The Pharmacist Activist

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Editorial

Medications that Must Be Available without a Prescription from a Pharmacist

The title of my editorial in the October 2007 issue of *The Pharmacist Activist* was "Behind-the-Counter (BTC) – Long Overdue but, Let's Seize the Day." In the introductory comments in that editorial I noted that the efforts over many decades of some pharmacists and pharmacy associations to establish a class of medications that would be available without a prescription from a pharmacist had been an exercise in futility. However, that editorial was prompted by two events. In late 2006, the Food and Drug Administration (FDA) approved the nonprescription behind-the-counter availability in pharmacies of levonorgestrel (Plan B) for use as emergency contraception. The FDA also announced that there would be a public meeting on November 14, 2007 to address the topic, "Behind the Counter Availability of Certain Drugs."

What has happened with respect to switches of prescription medications to OTC or BTC status since 2007? My response is "far too little!" Yes, there have been some additional switches of prescription medications to OTC status and the FDA has held two more public hearings on March 22, 2012 and March 26, 2014 (my testimony at these hearings is included in the March 2012 and March 2014 issues of *The Pharmacist Activist*, accessible at www.pharmacistactivist.com). However, the present situation can be summarized in the following observations:

1. Some important Rx to OTC switches have occurred.

2. We are not close to the potential that exists for switching medications from prescription to nonprescription status.

3. Pharmaceutical companies, the FDA, and associations of pharmacists can do much more to increase the number of switches.

4. There should be formal recognition and support for a category of medications that are available without a prescription from a pharmacist.

Selected examples and commentary regarding these observations are provided in the following discussion.

Recent switches

The recent switch to OTC status of the intranasal corticosteroids triamcinolone acetonide (Nasacort Allergy 24HR) and

fluticasone propionate (Flonase Allergy Relief) for the treatment of allergic rhinitis is an important switch, as is oxybutynin (Oxytrol for Women) for the transdermal treatment of overactive bladder. In California and Oregon, legislation has been passed that will permit oral contraceptives to be available without a prescription from a pharmacist. However, this is an initiative that has been considered by individual states rather than by the FDA for implementation on a national basis.

Notwithstanding the several positive steps that have been taken, we are not even close to achieving the potential that continues to exist for switching prescription medications to nonprescription status. There are more than a dozen prescription medications in different pharmacologic/therapeutic classes for which I can strongly support a switch to BTC or OTC status.

Much more should be done

Pharmacists and our associations, the FDA, and pharmaceutical companies should be doing much more to provide the initiative, justification, and support for switching prescription medications to nonprescription status. Both individual consumers/patients and society in general will benefit from increased access to medications that have been demonstrated to be effective and can be used safely. Why has more not been done?

Let's start with the pharmacy associations. Although this is a topic of interest for the associations, they have not given it a high priority and strong support. Yet this is a subject that has far greater implications and opportunities for the profession of pharmacy than any other health profession. It is not enough for the pharmacy associations to be providing statements at hearings and supportive commentary. The pharmacy associations should be providing strong *leadership* in addressing these initiatives that will result in substantial societal benefit. Although I have provided testimony at FDA hearings and written editorials on this subject, I have not done enough as an individual pharmacist. Accordingly, I intend to introduce an item of new business that addresses this topic for consideration by the House of Delegates of the American Pharmacists Association (APhA) at its annual meeting in March.

I commend the FDA for its apparent interest in increasing the number of medications available without a prescription, and for holding the public hearings. However, eight years have gone by since the first of these hearings and, to my knowledge, no conclusions have been reached and no actions taken with respect to formal recognition for a category of medications that are available without a prescription from a pharmacist. The FDA is too timid and too slow in addressing this situation although I will acknowledge that it is "handcuffed" by excessive regulation, has insufficient resources, and has not received strong enough support from the pharmacy associations.

The pharmaceutical companies have not been supportive of switching medications from prescription to nonprescription status UNLESS the timing and circumstances of such a decision correspond with their financial interests. A company will typically derive much greater revenues from a medication that is available only on prescription than if that medication is available without a prescription. Therefore, a company's interest in switching one of its prescription medications to nonprescription status usually occurs close to the time that the patent will expire and less expensive generic products will greatly reduce its prescription sales. It is at this time that a company may offset some of its anticipated financial losses for the prescription product by obtaining approval to make the medication available without a prescription and perhaps also obtain a period of marketing exclusivity for the OTC product. Claritin, Allegra, Prilosec, and Nexium come quickly to mind as medications that were switched to OTC status at about the same time that their patents expired, and have been very successful in the OTC marketplace.

With respect to the official recognition and support for a category of medications that are available without a prescription from a pharmacist, the associations of pharmacists must provide strong justification and support for this initiative and, where appropriate, establish criteria and guidelines for pharmacists to use in the provision, counseling, and use of these medications. Because of its willingness to hold hearings on this subject, I would like to think that the FDA would be supportive of approving on a timely basis selected medications for nonprescription availability from a pharmacist. I would welcome, but do not expect, support from pharmaceutical companies for this category of medications. For products that are available without a prescription, their priority has been to have them be available from as many retail sources as possible to maximize their revenue and to not have sales restricted by limiting availability to pharmacies. This initiative, however, addresses the needs and interests of patients and society, and I am confident that a strong position of the profession of pharmacy and the FDA will prevail.

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New Drug Review

Brexpiprazole (Rexulti – Otsuka)

Antipsychotic Agent

New Drug Comparison Rating (NDCR) = 2
(significant disadvantages)
in a scale of 1 to 5 with 5 being the highest rating

Indication:
Treatment of patients with schizophrenia, and as adjunctive treatment of patients with major depressive disorder (MDD).

Comparable drugs
Aripiprazole (e.g., Abilify).

Advantages:
- May be effective in some patients who have not experienced an adequate response with other agents;
- May be less likely to cause extrapyramidal reactions.

Disadvantages:
- Has not been directly compared with comparable drugs in clinical studies;
- Labeled indications are more limited (aripiprazole also has labeled indications for the acute treatment of patients with manic and mixed episodes associated with bipolar I disorder, the treatment of Tourette's disorder, and irritability associated with autistic disorder);
- Has not been evaluated in pediatric patients (whereas aripiprazole is indicated for use in pediatric patients as young as 6 years for certain conditions);
- Dosage forms are more limited (aripiprazole is also available in an oral solution formulation, and in a parenteral formulation for intramuscular injection for the treatment of agitation associated with schizophrenia or bipolar mania);
- May be more likely to cause weight gain.

Most important risks/adverse events:
Increased risk of death in elderly patients with dementia-related psychosis (boxed warning), and a higher incidence of cerebrovascular adverse events (e.g., stroke, transient ischemic attack) in these patients; increased risk of suicidal thoughts and behaviors in patients 24 years of age and younger (boxed warning); neuroleptic malignant syndrome; tardive dyskinesia; seizures; orthostatic hypotension and syncope; body temperature dysregulation; dysphagia; metabolic changes (e.g., hyperglycemia/diabetes, dyslipidemia, weight gain); leukopenia, neutropenia, and agranulocytosis; potential for cognitive and motor impairment (patients should be cautioned about operating hazardous machinery); is a substrate for the CYP3A4 and CYP2D6 metabolic pathways and activity is increased by the concurrent use of a strong CYP3A4 inhibitor (e.g., clarithromycin), a moderate CYP3A4 inhibitor (e.g., fluconazole), a strong CYP2D6 inhibitor (e.g., fluoxetine, paroxetine), or a moderate CYP2D6 inhibitor (e.g., duloxetine); action is reduced by the concurrent use of a strong CYP3A4 inducer (e.g., rifampin, St. John's wort); has not been evaluated in pediatric patients (boxed warning); may cause extrapyramidal and/or withdrawal symptoms in neonates with third trimester exposure.

Most common adverse events:
Weight gain (4%) in patients with schizophrenia; akathisia (9%) and weight gain (7%) in patients with MDD.

Usual dosage:
In the treatment of patients with schizophrenia, the recommended starting dosage is 1 mg once a day on Days 1 through 4; the recommended target dosage is 2 to 4 mg once a day; the dosage should be titrated to 2 mg once a day on Days 5 through 7, then to 4 mg once a day on Day 8; the maximum recommended daily dosage is 4 mg; when used as adjunctive treatment in patients with MDD, the recommended starting dosage is 0.5 mg or 1 mg once a day; at weekly intervals the dosage should be titrated to 1 mg once a day, and then to the target dosage of 2 mg once a day;the maximum recommended daily dosage is 3 mg; the product labeling should be consulted for the recommended dosage adjustments in patient with hepatic or renal impairment, in patients also being treated with potentially interacting medications, and in CYP2D6 poor metabolizers.

Products:
Tablets – 0.25 mg, 0.5 mg, 1 mg, 2 mg, 3 mg, 4 mg.

Comments:
Brexpiprazole is an atypical antipsychotic agent with properties and uses that are most similar to those of aripiprazole. It is thought to have partial agonist activity at serotonin 5-HT1A and dopamine D2 receptors, and antagonist activity at serotonin 5-HT2A receptors. It has been demonstrated to be more effective than placebo in reducing the occurrence of symptoms of schizophrenia, and in reducing symptoms of depression.

Daniel A. Hussar

Specific recommendations

There are medications for which the need for use is urgent and I strongly recommend that the FDA take action to designate the following medications to be available without a prescription from a pharmacist:

- Naloxone for opioid overdosage
- Epinephrine auto-injectors for severe allergic reactions
- Albuterol for oral inhalation for acute asthma attacks
- Nitroglycerin for sublingual use for symptoms of a heart attack

The epidemic of abuse of opioids (narcotics) and the tragedies of deaths from overdosage warrant the most timely availability of naloxone. Naloxone is a life-saving intervention that reverses the action of opioids, but it must be administered as soon as possible following overdosage. In Pennsylvania, police revived 289 people who experienced opioid overdosage within less than a year following approval for the police to carry naloxone. On a state-by-state basis police, first responders, school authorities, and/or pharmacists are being provided the authority to use and/or provide naloxone without a prescription. However, this is a grossly inefficient waste of time, effort, and resources for states to address this matter on an individual basis. The FDA must take urgent action to designate naloxone as a medication that may be obtained without a prescription from a pharmacist, and this will markedly increase the accessibility of this antidote that must be administered on an urgent basis. This national policy will avoid the need for states to consider and take action on an individual basis, and can be extended to provide the authority for individuals such as police and first responders to carry the medication for emergency use.

Other emergencies such as severe allergic reactions, acute asthma attacks, and heart attacks warrant timely availability of epinephrine, albuterol, and nitroglycerin, respectively. These agents must also be available without a prescription from a pharmacist. In these situations, as well as opioid overdosage, individuals may die if the medication that rapidly resolves acute symptoms or overdosage is not quickly administered. The legal barrier that prevents a pharmacist from providing these medications without a prescription must be removed.

There is another situation that mandates rapid action to address the most important public health challenge in the United States – the consequences of smoking cigarettes. Although nicotine gum, lozenges, and transdermal patches are available without a prescription, products like nicotine nasal spray, nicotine inhalation system, and varenicline (Chantix) require a prescription. In my opinion, Chantix is more effective than any other medication/product in helping individuals stop smoking. It is ludicrous that cigarettes with their toxins can be purchased by only providing proof of age while there are restrictions on the availability (i.e., need for a prescription) of products that will help people stop smoking. Some will respond that there are risks associated with the use of Chantix but I contend that pharmacists are prepared to keep the risks at a minimum. Let's consider the following questions:

> How many Americans will die in 2015 from medical problems in which smoking cigarettes is a contributing factor? The answer is **MORE THAN 440,000**.
>
> How many Americans will die in 2015 from medical problems resulting from the use of Chantix? The answer is **NONE!**

This comparison certainly has limitations but it also provides an important message.

Naloxone, epinephrine, albuterol, nitroglycerin, varenicline, nicotine nasal spray, and nicotine inhalation system must be available without a prescription from a pharmacist! Action to make these changes is long overdue to the peril of many.

Daniel A. Hussar

Author/Editor - Daniel A. Hussar, Ph.D.
Philadelphia College of Pharmacy, University of the Sciences in Philadelphia
Publisher - G. Patrick Polli III
Publications Director - Jeff Zajac

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The Pharmacist Activist, 15 Shoemaker Rd., King of Prussia, PA 19406
610-337-1050 • Fax: 610-337-1049
E-mail: pharmacistactivist@news-line.com

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