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Making the Switch from Rx to OTC

Making the Switch from Rx to OTC

By Suzanne Elvidge

The Switching drugs from prescription to over-the-counter (OTC) status is a marketing strategy that has been growing in popularity over the past few decades. Under pressure from patent losses and rising R&D costs, several pharma companies are considering the feasibility of this approach, including Sanofi ($SNY) and Eli Lilly ($LLY), which are collaborating to develop an OTC version of the erectile dysfunction pill Cialis (the PDE5 inhibitor tadalafil).

However, companies must overcome a number of challenges if they hope to turn the decision to switch into the success of earning shelf space at the pharmacy or gas station. "Switching from prescription to OTC is an art rather than a science, especially as it's different for every drug and every country," says Laura Mahecha, industry manager for healthcare and industrial and institutional markets at Parsippany, NJ-based Kline & Company, a management consulting and market research agency.

Between 9 September 1976 and 28 July 2014, 110 ingredients or doses were approved as OTC drugs by the FDA. The most common product categories were antihistamines and agents to treat acid indigestion or heartburn, according to the Consumer Healthcare Products Association. Recent successes have included AstraZeneca's ($AZN) heartburn treatment Prilosec (omeprazole), and a number of allergy treatments including Schering-Plough's Claritin (loratidine), Sanofi's Allegra (fexofenadine) and UCB's Zyrtec (cetirizine).

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In Europe, one in two packs of medicines sold is a non-prescription medicinal product, according to the Association of the European Self-Medication Industry.

There are a number of drivers behind this move from prescription to something that can be sold directly to consumers. Many major blockbuster drugs are approaching, or have already passed, their patent expiry in major markets. OTC offers an add-on to remaining in the prescription market and battling low cost generics, by providing access to another, sizeable market.

"Switches may be viewed by big pharma as an initiative to be considered at the end of the product's lifecycle, but actually it should be seen as the beginning of a new R&D phase and the creation of a new consumer brand.."

ANNA MAXWELL, CEO, MAXWELLIA

Introducing the first OTC drug in a particular category can actually expand the market by up to 30%, according to Washington, DC-based consulting firm Bates White. That's particularly true for conditions that can be managed easily by the patients themselves, such as heartburn. "The introduction of OTC Zantac increased the heartburn market rather than taking away market share from antacids like Tums or Pepto-Bismol," says Mahecha. "This is because patients previously taking [Zantac] as a prescription drug followed it onto the OTC market."

What's more, drugs that are switched in the U.S. have three years exclusivity if they are very different from anything else on the market, which allows the developer a degree of protection against competition and provides an incentive to switch to OTC in new areas, which could improve market access for patients.

In the case of erectile dysfunction drugs like Cialis, developing an OTC product may help drug developers combat counterfeit and falsified medicines sold illegally via the Internet. Switching to OTC allows companies to provide safe and reasonably priced access to legitimate drugs, gaining control over rivals and protecting consumers.

Another issue motivating pharmaceutical companies to convert prescription drugs to OTC products is the pressure they're facing from international health systems. As the population ages and levels of dementia, cardiovascular disease, cancer and diabetes increase, drugmakers are increasingly getting pushback on pricey drugs from private and public insurers. By placing more of the cost burden directly on consumers, certain OTC drugs could save healthcare systems billions. In a study presented in 2004, Northwestern University researchers showed that switching from Rx to OTC for drugs to treat respiratory infections could save the U.S. $4.75 billion a year.

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A key factor in the success of an OTC switch is ensuring that the product will appeal to consumers. While the optimal dosage form is important in successful administration of a drug product, when it's the consumer who chooses which version of a drug to take rather than the pharmacist, this practical appeal is important.

Consumers are looking for products that are fast acting, effective and easy to take. In a global consumer study conducted by Catalent Pharma Solutions, consumers rated softgel capsules as a highly desirable form. 82% rated softgels as fast acting and effective, plus 89% found them easy to digest. Choosing a consumer-preferred format such as a softgel may give a product a competitive advantage with consumers.

With 80 years of history, there is a huge amount of softgel manufacturing and formulation experience in dissolving drug actives in an excipient and encapsulating the solution within a gelatin shell. As most Rx products that are ripe for an OTC switch predate the solubility problems that have come to the industry recently, there is a good chance that a softgel formulation will be possible. Successful examples include OTC versions of the antihistamine drugs loratadine and cetirizine.

New non-gelatin alternatives are also available. Catalent's Vegicaps® technology uses ribbons made from natural seaweed extract carrageenan and a modified starch to form the capsules. First developed in response to the BSE problem, they are appropriate for consumers seeking all natural products, vegetarians and those with religious dietary requirements. The technology is proven – many plant based supplement products are already on the market, notably in Asia.

These non-gelatin softgels have other advantages that can make for a more attractive OTC product. The shell can successfully encapsulate a wider range of excipients, tolerate a wider pH range, and be filled at a much higher temperature (up to 70°C).

Indeed, Catalent's OptiGel™ Mini technology allows for higher API concentrations in smaller sized softgels. Softgels can be 30–50% smaller than a traditional product, making them easier to swallow and significantly more appealing to the consumer. This makes it possible to make much smaller softgels, particularly useful for those who dislike taking large capsules.

Much smaller softgels can also be made, which could have potential in enabling dose flexibility. Catalent first developed its OptiGel™ Micro for the Japanese fish oil market, minuscule capsules the size of fish eggs can be made. These are incredibly easy to swallow, convenient, and allow for greater flexibility in dosing products to consumers.

From a more commercial standpoint, combining an innovative fill formulation with commercially proven technology can potentially provide IP protection to the product, making it more difficult (if not impossible) for competitors to copy. If the leading brand switches to OTC in such a format, while rival products might appear if the active were off patent, it would not be the same as the leading brand. And if that leading brand were an easy-to-take softgel, it would stand a great chance of beating the competition. ■

"In times when all healthcare payers are struggling to contain their budgets, the financial relief provided by OTC medicines will enable shifting their resources towards more expensive and medically intensive life-saving technologies," says Charles Billard, vice president for strategic development for Sanofi's global consumer healthcare division.

"Regulatory authorities demand appropriate evidence from applicants of a wide margin of safety, along with sound evidence of effectiveness, before granting a medicine non-prescription status."

CHARLES BILLARD, VICE PRESIDENT FOR STRATEGIC DEVELOPMENT, SANOFI

This is about more than just easing the impact on drug budgets, of course. Drug switches can make access to treatments much easier for patients, too. When a migraine strikes on a Friday night and there is no appointment available with a general practitioner until Monday morning, the patient can self-select OTC drugs at a pharmacy, often with pharmacist support available around the clock. This offers the added benefit of freeing general practitioners from wasting precious office time on minor issues or chronic conditions that patients can manage on their own.

Making the leap to OTC

For the pharmaceutical industry, converting products to OTC status can offer attractive new business opportunities. "Switches may be viewed by big pharma as an initiative to be considered at the end of the product's lifecycle, but actually it should be seen as the beginning of a new R&D phase and the creation of a new consumer brand," says Anna Maxwell, CEO of Maxwellia, a U.K. consultancy that specializes in the reclassification of drugs from Rx to OTC.

Switching from prescription to OTC is a strategic decision that requires companies to assess the value of investing resources--and potentially running additional clinical trials--to support the switching process. That forces companies to answer two key questions: can you switch and should you switch?

Answering the "can you switch question" brings up a host of other questions: Is the drug is safe and effective when used without doctor or pharmacist support? Can patients diagnose the condition themselves and then select the right drug? Can the label and the packaging be made clear enough so patients can understand them?

The "should you switch" question is more about the overall market and determining the value that the product would add to it. This includes determining whether there is an unmet need, what the competition is, and how much the drug would cost. Just because a product can be switched, it doesn't always mean it should be switched, says Morris Lewis, senior

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director for external affairs at Pfizer ($PFE) Consumer Healthcare. "If for example you will be the fifth [proton-pump inhibitor] to market, is it worthwhile switching?" Lewis says.

A company's switching strategy will vary globally depending on foreign rules and regulations. For example, in the U.K., prescription drugs (known as prescription-only medicines or POMs) generally change to pharmacy-only medicines (P), which are sold under the supervision of a pharmacist. After a few years, companies can apply to switch to the general sales list (GSL) designation, which means the drugs can be sold in general retail outlets, from gas stations to supermarkets. To grant GSL status, the authorities need proof that the drug has been used safely, and that it can be sold freely with no harm to public health.

New Zealand has a similar system, with pharmacist, open sales, and dual labelling, where only a registered nurse or a pharmacist with additional training can dispense the drug.

The existence of the "third class" (P) in countries like the U.K. can give authorities a little more flexibility in approving products for OTC use. That's because there is an intermediary (the pharmacist) actually handing over the drugs, and both asking and answering questions about their use. This is in contrast with the United States, where OTC drugs are usually available for self-selection on open shelves, with just a few being restricted to "behind-the-counter" sales. These restricted medications include pseudoephedrine, which can be used in the manufacture of illegal drugs; emergency contraception; and some controlled substances. These need to be dispensed by a pharmacist, and require the customer to produce identification, verify his or her age, and confirm that they understand the use of the drug.

Outside this group of drugs, there is less supervision, which may make the FDA more cautious in its approval choices. "The U.S. is a bigger OTC market, but more needs to be spent on awareness marketing as [for many drugs] there is no learned intermediary such as a pharmacist to recommend it," says Richard Holme, senior partner at Thrive Unlimited, a U.K.-based brand and innovation consultancy, and previously the global expert marketing director for GlaxoSmithKline ($GSK) Consumer Healthcare. "However, because of direct-to-consumer marketing on the pharma side, existing brand identities can be successfully leveraged when switched into OTC."

Companies have a few choices in making the decision to move a product over the counter. They can do a full switch for all indications and doses, which was the tactic chosen for many non-sedating antihistamines. Or they can choose a partial switch, changing certain indications or doses to OTC status, as was the case for some low-dose painkillers. If there are a number of strengths of a drug available for an indication, companies often start with the lowest strength, keeping the higher dose for prescription use, as OTC doses tend

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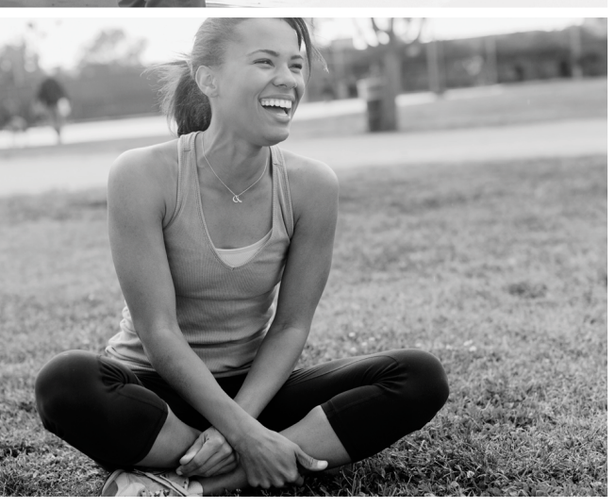

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to include a bigger margin for safety in the maximum dose. Alternatively, the company may switch just one of the existing indications, or even create a new indication for the OTC market, because it is deemed an indication that's safer for patients to manage on their own.

"One approach is to look at existing categories where there are OTC drugs, such as skin disorders or heartburn, and find a better solution, something that is genuinely different," says says Paul Lowndes, managing director at U.K.-based consulting company Mediapharm,.

"Manufacturers would prefer to see the decision to switch from prescription to OTC driven by science rather than politics."

MORRIS LEWIS, SENIOR DIRECTOR FOR EXTERNAL AFFAIRS, PFIZER CONSUMER HEALTHCARE

In recent years, the list of popular OTC indications has expanded to include migraine headaches, psoriasis, eczema, fungal skin infections, and thrush.

The Regulatory Challenge

The process of switching a drug to OTC status is highly regulated, and authorities will look at balancing the benefit for patients--and public health as a whole--with the risks posed by self-selection. To gain regulatory approval, the drug has to be confirmed as safe for use as self-care, and this may require additional data. "Regulatory authorities demand appropriate evidence from applicants of a wide margin of safety, along with sound evidence of effectiveness, before granting a medicine non-prescription status," says Sanofi's Billard.

Broadly speaking, the approaches to OTC switches are similar throughout the developing world, but nitty gritty details can differ widely, says Mike Munley of Medical Technology Association of New Zealand. Munley has worked in marketing and OTC switching for a variety of companies, including GlaxoSmithKline Consumer Healthcare. "The Japanese Pharmaceuticals and Medical Devices Agency is very risk averse and conservative, and is more akin to the Western authorities 30 or 40 years ago," Munley says. "In New Zealand, the environment is really progressive and liberal, but in Australia, the system is very complex, with nine different health departments to negotiate."

Munley describes the approach of New Zealand authorities as being "open source," which can be a positive for companies. "Organizations other than the license holder can initiate the switch," he says, including individuals, major grocery retailers and pharmacy chains.

In the European Union, by contrast, all 27 countries have to approve the switch, which can cause issues if there are cultural differences that affect a specific drug or category. There are often quite different regulatory requirements in different countries, explains

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Harm-Jan Schuurman, a Big Pharma veteran who is now a management consultant at Dutch healthcare consultancy OTC-LABS. "For example, the regulatory authorities in the Netherlands are more stringent, and may reject drugs with additional ingredients," such as Nurofen Plus [ibuprofen with added codeine, available in the U.K.], or Wick Medinait [paracetamol, dextromethorphan, ephedrine, and doxylamine, available in Germany], he says.

Switching can be a challenging process, with many roles involved, from marketing to regulatory, and from R&D teams to medical groups. Companies that have found the most success don't just hand off projects from function to function chronologically, like passing on a baton in a race, which can lead to problems with positioning and labelling. "The set up of a switch should be arranged more like an orchestra, with many players involved in different parts simultaneously but all working from the same score," says Maxwell, who has worked in consumer healthcare marketing at Boots, Nelsons, and Boehringer Ingelheim. "It helps if there is a 'conductor' with overall accountability for the project to keep it on track."

There can also be many stakeholders weighing in on a company's decision to switch a drug from prescription to OTC status, including pharmacists, doctors and charities. This is particularly true in first-in-class or controversial switches, and can have either a positive or a negative impact. "General practitioners can be resistant to the OTC pathways," says Maxwell. "However, a growing number of clinicians are positive about the role of over-the-counter drugs because of the potential of reducing the footprint of state health schemes, and I think this will increase."

An example of a switch where stakeholders had an influence was the first OTC emergency contraceptive, Barr Laboratories' Plan B. "There was a lot of lobbying from women's groups and medical groups, and from Congress and the Administration concerning Plan B," Lewis says. "Manufacturers would prefer to see the decision to switch from prescription to OTC driven by science rather than politics."

The pharmacist is another key stakeholder. In Europe, regulators require that pharmacists be trained in risk management when a drug is switched from prescription to OTC status. That training includes explaining the rationale behind the switch, and instructing pharmacists to recognize when it's appropriate to recommend the drug, and when they should instead refer patients to their doctors. "Pharmacy training will encourage pharmacy staff to give recommendations. If it is done well, it can generate sales," Lowndes says. However, if the training is badly written or too technical, or simply created as a [menial] exercise, it can act as sales prevention rather than sales support. This is because the members of staff lack the confidence to recommend the product, and may actually recommend the competition instead because they understand it better."

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There is a rising tide of interest in Big Pharma in giving pharmacists a bigger role in managing patients with chronic conditions such as diabetes, high cholesterol, and high blood pressure--and possibly making OTC therapeutics part of that. There will be challenges in making this ambition a reality, however, because some of these conditions are asymptomatic, making it difficult for consumers to determine whether a drug is working without monitoring from a physician. Compliance could also be an issue. "Preventative therapies such as lipid lowering could work as an OTC indication, but the likelihood that the patient would take it long-term needs to be considered," says Sven Stegemann, director of pharmaceutical business development at Capsugel and professor in patient-centric drug development and manufacturing at Graz University of Technology.

Still, many experts envision a day when the pharmacist becomes a full-fledged member of the medical team for any patient with a chronic, self-managed condition. "If a doctor is who you see when you are unwell, a pharmacist could be considered as the person you see to help you stay healthy," says Lowndes.

To make that a reality, however, there's little doubt that pharmacists will need additional infrastructure, such as interactive displays in pharmacies to support diagnosis, decision making and monitoring. Whether the average pharmacy chain will support such additions remains to be seen.

OTC Switching for the Next Generation

Many companies use the prescription-to-OTC switch as a lifecycle management tactic, triggering the switch towards the end of a drug's patent life to maximize its value over the long run. "Even though the margins are narrower, launching on the OTC market provides an additional way to recoup money invested in R&D, especially as the OTC drug is likely to have a greater longevity than the prescription version," says Kline & Company's Mahecha.

Historically, companies tried to keep drugs as prescription products as long as possible, and then switched just before the patent expired, perhaps as an afterthought. Now manufacturers are becoming increasingly proactive, starting to plan switching opportunities earlier in the lifecycle of products, and even looking to capture data useful for switching in parallel with other information gathering during Phase III studies.

Some companies have limited marketing experience on both sides of the fence, so they're striking up partnerships with other companies that are well established in the OTC market. For example, in 2012 AstraZeneca granted Pfizer, global marketing rights to AstraZeneca's Nexium (esomeprazole magnesium) for OTC indications.

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"To be successful, companies need to understand the strengths and weaknesses of the prescription brand but also be good at seeing the OTC brand opportunity sitting within it," says Holme.

Erectile dysfunction is the latest target of OTC switching. In May 2014, Sanofi and Eli Lilly signed an agreement to pursue OTC regulatory approval for Cialis, Lilly's oral erectile dysfunction drug. Cialis is available worldwide by prescription but is losing patent protection in certain markets. Under the terms of the agreement, Sanofi gains exclusive rights to apply for approval and then market Cialis OTC in the U.S., Europe, Canada and Australia. Sanofi Consumer Healthcare brings experience in OTC switches, as well as in consumer marketing.

Despite labelling restrictions and pharmacist training, there are both medical and societal concerns over the prospect of Cialis becoming available on store shelves. "Erectile dysfunction is a huge potential OTC market, but there are concerns about cardiovascular side effects if the drug is taken by the wrong population," Mahecha says. "There are also potential social implications if the drug is used by men who do not suffer from erectile dysfunction."

Despite such worries, as the population ages and healthcare costs rise, OTC therapeutics are likely to become more prominent. Regulatory agencies seem to be catching on to the trend, approving a host of new OTC switches. For example, in January 2013, the FDA approved Oxytrol for Women, the first OTC treatment for overactive bladder in women. The approval came just a few months after the FDA gave the thumbs-up to Nasacort Allergy, the first topical nasally-inhaled corticosteroid to be approved as an OTC treatment for allergies.

Munley suggests that a shortage of general practitioners in U.S. and other countries may be increasing the pressure on regulatory agencies to approve products that will make it possible for patients to manage chronic conditions without physician involvement. "A push to OTC in the future may be simply be out of necessity," he says. ■

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