The Pharmacist Activist

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Editorial

Editor's note: The following testimony was presented by the editor at an FDA public hearing on March 26, 2014.

Over-The-Counter Drug Monograph System – PAST, PRESENT AND FUTURE

Food and Drug Administration Public Hearing | March 26, 2014

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I commend the Food and Drug Administration (FDA) for convening this hearing to receive comments and opinions on a topic that I believe represents an important opportunity to improve the effectiveness and safety of medications for millions of individuals. The perspectives and recommendations I am providing are based on my responsibilities as a pharmacist and faculty member at the Philadelphia College of Pharmacy that include teaching our required Nonprescription Therapeutics course, having taught every other area of drug therapy, and having written and spoken about every new drug marketed in the United States in the last 40 years.

I commend the FDA for its recent approval of over-the-counter (OTC) availability of the oxybutynin transdermal system for overactive bladder (Oxytrol for women) and triamcinolone acetonide nasal spray for allergic rhinitis (Nasacort Allergy 24HR). The extended availability of these products increases the opportunity for consumers to increase their responsibilities for their own health care.

Also noteworthy is the FDA's approval last year to permit companies that market OTC nicotine replacement therapy (NRT) products to revise the labeling for these products to reflect the safety of using more than one OTC NRT at the same time, or using an OTC NRT at the same time as another nicotine-containing product—including a cigarette. I applaud this action—BUT—there has been enough known about the properties and use of these products to have permitted this action to have been taken 20 years ago. The following example illustrates how the previous excessively-restrictive labeling/warnings have actually worked against the optimum use of these products. The labeling for the OTC NRT products included a statement that individuals should not use a second NRT product concurrently. However, this statement may preclude what I would contend is the best strategy in using NRT products—using the transdermal patch to provide a sustained low concentration of nicotine, and the lozenge or gum to provide a prompt, but brief, action when cravings to smoke are experienced.

Pharmacists have the knowledge and ready accessibility to assume an increased role in the provision of medications, as well as pertinent information and recommendations regarding their use. In my opinion, there are numerous medications that currently require a prescription that can be provided without a prescription upon consultation with a pharmacist in a manner that will assure effective and safe use. The following are examples:

SELECTED MEDICATIONS THAT SHOULD BE CONSIDERED FOR AVAILABILITY WITHOUT A PRESCRIPTION FROM A PHARMACIST

Varenicline (Chantix)

Varenicline is more effective than any other medication/product in helping individuals stop smoking. However, for a variety of reasons, many individuals who smoke will not make an appointment to see a physician and, as a consequence, do not have access to this medication. A paradox is perpetuated in which the toxin (cigarettes) is readily available requiring only proof of age to purchase, whereas the availability of the potential cure is restricted.

When I have made this recommendation that varenicline should be available without a prescription from a pharmacist, the almost immediate response of some is that the FDA will never approve availability without a prescription of a medication that includes a boxed warning in the labeling for the prescription product. However, such situations already exist, and with the most widely used of all therapeutic agents—acetaminophen. For example, the prescription product Vicodin contains a combination of hydrocodone and acetaminophen, and its labeling/package insert includes a boxed warning. The boxed warning does not address a risk with hydrocodone, but rather a risk of hepatotoxicity with acetaminophen.

More than 480,000 Americans die each year as a consequence of complications from smoking-related illnesses. The most effective medication to help people stop smoking must no longer be excessively restricted in its availability. I urge the FDA to take prompt action to approve its availability from a pharmacist!

Oseltamivir (Tamiflu)

Oseltamivir is one of a very small number of medications that is effective for the treatment of influenza. However, for this drug to be optimally effective, it is very important that treatment be initiated as soon as possible following the onset of symptoms (within 2 days). Patients who experience influenza symptoms should be provided the fastest access possible to medication that can be of significant benefit. Pharmacists can make the distinction between the symptoms of influenza and the symptoms of the common cold and other respiratory conditions, and identify the patients for whom the use of oseltamivir is appropriate.

Epinephrine auto-injectors for severe allergic reactions

Severe allergic reactions require emergency treatment. Even patients who have previously used an epinephrine auto-injector may not have one readily available when they experience an acute, severe allergic reaction. A pharmacist may be more quickly accessible than a physician or hospital when such emergencies occur, and pharmacists should have the authority to provide this product without a prescription.

Naloxone for narcotic overdosage

The acute overdosage of a narcotic is a life-threatening event. Naloxone is a specific antidote that acts rapidly and there have been initiatives to increase its availability to paramedics, police officers, and others for emergency use. Pharmacists should also have the authority to provide this product without a delay to receive a prescription.

THE NAME GAMES

Many OTC products have trade names that are well known to consumers. When companies that make certain of these products develop new products—even for different symptoms and uses—they sometimes use the same trade name because of the name recognition and popularity of the product already on the market. Thus, situations exist in which the same trade name is used for products with different active ingredients and uses. This can result in situations in which consumers unknowingly use a product that contains

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New Drug Review

Dolutegravir sodium
(Tivicay – GlaxoSmithKline; ViiV)

Antiviral Agent

New Drug Comparison Rating (NDCR) = 3

(no or minor advantages/ disadvantages) in a scale of 1 to 5 with 5 being the highest rating

Indication:
In combination with other antiretroviral agents for the treatment of HIV-1 infection in adults and children aged 12 years and older and weighing at least 40 kg.

Comparable drug:
Raltegravir (Isentress).

Advantages:
- Is administered once a day in most patients (whereas raltegravir is administered twice a day);
- Effectiveness and safety have been demonstrated in children as young as 12 years of age (raltegravir has subsequently been approved for use in patients 4 weeks of age and older);
- May be less likely to cause severe skin reactions;
- May be less likely to cause musculoskeletal effects.

Disadvantages:
- Poor virologic response has been observed in patients with certain integrase strand transfer inhibitor (INSTI)-resistant substitutions;
- May cause transaminase elevations in patients with hepatitis B or C co-infection;
- Interacts with more medications;
- Should be administered 2 hours before or 6 hours after medications/products containing polyvalent cations.

Most important risks/adverse events:
Increases the action of dofetilide and concurrent use is contraindicated; hypersensitivity reactions; transaminase elevations in patients with hepatitis B or C co-infection (patients should be monitored for hepatotoxicity); fat redistribution; immune reconstitution syndrome; breastfeeding is not recommended because of the potential for HIV transmission; action may be reduced by enzyme inducers (e.g., certain antiretroviral agents, rifampin, carbamazepine, St. John's wort); action is reduced by polyvalent cation-containing medications/products, and should be administered 2 hours before or 6 hours after such products.

Most common adverse events
(of at least moderate intensity – grades 2 to 4):
Insomnia (3%), headache (2%).

Usual dosage:
50 mg once a day in treatment-naïve or treatment-experienced INSTI-naïve patients; 50 mg twice a day in treatment-naïve or treatment-experienced INSTI-naïve patients when coadministered with the potent UGT1A/CYP3A inducers efavirenz, fosamprenavir/ritonavir, tipranavir/ritonavir, or rifampin; 50 mg twice a day in INSTI-experienced patients with certain INSTI-associated resistance substitutions or clinically suspected INSTI resistance.

Product:
Tablets – 50 mg.

Comments:
Dolutegravir is the third HIV-1 integrase strand transfer inhibitor (INSTI), joining raltegravir and elvitegravir (included with cobicistat, emtricitabine, and tenofovir in the combination product Stribild). It is used in combination with other antiretroviral agents and its effectiveness in clinical studies was considered similar to or slightly greater than that of raltegravir. However, poor virologic response was observed in patients treated with dolutegravir (50 mg twice a day) with an INSTI-resistance Q148 substitution plus 2 or more additional INSTI-resistant substitutions.

Dolutegravir inhibits the renal organic cation transporter, OCT2, and increases plasma concentrations of dofetilide and metformin that are eliminated via OCT2. The concurrent use of dofetilide is contraindicated and it may be necessary to adjust the dosage of metformin. Dolutegravir is primarily metabolized via UGT1A1 with some contribution from CYP3A. Other drugs that induce these metabolic pathways (e.g., efavirenz, rifampin) may decrease the plasma concentration and action of dolutegravir, necessitating an increase in dosage. Products containing polyvalent cations (e.g., antacids, laxatives, iron supplements, calcium supplements) may reduce the absorption of dolutegravir and the new drug should be administered 2 hours before or 6 hours after these products.

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an ingredient that might put them at risk, or is used for a condition that is different than what they are experiencing.

A recent example involves the new product Mucinex Allergy. The original Mucinex product contains the expectorant guaifenesin that is used for certain respiratory conditions, and this is the active ingredient that both health professionals and consumers expect a product with the name Mucinex to contain. However, Mucinex Allergy contains the antihistamine fexofenadine, but no guaifenesin. It can be expected that some consumers will use both Mucinex Allergy, and Allegra, the original fexofenadine-containing product, without recognizing they contain the same active ingredient.

The FDA should not permit a company to use a trade name that has a well-established identity with a particular active ingredient for a product that does not contain that active ingredient.

EQUIVALENCY OF ACETAMINOPHEN-CONTAINING PRODUCTS

The FDA has recently requested that companies that market combination products containing an opioid analgesic plus acetaminophen limit the amount of acetaminophen included in a tablet or other dosage unit to no more than 325 mg. The Vicodin formulations containing hydrocodone and acetaminophen are very widely prescribed, and these products have been reformulated to contain 300 mg of acetaminophen. Generic products containing these same two analgesics are available at a much lower price than Vicodin, but they may contain 325 mg of acetaminophen per tablet. This raises a question as to whether a pharmacist has the authority to substitute a much lower-priced combination formulation that includes 325 mg of acetaminophen for prescriptions for Vicodin that contain 300 mg.

The FDA should take the position that there is not a clinically important difference in the analgesic effect of 300 mg and 325 mg quantities of acetaminophen and that products containing quantities of acetaminophen within this range of difference may be considered to be therapeutically equivalent and interchangeable.

HERBAL PRODUCTS AND DIETARY SUPPLEMENTS

The FDA does not have regulatory authority for products such as herbal products, dietary supplements, and other natural products unless therapeutic claims are made for their use. However certain of these agents are recognized to have pharmacologic activity and the potential to interact with medications that do come under the authority of the FDA. For example, St. John's wort is known to increase the action of metabolic pathways that can result in significantly reduced activity of many prescription medications with which it might be used concurrently. Although St. John's wort may be identified as an interacting product in the labeling for prescription medications, there is little or no additional information regarding the properties and use of St. John's wort that carries the authority of the FDA.

I recommend that actions be taken that will provide the FDA with the authority to regulate the herbal products, dietary supplements, and other natural products that have risks that are of sufficient importance to identify them in the labeling of prescription medications.

I recognize that the initial response to certain of my recommendations might be that the FDA does not have the authority to take the action requested. However, even if that is the case, I would hope that my recommendations and supportive rationale are sufficiently persuasive that FDA would contribute to the identification of legislative and other initiatives that would be needed for further attention and action to be taken.

Thank you for your consideration of these recommendations.

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