

11-13-2017

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Recommended Citation

Shah RM, Holmes ER, West-Strum DS, Patel A. Community Pharmacists' Classification of Prescription Drugs into an Expanded Class of Nonprescription Drugs under the FDA's Proposed NSURE Initiative. *Inov Pharm*. 2017;8(4): Article 6. <https://pubs.lib.umn.edu/innovations/vol8/iss4/6>

Community Pharmacists' Classification of Prescription Drugs into an Expanded Class of Nonprescription Drugs under the FDA's Proposed NSURE Initiative

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Abstract

Objectives: There has been considerable debate over the last few decades about creating a third class of drugs that would not require a prescription or not be available freely over the counter, but require a pharmacist's consultation upon purchase. These debates reignited again in 2012, when the Food and Drug Administration (FDA) held a hearing about a third class of drugs positioned as an expanded nonprescription drug class under the FDA's Nonprescription Safe-Use Regulatory Expansion (NSURE) Initiative. The objective of this study was to determine which prescription drugs community pharmacists believe are acceptable additions to an expanded definition of nonprescription drugs that would be available pending pharmacists' consultation with a patient.

Methods: This cross-sectional study was conducted using a self-report, web-based survey administered to a national panel of community pharmacists. The survey contained a list of 24 current "prescription-only" drugs which may be potential candidates for an expanded nonprescription drug class, based on criteria outlined by the FDA, and questions related to respondent demographic and practice characteristics. The respondents were asked to indicate whether a particular drug should be marketed as a prescription drug, nonprescription drug or as part of an expanded non-prescription drug class. Descriptive analyses were conducted to determine the drugs that community pharmacists believed would be suitable additions to an expanded non-prescription drug class under the NSURE initiative.

Results: 462 completed surveys were received. Most respondents indicated that clopidogrel bisulfate (85.3%) and zolpidem (86.6%) should continue to be dispensed as prescription drugs. Atorvastatin, metformin, and sildenafil (among others) were considered appropriate to be marketed as an expanded nonprescription drug, in other words, dispensed without a prescription but upon pharmacist consultation. Desloratadine (64.6%) and pre-natal vitamins (50.2%) were considered appropriate for nonprescription status (over-the-counter, without pharmacist intervention).

Conclusions: Respondents suggested that 18 out of 24 drugs (75%) on the list provided could be categorized into an expanded class of nonprescription drugs. Adding more drugs to an expanded nonprescription drug class has the potential to expand pharmacists' provision of patient care under the FDA's proposed NSURE program.

Background

Limited access to prescription medications due to the time and cost associated with a prescriber visit and safety issues associated with prescription to over-the-counter substitutes continue to be a cause for concern.¹⁻³ As a result, there has been much debate over the last few decades about creating an expanded class of nonprescription drugs (also known as a third class or a "behind-the-counter (BTC)" class of drugs).⁴ Such a class of medications would include those drugs that do not require a prescription, but require a pharmacist's consultation upon purchase.⁵ An overview of the various drug classes in the United States can be found in **Table 1**.

The third-class debate came to the forefront again with a Food and Drug Administration (FDA) hearing in March 2012 entitled "Using Innovative Technologies and Other Conditions of Safe

Use to Expand Which Drug Products Can Be Considered Nonprescription," also known as the FDA's Nonprescription Safe-Use Regulatory Expansion (NSURE) Initiative. This hearing repositioned a third class of drugs not as a BTC class, "but rather as a 'new paradigm' under which FDA "would approve certain drugs that would otherwise require a prescription for nonprescription use."⁴ These drugs would be approved under conditions of safe use.⁴ According to the FDA, these "conditions of safe use, would be specific to the drug product and might require sale in certain pre-defined health care settings, such as a pharmacy" and would be decided on a case-by-case basis.⁴ For example, the patient might be required to consult a pharmacist, or have a diagnostic test performed or talk to a prescriber for the first prescription of the drug, but obtain subsequent refills as non-prescription.

Under NSURE, it has been proposed that various technologies such as kiosks at pharmacies, computer algorithms or questionnaires on the internet, would help the patient self-diagnose correctly. Such technologies would be able to recommend appropriate medications to the patient for the specific condition along with the drug specific conditions for safe use. Alternatively, pharmacists would dispense the drug based on the patient's medical records and inform the patient about the conditions for the safe use of the drug.⁶

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NSURE has not gained a strong foothold at this point. Additionally, the FDA denied requests to reclassify atorvastatin, varenicline, and sildenafil as over-the-counter in 2015.⁷ The profession of pharmacy has seen, in some states, prescription drugs re-categorized into an expanded nonprescription drug class. One example includes the administration of oral contraceptives in Oregon and California by community pharmacists without a prescription after pharmacists have received relevant training and conducted a health screening for the patient.⁸ Regardless, it is argued that pharmacists are ready for the transition of some prescription drugs to an expanded nonprescription class given their current provision of patient-care services in the form of medication therapy management, vaccinations, and disease state management.⁷ The opportunity for pharmacists to dispense drugs in an expanded nonprescription class may be an answer to concerns about limited access to some prescription medications. As such, community pharmacists are critical stakeholders when considering which drugs are appropriate for an expanded nonprescription drug class.

Objective

The objective of this study was to determine which drugs community pharmacists believe would be acceptable additions to an expanded class of nonprescription drugs.

Methods

This study utilized a cross-sectional non-experimental descriptive design by means of a self-administered web-based survey that was distributed to a national convenience sample of community pharmacists obtained from Delta Marketing Dynamics (DMD) Healthcare. Before data collection, exemption status was granted by the respective university's Institutional Review Board.

This study was a part of a larger study that assessed community pharmacist's attitudes toward an expanded class of non-prescription drugs. The survey contained a list of 24 current "prescription-only" drugs that may be potential candidates for an expanded nonprescription drug class, based on criteria outlined by the FDA under the NSURE initiative. The list of drugs was developed using the criteria for an expanded non-prescription drug class outlined by the Department of Health and Human Services (DHHS) February 2012 federal register notice⁹, based on input from content experts, and based on existing literature.¹⁰ Preliminary qualitative interviews were conducted with six local community pharmacists to develop a list of drugs which would suffice the FDA's criteria for "conditions of safe use" under NSURE. This list of drugs was further refined and validated through a focus group including three community pharmacists, two-pharmacy practice faculty, and one pharmacy administration faculty at the university. Clopidogrel and zolpidem were added to the survey as validity checks to assess whether respondents understood the concept of an expanded definition of non-prescription drugs. It was expected

that under no circumstance should these two drugs be considered as potential additions to an expanded non-prescription drug class under the NSURE program. Respondents were asked to indicate whether a particular drug should be marketed as a prescription drug, nonprescription drug or as a drug in an expanded non-prescription drug class. The list of drugs contained the generic name, brand name, and the dosage form for each drug. Definitions for the three response categories, "Dispensed as Prescription Only", "Dispensed as an Expanded Nonprescription Medication" and "Sold as Nonprescription Only" were provided to the respondents as follows:

- Dispensed as prescription only: A prescription is required before the pharmacist may dispense the medication.
- Dispensed as an expanded nonprescription medication: A medication dispensed under the expanded nonprescription drug class that would require a confirmation of diagnosis by the pharmacist.
- Sold as nonprescription only: The patient may purchase the medication over-the-counter without pharmacist intervention.

Frequencies were calculated in order to determine the number of pharmacists that appropriated the sale of a particular drug under each of the three categories (i.e., prescription-only, nonprescription, and expanded nonprescription drug).

Results

Participant Response. A total of 462 completed, useable responses were obtained for a resultant 16.5% response rate. Participants were eligible for the study only if they were community pharmacists (potential respondents were screened at the start of the survey).

Respondent Demographics. The average age of the respondents was 49 years. The sample consisted of 272 males (61.4%) and was predominantly Caucasian (87.2%). Just over 66% of respondents had a Bachelor of Pharmacy (BPharm; practice degree) while almost 28% had a Doctor of Pharmacy (PharmD). 297 (64.28%) respondents were affiliated with a national, state, or local professional pharmacy organization. A full description of respondents' demographic characteristics is provided in **Table 2**.

Respondent Practice Characteristics. Most of the respondents were pharmacy managers/ pharmacists-in-charge (54.3%) and worked in an independent pharmacy (37.8%) in a self-reported urban location (57.9%). The sample was representative of all four-census regions in the United States.¹¹ On average, respondents reported to have been actively practicing pharmacy for nearly 24 years. In a typical week respondents worked an average of almost 42 hours. Respondents reported

that their stores fill an average of 450 prescriptions on a typical weekday.

Respondent Classification of Drugs into Dispensing Categories: Majority of respondents (~85%) indicated that clopidogrel and zolpidem should still be dispensed as prescription drugs despite the presence of an expanded nonprescription drug category. Atorvastatin, metformin, sildenafil, montelukast, proscar, promethazine and tamiflu (among others) were considered appropriate to be marketed as drugs in an expanded non-prescription drug class. Desloratadine and prescription pre-natal vitamins were considered appropriate for nonprescription status. Complete results can be found in **Table 3**, below.

Discussion

As the FDA continues to explore ideas on expanding access to prescription medications, it is imperative to determine the drugs which would be acceptable additions to an expanded non-prescription drug class from a patient safety/abuse potential standpoint. This is the first study to determine suitable prescription drugs, which could be dispensed without a prescription under conditions of safe use as per the NSURE initiative. A study by Segal and Sullivan (2010) had assessed drugs, which would be appropriate for inclusion in a BTC category. However, the legislation for a BTC category is different from the considerations for NSURE (**table 1**) and therefore an examination of suitable additions to an expanded non-prescription drug class under NSURE is warranted. Respondents indicated that most drugs on the list would be acceptable to dispense as part of an expanded nonprescription drug class.

As expected, community pharmacists indicated that clopidogrel and zolpidem should continue to be dispensed as prescription drugs. Typically, clopidogrel is indicated to prevent clotting of blood in the heart or any other blood vessels. However, side effects of this drug include internal bleeding. Clopidogrel is contraindicated for use with common drugs such as aspirin and other NSAIDs (Non-Steroidal Anti-Inflammatory Drugs). While, zolpidem is a sedative and is used to treat insomnia. It is habit-forming schedule IV controlled substance and therefore has a potential for abuse. Additionally, the use of this drug may lead to severe allergic reactions in certain patients. Therefore, community pharmacists indicated that clopidogrel and zolpidem should remain prescription-only.

On the other hand, there were two prescription-only drugs (desloratadine and prescription pre-natal vitamins) that community pharmacists suggested should be switched to over-the-counter (OTC) status. This indicates that respondents believed that there is little or no need to monitor the usage of these drugs in the form of a prescription or nonprescription with pharmacist-monitoring. Desloratadine is indicated for allergic rhinitis and it does not have a severe adverse events

profile unlike some of the above-mentioned drugs. Additionally, other allergy medications such as cetirizine (which were formerly prescription-only) are now available as a nonprescription drug. Therefore, it is not surprising that respondents advocated for nonprescription sale of this drug.

Community pharmacists also indicated that prescription prenatal vitamins should be switched to OTC status. This may have been because several prenatal vitamins are already available on the market as OTCs. These OTC prenatal vitamins contain smaller quantities of essential micronutrients such as folic acid, iron, and omega-3 fatty acids as compared to their prescription counterparts. Community pharmacists may have considered that higher quantities of these micronutrients may not impact pregnant women. Also, given the higher demand for these micronutrients during the peri-conceptual stage, sometimes it may be convenient for pregnant women to consume a higher dose once daily rather than smaller dose two or more times a day.

Finally, the majority of community pharmacists surveyed indicated that ~75% of the drugs on the list would be acceptable additions to an expanded nonprescription drug category. Community pharmacists may have viewed most of the topically applied medications to be safe based on previous experience and therefore were comfortable dispensing them without a prescription. Pharmacists also indicated that epinephrine injections, asthma-rescue inhalers should be dispensed under an expanded non-prescription drug class. This may have been because these are used to rescue patients in life-threatening conditions. These results are in line with findings from the Segal and Sullivan (2010) study, which was conducted among pharmacists in Ohio.

Results from the current study also indicated that respondents were comfortable dispensing statins and erectile dysfunction (ED) drugs without a prescription under NSURE. These results contrast with the findings by Segal and Sullivan where pharmacists did not agree with the inclusion of these drugs into a BTC category.¹⁰ Previously under BTC, pharmacists did not have access to patient medical records and therefore they may have not been comfortable dispensing these drugs without a prescription. The expanded access to these drugs was acceptable to community pharmacists because under NSURE these drugs will be potentially dispensed under conditions of safe use, which may include providing pharmacists access to patient's medical history, laboratory records, and even the ability to order routine lab tests to monitor patient's health status. Recently there has been a widespread push to increase access to cholesterol-lowering and ED medications especially for drugs which are nearing loss of patent exclusivity.⁷ In fact in 2007, manufacturers of an ED drug conducted an experiment in the United Kingdom (UK) where certain pharmacies could dispense the drug without a prescription. The patients had to present the pharmacists with

their medical history including cholesterol and glucose levels before acquiring the drug. If there is a need then pharmacists referred the patient to a prescriber. However, the European Medicines Authority (EMA) stopped the experiment citing that dispensing the drug without a prescription could delay the diagnosis of ED.¹² Respondents in the current study believed that placing such drugs into an expanded nonprescription category under the NSURE initiative would put them on a continuum of average risk. Pharmacists are trained and are largely responsible for providing clinical interventions for conditions such as hyperlipidemia and diabetes especially in the asymptomatic early stages. A growing roster of states are expanding the role of community pharmacists in patient management especially while dealing with chronic diseases. This may have been a key factor due to which respondents felt comfortable and confident listing these medications as expanded nonprescription drugs.

Limitations

A national community pharmacist panel was used to collect data for this study. Despite our recruitment letter stating that this study was being conducted for academic purposes, there is potential of self-selection bias in this study. Also, generalizability of this study to all pharmacists across the United States may be limited because this study employed a national convenience sample of community pharmacists. However, the sample was stratified by region of the country where the respondents practiced in order to ensure that the distribution of the respondents was representative of the distribution of community pharmacists nationally based on the region of practice (i.e. northeast, south, mid-west and west). Finally, this study employed a cross sectional and descriptive design and therefore causal relationships among the variables cannot be drawn.

Conclusions

Respondents thought most drugs on the list provided can be categorized into an expanded nonprescription drug class whereby prescriptions were not needed, but pharmacist intervention still was. The existence of more drugs in such a class has the potential to expand pharmacists' role in the provision of patient care. It has been argued that the groundwork for pharmacists' provision of drugs in a nonprescription drug class had already been laid.⁷ Making more drugs available in this category may also increase access to drugs currently only available by prescription. As the FDA continues to seek feedback from stakeholders in regard to which medications should be a part of an expanded class of nonprescription drugs, feedback from pharmacists is critical.

Acknowledgements: The authors would like to acknowledge Delta Marketing Dynamics (DMD) Healthcare Research for providing our community pharmacist panel gratis.

Declaration of financial/other relationships/conflicts of interest: None

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Table 1. Definitions of drug classes in the United States with examples

Drug Category	Definition	Examples
Prescription drugs	A prescription drug requires a medical prescription from a physician/nurse practitioner in order to be dispensed	e.g. statin medications
Over-the-counter drugs (OTC)	OTC drugs does not require a medical prescription to be dispensed	e.g. multivitamin tablets
Behind-the-counter (BTC)	BTC drugs do not require a medical prescription but do need pharmacist approval before being dispensed	e.g. pseudoephedrine, Plan B (among adult women), dextromethorphan
Non-prescription safe use regulatory expansion (NSURE)	NSURE drugs would not require a medical prescription but would be approved by the FDA to be dispensed under certain conditions of safe use (e.g. pharmacist reviewing patient medical records). This class of drugs is not yet approved and is still under consideration by the FDA.	To be determined by the FDA

Table 2. Demographic and Practice Characteristics of Respondents *

Variable	Number (%)
Gender	
Men	272 (61.4)
Women	171 (38.6)
Race/Ethnicity	
White/Caucasian	381 (87.2)
Asian/ Asian Indian	32 (7.3)
Hispanic	4 (0.9)
African American/Black	9 (2.1)
American Indian/Alaska Native	3 (0.7)
Other	8 (1.8)
Pharmacy Training	
Bachelor of Pharmacy (practice degree)	320 (66.12)
Doctor of Pharmacy	133 (27.48)
Master of Science	6 (1.24)
Doctor of Philosophy	3 (0.62)
Other	22 (4.54)
Membership of Professional Pharmacy Organization	
American Pharmacists Association	118 (22.01)
National Community Pharmacists Association	81 (15.14)
American Society of Health-System Pharmacists	9 (1.68)
National Pharmaceutical Association	10 (1.87)
State Pharmacy Association	226 (42.24)
Other	91 (17.01)
Type of Pharmacy	
Independent	168 (37.8)
Franchise	23 (5.2)
Traditional Chain	72 (16.2)
Supermarket with a pharmacy	130 (29.3)
Mass merchandiser with a pharmacy	41 (9.2)
Other	10 (2.3)
Position in the Pharmacy	
Staff/Floater/Relief pharmacist	128 (29.0)
Manager/Pharmacist in-charge	240 (54.3)
Owner	70 (15.8)
District manager	3 (0.7)
Regional manger	0 (0.0)
Other	1 (0.2)
Location of Pharmacy	
Urban	256 (57.9)
Rural	186 (42.1)
Geographic Region of practice	
South	152 (34.1)
Mid-West	104 (23.3)
North East	108 (24.2)
West	82 (18.4)
Variable	Mean (SD)
Age (in years)	48.76 (11.27)
Years of actively practicing pharmacy (in years)	23.59 (11.50)
Number of hours practiced in a typical week	41.51 (7.81)
Number of prescriptions store fills on an average weekday	449.93 (554.26)

*Fewer than 462 responses for a given question was indicative of nonresponse for that particular category.

Table 3. Respondent Classification of Drugs into Dispensing Categories

Drug Name	Category under which the Drug should be Dispensed						Total*	
	Dispensed as Prescription Only		Dispensed as Expanded Nonprescription		Sold as Nonprescription Only		N	%
	N	%	N	%	N	%		
atorvastatin oral	175	39.0	266	59.2	8	1.8	449	100
metformin oral	201	44.8	242	53.9	6	1.3	449	100
clopidogrel bisulfate oral	383	85.3	63	14.0	3	0.7	449	100
hydrochlorothiazide oral	106	23.6	316	70.4	27	6.0	449	100
lisinopril oral	152	33.9	288	64.1	9	2.0	449	100
sildenafil oral	122	27.2	298	66.5	22	6.3	448	100
finasteride oral	154	34.4	259	57.8	35	7.8	448	100
valacyclovir hydrochloride oral	142	31.7	279	62.3	27	6.0	448	100
zolpidem oral	388	86.6	56	12.5	4	0.9	448	100
clindamycin benzoyl peroxide topical gel	22	4.9	277	61.8	149	33.3	448	100
bupropion SR oral	210	47.0	221	49.4	16	3.6	447	100
Prescription pre-natal vitamins oral	18	4.0	205	45.8	225	50.2	448	100
Eflornithine cream	101	22.5	231	51.6	116	25.9	448	100
montelukast sodium oral	159	35.7	248	55.6	39	8.7	446	100
albuterol inhaler	97	21.7	315	70.6	34	7.6	446	100
desloratadine oral	9	2.0	149	33.4	288	64.6	446	100
fluticasone cream	42	9.4	298	66.8	106	23.8	446	100
oseltamivir oral	177	39.7	255	57.2	14	3.1	446	100
betamethasone cream	110	24.7	287	64.3	49	3.1	446	100
methyl prednisolone oral	243	54.5	199	44.6	4	0.9	446	100
ondansetron oral	149	33.4	271	60.8	26	5.8	446	100
sumatriptan oral	278	62.3	160	35.9	8	1.8	446	100
epinephrine injection	117	26.2	288	64.6	41	9.2	446	100
promethazine oral	124	27.8	276	61.9	46	10.3	446	100

*Fewer than 462 responses for a given question was indicative of nonresponse for that particular category.