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What's Inside…

PUBLIC HEALTH ADVISORY

The FDA has issued a public health advisory concerning **Chantix** (varenicline). As reported in December's ***PRN***, the agency has been conducting an ongoing safety review of the smoking cessation product due to post-marketing reports of changes in mood and behavior. That review has resulted in changes to the product labeling and approval of a medication guide. The key points highlighted by the FDA include:

Patients should inform physicians of any prior psychiatric illness

Healthcare professionals, patients and their families, and caregivers should be alert to changes in mood and behavior of patients taking Chantix, such as:

Anxiety, nervousness, tension, depressed mood, unusual behaviors, and thinking about or attempting suicide

Patients should report changes in mood or behavior to their physician

Patients taking Chantix may experience vivid, unusual, or strange dreams

Patients taking Chantix may experience impairment of the ability to drive or operate machinery

……RX NEWS……RX NEWS……RX NEWS……RX NEWS……

Patanase Nasal Spray: Alcon, Inc, maker of olopatadine ophthalmic solutions (**Patanol** and **Pataday**), has been granted approval for **Patanase** (olopatadine) nasal spray. Patanase is indicated for the relief of symptoms of seasonal allergic rhinitis in patients 12 years of age and older. Patanase is a histamine H_1 receptor antagonist and inhibitor of histamine release from mast cells. The recommended dose is two sprays per nostril twice daily. The spray pump should be primed before initial use and after periods of non-use greater than 7 days. The most common adverse effects noted in clinical trials were bitter taste (12.8%), headache (4.4%), and epistaxis (3.2%).[1] Since some subjects experienced somnolence, patients should be cautioned about driving or operating machinery. (*Historical Note:* Alcon, best known for its ophthalmic products, was formed in 1945 by two pharmacists, Robert Alexander and William Conner, who owned a small pharmacy in Fort Worth, Texas. The pair combined the first syllables of their last names to create the company name. Alcon is now majority-owned by Nestle, with headquarters in Switzerland.)

New Migraine Combo: GlaxoSmithKline (GSK) has received FDA approval to market a new combination drug for the treatment of migraine headache. **Treximet** is a fixed-dose regimen of **Imitrex** (sumatriptan) 85 mg and naproxen sodium 500 mg. The recommended dose of Treximet is 1 tablet for acute migraine. A second dose may be administered, separated by at least 2 hours from the initial dose (maximum daily dose is 2 tablets). Treximet may be taken with or without food. Tablets should not be split, crushed, or chewed.[2] Treximet labeling contains **black box** warnings for cardiovascular and GI risks.

Amitiza Approved for IBS: The FDA has approved an additional indication for Sucampo's **Amitiza** (lubiprostone): irritable bowel syndrome with constipation (IBS-C) in women aged 18 and over. Amitiza is a chloride channel activator which increases intestinal fluid secretions. Amitiza was originally approved in 2006 for the treatment of chronic idiopathic constipation in adults, at a dose of 24 mcg BID. For the treatment of IBS-C, the recommended dose is 8 mcg BID. Amitiza should be taken with food and water. In clinical trials for IBS-C, the most common adverse effects were nausea (8%), diarrhea (7%), and abdominal pain (5%).[3] Amitiza is the third drug approved specifically for the treatment of IBS. The two previously approved agents have had troubled histories. **Lotronex** (alosetron), the first IBS drug, indicated for diarrhea-predominant IBS (D-IBS), was withdrawn from the market in November, 2000 due to reports of ischemic colitis leading to hospitalizations and deaths. In June, 2002, Lotronex was re-introduced as a restricted-access drug through the Prescribing Program for Lotronex (go to *www.Lotronex.com* for program details). **Zelnorm** (tegaserod) was introduced in 2002 for treatment of IBS-C, but was withdrawn in 2007 following reports of increased risk of serious cardiovascular adverse events. A restricted-access program for Zelnorm was instituted, but the program was discontinued as of April 2, 2008.

FDA Advises Switch to HFA: In a statement released on May 30, 2008, the FDA advises patients, caregivers, and health care professionals to switch to HFA-propelled albuterol inhalers because CFC-propelled products will no longer be available after December 31, 2008. To help pharmacists prepare their patients for the change, ***PRN*** has prepared an article about the upcoming switch (see pg. 3).

No More ABC's (or D's or X's): FDA Announces Proposal to Change Pregnancy Ratings

The FDA has proposed a new rule that would lead to a major revision in the labeling of prescription drugs as they relate to pregnancy and lactation. For starters, the agency will do away with the familiar letter ratings, A,B,C,D, and X, which have served to categorize drugs ranging from safe to contraindicated. The new labeling would consist of two subsections: Pregnancy (including labor and delivery) and Lactation. Each subsection would contain three principal components: Risk Summary, Clinical Considerations, and Data. For more information, go to *www.fda.gov/cder/regulatory/pregnancy_labeling/default.htm* Comments on the proposed rule may be submitted to *www.regulations.gov* by the deadline of August 27, 2008. To see samples of the proposed Pregnancy and Lactation labels, visit our website at *www.prnnewsletter.com* and click on "This Month's Issue" and then on "FDA Sample Label."

MEDICAID UPDATE

Information Regarding the New York State Medicaid Program

Clinical Drug Review Program

In October, 2006, New York State Medicaid initiated the Clinical Drug Review Program (CDRP). CDRP was designed to ensure that specific drugs be used in a medically appropriate manner. Currently, there are 3 drugs covered by the program:

Revatio (sildenafil): authorized when prescribed by a board certified cardiologist or pulmonologist solely for the treatment of primary pulmonary arterial hypertension

Serostim (somatropin): authorized for a maximum of 28 days with no refills allowed when prescribed for the treatment of HIV patients with wasting or cachexia. A new prior authorization will not be issued unless75% of the original prescription has been used. Continuation beyond 12 weeks requires validating documentation upon request.

Zyvox (linezolid): authorized for 14 days with no refills when prescribed for appropriate infections. If additional Zyvox is needed, the prescriber must write a new prescription and obtain a new prior authorization.

Prescribers

In order to obtain CDRP authorizations, prescribers must call the prior authorization line at 1-877-309-9493 and choose option 1. If approved, a prior authorization number, ending in "W", will be issued and should be written on the prescription.

Pharmacists

Upon receiving a prescription for a CDRP drug, pharmacists must call the prior authorization line at 1-877–309-9493 and choose option 2. The pharmacist will be prompted to enter the prior authorization number (without the "W"), as well as all the pertinent patient and pharmacy ID numbers.

LAW REVIEW

Regulatory Issues Affecting Pharmacy in New York State

Buprenorphine for Treatment of Opioid Dependence

The Federal Drug Addiction Treatment Act of 2000 (DATA 2000), codified in 21 USC 823 (g), provided a waiver for physicians to prescribe Schedule III-V medications for the treatment of opioid dependence outside the context of a hospital or registered methadone clinic. The first drugs approved for this office-based treatment were **Suboxone** (buprenorphine/naloxone) and **Subutex** (buprenorphine). In order to obtain a waiver, physicians must meet one or more of the following qualifications:

- Hold a subspecialty board certification in Addiction Psychiatry or Addiction Medicine
- Hold an addiction certificate from the American Society of Addiction Medicine
- Have completed not less than 8 hours of authorized training on the treatment or management of opioid-dependent patients

In addition, physicians must have the capacity to provide or to refer patients for necessary ancillary services, such as psychosocial therapy, and must agree to treat no more than 30 patients at any one time in their individual or group practice. Physicians qualifying for a waiver will be issued a unique identification number by the Drug Enforcement Agency (DEA). These DATA 2000 identification numbers are similar to DEA numbers, except that the always begin with the letter "X".

Dispensing Prescriptions under DATA 2000

Federal law (21 CFR 1306.05[a]) requires that prescriptions for the treatment of opioid dependence contain both the DEA number *and* the unique identifier, or "X" number, of the prescribing physician. As per New York State law (80.74(g) of Title X), pharmacists may obtain the physicians DEA by phone if it is missing from the prescription. Pharmacists wishing to obtain or verify the physician unique identifier, or "X" number, may:

- Call SAMHSA directly at **866-BUP-CSAT** (866-287-2728)

OR

- Check the Substance Abuse and Mental Health Services (SAMHSA) physician locator at ***www.buprenorphine.samhsa.gov*** (some physicians may choose not to be listed on this site)

If a prescription is issued for an off-label use of Suboxone or Subutex, unrelated to opioid dependence (e.g., treatment of pain), an "X" number is not required. In such cases the pharmacist should verify and document the off-label use.

Confidentiality

When discussing prescriptions for opioid dependence treatment, even with prescribing physicians, it is a violation of Federal regulations (42 CFR Part 2) to disclose any patient-identifying information unless the patient has signed a consent form allowing such disclosures. Obtaining patient consent allows physicians to phone or fax prescriptions to pharmacies, as well as verify patient's prescriptions over the phone. Consent forms are usually filled out in the physician's office during the patient's first visit.

New York State Regulations

In November, 2002, New York State Department of Health regulations on Buprenorphine (Title X, 80.84 and 80.86) took effect. Originally, pharmacies were required to register with the state to be authorized to dispense buprenorphine for the treatment of opioid dependence. The Bureau of Narcotic Enforcement announced in December, 2006 that ***registration is no longer required***.

Feature Article..

Transition from CFC to HFA Albuterol Inhalers: Getting Ready for January, 2009

In response to the Montreal Protocol on Substances that Deplete the Ozone Layer, a 1987 treaty, the FDA has ruled that the sale of single ingredient albuterol inhalers containing chlorofluorocarbons (CFCs) must end on December 31, 2008. Beginning January 1, 2009, pharmacists may only dispense albuterol inhalers using hydrofluoroalkanes (HFAs) as the propellant. To date, four such inhalers have been approved and marketed in the United States (see table below). There are a number of important differences between CFC and HFA inhalers which pharmacists must understand in order to properly counsel their patients as they switch products over the next six months. HFA inhalers have a softer and warmer spray than CFC products, and patients may notice this difference and fear their inhaler is not working. Pharmacists should prepare patients for this difference when counseling them on their new inhalers. HFA inhalers are more likely to clog, due to the chemical nature of the propellant, and therefore the plastic mouthpiece must be washed in warm water at least once a week (see Cleaning Instructions below). Priming the inhaler is more important to proper functioning than with CFC inhalers, and different HFA products vary in their recommendations (see table below). Finally, all HFA albuterol inhalers are rated **BX** by the FDA, and therefore have no generic substitutes, meaning the cost for patients will be higher than with their generic CFC inhalers. All four manufacturers of HFA albuterol inhalers offer patient assistance programs to help those who cannot afford the higher cost. Pharmacists should direct these patients to call the specific program for their inhaler or the Partnership for Prescription Assistance (www.pparx.org or 1-866-4PPA-NOW):

Proventil HFA patients call…….1-800-656-9485
Ventolin HFA patients call……..1-866-475-3678
ProAir HFA patients call……. 1-877-254-1039
Xopenex HFA patients call……. 1-888-878-6266

INSTRUCTIONS FOR WEEKLY CLEANING OF HFA ALBUTEROL INHALERS

1. **Remove the canister and mouthpiece cap from the mouthpiece**
2. **Wash the mouthpiece through the top and bottom with warm running water for at least 30 seconds**
3. **Shake off excess water and allow the mouthpiece to air dry (this can be done overnight, for example)**
4. **If you need to use the inhaler before the mouthpiece is completely dry, shake off excess water, replace the canister, shake well, test spray twice into the air to remove most of the remaining water, and then take dose as prescribed**

PRODUCT (Active Ingredient)	FDA INDICATION	AGE RANGE	WHEN TO PRIME	NUMBER OF SPRAYS TO PRIME	A.W.P.	PRODUCT PHOTO
PROVENTIL HFA (Albuterol Sulfate 90 mcg/spray)	1. Treatment or prevention of bronchospasm in reversible obstructive airway disease 2. Prevention of exercise-induced bronchospasm	Adults & children 4 years of age and older	1. Before initial use 2. When not used for more than 2 weeks	4	$42.20	
VENTOLIN HFA (Albuterol Sulfate 90 mcg/spray)	1. Treatment or prevention of bronchospasm in reversible obstructive airway disease 2. Prevention of exercise-induced bronchospasm	Adults & children 4 years of age and older	1. Before initial use 2. When not used for more than 2 weeks 3. If dropped	4	$36.12	
PROAIR HFA (Albuterol Sulfate 90 mcg/spray)	1. Treatment or prevention of bronchospasm in reversible obstructive airway disease 2. Prevention of exercise-induced bronchospasm	Adults & children 12 years of age and older	1. Before initial use 2. When not used for more than 2 weeks	3	$36.72	
XOPENEX HFA (Levalbuterol Tartrate 45mcg/spray)	Treatment or prevention of bronchospasm in reversible obstructive airway disease	Adults & children 4 years of age and older	1. Before initial use 2. When not used for more than 3 days	4	$52.49	

A.W.P. = Average Wholesale Price. Source: Redbook; May, 2008 Edition

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NATURAL PRODUCTS: RESVERATROL

What would you do if you knew of a substance, naturally occurring and seemingly safe, which promised to lower blood sugar, ward off cancer, and increase both the length and quality of life? Well, if you're the British pharmaceutical giant **GlaxoSmithKline**, you plunk down $740 million dollars in cash to acquire Sirtiris Pharmaceuticals, an American biotech company specializing in the development of synthetic versions of **resveratrol**, a chemical found in the skin of grapes and in red wine.[4] In addition to the claims listed above, resveratrol is also claimed to allow users to enjoy all the pleasures of a high fat diet without facing any of the consequences; some have claimed it to be a partial explanation of the mystery of the "French Paradox," the fact that the French, with a diet rich in fats, suffer less heart disease than Americans. The only problem with all this good news is that it has so far been proven only in studies of mice given doses equivalent to a human drinking 1,000 bottles of red wine a day! Even the CEO of Sirtiris, Dr. Christoph Westphal, has been quoted as saying therapeutic levels of resveratrol cannot be reached in humans.[5] The company hopes to soon be able to start trials of a more potent, synthetic version of the compound. In the meantime, there are a number of natural sources of resveratrol which can be added to one's diet in the hope of obtaining at least a little of the magic promised by the studies: in addition to grapes and red wine, peanuts, peanut butter, blueberries, bilberries, and cranberries contain resveratrol.

DID YOU KNOW?

DID YOU KNOW that the symbol of pharmacy, the Bowl of Hygeia (seen here at right), is based on figures from ancient Greek mythology? Hygeia, the goddess of health, was one of the daughters of Asclepius, god of medicine and healing. Hygeia is usually depicted with a serpent, the symbol of healing and renewal, and a bowl, perhaps containing a medicinal potion. Hygeia is also the source of the word "hygiene," and one of her sisters was Panacea, whose name became the word for a "cure-all." Asclepius is also associated with a well-known emblem, the serpent entwined around a staff, which is the international symbol of medicine.

PHARMACY FUN

Speaking of ancient mythological types, the Roman figure Janus was the god of both beginnings and endings, as well as lending his name to the first month of the year. In his honor we present a puzzle matching beginnings and endings, alphabetically speaking. There are a number of prescription drugs for which the generic name begins with the letter "A", while the brand name begins with the letter "Z", or vice-versa. For example, the macrolide antibiotic *Azithromycin* goes by the brand name *Zithromax*. We can think of five other examples of this Alpha-Omega situation. The first reader to submit all five (or more?) correct answers to *puzzle@prnnewsletter.com* wins a custom-printed *PRN* binder.

Hint: For those of you stuck on four correct answers, here's a little help:

One of the five is actually a *prescription* version of a well-known over-the-counter drug!

We welcome your ideas for Pharmacy Fun. Forward any pharmacy-related puzzles, games, riddles, etc., to *puzzle@prnnewsletter.com*. If we use your submission, you will be credited in this column and receive a custom-printed *PRN* binder as well.

References:
1. Patanase [package insert]. Fort Worth, TX: Alcon Laboratories, Inc.; revised March, 2008.
2. Treximet [package insert]. Research Triangle Park, NC: GlaxoSmithKline ; April, 2008.
3. Amitiza [package insert]. Bethesda, MD: Sucampo Pharmaceuticals, Inc.; revised April, 2008.
4. Andrew Pollack, "Glaxo Says Compound in Wine May Fight Aging," *New York Times*, April 23, 2008.
5. Nicholas Wade, "Yes, Red Wine Holds Answer. Check Dosage," *New York Times*, November 2, 2006.

Credits: Photographs by James Murphy