans to only the OTC (prescription) equivalent. Specific categories of OTC products are covered by a number of HMOs, including

- acid reducers: 13%,
- antifungals, smoking cessation aids, and vitamins: 7.4%,
- antihistamines: 11.1%,
- nonsteroidal anti-inflammatory agents: 8.3%, and
- diabetic supplies: 27.8%.³⁵

In a report by Aventis Pharmaceuticals in 2000, it was noted that the percentage of HMOs that covered OTC medications had doubled from 6.6% in 1998 to 12.3% in 1999.⁴⁷ The trend toward increased coverage of OTCs was most notable for network-model HMOs, 20.5% of which extended coverage in 1999 as compared to 7.3% in 1998. In 1999, network-model HMOs comprised 18.2% of the HMO sector. In contrast, only 9.1% of IPA-model HMOs, which comprised 66.7% of operating HMOs in 1999, offered coverage of OTC medications.⁴⁷ The discrepancy between the Novartis and Aventis reports regarding percentage of HMO plans covering OTCs may reflect differences in perception between organizations as to what constitutes an OTC product.^{46,47}

In a study involving 1.5 million HMO members in 3 drug plans for the period 1999-2000, it was found that spending increased on prescription antifungals following the switch from prescription to OTC status of Lamisal cream and Nizoral shampoo in spring 1999.⁴⁸ While coverage of these OTC products was excluded, the overall net increase in cost of antifungal agents to the HMO was \$0.26 per member per month. The impending switch of Claritin and Prilosec to OTC status may force HMOs to reconsider their position in relation to coverage of OTC products. Currently, in the absence of insurance coverage of OTC products, insured individuals experience increases in out-of-pocket expenses as a consequence of prescription-to-OTC switches. This is likely to be detrimental to consumers even if savings by the third-party payers are passed on to the consumer in the form of premium reductions.

One additional consideration is the rising copayments in managed care. For those OTC products that are not included in the managed care plan, the possibility exists that the price of some OTC products will be less than the copay amounts for the prescription drug product. Obviously, some consumers will opt for the OTC product to save out-of-pocket expenses, and some physicians may even recommend the OTC product to the patient knowing the copayment requirements. One major limitation of this approach is that health care practitioners, including pharmacists, may not realize that patients are taking an OTC product for their condition. The product may not be listed within the patient's medication profile or electronic medical record, increasing the risk of drug-drug or drug-disease adverse events. Therefore, one advantage of including OTC products as part of the managed care plan is the documentation of patient use and improved ability to monitor all drug use for patient safety.

■ The Industry Perspective on Prescription-to-OTC Switches

From a pharmaceutical industry perspective, having a monopoly on the prescription market is preferred. However, the OTC sector, while less profitable than the prescription market, is evidently still viewed as being immensely profitable by the industry. In its first year of sales after an April 1995 switch to OTC status, Pepcid AC had sales of more than \$200 million, making it the most profitable switch of its era.⁶ In 1996, Warner-Lambert spent \$125 million in a marketing blitz of Zantac 75, the OTC version of Zantac, the world's largest selling prescription drug at the time.⁴⁹ Companies market the drugs accordingly, with budgets of \$50 to \$100 million allocated to many new OTC products.⁵⁰ Marketers are taking a dual strategy—marketing directly to consumers and persisting in detailing physicians in order to gain advantage from additional credibility of an OTC recommended by a physician. Warner Lambert was estimated to have spent \$11 million in detailing physicians about OTC Zantac 75.⁵⁰

If a drug is switched to OTC status prior to patent expiration, it can be difficult to maintain the same market share and profit levels. Drug manufacturers typically do not submit their own product for consideration for OTC status until a patent is close to expiration. Recouping the expense of research and development of a product and the payment of FDA fees (\$937,000 per dosage per drug for 5 years) are factors.⁵¹ In a study published in 1999, Christopher Hollenbeak presented a model of the effect of generic competition on prescription-to-OTC switches.⁵² He concluded that it was in the best interest of the pioneer company to keep its drug in the prescription market for as long as possible in order to maximize its monopoly profits and to reveal harmful side effects. He noted that the best time to switch a product is just before the patent expires so that the pioneer has a period of marketing exclusivity to build brand loyalty and name recognition in the OTC market. While elasticity of demand and per-unit prices may be higher in the prescription market, total quantity demanded may be much higher in OTC, where access is less limited and the costs of obtaining the drug may be lower. A pioneer drug manufacturer may switch its prescription product to OTC status as a response to generic entry if it believes the holder of the generic will apply for the switch if it does not. The belief here is that within the pharmaceutical market there is "first-mover advantage," which is defined as product differentiation advantages that allow the first firm in the market to charge high prices and maintain significant market share despite subsequent market entry by competitors.

Managed care is another factor that influences pioneer drug manufacturers in deciding to move a drug from prescription to OTC status. In particular, MCOs commonly attempt to contain costs by allowing full or partial reimbursement only for generic versions of prescription drugs that have lost patent protection. As managed care generally does not cover OTC preparations, these preparations are more immune to the influences of managed care policies, potentially encouraging pioneer drug companies to switch their products to OTC status once a generic prescription drug competitor emerges.

Conclusion

The prescription-to-OTC switch movement is complex and multifactorial. Forces impacting on the movement of prescription drugs to OTC status include the market expansion motives of the pharmaceutical industry, a national trend toward deregulation, the growth of the self-help movement among consumers, and cost-containment efforts by the health care industry. Actions by MCOs such as WellPoint Healthcare, Inc., signify a new aggressive trend in the switch process. As noted by Bert Spilker, former senior vice president for science and regulatory affairs of the Pharmaceutical Research and Manufacturers of America, "it is likely that many products will be proposed for such changes of status on a very frequent basis by those who have a strong self-interest in the change."³³ Given the number of interested parties and the monetary value of both the prescription and OTC markets in the United States, it is likely that the volume of prescription-to-OTC switches will continue to grow in the years to come.

DISCLOSURES

No outside funding supported this study. Author Patricia Harrington served as principal author of the study. Drafting of the manuscript and critical revision of the manuscript was the work of Harrington and author Marvin D. Shepherd.

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Analysis of the Movement of Prescription Drugs to Over-the-Counter Status

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A large common snapping turtle (*Chelydra serpentina*) investigates a rustic “live well” in the Boundary Waters Canoe Area of Northern Minnesota. —Photo by Daniel J. Pepin