The Pharmacist Activist

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"Enter into His gates with thanksgiving and into His courts with praise! Give thanks to Him and bless his name!" Psalm 100:4

Editorial

CIGARETTES AND VAPING PRODUCTS - MUCH SMOKE AND RHETORIC, BUT NO ACTION

With each additional report of vaping-related lung injuries and deaths, the media seems compelled to report the event with a background video showing a vaper in a cloud of smoke. The smoke obscures the identity of the vaper, but apparently also spreads a contagious fog that prevents those with the authority and responsibility to address these concerns from experiencing the clarity of thinking necessary to take decisive actions.

As of November 13, 2019, the Centers for Disease Control and Prevention (CDC) have received reports of 2,172 cases of e-cigarette, or vaping, product use associated lung injury (EVALI) and 42 confirmed deaths. The vaping products implicated in causing EVALI contain tetrahydrocannabinol (THC) and/or nicotine. The specific cause(s) of EVALI have not been conclusively determined, but there is a strong focus of attention on vitamin E acetate that was identified in all of the fluid samples collected from the lungs of 29 patients who experienced EVALI. Vitamin E acetate is an oily material that does not cause harm when used orally in supplement products or when applied to the skin. However, if it is included as an additive (e.g., as a thickening agent) in certain vaping products that work by heating a liquid to produce an aerosol that is inhaled into the lungs, it may congeal as it cools and cause injury to lung tissues that are not able to metabolize or eliminate the oily material. The potential risks of other ingredients, and the vaping process itself, are also being investigated.

The CDC and other agencies have provided helpful information and warnings about the use of vaping products, and some have called for a ban on the sale of vaping products, or at least flavored vaping products. However, no substantive actions have been taken.

FDA hearing

Prior to the awareness of vaping-related lung injuries and deaths that have been so frequently reported in recent months, the Food and Drug Administration (FDA) and many others already had strong concerns regarding the extent to which young people were using and becoming addicted to nicotine as a consequence of using electronic cigarettes/vaping products. The FDA convened a public hearing on January 19, 2019 to address the topic, "FDA's Eliminating Youth Electronic Cigarette and Other Tobacco Product Use: The Role for Drug Therapies." Based on my long-standing advocacy for smoking prevention and cessation initiatives, I requested the opportunity to participate in the hearing.

The following are excerpts from my comments at the FDA hearing:

> Nicotine replacement therapies (NRTs) that include nicotine have been approved by the FDA to help individuals stop smoking. NRTs are available in five

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delivery systems (gum, patch, lozenge, nasal spray, oral inhalation system) that have been thoroughly studied by pharmaceutical companies, and subsequently approved by the FDA in a comprehensive review process.

Nicotine is no less of a drug when it is administered in other ways such as electronic nicotine delivery systems (ENDS), such as Juul and related products. Like the NRTs, Juul and related products are nicotine delivery systems. However, unlike the NRTs, these products have been permitted to escape regulation! Why has the FDA not exercised its authority with respect to the marketing of these products that it has insisted on with respect to the approval and marketing of the NRTs? Why has the FDA not required these products to be available only on prescription in the same manner in which it has restricted the availability of nicotine nasal spray and nicotine oral inhalation system? Insufficient action with respect to the present situation has resulted in thousands of teenagers, many of whom may have not even smoked one cigarette, now being addicted to nicotine!

Under current regulations and policies, I contend that the FDA has no other option but to rule that Juul and other nicotine delivery systems (with the exception of the gum, lozenges, and patches that are OTC) will only be available on prescription!

My testimony at the hearing included strategies for addressing the existing concerns which are included among my recommendations later in this editorial. I attended the entire hearing and learned from the information and perspectives provided by other participants. However, the most compelling testimony was provided by two teenagers who described their personal experiences in dealing with their addiction to nicotine as a consequence of using electronic cigarettes, and the prevalence of use of these products by their peers.

The hearing was in January, it is now November, and the FDA response has consisted only of more statements and warnings. The numerous vaping-related lung illnesses and deaths that have been reported even more recently make the need for substantive *actions* even more urgent!

Some pharmacy responses

Many pharmacies never sold tobacco products, and many others have discontinued doing so. They are to be commended for their recognition of the health risks of these products. However, Rite Aid, Walgreens and Walmart continue to be among the largest retailers of tobacco products. These three companies now require customers to be at least 21 years of age to purchase tobacco products and have stopped the sale of electronic cigarettes, although the implementation of the Walmart action is "after selling its existing inventory." However, these companies *still* sell tobacco products! The CEO of Walgreens defends that position by stating, "The safety of our patients is very important, but we also have to do what our customers are requiring us to do." The greedy, disingenuous hypocrisy of the executives of Rite Aid, Walgreens, and Walmart must be exposed and rejected!

On February 5, 2014, CVS announced that it would stop selling cigarettes and other tobacco products in its stores by October 1, 2014. I was among the first to commend CVS for this important decision (please see my editorial, "Commendation for CVS!" in the February 2014 issue at www.pharmacistactivist.com). This was a great decision with near-unanimous support (the tobacco companies being the exception) for the CVS declaration that the decision "…is the right thing for us to do…"

CVS should have been satisfied to receive the extensive accolades of so many others for this decision. However, its hubris in its self-congratulatory press release and advertisements to celebrate the 5th anniversary of this decision is almost enough to induce the medical entity with the same acronym – cyclic vomiting syndrome. CVS claims credit for its "bold move" and reduced cigarette smoking, and brags that it is the only national pharmacy to have made this decision and that it "…is also bringing its smoking cessation *expertise* (my emphasis) to areas across its businesses..." Given the importance that CVS claims for its decision, the question must be asked – "Why did it take more than 50 years for CVS to discover 'the right thing to do?'" – particularly when it was urged by many to make that decision at a much earlier time.

CVS has committed millions of dollars to organizations and initiatives for the purpose of preventing/reducing smoking and vaping. (This financial commitment should not be viewed as reparations for survivors of its former customers who died as the result of smoking-related complications from products purchased at CVS.) In its press release of September 3, 2019, CVS notes that its CEO "…wrote to State Governors asking those leaders to discourage the sale of harmful tobacco products in pharmacies…"

I wish to be clear that I highly support and commend the CVS decision to discontinue the sale of tobacco products and its provision of financial support for programs to reduce smoking and vaping. However, its self-serving promotion and claims

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New Drug Review

Omadacycline tosylate
(Nuzyra – Paratek)

Antibacterial Agent

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

Indications:
Administered intravenously or orally for the treatment of adults with community-acquired bacterial pneumonia (CABP) caused by the following susceptible microorganisms: *Streptococcus pneumoniae, Staphylococcus aureus* (methicillin-susceptible isolates), *Haemophilus influenzae, Haemophilus parainfluenzae, Klebsiella pneumoniae, Legionella pneumophila, Mycoplasma pneumoniae*, and *Chlamydophila pneumoniae*; is also indicated for the treatment of adults with acute bacterial skin and skin-structure infections (ABSSSI) caused by the following susceptible microorganisms: *Staphylococcus aureus* (methicillin-susceptible and –resistant isolates), *Staphylococcus lugdunensis, Streptococcus pyogenes, Streptococcus anginosus* group (includes *S. anginosus, S. intermedius*, and *S. constellatus*), *Enterococcus faecalis, Enterobacter cloacae*, and *Klebsiella pneumoniae.*

Comparable drug:
Tigecycline.

Advantages:
- Labeled indications include a larger number of susceptible bacteria;
- May be effective in some patients whose infections are resistant to other agents;
- Is available for both intravenous and oral use (whereas tigecycline is only administered intravenously);
- Labeling does not include a boxed warning regarding all-cause mortality.

Disadvantages:
- Labeled indications are more limited (tigecycline is also indicated for the treatment of complicated intra-abdominal infections).

Most important risks/adverse events:
Contraindicated in patients with a known hypersensitivity to any of the tetracyclines; may cause adverse developmental effects if used during pregnancy; may cause permanent discoloration of the teeth, and inhibit bone growth, if it is used during the second and third trimesters of pregnancy, infancy, childhood up to the age of 8 years, and in nursing mothers; photosensitivity; Clostridium difficile-associated diarrhea; mortality imbalance in patients with CABP; may depress plasma prothrombin activity and, in patients being treated with an anticoagulant, it may be necessary to reduce the dosage of the anticoagulant; activity may be reduced by multivalent cation-containing products (e.g., aluminum, magnesium, calcium, iron; should not be administered intravenously with any solution containing cations such as calcium and magnesium through the same intravenous line; when omadacycline is administered orally, cation-containing products should not be taken for 4 hours).

Most common adverse events:
In patients with CABP: hypertension (3%), insomnia (3%), increased ALT (4%), increased gamma-glutamyl transferase (3%); in patients with ABSSSI: nausea (22%), vomiting (11%), infusion site reactions (5%), headache (3%), diarrhea (3%), increased ALT (4%), increased AST (4%)

Usual dosage:
Exposure is similar between a 300-mg oral dose and a 100-mg intravenous dose; patients should fast for at least 4 hours prior to oral administration, and the dose should be taken with water; following oral administration, no food or beverage (except water) should be consumed for at least 2 hours; in patients with either CABP or ABSSSI, the dosage on Day 1 is 200 mg by intravenous infusion over 60 minutes or 100 mg by intravenous infusion over 30 minutes twice during Day1; maintenance dosage is 100 mg by intravenous infusion over 30 minutes once a day, or 300 mg orally once a day; an alternative oral regimen for patients with ABSSSI is a loading dose of 450 mg once a day on Days 1 and 2, followed by a maintenance dosage of 300 mg once a day; treatment is continued for 7-14 days.

Products:
Capsules – 150 mg; single-dose vials – 100 mg - lyophilized powder to be reconstituted and then diluted.

Comments:
Omadacycline is an aminomethyltetracycline with activity against certain bacteria that have mechanisms to resist the action of most other tetracyclines. In patients with CABP, it was noninferior to moxifloxacin, with clinical response rates of 88% and 85%, respectively. In two studies in patients with ABSSSI, it was noninferior to linezolid, with clinical response rates for both agents in each study between 81% and 86%.

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are inappropriate, and its hypocrisy in claiming a commitment to improve the health of its customers continues to be exposed through the understaffing and working conditions in its pharmacies, as well as the terms and conditions of its prescription benefit plans that are a disservice and compromise the quality of care and services for patients.

Other responses

Dr. Scott Gottlieb was the Commissioner of the FDA until he left that position earlier this year. During his service as Commissioner he voiced strong concerns about the health risks of electronic cigarettes and, most recently, has called for a ban on pod-based electronic cigarettes such as those sold by companies like Juul. His concerns and his passion in communicating them are highly commendable, but it is very unfortunate that he did not take stronger actions to address these concerns when he had the authority to do so as FDA Commissioner. Even before the awareness of vaping-related lung injuries and deaths, could any issues that the FDA must address be more important than smoking and its complications that are factors in the deaths of approximately 480,000 Americans each year, and addictions and illnesses in many thousands of others? Is it possible that the bureaucracy and politics within which the FDA functions prevent it from taking actions that will save lives?

Recommendations

The following recommendations are provided for reducing the use and risks of tobacco, vaping, and related products:

1. The minimum age for purchasing tobacco and related products should be increased to 21 years in all states.
2. State Boards of Pharmacy should not issue licenses to new pharmacies that sell tobacco products or that are in facilities that sell tobacco products, or renew the licenses of existing pharmacies that sell tobacco products.
3. Nicotine nasal spray, nicotine oral inhalation system, and varenicline (Chantix) should be designated as products that may be provided by pharmacists without a prescription. The continued restricted availability of these products with little risk is an unjustifiable barrier to greater access that will result in reduced use of tobacco products with great risk.
4. Electronic cigarettes and other nicotine delivery systems should be regulated in the same manner by the FDA in which the NRT products currently available have been regulated. A 2-year "grace period" should be provided in which electronic/vaping nicotine delivery systems that are currently on the market may continue to be available, but only through pharmacies as noted in #5 below, while appropriate studies are being conducted and FDA approval is requested.
5. Currently marketed electronic/vaping nicotine delivery system products should only be available to adults in pharmacies without a prescription from a pharmacist. This would permit confirmation by a health professional of the appropriate use of the product to help the purchaser stop smoking cigarettes. Flavored products that smokers have found to be helpful in discontinuing smoking cigarettes could continue to be available through this distribution system.
6. The greedy hypocrisy of the executives of Rite Aid, Walgreens, and Walmart in wanting consumers to view their stores as health centers while they are also selling harmful tobacco products must be exposed and rejected. Consumers should be urged to use other pharmacies that do not sell tobacco products!

Heroes

Fred Mayer, Robin Corelli, Karen Hudmon, and the late Linwood Tice have been pharmacist heroes in their exceptional advocacy for smoking cessation programs and initiatives. Fred Mayer initiated the Great American Smokeout more than 50 years ago, which is observed on the third Thursday of November (November 21 this year). On November 4 at the annual meeting of the American Public Health Association, Fred was honored by the Pharmacy Section with its Lifetime Achievement Award. Congratulations to Fred who, at 87 years young, continues his passionate advocacy for public health and pharmacy services that will benefit consumers!

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