Manufacturers and consumers alike benefit when prescription drug products become available over the counter. This article summarizes those benefits, describes how Rx-to-OTC switches come about, and describes why more products are likely to migrate from the shelves of pharmacies to the aisles of drug stores and other retailers.

To receive prescription (Rx) drug products, you must present a valid prescription from a healthcare professional (HCP), while over-the-counter (OTC) drugs are sold directly to consumers without a prescription. The FDA has issued guidance documents specific to OTC medicines [1]. How each drug product is sold is for the FDA to decide. For it to be sold as an OTC, the product must:
Furthermore, consumers must be able to adequately recognize their own medical condition without the intervention of a learned intermediary (e.g., an HCP) [7]. To that end, the FDA created the “Drug Facts” label, which gives consumers easy access to important information about an OTC drug, such as its API(s), directions for use, and warnings. This enables appropriate self-selection.

Rx-to-OTC switches are an important business driver in the OTC industry, opening up new treatment categories and new classes of drugs, brands, and technologies to give consumers more choice in managing and improving their health. In 2014, the FDA approved two Rx-to-OTC switches (Flonase Allergy Relief and Nexium 24HR) in two different but established OTC categories. In fact, two Rx-to-OTC approvals per year has roughly been the average since 2000.

### Part of lifecycle management strategy

A pharmaceutical company will often consider switching an Rx drug to optimize its product lifecycle. The product could be a heritage brand managed by an affiliated prescription drug company, or it could be a licensed product from another prescription drug company that lacks the resources to switch or is not interested in OTC medications. Frequently, Rx-to-OTC switches take place as a drug product nears its patent expiration, and has sufficient market exposure and favorable safety data to make it a good candidate for OTC status.

But in recent years, sponsors have begun planning to switch some or all of the Rx indications to OTC status earlier in the product lifecycle. This strategy often requires companies to plan for the switch while the program for a new Rx product is in development. It may even encompass considering OTC-type packaging design and convenient product handling during the design of the Rx product in anticipation of the patient becoming a retail consumer (e.g., Veramyst, an Rx that has not yet switched). In so doing, the manufacturer may be able to obtain 3 years of Hatch-Waxman exclusivity (i.e., added patent life) for the OTC product if it requires additional clinical studies. It

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<td><strong>Top 10 OTC brands by sales revenue (millions of dollars)</strong> [2]. Boldfaced brands are Rx-to-OTC switches.</td>
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<tr>
<td><strong>1. Advil</strong></td>
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<td><strong>2. Nature Made</strong></td>
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<td><strong>3. Mucinex</strong></td>
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<td><strong>4. Tylenol</strong></td>
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<td><strong>5. Vicks</strong></td>
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<td><strong>6. Nature’s Bounty</strong></td>
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<td><strong>7. Claritin</strong></td>
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<td><strong>8. Aleve</strong></td>
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<td><strong>9. Zyrtec</strong></td>
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<td><strong>10. Centrum</strong></td>
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<td><strong>All OTCs</strong></td>
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may also be possible to achieve dual status, in which some indications for the product remain in the Rx realm after others are switched to OTC (e.g., Pepcid AC for heartburn and Pepcid Rx for peptic ulcer disease, etc.). Clinical studies can also give the OTC product a better market introduction by allowing the marketer to make differentiated claims versus existing OTC products.

**Forces driving Rx-to-OTC switches**

The macro-environment of healthcare is evolving, and several factors—the growing ranks of baby boomers reaching retirement age, an increase in healthcare consumption, and a shrinking number of HCPs to provide care—explain why better access to OTC medicines is needed. Indeed, making OTC treatments more accessible meets the need for cost reductions in the healthcare system and meshes with the trend of shifting costs and responsibility for people’s healthcare to patients/consumers [8].

Another trend is the growing importance of pharmacists, physician’s assistants, and nurses in managing patients with chronic conditions (diabetes, high cholesterol, high blood pressure, etc.). Concurrent to that trend is yet another: Moving some Rx medicines for treating these chronic conditions to OTC status. In this and other ways, Rx-to-OTC switches align with the goals of the Affordable Care Act.

In the last two decades, a variety of new OTC drugs, therapeutic categories, and market segments have come from switching an Rx drug to OTC status. They include H2-receptor antagonists and proton pump inhibitors (both Rx anti-ulcer drugs), osmotic laxatives, non-sedating antihistamines, and nasal steroids. Consider the nicotine-replacement therapies that help consumers quit smoking. When switched to OTC status, sales nearly doubled in the first year [8, 9]. In addition, a number of switched brands have become leaders within their segments, and some rank among the top 25 drugs within the entire OTC market.

**The complexity of switches**

Improving the probability that an Rx product can be switched into a new category of OTC status may require a wide circle of stakeholders beyond the FDA team, including technology experts, pharmacists, physicians, consumers, retailers, and payers. This is especially important when the switch would be the first drug in a therapeutic class (e.g., Oxytrol for overactive bladder, Figure 1) or when it engenders controversy (Plan B contraceptives). In such cases, resistance must be met with scientific data and persuasive arguments.

**The marketing side**

Establishing a successful switch franchise brings a number of factors into play. They include consumer awareness of the Rx product, product performance, order of entry into the OTC market segment, exclusivity within the category based on some intellectual property, a patent, or Hatch-Waxman exclusivity; launch execution; amount spent to support the launch (consumer advertising and promotion, physician detailing); and brand expansion and innovation through new forms and indications.

To understand what can happen when an Rx product is switched into a new OTC category, consider the new
class of anti-ulcer drugs (so-called H2 blockers) that were launched as OTCs in the mid-1990s. Each brand used a different API within the same class of histamine H2 antagonists and performed well for patients. Pepcid, the first to launch as an OTC, still had some patent life available to protect its novel API from being used in store brands. Aggressive marketing to physicians and consumers—combined with product innovation for several years after the OTC launch—made the product a successful OTC brand. Shortly after Pepcid AC came Tagamet HB, followed somewhat later by Zantac 75 and Axid AR. Of these last three, Zantac 75 was most aggressive in parlaying its popularity as an Rx drug into the OTC realm, spending in support of the brand, developing new product forms (including a maximum-strength version, Zantac 150), and establishing a solid long-term franchise (Figure 2). Tagamet HB, despite a strong Rx heritage, did not fully establish a significant US business, and Axid AR, the last to market, had no key point of differentiation, and its manufacturer eventually pulled it from the US market.

These examples show the importance of order of entry, Rx-history, and marketing, with two brands establishing long-term franchises and two underperforming. In short, this type of switch—a new class of drug, especially when several compounds in that class are entering the OTC market—entails more risk and requires more effort than typical OTC product line extensions. It also requires more time and investment.

**Future of Rx-to-OTC switches**

Switching more powerful medicines, lifestyle drugs, and treatments for more complex health targets started in the 1990s. Since then, several new OTC categories and successful OTC brands have emerged, including treatments for allergies, products for smoking cessation and, more recently, a drug to manage overactive bladder in women.

However, some switch programs were not successful. Despite substantial efforts since the early 1990s, switching cholesterol-lowering drugs to OTC status has, to date, been unsuccessful. This is primarily because high cholesterol is asymptomatic (“silent disease”), and consumers cannot easily determine lipid levels before and during treatment. But due to this disappointing experience and the desire to expand the OTC categories for treating chronic disease, the FDA and others are considering how new technologies can help ensure “conditions of safe use” for more OTC treatments.

**FDA’s NSURE initiative**

In 2012 the FDA introduced the Nonprescription Drug Safe Use Regulatory Expansion (NSURE) initiative, a framework for assessing whether several medical disorders and Rx drug classes could be suitable for a switch to OTC status [10]. Among the new therapeutic classes and their respective drug classes under review are cholesterol-lowering drugs, erectile-dysfunction treatments, migraine medicines (e.g., triptans), certain sleep aids, as well as...
drug products that treat various chronic conditions. By incorporating technology to create “conditions of safe use,” NSURE seeks to expand the Rx-to-OTC switch paradigm. While the Agency has indicated that it is open to novel ideas in switch applications, it does not intend to introduce a third class of drug products, namely behind-the-counter drugs, a system that is used in many other countries. Rather, NSURE is intended to facilitate the development of technologies that improve the consumer’s ability to self-recognize the medical condition to be treated and appropriately self-select/de-select before using a new OTC medicine.

It is expected that initiatives like NSURE will encourage companies to develop mobile-device apps, sensor technology, and/or other rapid diagnostic testing-monitoring technologies; smart kiosks offer another avenue to integrate HCP knowledge into decision-making before a consumer is allowed to purchase an OTC treatment for an asymptomatic condition or use an OTC medication for an extended period.

**Expectations**

Although the easy switches may have essentially been done, there is significant societal need and pressure to give consumers access to more OTC treatments by developing new OTC categories and switching more Rx drugs to OTC status. The switch space promises to be busy, creative, and competitive.

Various new technologies could facilitate switches and ensure “conditions of safe use,” and the FDA is poised to support new initiatives and technologies. But consumer safety will remain the Agency’s ultimate requirement for companies to obtain regulatory approval of new Rx-to-OTC switches.

Rx-to-OTC switches will continue to be a demanding—but also promising and lucrative—business target. To succeed, manufacturers must be willing to invest in and empower experienced teams to run the switch programs. Finally, for even the most innovative Rx-to-OTC switch to succeed, it must include continuous product and packaging innovation that drives brand growth and consumer engagement.

**References**


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