The Pharmacist Activist

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Editorial

Nicotine, Cigarettes, JUUL, Chantix, FDA Talk, Chain Pharmacy Hypocrisy, and Boards of Pharmacy Inertia

As with opioids, alcohol, and other addictive chemicals/drugs, it is extremely difficult for an individual to stop using nicotine-containing products without a combination of a strong personal commitment to do so, effective interventions, and a support system to help avoid relapses.

Cigarettes are the most commonly used nicotine-containing product, and it is estimated that approximately 480,000 Americans die each year as a consequence of diseases (e.g., cancers, cardiovascular disease, pulmonary disease) in which long-term use of cigarettes and other tobacco products is a causative factor. Although it is the toxins in tobacco and cigarette/cigar smoke that are the components directly implicated in associated diseases and deaths, nicotine is the addictive component that results in continued and long-term smoking of tobacco products, and the great difficulty in attempting to discontinue their use.

Products such as nicotine replacement therapies (NRTs) that include nicotine have been approved by the Food and Drug Administration to help individuals stop smoking. NRTs are available in five delivery systems that include gum, lozenges, transdermal patches, nasal spray, and oral inhalation system. Nicotine gum, lozenges, and transdermal patches are available without a prescription, whereas nicotine nasal spray and oral inhalation system require a prescription. The goals of use of NRTs are to avoid/reduce withdrawal symptoms and cravings as an individual discontinues smoking, and to gradually reduce the dosage of the NRT with the resultant discontinuation of its use. However, the reality of this experience for many is that the continuing addiction to nicotine results in the use of the NRT for years/decades. Nevertheless, the continued use of a NRT is far safer than continuing to smoke cigarettes.

Newer nicotine-containing devices/delivery systems

E-cigarettes and other nicotine-containing device/delivery systems have experienced rapid growth in the marketplace. The most popular product of this type is JUUL, a closed system vapor product not designed to be refillable, that is rechargeable via a USB port. JUUL uses changeable JUULpod cartridges that contain a salt-based nicotine e-liquid and a heating mechanism that creates an aerosol. JUULpods are supplied in different flavors and each JUULpod has a nicotine content approximately equivalent to that in one pack of cigarettes.

JUUL Labs states that it "is on a mission to improve the lives of the world's one billion adult smokers by eliminating cigarettes." The advertising for the product includes a bold warning: "This product contains nicotine. Nicotine is an addictive chemical." It also states: "JUUL is for adult smokers. If you don't smoke or vape, don't start." The company can validly claim that it is helping adults stop smoking cigarettes, and that its statements include clear warnings and the message that its products are "not for youth or non-smokers." The actual use of JUUL and related products, however, is very different from their stated purpose and limitations.

A story in the October 26 edition of *The Wall Street Journal* ("Altria Trims E-Cigarette Line" by Jennifer Maloney; page B1) includes the following observations:

> "After years of declining U.S. smoking rates, sales of e-cigarettes have jumped in the past year, fueled in part by online startups selling vaporizers and nicotine-laced liquids.
>
> The number of high-school students who used e-cigarettes in the past 30 days has risen roughly 75% since last year, according to preliminary federal data. That would equate to about three million or about 20% of high-school students. Meanwhile, use among middle-schoolers has increased nearly 50%.
>
> Nearly a third of 13-to-18-year-olds who responded to a survey conducted in May by The Wall Street Journal with research firm Mercury Analytics said they currently vape. Most of the teens who vape said they are doing it for reasons other than to quit smoking, according to the Journal's study conducted in 49 states. More than half said they do it because they like the flavors that e-cigarette liquids come in and they think vaping is fun."

The inescapable conclusion is that many thousands of teenagers, many of whom may not have even smoked one cigarette, are now addicted to nicotine. These products are nicotine delivery systems, as is the nicotine oral inhalation system (Nicotrol). However, the latter product requires a prescription. Why have JUUL and related products been allowed to escape regulation? Why do they not require a prescription?

Chantix

Varenicline (Chantix) is the most effective smoking cessation intervention. By selectively binding at certain nicotinic receptors, it stimulates activity at these receptors while simultaneously preventing the binding of nicotine to these receptors. Varenicline has important advantages over NRTs because it is not addicting, and successful use results not only in discontinuation of smoking cigarettes, but also in discontinuation of the medication. However, the availability and use of varenicline is significantly restricted, notwithstanding Pfizer's extensive direct-to-consumer advertising, because it requires a prescription.

Although some questions have been raised regarding the safety of varenicline, the vast majority of individuals tolerate it well. However, there is no question that varenicline is much safer than continuing to smoke cigarettes, the purchase of which only requires proof of age. It is ludicrous that cigarettes and their toxins are so readily available while there are barriers to the access to the most effective intervention. Some have urged that varenicline be made available without a prescription from pharmacists (please see my letter to then FDA Commissioner Califf, "The FDA Should Provide Pharmacists with the Authority to Dispense Chantix Without a Prescription," in the April 2016 issue of *The Pharmacist Activist* at www.pharmacistactivist.com). The FDA has taken no action in this direction, but I commend the pharmacy leaders in states such as New Mexico and Idaho for their success in attaining this authority for pharmacists for the benefit of the residents of those states.

As the manufacturer of Chantix, Pfizer has given the highest priority to its own profits which are greater with the higher prices it can charge when the drug is available only on prescription. However, as the expiration of the patent for Chantix approaches and lower-priced generic products are anticipated, there are some indications that Pfizer may decide that it is 1) in its own best interest, and 2) in the best interest of smokers to seek approval of an Rx to OTC switch for Chantix.

The FDA

During the last several years the FDA has approved record numbers of new drugs and generic products, and has issued an unprecedented number of statements and communications to health professionals and consumers, including a news release of October 12, 2018 titled, "FDA advances investigation into whether more than 40 e-cigarette products are being illegally marketed and outside agency's compliance policy." However, with respect to the devastating health consequences of smoking, there has been a lot of talk but little action from FDA.

Why does the FDA restrict the availability of nicotine oral inhalation system to prescription-only status, while at the same time it takes no action on a nicotine delivery system industry enjoying billions of dollars a year in profits at the expense of thousands of teenagers addicted to nicotine?

Why does the FDA refuse to consider the classification of medications in a manner that extends beyond the traditional, but outdated, classification as prescription and nonprescription medications? Why does the FDA not take action to reclassify certain prescription medications such as smoking cessation products and medications that are needed on an urgent basis (e.g., epinephrine injection) to permit availability without a prescription from pharmacists who are prepared to assess and assure the appropriate, effective and safe use of these medications?

Chain pharmacy hypocrisy

A large majority of independent pharmacies have either never sold, or have discontinued the sale of tobacco products. Some chain/supermarket pharmacies such as CVS, Target, and Wegmans have discontinued the sale of these products. However, executives of many chain pharmacies continue their hypocrisy in wanting to be viewed as having a commitment to health care

(Continued on Page 4)

New Drug Review

Baloxavir marboxil
(Xofluza – Genentech; Shionogi)

Antiviral Agent

New Drug Comparison Rating (NDCR) = 4
(significant advantages)
in a scale of 1 to 5 with 5 being the highest rating

Indication:
Treatment of acute uncomplicated influenza in patients 12 years of age and older who have been symptomatic for no more than 48 hours.

Comparable drug:
Oseltamivir (e.g., Tamiflu).

Advantages:
- Is a single-dose treatment (whereas oseltamivir is usually administered twice a day for 5 days);
- Has a unique mechanism of action (is a polymerase acidic endonuclease inhibitor);
- May be effective in some patients with influenza that is resistant to oseltamivir;
- Use has not been associated with neuropsychiatric adverse events;
- Dosage adjustment is not necessary in patients with renal impairment.

Disadvantages:
- Effectiveness and safety have not been evaluated in patients less than 12 years of age (whereas oseltamivir is indicated for the treatment of patients 2 weeks of age and older);
- May be less effective against influenza B viruses;
- Has not been evaluated for the prophylaxis of influenza (whereas oseltamivir is indicated for the treatment and prophylaxis of influenza);
- Absorption and activity may be reduced by coadministration with polyvalent cation-containing products.

Most important risks/adverse events:
Bacterial infection (may coexist with or occur as a complication of influenza); absorption and activity may be reduced by polyvalent cation-containing products (e.g., antacids), and coadministration should be avoided; may decrease the effectiveness of intranasal live attenuated influenza vaccine.

Most common adverse events:
Diarrhea (3%), bronchitis (2%).

Usual dosage:
For patients weighing 40 kg to less than 80 kg – single dose of 40 mg; for patients weighing at least 80 kg – single dose of 80 mg.

Products:
Film-coated tablets – 20 mg, 40 mg; supplied in blister card packaging.

Comments:
Baloxavir marboxil is a prodrug that is almost completely converted by hydrolysis to its active metabolite, baloxavir, that exerts activity against influenza A and influenza B viruses. Baloxavir inhibits the endonuclease activity of the polymerase acidic protein, an influenza virus-specific enzyme in the viral RNA polymerase complex required for viral gene transcription, resulting in inhibition of influenza virus replication. Oseltamavir and related agents act by inhibiting influenza neuraminidase.

The effectiveness of baloxavir was evaluated in two clinical studies in which the primary endpoint was the time to alleviation of symptoms, defined as the time when all seven symptoms (cough, sore throat, nasal congestion, headache, feverishness, myalgia, and fatigue) had been assessed by the patient as none or mild for a duration of at least 21.5 hours. The first study was conducted in 400 adult patients and was placebo-controlled. The median time to alleviation of symptoms in patients treated with a single dose of 40 mg of baloxavir was 50 hours, compared with a median time of 78 hours in those receiving placebo. The second study was an active- and placebo-controlled trial in 1,436 adult and adolescent patients. The median time to alleviation of symptoms in patients treated with a single dose of 40 mg or 80 mg of baloxavir was 54 hours, compared with a median time of 80 hours in those receiving placebo. The second study included a group of patients who were treated with oseltamivir (twice a day for 5 days). There was no difference in the median time to alleviation of symptoms (i.e., 54 hours) between patients who received a single dose of baloxavir and those who received oseltamivir. The infections of most patients in the clinical studies were caused by influenza A viruses. The subset of patients with influenza B infections in the first study had a shorter median time to alleviation of symptoms than those in the placebo group, but in the subset of patients in the second study with influenza B infections, the median time to alleviation of symptoms was longer in those receiving baloxavir than in those receiving placebo.

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at the same time they place their customers at risk by the sale of tobacco products. On numerous occasions, I have attempted to personally meet or have a telephone discussion with the CEOs of Rite Aid, Walgreens, and Walmart to discuss their sale of tobacco products. I have not been successful even once in reaching these individuals, and the discussions with individuals in these companies who have been tasked with defending these sales have been exercises in futility.

In a recent interview, the CEO of Walgreens Boots Alliance stated that Walgreens wants to be seen as a health-care company, not just a retailer. When asked about the steps taken by CVS in this direction, he responded," I don't say [ours] is the better strategy. I don't have the arrogance to criticize what our competitors are doing – we are a true health-care company." NO! Walgreens can't be viewed as having a commitment to health care when it places the health of its customers at risk by selling them cigarettes, and its CEO IS arrogant in trying to disguise this deceptive hypocrisy.

In September Rite Aid distributed a press release about its policy for addressing "chemicals of consumer concern" that are included in some of the products they sell. This follows an earlier initiative of Walmart and some other companies that were at least more forthright in referring to these materials as "toxic chemicals" (please see my editorial, "Many Walmart Customers Will Stop Smoking Today! Their Funerals Will be Held Sometime in the Next Three or Four Days," in the March 2017 issue of *The Pharmacist Activist*). The priorities of these companies are grossly misdirected. I am not aware of even one death associated with the use of a consumer product containing one of these chemicals, but these companies voicing this concern. without any consideration of their sale of tobacco products that are causative factors in hundreds of thousands of deaths each year, destroys their credibility.

This hypocrisy must be exposed and consumers should be encouraged to use pharmacies that have a commitment to their health care, and that do not sell tobacco products.

Boards of pharmacy inertia

The most important responsibility of boards of pharmacy is to protect the health and interests of the public with respect to the practices and operations of the pharmacists and facilities for which it issues licenses. The sale of cigarettes and the resultant harm to the purchasers severely compromise the fulfillment of that responsibility. State boards of pharmacy should not issue new licenses or renew current licenses for pharmacies or stores that include pharmacies that sell tobacco products. Board of pharmacy members who are employed in pharmacies that sell tobacco products should not participate in these decisions.

Governments of large cities such as San Francisco and Boston and numerous smaller communities have recognized the importance of preventing the sale of tobacco products in pharmacies. Boards of pharmacy and the National Association of Boards of Pharmacy must not consider inaction or any lesser action to be acceptable.

Recommendations

1. The FDA should take action at the earliest possible time to establish a class of medications that are available without a prescription from a pharmacist.

2. The FDA should designate nicotine oral inhalation system, nicotine nasal spray, and varenicline as products that may be dispensed without a prescription from a pharmacist.

3. The FDA should require that JUUL and other nicotine-containing products/delivery systems only be available in pharmacies from a pharmacist to adults who smoke cigarettes.

4. Executives of chain pharmacies, supermarkets, and other stores that include pharmacies and sell tobacco products should discontinue the sale of these products.

5. Boards of pharmacy should not issue new licenses or renew current licenses to pharmacies or stores that include pharmacies that sell tobacco products.

Fifty years ago, Pharmacist Fred Mayer of California started the Great American Smokeout. Observed on the third Thursday in November, the date for this year is November 15. Our patients and our communities deserve and need the health protection and services we are in a position to provide. Let's not waste any more time!

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