Rx-TO-OTC SWITCH TIPS

Identifying the Right Timing, Conditions, and Approach for Rx-to-OTC Conversion

Tanuj Mehra, *Senior Principal,*
EVERSANA™ MANAGEMENT CONSULTING

Hai Nguyen, *Senior Consultant,*
EVERSANA™ MANAGEMENT CONSULTING

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Rx-to-OTC Switch Tips: Identifying the Right Timing, Conditions, and Approach for Rx-to-OTC Conversion

Exploring the idea of converting a prescription (Rx) drug to an over-the-counter (OTC) product can be a useful part of life cycle management and loss of exclusivity planning. However, while an Rx-to-OTC switch could provide significant benefits to patients and a potential revenue source for drugs facing loss of exclusivity (LOE), manufacturers considering this strategy must overcome a number of hurdles.

This white paper will:

- Review the current state and examine the potential reasons behind the limited number of recent Rx-to-OTC switches.
- Outline conditions a product must meet to be a viable contender to switch.
- Highlight the regulatory requirements for such a switch.
- Detail considerations for manufacturers exploring this strategy for their assets.

Current State

The current U.S. OTC market is dominated by products to manage upper respiratory issues (e.g., Zyrtec, Flonase, Claritin), pain (e.g., Advil, Tylenol), and digestive symptoms (e.g., Nexium). OTC is traditionally not a large market relative to prescription pharmaceuticals, and in recent years few Rx-to-OTC switches have taken place. Meanwhile, the margins are low in the OTC market, and a recent generic collusion crackdown makes it harder for authorized generics to generate as many sales as before. In addition, while the digital retail channel is growing rapidly, it is small and unlikely to have a major impact on branded OTC product prices or sales in the near future.

Despite the small OTC market, a successful Rx-to-OTC conversion could provide significant health benefits to patients by facilitating access to drugs and improving quality of life. In general, an OTC product launch has a positive and economically meaningful influence on drug class utilization. Overall, Rx-to-OTC switches resulted in a 25%-42% increase in utilization across drug classes (1999-2010). There is notable evidence of within-class substitution effects upon OTC launch for some drug classes, such as antihistamines; and Rx-to-OTC conversion leads to increased access to drugs and usage, especially among untreated patients, due to the removal of barriers related to insurance coverage and costs of physician visits. The most significant cost savings come from averted serious health events.[1]

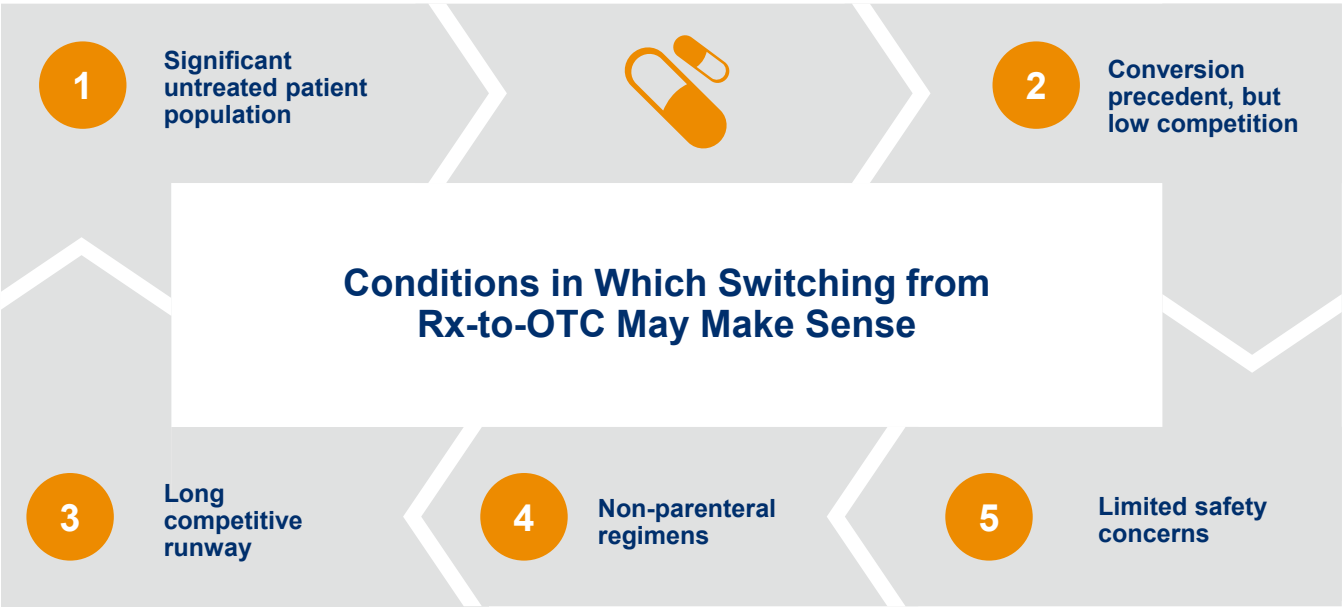
There are 41 total NDAs approved for Rx-to-OTC switches this century. The longest gap in FDA approvals for such switches was from 2017 to early 2020, but there has been substantial activity since 2020. Between January 2020 and June 2021, FDA approved six Rx-to-OTC switches (four allergy-related drugs, one arthritis pain medication, and one head lice infestation medication). Rx-to-OTC switches so far remain heavily concentrated in allergy.

One potential reason for the infrequency of such approvals is concern about safety risks (e.g., overdose, misuse) due to ease of access to the medication and lack of physician supervision. To address these concerns, FDA set out data requirements for different types of studies to establish evidence of safety and ease of use for Rx-to-OTC applications. Due to these data requirements, few drugs have been able to meet the bar.

All complex diseases, such as oncology or therapeutic areas that require infusion therapies, are automatically ruled out of an Rx-to-OTC switch, leaving only a limited subset of therapeutic areas in which patients can easily self-diagnose and self-treat without harm. These areas include allergy, pain, weight loss, and antifungal. In other words, the requirements for OTC approval will lead to very specific use cases.

Switch Conditions

An RX-to-OTC switch is an option worth considering for some brands, especially if the medication addresses a significant untreated patient population, is in a therapeutic area with a precedent for OTC switching, has limited safety concerns, has non-parenteral regimens, and has a long competitive runway. If a brand is able to meet at least a few of these conditions, switching from Rx to OTC may make sense.



1. Signficant untreated patient population

If a significant portion of patients are silently suffering from a disease and they are not seeking treatments due to stigma or lack of access to care, availability of an affordable OTC option may tip the scale in favor of the manufacturer due to the potential to tap into a significant patient volume.

2. Conversion precedent, but low competition

Being in a therapeutic area with a precedent of OTC conversion but without intense OTC competition would be an important factor. Having a precedent of Rx-to-OTC approval would significantly accelerate an approval for subsequent applicants, as the FDA often refers to prior similar cases for decision-making. However, if the market is already inundated with OTC options, putting another OTC product on that market might not be a good financial move for the manufacturer.

3. Limited safety concerns

An ideal therapeutic area or indication would be one without significant safety concerns. If the therapeutic area or indication has extremely minor and manageable safety issues, it could be a potential candidate for Rx-to-OTC switches.

4. Non-parenteral regimens

Drugs with simple, straightforward dosing regimens and administrations that are available primarily through retail pharmacies can be good candidates. There have been Rx-to-OTC switches for drugs with multiple doses, but none of them requires titration or complicated administration schedules. (Any potential for titration could be interpreted as requirement for healthcare professional supervision, hence representing a barrier to OTC approval).

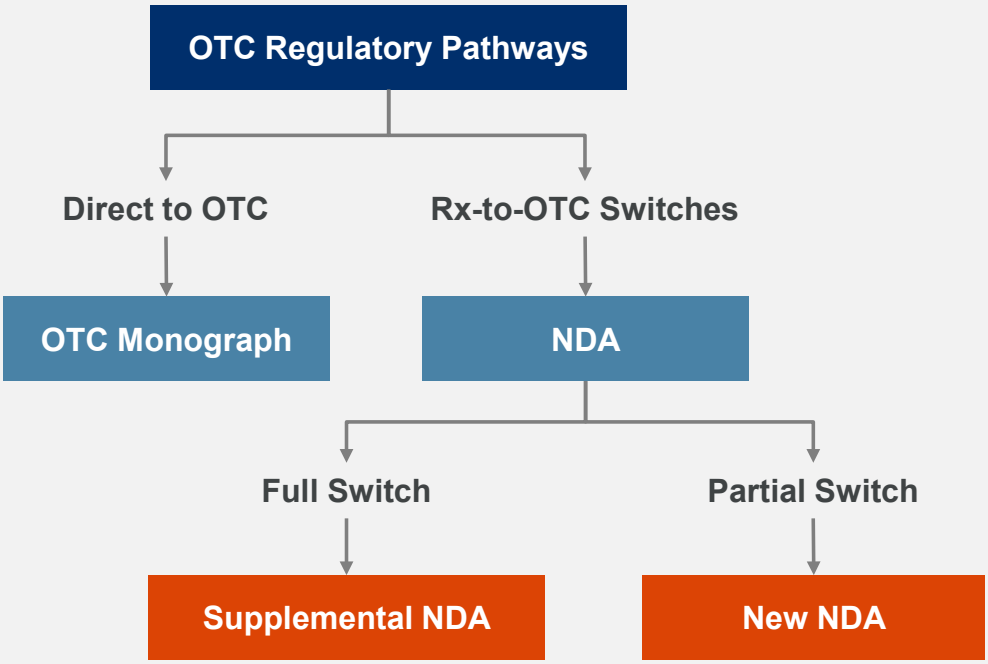
5. Long competitive runway

A competitive timeline with a few years of runway prior to loss of exclusivity will be extremely beneficial, as going through the regulatory process may take time. The standard review timeline is 10 months. However, multiple studies may be required prior to NDA submissions, each of which can take three months to a year to complete and meet FDA requirements, which can push the timeline out much further. If partnership is required, more time needs to be allotted for partner vetting and engagement.

On the other hand, manufacturers should not launch the OTC product too early, due to the vastly different economics of OTC. In fact, it will almost always be best to wait until LOE to launch the OTC product and then to launch it quickly upon LOE to maintain the brand strength.

Regulatory Pathways

Depending on the product, either a new drug application (NDA) or a supplemental new drug application (sNDA) will need to be submitted to FDA for the proposed Rx-to-OTC switch. If no changes are made to the dosage form, route of administration, or indication, a manufacturer may submit an sNDA. However, if any differences exist between the marketed product and the proposed OTC product, including narrowing the OTC indication, a new NDA will be required. Sponsors are strongly encouraged to request milestone meetings with FDA during OTC development (pre-IND, end of Phase 2, pre-NDA). This will help manufacturers to be on the same page with the FDA in terms of potential study requirements for their products and avoid wasting time in back-and-forth revisions of study designs with the FDA. The standard FDA review timeline is about 10 months, and as long as new evidence is utilized in gaining approval, three years of OTC exclusivity will be granted.[2]



Efficacy data is not required for Rx-to-OTC NDAs, and most of the required evidence for FDA approval could come from post-marketing data or from non-clinical trials, such as label comprehension studies, self-selection studies, or actual use studies.

Label comprehension studies: assess consumers' ability to understand the OTC label

Self-selection studies: test consumers' ability to determine if the OTC product is appropriate for themselves based on label information

Actual use studies: examine consumers' ability to use the drug correctly and safely

Data Requirements for FDA Approval		
Diagnostic	Symptom Recognition	Symptoms targeted for treatment should be easily recognizable by a person of average intelligence
	Disease Identification	The drug must be used for easily recognizable diseases
	Disease Masking	Utilization of the drug should not hide any potentially dangerous underlying diseases
Usage	Difficulty of Administration	Drug administration must be easy
	Route of Administration	Drugs must be administered non-parenterally (not intravenously, subcutaneously, or intramuscularly)
	Regimen Complexity	The treatment regimen should be simple enough for a layman to follow
Safety	Error Margin	The drug must possess a very high safety margin
	Addictiveness	The drug must be non-addictive and non-narcotic
	Speed of Onset	Drug effects must rapidly exert themselves post-administration, and the effects must be easily noticeable

Considerations for Manufacturers Exploring a Switch

When pursuing an Rx-to-OTC strategy, manufacturers should keep several factors in mind. An Rx-to-OTC strategy should consider the organization's OTC marketing and regulatory capabilities, the timeline from initial market assessment to approval, and implications of issues such as IP and dosing.

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Go Alone *OR* **Partner** *OR* License

- Branded Pharma
- Consumer Health
- Private Label

Go-To-Market Capabilities

2

1. **Competitive Market Events**—LOE, competitive launches
2. **Regulatory Process**—Regulatory studies + FDA review
3. **Partner Engagement**—Finding, vetting, finalizing

Timeline

3

OTC Dosing: Multiple doses vs. single dose complications

- Pricing
- Patient volume
- Medication onset and overdose / patient drop-off
- Regulatory studies

Manufacturing: IP and cost concerns

Other Considerations

Go-to-market capabilities are a major consideration. The decision must be made whether to establish in-house capabilities, partner, or license the product. Each decision has its own set of parameters to consider, including existing OTC capabilities, potential costs, and financial benefits.

Manufacturers should also be aware that OTC a life cycle management (LCM) strategy, and even if successful, it is likely to be associated with a dramatic decline in **net revenue**. Rx-to-OTC cash flow potential is influenced by patient volume, value per purchase to the pharma company, and duration of therapy. There is limited precedent for an OTC medication to cost more than $1 per day. Depending on the type of partnership, a pharma company could expect to retain roughly 5%-10% earnings from top-line OTC product sales. The key to an Rx-to-OTC switch being high value is to unlock patient pools that are not currently on the Rx treatment.

The **timeline** is also key. Manufacturers should maintain multiple exit/decision points at low incremental dollar values. The timeline will also be affected by the type of partnership that is employed. A manufacturer can engage a partner either at the beginning of the regulatory process or after a few studies have been conducted.

Competitive entries are something to watch out for, as they will significantly impact the forecasting model for the OTC product's potential value. Be aware that, in general, an Rx-to-OTC product's potential upside could be fairly limited due to the low price per pack, lack of initial patient awareness, availability of competitive options (e.g., generics, new branded products), and high regulatory and partnership costs. Intellectual property issues (i.e., who gets to retain the right to the molecule) are another major consideration.

Conclusion

While Rx-to-OTC conversion could provide significant benefits to patients and a revenue source for drugs facing loss of exclusivity, only certain products are well positioned to make the transition after clearing the necessary regulatory hurdles. EVERSANA™ MANAGEMENT CONSULTING has experience partnering with manufacturers to help them understand and evaluate the viability of pursuing an OTC approval by assessing the feasibility, value potential, and requirements of an Rx-to-OTC switch. EVERSANA can also work with manufacturers to identify analogs within their therapeutic area or indication in order to get a better view of the potential regulatory challenges down the road for their Rx-to-OTC application.

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1. Stomberg et al. (2013), "Utilization effects of Rx-OTC switches and implications for future switches," Health, 5, 1667-1680.

2. FDA.gov. (https://www.fda.gov/drugs/types-applications/drug-applications-over-counter-otc-drugs; https://www.accessdata.fda.gov/scripts/cder/training/OTC/topic3/topic3/da_01_03_0005.htm; https://www.chpa.org/SwitchFAQs.aspx