Usage Patterns of Over-the-counter Phenazopyridine (Pyridium)

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OBJECTIVES: Little is known about how the public uses formerly prescription medications that are available over-the-counter (OTC). This study examines whether consumers inappropriately use and substitute a recently widely distributed OTC urinary analgesic, phenazopyridine, for provider care.

DESIGN/SETTING: We conducted a cross-sectional survey of a stratified cluster random sample of OTC phenazopyridine purchasers ($N = 434$) in 31 Los Angeles retail pharmacies over 5 months. Recruited by shelf advertisements, participants were 18 years or older who purchased a phenazopyridine product. Each completed a 25-item self-administered anonymous questionnaire. Inappropriate use was defined as 1) having medical contraindications to phenazopyridine, or 2) not having concurrent antibiotic and/or provider evaluation for the urinary symptoms.

RESULTS: The survey response rate was 58%. Fifty-one percent of the respondents used OTC phenazopyridine inappropriately, and 38% substituted it for medical care. Multiple logistic regression analyses revealed that inappropriate use was correlated with having little time to see a provider (odds ratio [OR], 1.57; 95% confidence interval [95% CI], 1.26 to 1.96), receiving friend's or family's advice (OR, 1.25; 95% CI, 1.05 to 1.47), having prior urinary tract infections (OR, 0.49; 95% CI, 0.30 to 0.80), having used prescription phenazopyridine, (OR, 0.40; 95% CI, 0.25 to 0.63), and having back pain (OR, 0.34; 95% CI, 0.16 to 0.74). Similar correlates were found in those who substituted OTC phenazopyridine for provider care. Respondents with incorrect knowledge about phenazopyridine's mode of action had 1.9 times greater odds of inappropriate use and 2.2 times greater odds of substitution than those who had correct knowledge about this drug.

CONCLUSION: Inappropriate use of OTC phenazopyridine appears common. Increasing the public's knowledge about reclassified drugs may help to mitigate this problem.

KEY WORDS: pharmacy; survey; over-the-counter; phenazopyridine.

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Reclassifying prescription medicines to over-the-counter (OTC) status has become increasingly common.¹⁻⁶ Nearly one third of new OTC drugs marketed between 1975 and 1994 were previously available by prescription only.⁷ Since 1995, the U.S. Food and Drug Administration (FDA) has reclassified other medications, such as histamine2-receptor antagonists, vaginal anti-fungal cream, nicotine patches, and some nonsteroidal anti-inflammatory drugs.^{1,8} In 1993, 9 of the "Top 10"-selling OTC drugs were reclassified products.⁹ Sales of OTC drugs are predicted to double from \$11 billion in 1993 to \$22 billion by the year 2010.⁹ Although reclassified drugs are enormously popular, substantial challenges exist regarding their appropriate use by the public.¹⁰⁻¹⁴

These challenges are reflected in ongoing discussions between the FDA, health insurance companies, the pharmaceutical industry, consumers, and health care providers.^{15,16} Proponents of reclassification believe that switching prescription drugs to OTC status can lower drug costs, decrease health services utilization, and increase consumer access to self-care products.^{1,17-23} In contrast, critics of this process are concerned with improper self-diagnosis and self-medication, leading to misuse and adverse outcomes.¹⁷⁻²³ This controversy is illustrated in the current debate on whether to reclassify prescription allergy medications and cholesterol-lowering agents.^{24,25}

To date, most reclassification decisions have been based primarily on data collected prior to the conversion,^{26,27} and little is known about whether consumers used these drugs properly during the post-OTC marketing period. The few studies that have attempted to evaluate this gap used a convenience sample of clinic patients or took place outside the United States under different regulatory conditions²⁸⁻³¹ and therefore lack the generalizability necessary to inform U.S. policy decisions.

To address this knowledge gap, we conducted a study to evaluate the consumer use of an OTC urinary analgesic, phenazopyridine (pyridium) that is recently widely marketed. We chose to study phenazopyridine because urinary tract infection (UTI) is a common health condition and there is abundant direct-to-consumer advertisement of OTC phenazopyridine found in television commercials and women's magazines. In addition, the standard of treatment for UTI and the use indications for phenazopyridine are well

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described in current medical literature, thus allowing us to derive explicit criteria for appropriateness of use. In our study, we measured the rates of inappropriate use in 31 community pharmacies within the Los Angeles area and investigated factors that might be correlated with consumers using this drug inappropriately or substituting it for provider care.

METHODS

Overall Design

This study involved a cross-sectional survey of a stratified cluster random sample of OTC phenazopyridine purchasers ($N = 434$) in 31 Los Angeles pharmacies from September, 2000 to February, 2001.

Sampling

Stratified cluster random sampling was employed to obtain survey respondents with a uniform distribution of income levels. The corporate office of a major retail chain provided a list of their pharmacies located within Los Angeles County ($N = 79$). From this list, we chose as the sampling frame a subset of 48 pharmacies located within an approximate 20-mile radius from central Los Angeles. Four of these pharmacies with convenient geographic locations were sampled with certainty for pilot testing. Three of them also participated in the main study; the fourth dropped due to a change in management.

Since income has been shown to be associated with OTC medication use,³² the 1989 U.S. Census data were used to rank the remaining 44 pharmacies by the per capita income of their respective ZIP codes. Stratification was obtained by systematic random sampling from this rank list. First, the sampling interval was calculated as $44/30 = 1.467$. Then, a series of numbers was constructed by selecting a random number greater than zero and less than or equal to 1.467, and successively adding 1.467 until the cumulative sum surpassed 44. Finally, the numbers in this series were rounded up to the nearest higher integer. These rounded numbers designated which of the 44 pharmacies on the list would be included in the sample. Thirty pharmacies were selected, but 2 declined to participate. Thus, a total of 31 pharmacies (28 from random sampling and 3 from pilot sites) participated in the data collection.

Respondent weights were also calculated to correct for interpharmacy site differences in nonresponse rate and data collection start dates. Respondents from pharmacy sites with lower survey response rates received proportionally larger weights, and those from sites with earlier data collection start dates received proportionately smaller weights. We estimated the design effect from weighting to be $1 + CV^2$ where CV is the coefficient of variation for the weights. Using this formula, the design effect in our study is low, 1.001. Similarly, the design effect from clustering also was minimal because the sampling fraction for

clusters was high (30/44) and stratification by per capita income was employed in selecting clusters.

Survey Instrument

At the time of purchase, consumers completed an anonymous 25-item, self-administered questionnaire in either English or Spanish. The survey asked questions about respondent's (1) demographics, (2) symptoms prompting use, (3) prior history of UTI, (4) prior use of prescription phenazopyridine, (5) provider contact (e.g., through telephone, clinic visit, or future pending appointments), (6) concurrent therapy (e.g., antibiotic and/or other medications), (7) medical contraindications, (8) knowledge of phenazopyridine's effects, (9) reasons for purchasing OTC phenazopyridine (e.g., provider recommendation, pharmacy advice or self-medication), (10) factors influencing purchase (e.g., advertisement, friend/family, package information, barriers to access to care, financial tradeoff), (11) primary spoken language, and (12) global health status. The questionnaire required approximately 3 minutes to complete. It was pretested for readability and comprehension using one-on-one cognitive interviews with 90 convenient clinic patients and 30 actual OTC phenazopyridine customers in the pilot pharmacies. These pilot data were excluded from the analyses.

Data Collection

Data collection began at each of the 31 pharmacies on different days over a 3-week period beginning on September 24, 2000. The collection process ended at all sites on February 16, 2001. Customers were recruited by placing bilingual (English and Spanish) advertisements next to the OTC phenazopyridine products on the shelves. These advertisements directed the customers to the pharmacy counter, where they completed the questionnaires. Participants were 18 years or older and purchased any 1 of the 3 OTC phenazopyridine products (Azo-Standard, Prodiur, or Uristat) for their own use. Those who completed the survey received a \$5.00 discount on the purchase of the drug. This method ensured that only purchasers completed the questionnaire. Furthermore, the pharmacists anecdotally reported no spurious sales rise induced by our \$5.00 incentives, because this discount only covered a portion of the drug's entire cost. Adhering to a natural experiment, the pharmacists were neither encouraged nor prohibited from giving advice to consumers about the use of OTC phenazopyridine. Likewise, the consumers were not cued with specific instructions to read the package information prior to answering our questionnaire.

The survey response rate was calculated as the number of surveys returned divided by the number of products sold during the study period. Because the sales data were private, our research team tracked the denominator by labeling the boxes on the shelves and counting those that remained each week. This conservative calculation assumed that each phenazopyridine package was

purchased independently by a consumer and that no packages were lost or stolen during the study period.

Outcome Measures

Figure 1 summarizes the criteria for these measures.

Appropriate/Inappropriate Use. The explicit criteria for appropriate and inappropriate use of OTC phenazopyridine were derived separately using the Physician's Desk Reference,³³ and the package labels on OTC phenazopyridine describing its indications and contraindications as determined by the FDA, established medical literature on the standard of care for UTI,^{34,35} and an expert panel comprised of a prominent urologist and 5 primary care physicians.³⁶ We resolved differences of opinion through mutual discussion. This constructed criteria effectively

and exclusively differentiated almost all cases of appropriate and inappropriate use. Only 3 cases were indeterminate. These were excluded from the final analyses.

Substitution. Consumers' substitution of phenazopyridine for provider care was based on self-reported intentions at the time of purchase. Although our questionnaire measured anticipated use and intended substitution, it is commonly accepted in the research literature that intention is strongly linked to direct action.^{37,38}

Independent Variables

In order to conceptualize those factors that might affect a consumer's decision to use OTC phenazopyridine, a modified version of the Anderson Behavioral Model^{39,40} was applied. Among the *environmental* and *predisposing*

Appropriate use of OTC phenazopyridine (n = 207)

Scenario #1: UTI under treatment or interim symptom relief use

At least one of the triad UTI symptoms (i.e., burning, urgency, frequency), and
No medical contraindications to phenazopyridine (i.e., liver, renal disease), and
On concurrent antibiotic or had seen/spoken to a healthcare provider or awaiting medical appointment for urinary symptoms.

Inappropriate Use of OTC phenazopyridine (n = 224)

Scenario#1: Presumed UTI¹ undertreated with phenazopyridine alone (n=213)

At least one triad of UTI symptoms, and
No contact with a healthcare provider², and
No future appointments pending, and
No antibiotic.

Scenario#2: Contraindication to drug (n=18)

Medical contraindications to phenazopyridine.

Scenario#3: Presumed non-UTI condition requiring medical evaluation (n=52)

Non-UTI triad symptoms (i.e., fever, back pain, nausea/vomiting, genital discharge, hesitancy, dribbling, incontinence, swelling, others), and
No contact with a healthcare provider, and
No future appointments pending.

Substitution of OTC phenazopyridine for physician care (n = 166)

Scenario#1: Substituting self-care for physician care

No contact with a healthcare provider about the symptoms, and
No future medical appointment pending, and
Answers "yes" to the question "Are you using this medicine instead of going to to see a doctor?"
Answers "strongly agree" or "somewhat agree" to the statement "If I could not buy this medicine over the counter, I would go to see a doctor for my symptoms."

Footnote: Appropriate use of phenazopyridine is based on: 1) the package label containing approved indication for temporary symptom relief pending medical care, and 2) the current medical standard for the treatment of UTI using an antibiotic.

FIGURE 1. Definitions of outcome measures.

factors, we included advertising, waiting for a medical appointment, friend's and family's advice, pharmacist's advice, lack of time to visit a provider, attitudes toward providers, income, and knowledge about phenazopyridine (i.e., knew that it is an analgesic, not an antimicrobial agent). Young females and those with a history of UTI or of using prescription phenazopyridine were considered to be high-utilizing *populations*. We included health insurance as an *enabling* factor, noting that it could have differing effects on consumers' behavior: insured individuals might learn about phenazopyridine while visiting their provider and then purchase the product, whereas uninsured individuals might choose to self-medicate. Finally, for *need*, we included a provider's recommendation for phenazopyridine and duration of symptoms.

Statistical Analysis

Missing data, found in only 3 surveys, were imputed to be the mean. Zero order correlation matrices were used as an initial check for multicollinearity. Exploratory modeling of inappropriate use and substitution began with cross-tabulations between the predictors and the outcome variables. Pearson χ^2 coefficients and independent sample *t* tests were used to identify potential predictors of the outcomes. For each outcome, we entered variables with an association of *P* value $\leq .2$ into a multiple logistic regression model (16 variables for inappropriate use and 20 for substitution model). Those with *P* value $\leq .05$ were retained in the final models. Statistical analyses were performed using the Intercooled Stata 7.0 survey programs (Stata Corp., College Station, Tex). These programs produced estimates corrected for possible clustering effects within pharmacies and utilized the sampling weights accurately. Using the final regression models for inappropriate use and substitution, we also predicted expected probabilities of the 2 outcomes for an average consumer with and without correct knowledge of phenazopyridine by holding all other predictors constant at their mean value.⁴¹

RESULTS

Respondents

During the study period, a total of 746 boxes of OTC phenazopyridine were sold and 434 consumers completed our questionnaire. The overall survey response rate was 58%, which is similar to the adjusted rate of 54.3% that accounts for between-site and within-site rates. As Table 1 shows, 96% of the respondents were females, with a mean age of 35 ± 0.8 years. Their ethnic composition was 43% white, 25% Hispanic, 18% African American, 11% Asian/Pacific Islander, and 3% other. Over 70% had at least some college education, and 46% had annual household incomes between \$30,000 and \$70,000. Seventy-three percent had private insurance, 8% had public insurance, and 19% had no health insurance.

Table 1. Overall Population Characteristics (N = 434)

Characteristics	n	Weighted %
Gender		
Male	20	4
Female	414	96
Ethnicity		
White	199	43
Nonwhite	235	57
Education		
Below high school	6	1
Some high school	20	5
High school graduate	94	23
Some college	135	32
College graduate	132	29
Postgraduate	47	11
Annual household income		
<\$30,000	159	38
\$30,000–\$50,000	117	27
\$50,001–\$70,000	82	18
>\$70,001	76	16
Health insurance		
No	85	19
Yes	349	81
History of UTI		
No	155	37
Yes	279	63
Previous use of prescription phenazopyridine		
No	311	71
Yes	123	29
Symptoms		
Burning	346	81
Frequency	274	63
Urgency	254	57
Incontinence	28	6
Dribbling	45	11
Fever	16	4
Nausea/vomiting	8	2
Back pain	52	12
Swelling/bloating	29	6
Genital discharge/lesion	7	2
Other	10	2
Knowledge of phenazopyridine's action		
Incorrect	186	43
Correct	248	57

UTI, urinary tract infection.

At the time of purchase, a majority of respondents experienced the triad symptoms of UTI; however, some also reported symptoms indicative of other medical conditions. Over two thirds had a history of at least 1 diagnosed UTI, and close to one third had previously used the prescription form of phenazopyridine. Just 4% reported medical contraindications to phenazopyridine. Only 35% had seen a provider, 15% were awaiting appointments, and the rest had not seen a provider nor had any future plans to do so. Only 23% were on concurrent antibiotics.

Despite having access to the package label information at the time of the survey, only 57% had correct knowledge regarding the analgesic effects of phenazopyridine in a UTI. Fifty-one percent used OTC phenazopyridine

Table 2. Final Logistic Regression Model: Factors Associated With Inappropriate Use and Substitution

Factors	Inappropriate Use		Substitution	
	Adjusted OR* (95% CI)	P Value	Adjusted OR* (95% CI)	P Value
Health insurance (no insurance = 1, have insurance = 0)	—	—	1.86 (1.00 to 3.45)	.049
Back pain symptom (no = 0, yes = 1)	0.34 (0.16 to 0.74)	.008	0.29 (0.12 to 0.72)	.009
History of UTI (no = 0, yes = 1)	0.49 (0.30 to 0.80)	.008	0.37 (0.22 to 0.61)	.000
Previous use of Rx phenazopyridine (no = 0, yes = 1)	0.40 (0.25 to 0.63)	.000	0.48 (0.30 to 0.76)	.003
Influenced by friend/family's advice (strongly disagree = 1, strongly agree = 4)	1.25 (1.05 to 1.47)	.012	—	—
Little time to see the doctor (strongly disagree = 1, strongly agree = 4)	1.57 (1.26 to 1.96)	.000	1.89 (1.50 to 2.38)	.000
Knowledge of phenazopyridine's action (incorrect = 0, correct = 1)	0.52 (0.34 to 0.80)	.004	0.45 (0.27 to 0.77)	.005

* Adjusted for the effects of other variables in the model.

Exploratory modeling for inappropriate use included 16 variables: gender, frequency, incontinence, fever, back pain, genital discharge, history of UTI, previous use of prescription phenazopyridine, friend's or family's advice, drug cheaper than provider visit, no time to see provider, waiting too long for provider appointment, health insurance, education, duration of symptoms, and knowledge of phenazopyridine's action. Exploratory modeling for substitution included 20 variables: gender, urinary burning, incontinence, dribbling, back pain, swelling, genital discharge, history of UTI, previous use of phenazopyridine, friend's or family's advice, drug cheaper than provider visit, no time to see provider, dislike provider, health insurance, income, education, duration of symptoms, ethnicity, knowledge of phenazopyridine's action. OR, odds ratio; CI, confidence interval; Rx, prescription.

inappropriately. Most of these inappropriate cases had symptoms of UTI but had not seen a physician or had pending appointments, and were not on an antibiotic. More than a third of the respondents substituted OTC phenazopyridine for provider care.

Table 2 shows the results of our logistic regression models for inappropriate use and substitution. They shared the same important predictors, except in 2 cases in which the predictors were retained in a single model. That is, individuals who were influenced by friend's or family's advice to purchase phenazopyridine were more likely to use it inappropriately than were those who were not similarly influenced. However, friend's or family's advice was not found to be statistically important in affecting substitution behavior. Similarly, consumers without health insurance were more likely to substitute OTC phenazopyridine for medical care than were those with insurance, but this variable was not found to be important in predicting inappropriate use. Consumers who reported little time to see a provider had 1.5 times greater odds of inappropriate use and 1.9 times greater odds of substitution than did those who had time. Those who had no prior UTIs had twice the odds of inappropriate use and almost 3 times the odds of substitution compared to those who had a past history of UTIs. Those who had never used the prescription phenazopyridine had over twice the odds of inappropriate use and substitution compared to those who had used it before. Those without back pain symptoms had over 3 times greater odds of inappropriate use and substitution than did those who experienced this symptom. Consumers with incorrect knowledge about phenazopyr-

idine had 1.9 times greater odds of inappropriate use and 2.2 times greater odds of substitution than did those who had correct knowledge about this drug and its action.

The expected probabilities of inappropriate use by an average consumer with and without correct knowledge of phenazopyridine were 44% and 60%, respectively. Similarly, the expected probability of substitution for an average consumer with correct knowledge of phenazopyridine was 27% as opposed to 45% for the same consumers lacking correct knowledge.

DISCUSSION

This survey of OTC phenazopyridine consumers in 31 Los Angeles County pharmacies showed that over half were using this medication inappropriately and that more than a third were substituting it for provider contact. Poor knowledge was an independent predictor of both inappropriate use and substitution for provider care, despite the fact that most consumers had adequate levels of education, income, and private health insurance.

The study design has several unique features. First, instead of convenience sampling, we employed a stratified cluster random sampling of consumers who purchased phenazopyridine from a large, well-known national retail chain in an area with a diverse population. This method strengthens the generalizability of our results within the sampled area. Second, to our knowledge, this is the first U.S. study that collected data directly from community pharmacy consumers. This is significant in that it allowed us to study the entire range of OTC phenazopyridine users,

including those who self-medicate, ask pharmacists for advice, and purchase medications recommended by providers. We were able to surmount the logistical obstacles that have limited research in this field and gain insights into how the public used a recently available OTC drug to treat a common health condition. Third, in contrast to previous studies that used loosely defined criteria for judging appropriateness of use, we constructed detailed and explicit scenarios by incorporating relevant concepts from established literature, as well as authoritative sources.

Findings from this study have striking implications for the OTC treatment of urinary symptoms. The high rates of inappropriate use and substitution among the self-medicating population in this study suggest that UTIs often may be undertreated and that there may be delays in diagnosing or treating other mimicking conditions. While phenazopyridine is indicated for use in temporary or interim symptom relief pending further medical care,³³ most of the consumers go beyond this indication and are using this drug as the only initial treatment for their urinary conditions without plans to seek further medical evaluation. And because phenazopyridine is an analgesic that can mask dysuria, consumers may have the false notion that their conditions are cured. On the contrary, the low rate of antibiotic use among those respondents with triad UTI symptoms who had visited providers may suggest problems with suboptimal care. Although this study was not designed to evaluate the quality of care delivered by providers, our findings suggest that some investigation is warranted.

Our study suggests one approach for reducing inappropriate use of OTC phenazopyridine. Among the various factors, knowledge about the drug is a mutable one. Individuals who had correct knowledge about phenazopyridine's analgesic effects were less likely to inappropriately use it and substitute it for medical care, even when we controlled for previous use of prescription phenazopyridine and history of UTI. However, correct knowledge has only a moderate effect on decreasing inappropriate use and substitution behaviors. Even if all consumers had correct knowledge about phenazopyridine, there would still be substantial inappropriate use and substitution. Thus, increasing knowledge alone cannot provide a complete solution. Further studies are needed to determine if this drug should continue to be available over the counter, and if so, ways to ensure proper consumer usage.

This study has some limitations. First, due to the impracticality of collecting urine specimens in a community pharmacy setting, presumed UTI was based on the presence of the triad symptoms. Nevertheless, these classic triad symptoms have a proven high sensitivity for diagnosing UTI.³⁴ Second, because we studied 1 medication purchased by consumers from a particular chain of retail pharmacies in 1 county, our results may not be generalizable to other regions, pharmacies, or health conditions. However, this limitation is somewhat offset by the fact that we studied a well-known pharmacy, a common health

condition, and an ethnically diverse population. Third, because the study was cross-sectional and anonymous, we do not have follow-up with the respondents to determine whether their behaviors resulted in adverse outcomes such as pyelonephritis or other serious health conditions. Nevertheless, our data collection methods enabled us to overcome logistical problems that have hindered previous studies and to conduct the first consumer study of OTC drug use in community pharmacies. Finally, our methodology did not allow us to assess nonresponse bias, since we could not track those consumers who elected, perhaps due to illiteracy, not to participate in the study. However, our response rate of 58% is much higher than those of other similar studies in community pharmacy settings.⁴² Even if all nonrespondents in the sample used OTC phenazopyridine appropriately and did not substitute it for provider care, our findings would still imply that 30% (224/746) of OTC phenazopyridine purchasers used this medication inappropriately and nearly a quarter (165/746) of purchasers substituted it for provider care.

Our findings on the inappropriate use of OTC phenazopyridine raise concerns regarding this drug and perhaps other reclassified drugs (e.g., histamine2 receptor antagonist, nicotine patch) or potentially reclassified drugs (e.g., cholesterol-lowering agents, nonsedating antihistamines). It would be important to expand our methodology to examine these drugs as well. Currently, 2 of the criteria used by the FDA for approving OTC marketing include 1) low potential for misuse and abuse, and 2) labeling instructions that are understandable to the average consumer.^{26,27} While these preconversion criteria may demonstrate consumer safety information under simulated environments, they appear to be insufficient in the real-world setting to ensure proper consumer usage behavior. The high rates of inappropriate use and substitution that we found suggest a wide discrepancy between these intended guidelines and actual consumer usage patterns. Further research is needed to understand how consumers use OTC medications, and more guidelines are needed to ensure the safe distribution of OTC medications. Extensive resources devoted to public education on an ongoing basis and better post-OTC marketing surveillance may help ensure that these medications are used appropriately by the public.

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