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Potential Rx-to-OTC Switch Drug Candidates

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Abstract

The purpose of this study was to gain insight in what Rx legend drugs pharmacists think have a good enough safety profile to sell as OTC and, if any, what OTC drugs pharmacists think should be legend only. This study was performed as a non-directional survey asking the 2 following questions: "What are some prescription only medications that you think would be okay to sell as nonprescription (over-the-counter and behind the counter)" and following that "If any, what are some OTC/BTC medications that you think should be prescription only?" Pharmacists who were surveyed were those in the Philadelphia area within convenient traveling distance or whose contact information was available or accessible. There were three modes of collecting data. The first method was traveling to pharmacies in person and giving the pharmacist a physical survey to complete. The second method was the creation of a survey monkey, identical to the physical survey, which was sent electronically via email, text, or Facebook. The third method was telephoning pharmacies and conducting the survey over the phone. Demographics of respondents' age range, education, area of work, and gender were collected. All methods were done as similarly as possible; with the same greeting and wording of questions, etc. Data analysis was done based on noticeable trends of answers and tallying frequencies of responses. In all, 101 pharmacists were contacted. The most common suggestion for Rx-to-OTC switch was oral contraceptives.

Introduction

In 1951, the Durham-Humphrey Amendment was passed, requiring that any habit forming or potentially harmful drug must be dispensed under direct medical supervision by a healthcare practitioner. The amendment differentiated between legend (Rx) drugs and OTC drugs. Prescription drugs must carry the statement "Caution: Federal law prohibits dispensing without prescription." All other drugs have OTC status. Until this time, there was a lack of statutory direction and the responsibility of who designated what was a prescription or non-prescription, the FDA, regulated industry, or professional pharmacy, was undetermined.¹

In 1962, the Kefauver-Harris Amendments were passed, establishing a formal process that required drug manufacturers to clinically prove not only safety, but efficacy of medications and to report serious adverse events. This bill was likely in response to the crisis in 1962 of thalidomide, a morning sickness medication for pregnant women, which caused devastating birth defects in Europe. There were some limitations to the FDA. For example, the FDA couldn't prevent manufacturers from selling a drug if the FDA didn't act within 60 days of the drug's marketing. The FDA also

couldn't enforce good manufacturing processes and accurate prescription drug advertising before this act. More importantly, this act required FDA approval before a drug can be marketed in the US.^{1,2}

With the Kefauver-Harris expansion of FDA authority, the Drug Efficacy Study Implementation (DESI) project was launched to evaluate the efficacy of drug products, including OTC, which reached the drug market from 1938 to 1962 that were initially based entirely on safety, prior to the 1962 FDA regulation amendments.^{1,3}

In 1972, the FDA launched the OTC Drug Review to review the safety and efficacy of the ingredients, doses, formulations, and labeling used in medications available without prescription.³

Rx-to-OTC switch is when a drug with prescription status (Rx) transfers to nonprescription over-the-counter (OTC) status for either the same or a related indication. Rx-to-OTC switch is a highly regulated process that allows consumers to have easier access to medications without having to go to the doctor. Some examples include nicotine replacement therapies (gum, patch, and lozenge), ibuprofen 200mg, Benadryl (diphenhydramine), Claritin (loratidine), Nexium (esomeprazole), and Flonase (fluticasone).

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Some of the requirements for a drug to switch are that the drug must have a wide safety margin, efficacy, and easy to understand labeling and language to ensure proper use. Consumers must also be able to self-recognize and self-medicate a condition, and to understand warnings.⁴

There is definitely some conversation about the utility of the Rx-to-OTC switch. On the one hand, increasing access to frequently used medications with benign side effects that require prescriptions can lead to cost savings. The downside is that, even with benign side effects, many medications still require counseling or monitoring of some sort to maintain safety. In addition, patients need to be able to effectively self-diagnose to be successful in OTC therapy. One such study attempting to show the economic benefits was done estimating the potential switch of a triptan from Rx to OTC in France, UK, Spain, Italy, Germany, and Poland. This study took into account factors including time away from work, pathology, populations that tend to get migraines, and so on. What they found is that the overall spending for migraine attacks across the 6 countries came to \$661 million annually with potential savings of 13% if only one triptan were to go OTC. The model in this study may not necessarily correlate in the US because of different healthcare spending methods (single-payer vs. multi-payer).⁵

In a study of OTC Nicotine-Replacement-Therapy (NRT), it was found that the OTC availability of NRT increased access to and utilization of treatment with safe and efficacious use, and without substantial misuse or abuse. Prior to the switch, NRT was not widely used despite proven efficacy in smoking cessation. This study helped show that the Rx-to-OTC switch can increase utilization. This study may suggest potential for other switches to address public health needs.⁶

OTC medication sales make up 8% of total US pharma sales volume. The availability of OTC medications has great value in the US healthcare system in the form of \$102 billion in annual healthcare savings because of unneeded physician visits and diagnostic tests avoided. Currently, the OTC sector is about \$40 billion in size. Rx-to-OTC switch category drugs accounted for 19% of OTC sales in the past 5 years.⁷

Study Methodology

The purpose of the study described here was a pilot study to gain insight in what Rx legend drugs pharmacists think have a good enough safety profile to sell as OTC and, if any, what OTC drugs pharmacists think should be legend only.

Method: This study was performed as a non-directional survey asking the 2 following questions: “What are some prescription only medications that you think would be okay to sell as nonprescription (over-the-counter and behind the

counter)” and following that “If any, what are some OTC/BTC medications that you think should be prescription only?” Examples of drugs that went through the Rx-to-OTC switch were given including Plan B, Mucinex, Benadryl, Hydrocortisone 1% cream, and Allegra.

The survey was conducted from September 1, 2015 to November 30, 2015. Pharmacists who were surveyed were those in the Philadelphia area within convenient traveling distance or whose contact information was available or accessible. There were three modes of collecting data. The first method was traveling to pharmacies in person and giving the pharmacist a physical survey to complete. The second method was the creation of a survey monkey, identical to the physical survey, which was sent electronically via email, text, or Facebook. The third method was telephoning pharmacies and conducting the survey over the phone. Demographics of respondents’ age range, education, area of work, and gender were collected. All methods were done as similarly as possible; with the same greeting and wording of questions, etc. Data analysis was done based on noticeable trends of answers and tallying frequencies of responses.

In all, 101 pharmacists were contacted; 21 in person, 45 by telephone, and 35 by electronic means. A sample of the survey instrument is found in appendix A.

This convenience sample is not intended to be generalizable, but rather is a pilot study to determine whether a larger, more diverse study might yield interesting and actionable results.

Findings

The demographics of the 101 surveyed are found in Table 1. The results for the #1 question “What are some prescription only medications that you think would be okay to sell as nonprescription (over-the-counter and behind the counter)” are found in Table 2. The results for the #2 question “If any, what are some OTC/BTC medications that you think should be prescription only?” are found in Table 3.

Discussion

This discussion will focus mainly on the most frequent responses. By count, the most common response for Rx-to-OTC switch received was all oral contraceptives, where 40 out of 101 pharmacists responded. Of the 40 pharmacists, 26 were male and 14 were female. This finding may be potentiated due to the fact that oral contraceptives are a medication that females take, so males may not quite see the harm. It is also a possibility that since a majority of the respondents were from a retail setting, these suggestions were to ease the burden of refills and calls. However, 31 of the pharmacists had a Pharm.D. and 9 had a B.S. Pharmacists with a Pharm.D. degree have more extensive clinical

knowledge of disease states and medications, which may lend support in the safety profile of oral contraceptives to switch them to OTC since the majority of respondents held a Pharm.D. Although there was no distinction between over-the-counter and behind-the-counter, oral contraceptives would likely be sold behind-the-counter because there are major counseling points associated with them, including but not limited to selecting the dosage of either the estrogen or progesterone component, medication adherence, and what to do with missed dosages.

The three most frequent medications following oral contraceptives are life-saving medications albuterol, epi-pen, and naloxone. One reason for these suggestions may be that albuterol and Epi-pen medications may frequently run out of refills or the prescriptions expire when they are needed because these medications aren't used consistently.

Naloxone is an interesting suggestion; retail chains in PA are starting to obtain standing orders from physicians so that the pharmacist can prescribe naloxone. Nasonex nasal spray was the fifth most frequent, likely because Flonase is also OTC and they are similar.

The most frequent suggestion of OTC medications that should be moved to Rx was Plan B, with 10 out of 45 pharmacists that responded to this question. This is an interesting result because the most frequent suggestion for Rx-to-OTC switch was oral contraceptives. Of the 10 responses, 6 were males and 4 were females. 8 of the respondents had Pharm.D and 2 had B.S. 6 of the respondents included birth control as a suggestion, 5 of them being male and 1 female.

Although the suggestion of all herbals was second in frequency, this does not take into account specific herbal suggestions such as black cohosh, ginkgo biloba, ginseng, red yeast rice, and other herbals that may be thought of as supplements like weight loss supplements. This suggestion is likely due to the fact that there is little evidence of the efficacy of many herbal supplements. Many herbal supplements have known interactions with medications. There may also be many more unknown interactions with herbals alone or in combination with medications than the interactions known. Herbal supplements are less regulated than FDA approved medications and can pose a threat to patient safety.

Conclusion

There are many prescription medications that practicing pharmacists believe are safe to sell as OTC. The most common medication is of oral contraceptives. This finding is potentiated by the fact that California and Oregon have recently passed laws allowing pharmacists to prescribe both oral and hormonal contraceptives, being implemented in

2016.⁸ These two states serve as examples of the services that pharmacists can provide. If there is success with California and Nevada in the advancement of women's health by allowing pharmacists to prescribe contraceptives, we can expect that other states will follow suit. It is not unreasonable to expect that contraceptives have potential to be sold as non-prescription in the future.

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Table 1: Demographics of Pharmacists Surveyed

| Demographic | Frequency |
|---|-----------|
| Gender | |
| Male | 57 |
| Female | 44 |
| Education | |
| Pharm.D | 71 |
| BS | 30 |
| Age Range | |
| 20s | 35 |
| 30s | 33 |
| 40s | 7 |
| 50s | 23 |
| 60s | 2 |
| 70s | 1 |
| Employment Status | |
| Retail* | 72 |
| Hospital | 14 |
| Academia | 8 |
| Home infusion | 5 |
| Mail Order | 1 |
| Compounding | 1 |
| Number of Suggestions per Response | |
| One Suggestion | 27 |
| 2-3 Suggestions | 47 |
| Over 4 Suggestions | 27 |

*there was no distinction between retail chain and independent pharmacy

Table 2: Raw Data for Rx-to-OTC Suggestions by Frequency

| Drug Rx | Frequency |
|------------------------------|-----------|
| Oral Contraceptives, All | 40 |
| Albuterol | 27 |
| Epi Pen | 18 |
| Naloxone | 14 |
| Nasonex | 13 |
| Rx Toothpastes | 8 |
| Xyzal | 8 |
| Albuterol Spacer | 6 |
| Antihistamines, All | 6 |
| Clarinex | 6 |
| Naltrexone | 6 |
| Sumatriptan | 6 |
| PPI, All | 5 |
| Antabuse | 4 |
| Hydroxyzine | 4 |
| H2 Receptor Antagonists, All | 3 |
| Chlorhexidine | 3 |
| Humalog | 3 |
| Ibuprofen, All | 3 |
| Lovastatin | 3 |
| Nasal Steroids | 3 |
| Novalog | 3 |
| Triamcinolone Cream 0.025% | 3 |
| Clindamycin/Benzaclin Gel | 2 |
| Dexilant | 2 |
| Flonase | 2 |
| Ketoconazole 2% shampoo | 2 |
| Lantus | 2 |
| Latisse | 2 |
| Levemir | 2 |
| Lidocaine | 2 |
| Nystatin | 2 |
| Prednisone 1mg | 2 |
| Robitussin w/ codeine | 2 |
| Triamcinolone Cream 0.1% | 2 |
| Analpram | 1 |
| Apidra | 1 |
| Atorvastatin | 1 |
| Combivent Inhaler | 1 |

| | |
|---------------------------|------------|
| Clindamycin Cream 1% | 1 |
| Denavir | 1 |
| Fluoride drops | 1 |
| Hydrocortisone Cream 2.5% | 1 |
| Ketoconazole products | 1 |
| Lovaza | 1 |
| Denavir | 1 |
| Fluoride drops | 1 |
| Hydrocortisone Cream 2.5% | 1 |
| Low Dose steroid creams | 1 |
| Montelukast | 1 |
| Mupirocin 2% | 1 |
| Mycolog cream | 1 |
| Naproxen, All | 1 |
| NSAIDs, All | 1 |
| Pataday | 1 |
| Patanol | 1 |
| Permethrin 5% cream/rinse | 1 |
| Pravastatin | 1 |
| Prednisone | 1 |
| Prenatal Vitamins | 1 |
| Propranolol 10mg | 1 |
| Retin A mild strength | 1 |
| Santyl | 1 |
| Silver Sulfasalazine | 1 |
| Statins | 1 |
| Tessalon | 1 |
| Tylenol #3 | 1 |
| Valaciclovir | 1 |
| Voltaren Gel | 1 |
| Weak Corticosteroids | 1 |
| Zovirax | 1 |
| Z-Pak | 1 |
| TOTAL FREQUENCY RX | 253 |
| Responses | 101 |

Table 3: Raw Data for Current OTC to Rx Suggestions by Frequency

| Drug OTC | Frequency |
|-----------------------------|-----------|
| Plan B | 10 |
| Herbals, All | 6 |
| Sudafed | 5 |
| Dextromethorphan | 4 |
| Primatene | 4 |
| Bronkaid | 3 |
| Diurex | 3 |
| Prilosec | 3 |
| Weight loss supplements | 3 |
| Flonase | 2 |
| Nexium | 2 |
| Tylenol Combinations | 2 |
| Acetaminophen >500mg | 1 |
| Aspirin | 1 |
| Aspirin >81mg | 1 |
| Bisacodyl | 1 |
| Black Cohosh | 1 |
| Compression stockings | 1 |
| Estrogen supplements | 1 |
| Gingko Biloba | 1 |
| Ginseng | 1 |
| Hypodermic needles/syringes | 1 |
| Insulin syringes | 1 |
| Loperamide | 1 |
| Melatonin >5mg | 1 |
| Miralax | 1 |
| Motrin Products, All | 1 |
| Nasacort | 1 |
| Nicotine Patch | 1 |
| Pediatric APAP | 1 |
| Prenatal vitamins | 1 |
| Prevacid | 1 |
| Red yeast rice | 1 |
| Stimulants | 1 |
| Tylenol products, All | 1 |
| Weight lifting supplements | 1 |
| TOTAL FREQUENCY OTC | 72 |
| Responses | 45 |

Appendix A:

| Survey | |
|--|---|
| This short survey was created by Victor Phan for his economic research at Temple University School of Pharmacy. This research is about Rx-to-OTC-switch, where a prescription drug obtains OTC status. Pharmacists, please answer the following questions. | |
| What are some prescription only medications that you think would be okay to sell over-the-counter? Examples of medications that were once prescription are Hydrocortisone cream 1%, Allegra, Plan B, Mucinex, and Benadryl. | 1 2 3 4 5 |
| What are some over-the-counter medications that you think should be prescription only? | 1 2 3 4 5 |
| Please indicate gender | Male _____ Female _____ |
| Please indicate age group | 20s ___ 30s ___ 40s ___ 50s ___ 60s ___ 70s ___ |
| Please indicate degree | BS _____ Pharm D _____ |
| Please indicate if you are owner/manager or employee, and area of pharmacy (ex; retail) | |
| Thank you! Contact information: | |