2 Why Switch? Evaluating the Value of Switch Candidates

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Introduction

In the US, there are many reasons to switch a drug from prescription to OTC status, or to potentially launch a new chemical entity directly OTC. Improving access to medications provides a public health benefit and reduces overall healthcare costs. For drugs that have demonstrated safety and efficacy as prescription products, Rx-to-OTC switch also can provide an effective lifecycle management tool; when properly managed, OTC brands can live into perpetuity.

Not all Rx-to-OTC switches have been commercially successful; therefore, an assessment of the switch product's value must be carefully considered before expending organizational resources and external costs on the switch program. In addition to the relatively high R&D costs associated with the OTC development plan, significant commercial expenditures are required to ensure commercial success. Factors such as order of entry, exclusivity, and competitiveness within a given therapeutic category must be carefully considered to ensure both initial commercial success and the long-term viability of an Rx-to-OTC switch brand. In addition, companies with potential switch candidates much secure critical OTC-specific commercial capabilities and infrastructure. For pharmaceutical companies that have attractive switch candidates but no OTC infrastructure, a decision needs to be made about whether to "build, buy, or borrow" the organizational capabilities required for success.

Benefits of Switch

The Consumer Healthcare Products Association (CHPA) highlights the public health benefits, including convenience and access, that have occurred as a result of Rx-to-OTC switches. According to CHPA research:

- As more prescription allergy medicines have switched to OTC, there has been a clear shift toward more convenient, effective, and affordable options. The percentage of allergy sufferers who use OTCs increased from 66% in 2009 to 75% in 2015.
- When nicotine replacement therapies went OTC, there was a 150–200% increase in their purchase and use in the first year after the switch. Increased access enabled tens of thousands of smokers to use these products to help quit smoking, resulting in a $2 billion social benefit every year.

Additional research points to overall savings to the US economy as a result of Rx-to-OTC switches. A landmark 2019 study conducted by IRI and CHPA found that, on average, each dollar spent on OTC medicines saves the US healthcare system approximately $7.20, totaling nearly $146 billion in annual savings.[1] The estimated savings from unnecessary clinical visits is based on the study's finding that nearly 90 percent of consumers who treat a condition with an OTC medicine would seek professional medical treatment if OTC options were not available.

OTC medicines continue to be an extremely cost-effective option for millions of consumers each year. The value of Rx-to-OTC switches to US consumers includes more than just the cost of prescription co-payments, which vary greatly from insurance plan to insurance plan. Other additional expenditures, such as fees for doctor's visits, travel and time off from work, and reduced childcare costs, could be considered extra savings when implementing Rx-to-OTC switches. Even more alarming are the number of Americans who do not have healthcare insurance. The Congressional Budget Office says that as many as 60 million Americans may lack health coverage/insurance at some point in any year. And many of those Americans with health coverage do not necessarily have a drug plan.

Access to OTC medicines also benefits the economy by preventing productivity losses. The common cold is a leading cause of missed workdays and decreased productivity. A 2004 study by Northwestern University estimated the impact of this lost productivity at $25 billion, with $16.6 billion attributed to on-the-job productivity loss.[2] The study estimated that using nonprescription medications to treat common upper respiratory infection symptoms could save the US economy $4.75 billion per year.

And many Americans do not always have access to a medical professional. A 2019 study found that one in four Americans living in rural areas said that they could not get the healthcare they needed because their healthcare location was too far or difficult to get to.[3] In other cases, access to medical professionals is only available during certain times of the day, which may not be convenient for shift workers or for consumers who need symptomatic relief after hours. OTC medicines enable consumers greater access when distance or time of day would otherwise prohibit availability of prescription medications.

It must be recognized that marketing efforts for OTC medicines can help educate consumers about various self-treatable health conditions. For some therapeutic areas, OTC marketing and education can empower consumers with an acceptable vocabulary to "normalize" and destigmatize diseases or conditions. The OTC approval of Gyne-Lotrimin in 1990 enabled women to treat annoying, recurrent vaginal yeast infections. Access to Plan B has empowered women to control their reproductive health.

Despite the reduced cost to the US healthcare system (resulting from access to OTC medicines, improved work productivity, improved quality of life with access to better treatment options, etc.), NDA holders are unlikely to submit an application for an Rx to OTC switch, unless the business case justifies the investment.

For pharmaceutical products, Rx-to-OTC switch provides an effective lifecycle management tool. An EvaluatePharma report estimated $198 billion in prescription drug sales to be at risk between 2019 and 2024 due to patent expirations.[4] It is well established that the entry of generic drugs quickly and significantly erodes a prescription drug's sales, even when sponsors of those prescription drugs have spent millions in marketing costs to build brand equity.

Rx-to-OTC switches enable companies to introduce a "new to the world" consumer healthcare brand. Once available over-the-counter, brands that are well-maintained with marketing spend and innovation can live into perpetuity. Recent syndicated data shows that Advil, which was switched Rx-to-OTC in 1984, has US retail sales of $680 million.[5]

While prescription products are considered "blockbusters" when sales exceed $1 billion, Rx-to-OTC switches are typically deemed successful when annual sales exceed $100 million. There is no simple formula to predict the commercial success of Rx-to-OTC switches; however, a number of recent switches have failed to hit this $100 million threshold. **Table 2-1** provides a list of all brands launched via Rx-to-OTC switch since 2000 and their most recent annual retail sales in the US.

Assessing Rx -to-OTC Switch Value: Category Size

A number of factors must be assessed in the process of evaluating the commercial value of an Rx-to-OTC switch candidate. OTC category size is the first of these factors. It is possible to have multiple successful Rx-to-OTC switches

Table 2-1. Brands Launched via Rx-to-OTC Switch Since 2000 and Most Recent Annual US Retail Sales

Brand	Year of First Switch	Annual US Retail Sales (in Millions)
Abreva	2000	$133.3
Mucinex	2002	$899.7
Claritin	2002	$530.3
Prilosec	2003	$209.6
Plan B	2006	$274.0
MiraLax	2006	$237.8
Zaditor	2006	$35.8
Alaway	2006	$17.4
Alli	2007	$25.2
Zyrtec	2007	$510.0
Prevacid	2009	$17.4
Zegerid	2009	$17.7
Allegra	2011	$309.3
Oxytrol	2013	$1.7
Nasacort	2013	$66.7
Nexium	2014	$228.9
Flonase	2014	$227.4
Rhinocort	2015	$7.4
Differin	2016	$49.8
Xyzal	2017	$91.4
Lumify	2017	$87.4
Pataday	2020	$26.4
Voltaren	2020	$32.2
Sklice	2020	N/A

Notes: Abreva and Lumify were direct-to-OTC NDAs; reported sales for Pataday, Voltaren, and Sklice are for fewer than 52 weeks.

Source: Symphony IRI Latest 52 Week MULO sales for the period ending 12 July 2020.

in larger categories, whereas the challenges are greater in smaller OTC categories.

Although COVID-19 drove increases in some OTC categories (hand sanitizers, sleep aids) and decreases in others (lice treatments, motion sickness treatments), the relative size of OTC categories has been pretty consistent in recent years, with total US retail sales of $36.5 billion in 2020.[6] The size of OTC categories, relative to Rx categories, is worth noting, with the majority of these categories (not just brands) under $1 billion. **Table 2-2** provides a list of OTC categories and their most recent annual retail sales in the US.

Certain OTC categories are growing and present opportunities for multiple successful Rx-to-OTC switches. For example, global climate change is increasing pollen production. As a result, people who have never suffered from allergies are now succumbing to symptoms, and allergy sufferers are finding that their conditions are worsening. According to a study presented by at the Annual Scientific Meeting of the American College of Allergy, Asthma, and Immunology in 2012, pollen counts are expected to more than double by 2040.[7]

While increased pollen counts may not be a positive trend for allergy sufferers, the Rx-to-OTC switch of non-sedating antihistamines, and more recently, intranasal steroids (INS), has allowed allergy sufferers to prevent and treat their allergy symptoms without a visit to the doctor. With access to safe and effective OTC medicines, and with allergy medication patents expiring, managed care organizations have also reduced insurance coverage of allergy medications. **Table 2-3** provides a list of allergy brands that have launched in the US as a result of Rx-to-OTC switch and their most recent annual retail sales in the US. Given the size of the allergy category, multiple Rx-to-OTC allergy switch brands have been able to achieve commercial success.

Depending on the size of the OTC category, and whether there is significant Rx volume, newly switched products will source their volume from:

- Rx volume "switching" OTC
- "Stealing" from the existing OTC category
- New users entering the market
- More usage occasions (i.e., getting treaters to treat more often or for more days)

However, as Rx categories become generic and are less of a cost burden to managed care organizations, it may be more difficult to switch

Table 2-2. OTC Therapeutic Categories and 2020 Annual US Retail Sales

Category	Retail Sales (in Millions)
Upper Respiratory	$8,656
Internal Analgesics	$4,506
Toothpaste	$3,116
Antiperspirants	$2,491
Heartburn	$2,161
Oral Antiseptics and Rinses	$1,603
First Aid	$1,565
Laxatives	$1,540
Hand Sanitizer	$1,464
Eye Care	$1,289
Lip/Oral Treatment	$1,117
Suncare	$1,112
External Analgesics	$1,089
Anti-Smoking Products	$974
Female Contraceptives	$526
Sleeping Aids	$429
Foot Care	$372
Eczema and Psoriasis	$332
Multi-Symptom GI	$321
Feminine Itch and Yeast Treatment	$317
Antidiarrheals	$287
Hemorrhoid Treatment	$238
Acne	$221
Gas Relief	$179
Petroleum Jelly	$113
Lice Treatments	$105
Motion Sickness	$83
Jock Itch	$56
Enema	$43
Ear Drops	$43
Feminine Hygiene and Douche	$39

Note: A few categories include a combination of OTC medicines as well as health-related products that are not classified as medicines by FDA.

Source: OTC Use Statistics. Consumer Healthcare Products Association (CHPA) website. https://chpa.org/about-consumer-healthcare/research-data/otc-use-statistics. Accessed 6 July 2021.

the remaining prescription patients (who have low generic co-pays) to OTC consumers. It also is more difficult to switch Rx volume to OTC when the switch is a "partial" switch, and some indications remain available by prescription, such as was the case with Flonase. Taking a deeper look at the allergy category, the trends to source OTC volume from existing and new OTC users have intensified. **Table 2-4** provides data on the source of volume for many recent allergy Rx-to-OTC switches.

Nonetheless, there were enough new sufferers in the allergy category that the introduction of INS in 2013 brought enough new users to the OTC market to prevent sales of non-sedating antihistamines from declining (although behind-the-counter combination products of non-sedating antihistamines with the decongestant pseudoephedrine did decline slightly). One thing that the INS brands did well was to encourage use before the start of the allergy season as a preventative measure, thus getting allergy sufferers to treat for more days in the allergy season. **Table 2-5** demonstrates that the launch of INS brands did not steal category share from NSAs, but rather grew the overall allergy category.

With four OTC allergy brands in the US exceeding $200 million in sales, another new product in the OTC allergy category would need to either bring significant prescription sales volume, create a reason for existing OTC users to switch brands, or convince non-treaters to begin treating. In August 2018, Perrigo announced a deal with Merck and Co., Inc. to switch Nasonex (mometasone) to OTC.[8] Once a blockbuster prescription drug with sales in excess of $1 billion,[9] generic versions of Nasonex have been available since 2016.[10] It will be interesting to see what happens to Nasonex based on the order of entry theory above. Unless Nasonex can secure a differentiating claim, such as allergy prevention, it may be hard for this brand to be successful in spite of its latent equity.

While the allergy category is large and growing in size, thus providing favorable dynamics for multiple successful switches, other categories are smaller and declining, creating obstacles for companies considering new switches. One of these

Table 2-3. Allergy Brands Launched as a Result of Rx-to-OTC Switch and Their Most Recent Annual US Retail Sales

Brand	Drug	Drug Class	Year of First Switch	Annual US Retail Sales (in Millions)
Claritin	Loratadine	Non-sedating antihistamine	2002	$530.3
Zyrtec	Cetirizine	Non-sedating antihistamine	2007	$510.0
Allegra	Fexofenadine	Non-sedating antihistamine	2011	$309.3
Nasacort	triamcinolone acetonide	Intranasal steroid	2013	$66.7
Flonase	fluticasone propionate	Intranasal steroid	2014	$227.4
Rhinocort	Budesonide	Intranasal steroid	2015	$7.4
Xyzal	Levocetirizine	Non-sedating antihistamine	2017	$91.4

Note: The prescription drug Veramyst, which contained a different salt, fluticasone furoate, was switched to OTC in 2016 as Flonase Sensimist™; retail sales shown are for the entire Flonase franchise.

Source: Symphony IRI Latest 52 Week MULO sales for the period ending 12 July 2020.

categories is smoking cessation. The good news is that smokers can and do quit smoking for good. In fact, since 2002, there have been more former smokers than current smokers.[11]

Current smoking has declined from 20.9% (nearly 21 of every 100 adults) in 2005 to 14.0% (14 of every 100 adults) in 2019.[12]

The current total US retail category size for antismoking products is under $1 billion, at $974 million.[13] Recent drug store sales figures demonstrate that distribution in this channel is essentially limited to one brand and private label products. **Table 2-6** shows the dollar share that private label products have obtained in the smoking cessation category**.**

The high share of private label products indicates that many consumers do not feel that the branded products are significantly innovative or can justify a premium price. In this case, consumers could be very open to trying an Rx-to-OTC switch product that addresses unmet needs. For the switch sponsor, however, the decreasing size of the smoking cessation category and potential challenges in securing retail placement could limit the long-term value of the switch program; sponsors would need to move forward with caution.

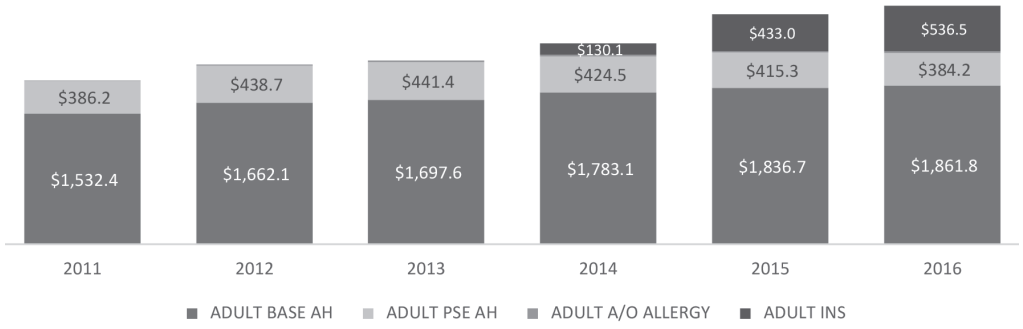
Assessing category dynamics becomes much more difficult for an Rx-to-OTC category that does not currently exist. Many marketers look at epidemiology when assessing the potential for new OTC categories to determine how many consumers need a particular solution and potential sources of volume. Certainly, many people suffer from overactive bladder (OAB). The size of the North American prescription OAB market is valued at $1.15 billion in 2020.[14] With 20 million OAB sufferers in the US,[15] Merck Consumer Care switched the OAB patch Oxytrol (oxybutynin) to OTC for women in early 2013. Oxytrol was not a well-known brand; from its original approval in 2003 through 2011, only 40 million patches had been sold.[16] As an OTC product, Oxytrol for women only garnered $29 million in sales in its first year in the market.[17] With disappointing OTC sales, the product was discontinued in early 2015.[18] There are a number of reasons why this first-in-class switch failed commercially, and it is difficult to assess whether a different, more well-established prescription drug for OAB would be commercially successful as an OTC.

Table 2-4. Source of Volume for Recent Allergy Rx-to-OTC Switches

Product	Year	Rx	OTC
Claritin	2002	49%	24%
Zyrtec	2007	53%	36%
Allegra	2011	46%	43%
Flonase	2014	20%	50%

Source: Year 1 volume data from Symphony IRI.

Table 2-5. US Retail Sales by Year of Allergy Products (NSAs versus INSs)



Source: Data courtesy Symphony IRI.

When considering categories that do not exist OTC today, another important factor to consider is whether the drug treats a (miserable) symptom that consumers want to eliminate or a chronic condition that presents with (virtually) no symptoms. Pfizer announced in 2015 that it was discontinuing efforts in the US to switch Lipitor (atorvastatin), sales for which had peaked at over $13 billion in 2006 prior to patent expiration in 2011.[19] While greater treatment of high cholesterol would have a tremendous public health benefit, the Centers for Disease Control and Prevention (CDC) reports that of the 93 million US adults who have high cholesterol, slightly more than half (55%) who could benefit from medicine, are currently taking it.[20] High cholesterol has no symptoms, and treatment is a preventative measure. Previous efforts in the UK to switch the cholesterol medication Zocor (simvastatin) from prescription-only to pharmacy-only (2004) did not result in commercial success; while generic versions remain available, the branded product was discontinued in 2010 due to low sales.[21]

Although treating high cholesterol may not be highly motivating for OTC consumers, other OTC categories that do not exist today could generate tremendous interest. One of these potential categories is erectile dysfunction (ED). ED affects 50% of men at age 50, and that number increases with age.[22] Sanofi signed a deal in 2014 to switch Eli Lilly and Company's drug Cialis (tadalafil) to treat ED.[23] Access to an OTC ED medication could improve access while reducing distribution of counterfeit or fake ED products. ED has the potential to be a "blockbuster" OTC category because existing prescription medications treat a highly bothersome symptom and can be highly efficacious for appropriate patients, whose numbers are significant. Nonetheless, the rise of telemedicine has enabled more consumers to access ED medications as well as oral contraceptives. Future switches, which will need to overcome

Table 2-6. Dollar Share of Retail Sales in Drug Stores (Branded Products Versus Private Label Smoking Cessation Products)

	Dollar Share
Nicorette	55.5%
Private Label Gum	43.8%
TOTAL	**99.3%**

	Dollar Share
Nicoderm CQ	49.9%
Private Label Patches	45.9%
TOTAL	**95.8%**

Source: DrugStore Management 2020-2021 Annual Drugstore State of the Industry Report.

the current labeling constraints and challenges, may need to be evaluated for convenience against these telemedicine alternatives.

Assessing Rx-to-OTC Switch Value — Ability to Build Awareness, Trial, and Repeat

When a product switches to OTC, consumers must be aware of its existence to consider making a purchase, as the healthcare professional no longer remains the gatekeeper. Well-known brands bring with them a strong prescription brand equity (and user base) and inherent trust ("millions of prescriptions have been written …") that help build instant awareness and commercial value.

For this reason, OTC brands keep some aspect of the Rx brand's trademark, even when only part of the Rx brand's indication, dose, population, or dosage form switches (a partial switch). Proton pump inhibitors (PPIs) like Nexium were approved OTC for treatment of frequent heartburn, but this indication was not an Rx indication; Nexium remains indicated as a prescription product for treatment of conditions that cannot be self-diagnosed, such as gastroesophageal reflux disease or H. pylori eradication to reduce the risk of duodenal ulcer recurrence. While consumers refer to the product as "Nexium," the OTC product is actually "Nexium 24HR." This name allowed Nexium to retain its brand equity and convey the long-lasting benefits of the product to consumers. "The purple pill" also transitioned its trademark color to the OTC product.

Imagery is key: when Rhinocort switched to OTC, it had relatively poor brand awareness. The OTC package relied heavily on the colors and imagery of Zyrtec as an attempt to generate consumer trust. However, brands cannot rely solely on the strength of their Rx equity.

Table 2-7 demonstrates that OTC brands need to continue to build awareness. By all rights, Prilosec and Prevacid should have been equally successful as OTC brands, given that they had similar levels of prescription sales. However, spending on the OTC Prevacid brand was reduced relatively quickly after launch. Today, Prevacid holds a smaller market share than Zegerid, which had a fraction of Prevacid's brand equity at the time of switch.

Prescription brand equity is therefore an important aspect of driving OTC commercial value. This is one reason that switches should ideally occur at or near the time of prescription drug patent expiration. The equity associated with prescription brand names erodes over time, particularly as volume switches to generic alternatives.

Brands that have little to no equity at the time of Rx-to-OTC switch can build equity, particularly if they offer meaningful consumer benefits. Abreva was a direct-to-OTC NDA and therefore had no existing prescription brand equity but delivered faster resolution of cold sores than previous OTC solutions. Today, Abreva has

Table 2-7. PPI Brands Launched as a Result of Rx-to-OTC Switch, Peak Rx Sales and Most Recent Annual US Retail Sales

OTC Brand	OTC Approval	US Rx Sales Prior to Patent Expiration[a]	Year 1 US OTC Retail Sales (in Millions)[b,c]	US OTC Retail Sales (in Millions)[d]
Prilosec OTC	6/20/03	$3.7B (2001)	$433	$209.6
Prevacid 24 HR	5/18/09	$3.4B (2007)	$220	$17.4
Zegerid OTC	12/1/09	$0.1B (2009)	NA	$17.7
Nexium 24 HR	3/28/14	$6.1B (2013)	$302	$228.9

Note: Nexium Year 1 sales are for first full calendar year.
a. Pharmaceutical Sales 2003. Drugs.com website. https://www.drugs.com/top200_2003.html. Accessed 6 July 2021.
b. Data courtesy Symphony IRI.
c. Recent OTC Innovation: Observations and Implications for Future Growth. IRI and Kline and Company website. https://klinegroup.com/articles/recent-otc-innovation-observations-and-implications-for-future-growth/. Accessed 6 July 2021.
d. Symphony IRI Latest 52 Week MULO sales for the period ending 12 July 2020.

US retail sales of $133.3 million.[24] The switch of Mucinex provided extended-release benefits for the expectorant guaifenesin. Prior to the switch, there were multiple extended-release guaifenesin products available as unapproved (desi) prescription products. Over time, the OTC brand has been extended with both NDA extended-release and OTC monograph products; total US retail Mucinex brand sales today are $899.7 million.[25] Imodium provided the benefit of rapid resolution of diarrhea. Sales of Imodium as a prescription product were not very strong because most patients experienced relief of symptoms before speaking with a healthcare provider. As an OTC product, US retail sales of Imodium are now $148.3 million.[26]

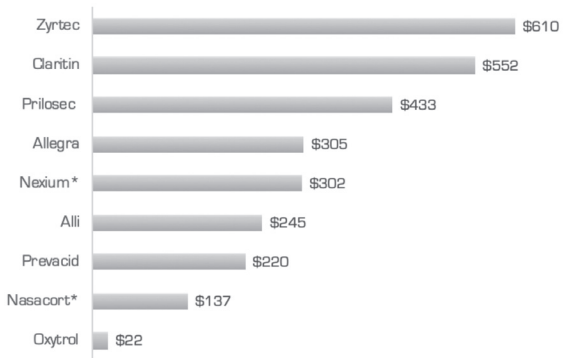
Appropriate media spending is a critical part of building switch awareness; business plans that have failed to consider this key point have been unsuccessful. **Table 2-8** provides Year 1 and Year 2 media spends for certain Rx-to-OTC switches and their resulting Year 1 retail sales.

The long-term success of Rx-to-OTC switches require heavy, continued spending. Generating awareness and garnering share-of-voice often requires first year spending of $50 million to $100 million, and/or 50% of 100% of first year sales. Brands that have underspent at this critical time in their lifecycle, including Oxytrol, have failed commercially. Brands that have cut back on spending too quickly, such as Prevacid, have also suffered. Ideally, spending for the switch should begin pre-launch to generate excitement and awareness.

While this high level of spending is not typical for prescription brands, which tend to be more profitable but whose sales diminish greatly upon patent expiration, OTC brands that are well-maintained, while less profitable, can live into perpetuity, e.g., Advil, which was initially switched to OTC in 1984 and today has US retail sales of $674.4 million, or Claritin, which was switched in 2002 and today has US retail sales of $530.2 million.[27]

Adequate spending is important for the long-term health of brands. Pepcid, part of a joint venture between Merck and J&J, was the first H2 antagonist approved in the US in 1995, followed quickly by Tagamet and Zantac within the same year. Pepcid initially secured the market-leading position. When J&J acquired Pfizer Consumer Healthcare (which marketed Zantac) in 2006, the Federal Trade Commission (FTC) required the divestiture of either brand for antitrust reasons. While Pepcid was the market leader, FTC noted in their analysis that the two

Table 2-8. Reported Media Spends and Year 1 US Retail Sales for Certain Recent Rx-to-OTC Switch Brands

Estimated Year 1 Sales (in millions)[a,b]	Media Spend (in Millions)		
	Year 1	Year 2	Brand
	$116	$93	Zyrtec
	$96	$109	Claritin
	$68	$105	Prilosec
	$134	$91	Allegra
	$60	$66	Nexium
	$118	$67	Alli
	$87	$43	Prevacid
	$70	n/a	Nasacort
	$29	n/a	Oxytrol

a. Data courtesy Symphony IRI.
b. Recent OTC Innovation: Observations and Implications for Future Growth. IRI and Kline and Company website. https://klinegroup.com/articles/recent-otc-innovation-observations-and-implications-for-future-growth/. Accessed 6 July 2021.

brands combined represented over 70% of the then $360 million OTC H2 antagonist category.[28] Boehringer-Ingelheim acquired Zantac, which held a smaller share of the market, for $509.5 million[29] and began to invest in the brand for growth. Although Zantac was removed from the market by FDA in 2020 due to a carcinogenic impurity,[30] by then, US OTC retail sales of Zantac had surpassed US OTC retail sales of Pepcid: $156.5 million versus $110.2 million.[31]

Building switch awareness is required for many different targets, not just the consumer themselves. Doctors, managed care organizations, and other healthcare professionals need to understand that a prescription is no longer required for the patient to purchase a particular product. Retail pharmacists need to learn where the product is now located in front of the counter so that they can direct customers there. In other cases, the OTC purchaser may be the caregiver, spouse, or parent of the person for whom the OTC drug is most appropriate.

Generating awareness, however, will only result in trial (purchase) of the Rx-to-OTC switch if the product is believed to deliver against an unmet consumer need. After its prescription approval in 1976, the H2 antagonist Tagamet was the first drug in the US to achieve blockbuster status, with more than $1 billion in sales.[32] Pepcid was a relatively late entrant (1986) to the prescription H2 market but was approved as an OTC product six weeks ahead of Tagamet. Both brands spent more than $100 million to generate initial awareness,[33] and Tagamet hoped to leverage its prescription heritage. While the advertising wars became contentious, with both parties suing the other for false claims,[34] consumers voted for Pepcid with their wallets. Despite Tagamet's stronger prescription heritage, Pepcid was better able to deliver against consumer needs with claims that it "prevents and relieves heartburn," whereas Tagamet at the time could only claim to relieve heartburn. Furthermore, the initially approved Tagamet dose was two tablets, twice daily, whereas Pepcid could provide greater benefits with a consumer-preferred dose of only one tablet.

Market research is key to discovering unmet consumer needs, and the marketing messages that worked for a prescription product (with physicians as the key target audience) may not work for consumers. Brands need a way to effectively communicate their meaningful difference. Prilosec, for example, claims "one pill, every 24 hours, zero heartburn." As the fourth entrant in the non-sedating antihistamine category, Xyzal created a differentiation by claiming that the product "works while you sleep…so you wake up more refreshed for a productive day."[35]

Communication starts with the product's indication and the principal display panel (PDP). When Differin was switched to OTC in 2016, the package failed to explain the product's benefits. It was indicated as an "acne treatment" and included key claims of "previously available only by prescription," "FDA approved," "dermatologist developed," and "once daily topical retinoid."[36] The package left the consumer to wonder how the newly switched product would provide better relief than previously existing acne treatments.

As a prescription product, Flonase was indicated for management of nasal symptoms of allergic rhinitis. The Rx-to-OTC switch sponsor proposed that the OTC product also be indicated to treat ocular allergy symptoms of "itchy, watery eyes."[37] Because clinical studies were required to support the OTC approval of this claim, FDA granted Hatch-Waxman exclusivity for the ocular allergy indications, which differentiated Flonase from other intranasal steroids and from private label versions of fluticasone in the OTC market.

Benefits that encourage trial must be delivered without unwanted side effects. Alli promised clinically proven weight loss, with the most common side effect being a change in bowel habits, which may include loose stools. The product's insert directs users to "make sure you wear dark pants." While the promise of weight loss was very enticing, and the product achieved sales of $155 million within a few weeks on the OTC market,[38] today US retail sales for Alli are $19.6 million.[39]

The OTC product also must be easy to use. Once a day dosing is preferred. Multiple doses per day and non-oral administration will limit compliance and reduce consumer satisfaction. Dosage forms that convey benefits, such as

Tylenol's rapid release gelcaps with "laser drilled holes," are consumer-motivating, even though one study found that this product did not dissolve as quickly as regular acetaminophen tablets.[40]

OTC is a business of "repeat" because the consumer must choose to buy the product again and again. Accordingly, the attributes that may have been tolerable when the product was available by prescription (side effects, palatability, dosage forms, onset, level of relief) may not be acceptable for the consumer without a doctor's insistence that the medication be used or the regimen be followed.

When Rx to OTC switches are launched, particularly for products in a new category, they can command a premium price, but there is a limit to what consumers will pay for a newer/better product. **Table 2-9** demonstrates average price increases for new waves of innovation based on class of OTC chemical entity versus the previous wave of innovation**.** Adjusting for number of doses per package or number of days of therapy provides similar results. The value that an OTC product provides includes the opportunity cost to the consumer, including the time (and time out of work) to visit the doctor and various co-pays. As the price of OTC drugs increases, however, consumers are more willing to seek prescription options or private label alternatives. Furthermore, high-priced OTC drugs risk enactment of anti-theft measures by retailers, including, but not limited to, being placed behind-the-counter or in lockboxes, thereby deterring access and trial.

Rx-to-OTC switches often command a price premium. Despite this price premium, an effort to drive awareness of a product that delivers against an unmet consumer need can generate trial. Brands that do not deliver on their promise, or that have unwanted side effects, may receive trial but will not generate repeat sales. For this reason, it is critical to use commercial input to guide the Rx-to-OTC switch development plan, including potential indications and motivating claims and strategies for gaining exclusivity.

Assessing Rx-to-OTC Switch Value—Does Order of Entry Matter?

Order of entry is not necessarily a strong determinant of (long-term) Rx-to-OTC switch value as evidenced in **Table 2-10.**

While Rx-to-OTC brands can take advantage of a "head start" in the market, this lead can be eroded when the brand cuts back on its advertising or fails to innovate. Failure to innovate (to be discussed further below) will result in a loss of sales not only to competitors, but to private label products as well. In well-developed and/or expensive OTC categories, such as the anti-smoking gum category, private label penetration can exceed 50% of unit sales.[41]

Table 2-9. Pricing Premiums for new Waves of Innovation (Based on Class of OTC Chemical Entity) Versus the Previous Wave of Innovation

	Innovation Wave	Class	Average Retail Price (Mass)[a]	Premium vs. First Wave	Premium vs. Second Wave
Heartburn	Original	Antacids	$4.90		
	First	H2 antagonists	$11.86	+142%	
	Second	PPIs	$17.21	+251%	+45%
Allergy	Original	Sedating antihistamines	$6.94		
	First	Non-sedating antihistamines	$17.47	+152%	
	Second	Intranasal steroids	$18.72	+170%	+7%

a. Research conducted by Susan B. Levy Consulting, LLC, July 2018.

Table 2-10. Order of Entry for Various Rx-to-OTC Switches (by Class) Versus Current Sales Rank

	Brand	Order of Entry	Current US Sales Rank
Non-sedating antihistamines	Claritin	1	1
	Zyrtec	2	2
	Allegra	3	3
	Xyzal	4	4
H2 antagonists	Pepcid	1	1
	Tagamet	2	2
	Zantac	3	Recently leading H2 until withdrawal
	Axid	4	Discontinued due to low sales
PPIs	Prilosec	1	2
	Prevacid	2	4
	Zegerid	3	3
	Nexium	4	1
Intranasal steroids	Nasacort	1	2
	Flonase	2	1
	Rhinocort	3	3

Source: Symphony IRI Latest 52 Week MULO sales for the period ending 12 July 2020.

Assessing Rx-to-OTC Switch Value—Ability to Innovate

The ability to innovate is a crucial consideration for the long-term success of an Rx-to-OTC switch brand. Driving innovation requires investments in market research, new product development, and NDAs. OTC innovation plans should be considered when the initial Rx-to-OTC switch plan is being developed. For large companies, global approval processes may need to be planned and coordinated. Innovation strategies can include combination products (Zantac Duo Fusion), new dosage forms (Nexium Clearminis™), novel packaging, use of trademarks for sub-branding (Claritin Eye), new claims (Claritin "alert and focused"), new uses and indications (Claritin Hives), adjacencies (Allegra Anti-Itch), extended-release, and/or higher doses (Zantac 150). (It is worth mentioning here that Claritin's follow-on strategy to gain the "hives" indication also enabled all Rx products to be removed from the market, which had remained available by prescription for the indication "chronic idiopathic urticaria.") Advil, originally switched to OTC in 1984, remains the internal analgesic brand leader by continuing to invest in the development of new (direct-to-OTC) NDAs. **Table 2-11** contains a list of new Advil products approved via NDAs since the original Rx-to-OTC switch.

One of the keys to success, therefore, is the ability to create a "billboard" at the retail shelf, as a single shelf keeping unit (SKU) would be

Table 2-11. Advil Products Approved via new NDAs (and Year of Approval)

Product	Year of Approval
Advil	1984
Advil Cold & Sinus	1989
Advil Liquigels	1995
Advil Migraine Liquigels	2000
Children's Advil Cold	2002
Advil PM	2005
Advil Congestion Relief	2010
Advil Dual Action	2020

visibly lost. Nexium, which was sold via prescription as a capsule, switched in 2014 and gained approval for tablets in 2015 and Clearminis in 2016. Flonase, which switched more recently in 2015, gained approval for children's packaging (same dosage) in 2016 and switched the prescription product Veramyst as Flonase Sensimist.

Retail trade partners, in fact, will expect a stream of innovations and "new news" every year, which can insulate the brand from private label competition (and thus preserve premium pricing).

A robust future innovation pipeline also may help general managers outside of the US commit to the launch and support of the new OTC product.

NDAs are not the only mechanism to extend Rx-to-OTC switch brands. Within the Mucinex product range, just over 50% of sales are from monograph (not extended-release NDA) formulations.

Other brands have turned to ancillary products. When Differin switched to OTC, it launched simultaneously with a cleanser and a moisturizer, both of which are governed by cosmetics regulations. Even further on this spectrum, Claritin licensed its name and equity to hypoallergenic bedding.

Assessing Rx-to-OTC Switch Value—Ability to Execute at Retail

A key difference between launching a prescription product and launching an Rx-to-OTC product is the ability to successfully execute at retail. Manufacturer and retailer partnership planning begins 24 months prior to launch to coordinate tactics such as appropriate shelf placement, prelaunch activity to drive awareness and excitement with consumers, rapid distribution at launch and retail launch ads, consumer education/activity at shelf, pharmacy education, and secondary store placement and retailer customization.

Unlike prescription products, in many OTC categories, retailers only reset their shelves once a year. Failure to hit this timing can significantly delay a launch and erode any period of exclusivity.

Shelf placement can be key to a product's success. Oxytrol was placed adjacent to products like pregnancy tests that were no longer relevant to the target consumer. The patch dosage form, coupled with a juxtaposition next to devices, may not have connoted "real medicine."

The package also needs to stand out at shelf, and the brand's colors and branding equities may need to be revised to provide shelf presence.

Recent launches have invested heavily to generate pre-launch awareness and excitement at shelf. Shelf blockers announcing, "Coming Soon!" are useful if the annual shelf reset precedes the Rx-to-OTC launch. Mock packages in the shelf blocker can be used to specify where to find the product when it does become available and can facilitate rapid distribution. Retailers find this tactic to be expensive, however, as no sales are generated from the space occupied by the "blockers."

Other tactics used to generate pre-launch excitement include store signage and pre-launch announcements, in-store, in circulars, and online. Prior to its launch, Voltaren announced a partnership with the American Arthritis Foundation and donated 100% of pre-order profits to the foundation's scientific research.[42]

Once the Rx-to-OTC switch is launched, however, speed to market is critical, especially if the product does not have protection from private label competition. For OTC products, distribution is retailer driven—retailers decide whether or not to stock the product. For a major Rx-to-OTC switch, it is not unrealistic to stock 100,000 retail outlets on the initial ship date. Given the need for speed, manufacturers must employ tactics that make it as easy as possible for stores to stock the shelves, both for open stock of the product and for potential displays.

OTC product volumes can exceed prescription product volumes. With different manufacturing configurations, including the need for inner packs and the potential need to "bright stock" prior to launch, expensive investments may be required for the manufacturing process, packaging equipment, or for other aspects of the supply chain.

Additional display opportunities, customized in multiple configurations to fit the needs of top retailers, can include endcaps, sidekicks, and displays at the point-of-purchase. The top eight to 10 retailers will expect customization

and will want to begin top-to-top discussions about the Rx-to-OTC switch up to two years before launch, which means initiating retailer conversations before the NDA is filed. In each case, however, additional retail display provides opportunities for more in-store signage.

After shelves are stocked, a variety of mechanisms may be used to bring attention to the newly available Rx-to-OTC switch product and to educate consumers without pharmacist intervention, including overhead signage, shelf talkers, floor talkers, undershelf signage, and even interactive video displays.

It is critical for retail pharmacists to be engaged in the launch. Pharmacists serve as a key reference in the Rx-to-OTC switch process and need to know what to recommend to patients when their prescription product is discontinued due to the switch. Furthermore, pharmacists need to know how to help consumers find the newly available OTC product at shelf. Pharmacists require a more scientific tone in communication materials than consumers and also need to be able to answer FAQs, particularly about contraindications and side effects, especially if the consumer does not have a primary care physician to ask. Similarly, clinics located in retail pharmacies also should be engaged in launch communications.

Assessing Rx-to-OTC Switch Value—A High Performing Team

The value of a switch can best be maximized with an experienced, high-performing team. Rx-to-OTC switch is a hybrid process: it contains some elements of an Rx approval and launch, some elements of OTC monograph launches, and some elements that are unique to switch. This combination makes it more complicated than a pure Rx or OTC project.

In addition, almost all switches are subject to "us" versus "them" thinking. Nearly all switches involve a transfer of power from a pharmaceutical division to a consumer healthcare division or are a joint venture between a pharmaceutical company and an OTC partner. Furthermore, many Rx-to-OTC switches operate with both global and local teams, despite geographic regulatory differences. Therefore, it is important to employ best practices with regard to alliance management, especially effective communication, to achieve alignment of expectations and goals. If partnering with a pharmaceutical company, the Rx team members will need appropriate recognition or, alternatively, some type of reward for providing effective help. Even without an external partner, the core team (R&D, marketing, manufacturing/supply chain, project management) needs to acknowledge the efforts of all extended team members.

A cohesive, creative, and collaborative team is therefore crucial to Rx-to-OTC switch success; for a $100 million Rx-to-OTC switch brand, every week lost represents $2 million in missed revenue. And missed timing for a seasonal product could represent an entire year of lost sales.

Implications for Strategy

With all of the work and investment required to develop and implement the Rx-to-OTC switch development plan, including the additional activities required to develop and implement a plan to ensure commercial success, organizations must carefully consider the value that a switch can generate. Rx-to-OTC switch may not be an appropriate lifecycle management strategy for all prescription drugs. A prescription drug that is the fourth (or fifth) in its therapeutic class to switch, does not offer additional, meaningful consumer benefits, and has little to no brand equity may not be worth the investment, even if the Rx-to-OTC switch pathway is straight-forward and well-defined.

Even for a "simple" switch, the investment plan should consider the initial switch and also the potential requirement to develop new primary packaging and an innovation plan (novel dosage forms, etc.).

A key strategic decision in the lifecycle plan is timing. Switches, particularly those that are first-in-class or the subject of a partnership, can take five years or more to plan and execute, not including the time to find a switch partner and negotiate a deal. Teams need to determine the value of exclusivity, either via remaining patent

life or by developing a plan to secure Hatch-Waxman regulatory exclusivity.

The Strategic Decision for Pharmaceutical Companies—Build, Borrow, or Buy?

Switch partnerships are relatively common because of the numerous key differences between prescription and consumer healthcare business models. **Table 2-12** provides some key differences.

Switch is an attractive lifecycle management option for may prescription products. For pharmaceutical companies, Rx-to-OTC switch provides an opportunity to leverage prescription assets by extending their lifecycle and to potentially gain a revenue stream via partnership payments. Nonetheless, pharmaceutical companies realistically cannot switch without OTC capabilities.

For consumer healthcare companies, Rx-to-OTC switch provides a mechanism to launch new consumer healthcare brands, often with market exclusivity, and the opportunity to offer "newer" active ingredients that will address unmet consumer needs. Nonetheless, consumer healthcare companies cannot switch without access to prescription assets.

As a result, classic pharmaceutical companies need to decide how they will secure OTC capabilities, either by building the capabilities internally, securing a joint-venture partner or licensee, or securing a company with OTC capabilities.

Switching a prescription asset without an OTC partner means that the pharmaceutical company is willing to prioritize the investment in the OTC program, with an up-front and long-term commitment to compete in the OTC market. There is a risk that the Rx-to-OTC switch program will fail, especially if the pharmaceutical company does not have experience with switch programs. Under this scenario, the pharmaceutical company will retain 100% of the financial returns upon product launch if the switch is approved, although the company may need to accept lower margins (compared to

Table 2-12. Key Differences Between Prescription and Consumer Healthcare Business Models

	Rx	OTC
Clinical Studies	Focus is on efficacy, although safety matters	Focus is on safety, although efficacy matters
	HCP makes diagnosis and treatment decision	Average consumer needs to self-diagnose and self-treat
	Can target very specific populations	Study endpoints are more behavioral
Marketing	Target is mainly HCPs	Target is mainly consumers
	Communicate clinical benefits	Often communicate emotional benefits
	Marketing involved later in development process	Marketing involved at beginning of development process
	Marketing importance decreases at/near patent expiry	Marketing can drive brand success into perpetuity
Sales/Distribution	Sell to drug wholesalers	Sell to retail and via ecommerce
	Control maintained by licensed pharmacists	Over 100,000 points of distribution, including convenience stores and dollar stores
	Launch when drug available	Trade dictates launch date based on shelf reset
P&L	Marketing spend is a fraction of revenue	At launch, marketing spend may be >100% of sales
	Nearly 90% sales lost within weeks of patent expiration	With innovation, sales can continue to grow
	Highly profitable	75% gross margin considered "good"

prescription products) and a negative profit and loss (P&L) for the first one to three years.

Barr Pharmaceuticals (later acquired by Teva) did an excellent job of building an organization around the switch product Plan B. As a prescription product, Plan B's revenue was $30 to $35 million and was not expected to more than double when it initially switched to an OTC product in 2006.[43] Although mainly a manufacturer of generic drugs, Teva sold Plan B One Step, its only OTC brand within its specialty medicines portfolio of prescription products to Foundation Consumer Healthcare in 2017 for $675 million. Today, Plan B One Step has US retail sales of $274 million[44] and is the number one selling OTC SKU at retail.

Switching a prescription asset with an OTC partner requires finding the right consumer healthcare company at the right time in the prescription product's lifecycle. While this strategy provides lower risk for the pharmaceutical company, it also can provide a lower return (compared to the pharmaceutical company commercializing the product itself). Nonetheless, up-front payments, milestones, and royalties can be used by the pharmaceutical company to fund more strategic prescription product programs.

Recent partnering deals include Sanofi's 2019 agreement with Roche to switch Tamiflu,[45] Perrigo's 2018 deal with Merck to switch Nasonex,[46] and an announcement from Eli Lilly in 2014 that it has provided Sanofi with the switch rights to Cialis.[47]

In most cases, the terms of these deals are not material to either party and are therefore not revealed. Nonetheless, in 2012, Pfizer paid $250 million up-front, plus milestone and royalty payments, to AstraZeneca for the global OTC rights on Nexium, plus the right of first refusal for Rx-to-OTC switch rights on Rhinocort.[48] On a much smaller scale, in 2006, Schering-Plough paid Santarus $15 million up-front, in addition to a potential $65 million in regulatory and sales milestones and a low double-digit royalty for the Rx-to-OTC switch rights on Zegerid.[49]

It is not unheard of for a pharmaceutical company to acquire a consumer healthcare company to secure Rx-to-OTC switch capabilities. While this strategy requires a major financial outlay and the availability of an OTC company to buy, it is a strategy that can make sense if the pharmaceutical company has a pipeline of viable switch candidates.

In 2009, Sanofi paid $1.9 billion to acquire the consumer healthcare company Chattem,[50] which provided capabilities to switch Sanofi's portfolio of upper respiratory assets: Allegra, Nasacort, and Xyzal. Subsequently renamed Sanofi Consumer Healthcare, the company has now demonstrated its capabilities to successfully switch and commercialize prescription assets, resulting in deals to switch Tamiflu and Cialis, as noted above.

Pharmaceutical companies seeking to assess the capabilities of potential consumer healthcare partners should consider not only the deal terms, but also the potential partner's ability to get the drug switched and the competency to maximize the drug's OTC sales. Currently, only three consumer healthcare companies have dedicated Rx-to-OTC switch teams that have successfully switched prescription products in the last 10 years (GlaxoSmithKline, Sanofi, and Bayer).

Rx-to-OTC switches do not occur that often, and there are dramatic differences between prescription and consumer healthcare capabilities. Identifying appropriate switch assets, finding the right partner, and securing OTC approval are time-consuming; for the right asset with the right partner, Rx-to-OTC switch programs enable significant public health benefits and produce brands that can live into perpetuity.

Conclusion

Not all Rx-to-OTC switches have been commercially successful. An assessment of the switch product's value must be carefully considered before expending organizational resources and external costs on the switch program. There are several factors that must be considered when evaluating the potential commercial value of an Rx-to-OTC switch; some of these factors are inherent in the drug itself (i.e., lack of side effects, benefits versus existing OTC therapies) and some of these factors are within the control of the company conducting the switch (i.e., media spend, ability to execute with excellence).

Long-term Rx-to-OTC switch success requires the ability to innovate and generate "new news" to maintain awareness, generate trial and drive brand loyalty. Successful Rx-to-OTC switches, however, can result in enduring brands that live into perpetuity.

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