

Asthma Medications Should Be Available for Over-the-Counter Use: Pro

Joe K. Gerald¹, Michael E. Wechsler², and Fernando D. Martinez³

¹Public Health Policy and Management, and ³Arizona Respiratory Center, BIO5 Institute, University of Arizona, Tucson, Arizona; and ²Department of Medicine, National Jewish Health, Denver, Colorado

Abstract

Medications that provide quick relief of symptoms and that control airway inflammation are the mainstays of asthma treatment. However, adherence to these medications is suboptimal. The inconvenience and costs associated with obtaining these prescription-only medications are factors that contribute to poor adherence. The Food and Drug Administration recently requested public comment on a new paradigm whereby specific prescription-only medications could be made available over the counter, provided that conditions for their safe use could be established. Many

organizations expressed opposition, including the American Thoracic Society and other societies representing patients with respiratory diseases. These organizations cited unsubstantiated benefits and unnecessary risks as reasons to oppose greater over-the-counter availability of current prescription-only medications. This article examines the rationale for, and potential ramifications of, making asthma medications available for nonprescription use.

Keywords: asthma; health policy; over-the-counter medications; medication adherence

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Correspondence and requests for reprints should be addressed to Joe K. Gerald, M.D., Ph.D., Assistant Professor, Public Health Policy and Management, University of Arizona, 1295 N. Martin Avenue, P.O. Box 245210, Tucson, AZ 85718. E-mail: geraldj@email.arizona.edu

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In March 2012, the U.S. Food and Drug Administration (FDA) proposed a new paradigm whereby specific, existing prescription-only medications could be made available for nonprescription (“over-the-counter”) use, provided that conditions for their safe use could be established (1). The FDA reasoned that reducing the monetary and nonmonetary costs associated with obtaining prescriptions could increase medication access for first-time and continuing users while freeing physicians to care for patients with more complex needs. Fewer prescription-seeking visits might also lower health care expenditures.

The American Thoracic Society, a professional medical organization, questioned the paradigm’s benefits and argued that unsupervised use of prescription-only medications might place patients at risk (2). In 2014, the FDA evaluated two respiratory medications for

potential nonprescription use. In February, the joint FDA Pulmonary Allergy Drug Advisory Committee and the Non-Prescription Drugs Advisory Committee voted against Armstrong Pharmaceuticals’ request to market Primatene HFA (epinephrine hydrofluoroalkane) to patients with asthma (3). While the committees acknowledged epinephrine’s efficacy, they concluded that its safety was unproven. In May, the Nonprescription Drugs Advisory Committee voted against Merck’s request to market Singulair Allergy (montelukast) to adults with allergic rhinitis (4). The committee cited the potential for off-label use (e.g., in children and in those with asthma), potential neuropsychiatric adverse effects (e.g., suicide), and labeling too difficult for the average adult to understand.

Despite the FDA’s implicit desire to make prescription-only medications more

readily available, its advisory committees have voted in opposition. While each decision must be considered individually, the process may be systematically biased such that risks are overstated and benefits are undervalued. This article will examine the general safety, access, and cost concerns that have been raised and will argue that asthma reliever and controller medications with favorable safety profiles should be available for nonprescription use.

The Asthma Treatment Gap

Asthma is a common chronic condition that affects approximately 10% of American adults and children (5). Nonadherence to controller medications, like inhaled corticosteroids, is an important impediment to better outcomes (6). Long-term adherence, even among clinical trial participants, may only reach 60% (7).

Pharmacy claims suggest that 12-month refill rates of controller medications may be as low as 20%, with fewer than 10% of patients continuing to fill their medications after a year (8). Only 34% of patients with asthma enrolled in the Tennessee Medicaid program ever filled a prescription for inhaled corticosteroids during 3 years of observation (9). Among those who did, refills were dispensed about once a year.

While barriers to adherence include social, attitudinal, and economic factors, nonprescription availability would primarily reduce economic barriers (10). Among chronic diseases in general, and asthma in particular, higher medication costs are associated with lower adherence (8, 11, 12). However, copayments represent only a fraction of the total acquisition costs. Annual out-of-pocket spending on prescription medications among children with asthma is approximately \$150 dollars per year (12). Patients actually spend 2 to 4 hours of time traveling to, waiting for, and completing a physician office visit to obtain a prescription (13). In the United States, this is equivalent to \$50–100 (2013 dollars) per prescription (14). Because of this, the time costs associated with obtaining a prescription may take on greater importance and essentially “function as prices in discouraging demand” (15). When the North Carolina Medicaid program reduced the supply of medication dispensed per prescription from 100 to 34 days, it had a larger impact on adherence than increasing copayments from \$1 to \$3 (16). Other benefits of nonprescription medication availability include locational convenience (goods closer to home or workplace), access convenience (goods available at right time and place), and choice (ability to make trade-offs between price and convenience) (13, 14). To the extent that these factors deter patients from filling prescriptions, nonprescription availability of asthma medications could increase access.

Nonprescription versus Prescription-Only Status

By statute, prescription-only status is required when a medication’s “toxicity or other potentiality for harmful effect, or the method of its use, or the collateral measures necessary to its use, [make it unsafe] for use except under the

supervision of a practitioner licensed by law to administer such drug” (1). Prescription-only medications tend to be used for chronic, serious conditions that require an initial physician diagnosis and subsequent monitoring (17, 18). Prescription-only medications may also have a narrow therapeutic index, potential for abuse, or require physiologic monitoring. Conversely, nonprescription medications are typically reserved for acute, self-limited conditions that can be readily diagnosed by the patient. Nonprescription medications must also be safe and effective (17, 18).

Since 1975, the FDA has approved more than 80 prescription-only medications for nonprescription use (19). To address anticipated safety concerns associated with expansion of nonprescription medications, the FDA emphasized “conditions of safe use” which “would ensure [certain prescription medications] could be used safely and effectively without the initial involvement of a health care practitioner” (1). Two example conditions included pharmacist supervision (e.g., behind-the-counter use) and electronic kiosks that would guide patients through self-diagnosis and treatment.

The American Thoracic Society opposed allowing pharmacists to dispense medications based solely on their evaluation and diagnosis (2). Previous efforts to establish a behind-the-counter class of medications supervised by pharmacists have been opposed by professional medical organizations on the grounds that the current two-class system is adequate, that there is insufficient evidence to suggest behind-the-counter medications would benefit patients, and that there are potential risks with pharmacist-only supervision (20).

Organized Medicine and the Political Process

The economic theory of government helps explain why organizations like the American Thoracic Society lobby legislators and regulators (21). The theory draws parallels to the free market in which individuals and firms act in accordance with self-interest. Legislators and regulators are “sellers” and interest groups are “buyers.” Buyers provide political support (e.g., campaign donations, block votes, and volunteers) to improve the re-election prospects of sellers. Sellers craft

legislation that provides economic benefits that cannot be otherwise obtained in the free market (e.g., monopoly power and tax breaks). Interest groups find it worthwhile to lobby because the obtainable benefits outweigh the costs. Conversely, the general public rarely finds it worthwhile to organize opposition because their costs are widely spread and often difficult to detect.

Adoption of the FDA’s proposed paradigm change would threaten the economic interests of physicians, as there might be fewer patient visits. When antifungal agents were made available for nonprescription treatment of vaginitis, physician visits and prescriptions fell (22). While opposition may not be driven purely by economic reasons, a conflict of interest exists. Professional medical organizations have been long criticized for their ties with and financial support from industry, particularly pharmaceutical manufacturers (23, 24).

Professional ethos can also bias decision-making (25). The most recognizable of these principles is “do no harm.” In the epinephrine and montelukast decisions, physician members cited the potential harms associated with unsupervised use of these medications. Some concerns were related to side effects, but others emphasized the possibility that consumers would use these nonprescription medications in unintended and inappropriate ways. When considering montelukast’s indication for treatment of allergic rhinitis in adults, a panelist stated: “If only 0.1% of [asthma] patients stopped taking their medications, it has a potentially significant risk” (4). Given that montelukast has effectiveness similar to that of inhaled corticosteroids (26) and is generally considered to be safe (27, 28), the panelist’s position shows the strength of this ethos.

The FDA has a reputation for protecting consumer safety and promoting public health. However, the FDA is a federal agency and needs legislative support to ensure future budget appropriations (29). The FDA faces asymmetrical risks such that approval of a medication that subsequently causes harm incurs substantial reputational damage, whereas denying a medication that might prove to be safe and effective typically does not (29). Taken together, physicians’ economic interests, the ethos of “do no harm,” and the FDA’s risk aversion systematically bias decision-making such that risks are overstated and benefits undervalued.

Public Acceptance of Nonprescription Medications

While many groups have opposed the FDA's proposed paradigm, the general public and many individual physicians appear to be comfortable with nonprescription medication use. Fifty-eight percent of primary care patients reported taking nonprescription medications in the past month (30). Thirty-eight percent of physicians recommended that patients switch to a nonprescription medication to reduce out-of-pocket costs (31). Considering asthma specifically, 71% of parents reported using a nonprescription medication (e.g., Vick's Vaporub, Sudafed, and Robitussin) to manage their child's asthma (32). Approximately 25% of adults and 50% of children with asthma may be using complementary and alternative medical treatments to control their asthma (33). Given patients' willingness to use existing nonprescription treatments with minimal efficacy and substantial harms (e.g., children's cough and cold medicine [34]), it seems somewhat hypocritical to withhold highly efficacious medications with similar or better safety profiles.

The American Thoracic Society argued that nonprescription treatment of asthma "assumes the condition can be successfully managed with minimal medical intervention" (2). Greater availability of nonprescription treatments would lead to less patient education, pulmonary function monitoring, and physician supervision. The notion that physician-directed management is superior to other strategies was addressed in part by the Best Adjustment Strategy for Asthma in the Long Term (BASALT) trial (35). Daily controller treatment was adjusted every 6 weeks based on physician, biomarker (exhaled nitric oxide), or patient (symptom) evaluation. Neither physician- nor biomarker-based adjustments were superior to patient-directed changes. While some patients may benefit from frequent physician monitoring, many would do no worse without it.

The Economics of a Prescription-Only to Nonprescription Switch

Pharmaceutical firms are unlikely to support nonprescription transitions unless they are profitable. Past transitions have been

initiated by pharmaceutical companies seeking to extend revenue from specific prescription-only medications, defend against generic competition, expand their nonprescription portfolio, or access larger consumer markets (18). The nonprescription market accounts for 6 of the 10 most frequently used medications (13), but only 6% of total pharmaceutical sales (18). Former prescription-only products actually account for 50% of nonprescription sales. To encourage firms to switch medications, firms are granted a 3-year period of market exclusivity.

The switch of Claritin (loratadine) from prescription-only to nonprescription status demonstrates how consumer prices can be affected. Prior to the switch, a 30-day supply of Claritin was \$96.30. Within 2 years, the price of nonprescription (but branded) Claritin was \$22.37 and the price of generic loratadine was \$1.17 (36).

Many opposed to the switch raised concerns that health insurers would remove Claritin from their formulary and push medication costs to patients (37).

This concern was not substantiated by health plan data representing 1.2 million covered lives (38). Plans were categorized as making no changes, moving all second-generation antihistamines to the highest co-payment tier, or imposing restrictions on prescriptions. Most plans, representing 75% of covered lives, made no changes. Beneficiaries in plans that changed antihistamine copayment prices paid about \$11 more per prescription. All plans, even those that did not change their benefit structure, observed less prescription-only antihistamine use (45%, 68%, and 69%, respectively) and lower medication costs (−144%, −136%, and −147%, respectively). Given that patients filled fewer prescriptions in plans that did not change benefits, it appears that many patients preferred nonprescription purchase. Ultimately, the Claritin switch was viewed as one of the most successful in history, as the nonprescription allergy market grew by \$500 million over several years (18).

Asthma Medications Potentially Amenable for Nonprescription Use

A number of current prescription-only asthma medications could be considered for

nonprescription use including albuterol, inhaled corticosteroids, and leukotriene receptor antagonists. While these medications have been found to be generally safe and effective, they are not without potential risks (27, 39, 40). Regular use of short-acting β -agonists have been associated with increased airway reactivity and blunted response to rescue therapy (39). Inhaled corticosteroids, particularly at high doses, have been associated with easy bruising, reduction in growth velocity, loss of bone mineral density, and adrenal suppression (40). Case reports have linked leukotriene receptor antagonists, particularly montelukast, with increased suicide risk; however, this finding has not been confirmed (28).

It is important to place these concerns into the context of existing harms associated with nonprescription medication use. Between 2004 and 2011, cough and cold medication use in children led to some 60,000 emergency department visits (34). Approximately three-quarters of these visits were triggered by nonprescription use. Nonprescription medications account for one-third of all unintentional medication overdoses among children seen in the emergency department (41). Among the elderly, aspirin accounted for 18% of all admissions for adverse drug events in two hospitals in the United Kingdom (42). While the risks of asthma medications should not be minimized, comparatively they seem to be substantially less worrisome than those associated with currently available nonprescription medications.

In a narrowly framed response, the American Thoracic Society argued that making albuterol available for nonprescription use would lead to albuterol monotherapy (2). Current data describing patient prescription-filling behavior suggests that, for many patients, albuterol monotherapy (supplemented by exacerbation-driven prescriptions for controller therapy) is already commonplace (9, 43). Greater nonprescription availability of both reliever and controller medications could reduce this phenomenon. Some have argued that combining short-acting β -agonists with inhaled corticosteroids could prevent this possibility altogether (44). Having a combination reliever/controller inhaler could also facilitate intermittent, symptom-directed treatment

in patients with mild-to-moderate asthma (45, 46). While concerns about albuterol monotherapy are warranted, holding asthma medications “hostage” has not been proven to effectively prevent this problem.

Nonprescription Use of Quick Reliever Medications in Australia

In 1985, Australia approved the sale of nonprescription quick reliever medications if purchased from a pharmacist (47). Early data raised concerns as nonprescription purchasers were twice as likely to be undertreated as prescription purchasers and they were much less likely to have visited a physician in the previous 6 months (48). However, controlling for prior physician visits eliminated the association between nonprescription purchase and undertreatment. Qualitatively, patients cited low perceived value of physician visits, greater convenience, and greater sense of control as reasons for nonprescription purchase (49). More recently, 40% of quick reliever purchasers obtained their medication without a prescription (50). Nonprescription purchasers tended to be younger (39 vs. 54 yr) and use controller medications less frequently (50% vs. 65%) than prescription purchasers. Despite less frequent controller use, nonprescription purchasers were not found to have worse asthma control, quality of life, or lung function than prescription purchasers. At the time of purchase, consultation with a pharmacist or pharmacy assistant occurred 84% of the time, but counseling was less common, only 24% of the time (51). Unfortunately, prospective exacerbation and health care utilization data are not available. Nonetheless, Australia’s experience with nonprescription quick reliever medications does not suggest reasons for alarm.

Behind-the-Counter Statin Use in the United Kingdom

To predict the impact of making asthma controller medications available for nonprescription use, we briefly discuss the United Kingdom’s experience with HMG-CoA reductase inhibitors (statins). In 2004, the United Kingdom approved low-dose simvastatin for behind-the-counter use by patients at moderate risk of cardiovascular disease. This transition raised concerns that the wrong people would take them, that many would skip needed doctor visits, and that some would fail to make necessary lifestyle changes. Data have since become available to evaluate some, but not all, of these concerns.

The Whitehall II study of British civil servants examined use of lipid-lowering medications among participants at moderate and high risk of cardiovascular disease (52). Three years after the switch, none of their participants reported obtaining simvastatin without a prescription (52). Use of lipid-lowering agents among this group remained suboptimal (20–44%). Making simvastatin more readily available did not seem to increase access for these study participants who were at moderate and high risk. Few (18%) Scottish pharmacists reported ever having dispensed behind-the-counter simvastatin, and only about one-half voiced support for the switch (53).

Integrated sales data from five countries (the United States, the United Kingdom, Canada, Spain, and New Zealand) examined simvastatin utilization, expenditures, and prices before and after the switch in the United Kingdom (54). In contrast to the Whitehall II data, the switch appeared to increase statin utilization by 60%, reduce overall expenditures by 60%, and decrease prices by 80%. Unfortunately, these data did not distinguish between prescription and nonprescription use, and

did not distinguish use among low- and high-risk patients. Nonetheless, it strongly suggests greater overall use of simvastatin, much lower prices, and overall lower expenditures. Consistent with this data, the United Kingdom’s General Practice Research Database covering 3.5 million lives suggested that statin prescriptions abruptly declined after the switch, from 437 to 281 per 100,000 patients per quarter (55). The authors concluded that many patients were making use of behind-the-counter simvastatin. Subsequent extrapolations to the United States market suggest that approximately 500,000 cardiovascular deaths could be prevented over 5 years if nonprescription simvastatin were made available (56).

Conclusions

Although making asthma medications available for nonprescription use is a well-intentioned and logically consistent strategy, the decision should be carefully considered. Extrapolating outcomes from other switches could be problematic. So far, no data have demonstrated that past switches have improved population-level health. Nonetheless, the switch of Claritin in the United States and of Zocor in the United Kingdom provide compelling evidence that prices would decrease and utilization would increase. Without actually making a switch and monitoring its impact, it will be impossible to conclude whether making a switch is beneficial. Conversely, the negative consequences of doing nothing are certain. From our perspective, making asthma medications like albuterol, inhaled corticosteroids, and leukotriene receptor antagonists available for nonprescription use is more likely to benefit patients than to cause them harm. ■

Author disclosures are available with the text of this article at www.atsjournals.org.

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