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What's Inside…

FDA NEWS

Counterfeit Alli Warning

The FDA has issued a Public Health Alert regarding counterfeit **Alli** (orlistat) being sold over the internet, particularly at online auction sites. Tests performed by GlaxoSmithKline, the maker of the genuine product, have revealed that the counterfeit product does not contain orlistat, but instead contains varying amounts of the schedule IV controlled substance **sibutramine**, sold by prescription under the brand name **Meridia**. This is of particular concern for those patients with cardiovascular disease who may have purchase counterfeit Alli, since sibutramine is now contraindicated in the presence of heart disease (see last month's ***FDA NEWS***). The agency listed several ways to differentiate the real product from the fake, including:

- **Genuine Alli expiration dates consist of the month/year only; counterfeit bottles list month/day/year and the outer carton has no lot number listed**
- **Genuine Alli capsules are filled with small white pellets; counterfeit capsules are slightly larger and are filled with a white powder**

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New GLP-1 Agonist: The FDA has approved Novo-Nordisk's **Victoza** (liraglutide) for the treatment of type 2 diabetes mellitus (T2DM). Victoza is glucagon-like-peptide-1 (GLP-1) receptor agonist, similar to **Byetta** (exenatide), which increases insulin secretion, decreases glucagon secretion, and delays gastric emptying. Like Byetta, Victoza may be associated with pancreatitis, and should be used with caution in patients with a history of pancreatitis. In addition, in animal studies Victoza caused thyroid cancer. While it is not known if Victoza would cause such cancers in humans, the drug's label will include a **black box warning** indicating that the drug is contraindicated in patients with a personal or family history of medullary thyroid carcinoma or in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2). The FDA has indicated that Victoza is not indicated as first-line therapy, and has required the manufacturer to conduct additional animal studies in mice to further evaluate the potential risk of thyroid cancer in humans. The most common adverse effects seen in trials were headache, nausea, and diarrhea. Victoza is administered once daily, without regard to meals, by subcutaneously injection into the abdomen, thigh, or upper arm. The initial dose is 0.6 mg daily for 1 week. The dose is then increased to 1.2 mg daily. If this dose does not result in acceptable glycemic control, the dose may be increased to 1.8 mg daily. Victoza will be available in a 3 mL pre-filled, multi-dose pen.

Long-Acting Trazodone: Labopharm, Inc., has been granted FDA approval to market **Oleptro** (trazodone) extended-release tablets. Oleptro is a once-daily formulation of the antidepressant trazodone, which is indicated for the treatment of major depressive disorder. The most common adverse effects noted in clinical trials were somnolence/sedation, dizziness, constipation, and blurred vision. Oleptro should not be taken concomitantly with or within 14 days of MAOIs. Use with CYP3A4 inhibitors may necessitate a lower dose of Oleptro; CYP3A4 inducers may necessitate a higher dose of Oleptro. Serotonin syndrome has been reported, especially in patients taking other serotonergic medications. As with all antidepressants, patients should be monitored for clinical worsening and suicidal thinking or behavior. The recommended starting dose of Oleptro is 150 mg once daily at bedtime on an empty stomach. The dose may be increased by 75 mg every 3 days to a maximum of 375 mg daily.

HIPAA Notification Rule: The U.S. Department of Health and Human Services (HHS) has issued regulations requiring HIPAA-covered entities, including pharmacies, to notify individuals whenever their protected health information is breached (e.g., disclosed without authorization). While the rule took effect on September 23, 2009, HHS has announced that enforcement will not begin until February 22, 2010. For a discussion of the rule, including details on how to comply with specific provisions, see ***Pharmacy Law*** on page 2 of this issue.

Cardiologists Warn of Problems with Herbal Products

Pharmacists are already aware of the possibility of drug interactions between popular herbal products and some prescription drugs, but an article in the current issue of the *Journal of the American College of Cardiology* points out that patients with cardiovascular disease are at particular risk for adverse effects from these over-the-counter remedies.[1] Cardiologists at the Mayo Clinic's Division of Cardiovascular Diseases reviewed 40 years of literature relating to herbal medicine and heart patients, and concluded that some of the most commonly used herbal products may present problems for patients being treated for heart disease. Some of their findings are summarized below:

- **Garlic, Ginger, and Ginkgo** can all **increase** bleeding risk in patients taking **Coumadin** (warfarin), **Plavix** (clopidogrel), or **Effient** (prasugrel).
- **Ginseng** can also **increase** bleeding risk in patients taking **Plavix** or **Effient**, but has been shown to **decrease** the effectiveness of **Coumadin**, likely due increased metabolism of the blood thinner. Ginseng abuse may also cause hypertension.
- **Green Tea** contains Vitamin K and may **decrease** the effects of **Coumadin.**
- **St. John's Wort** may **decrease** effects of **Coumadin**, **Digoxin**, and **Statins**, and may **increase** bleeding risk in patients taking **Plavix** or **Effient**.

MEDICAID UPDATE

Information Regarding the New York State Medicaid Program

Pharmacist's NPI Required

Effective April 1, 2010, all electronic claims submitted for payment to Medicaid must include the dispensing pharmacist's National Provider Identifier (NPI) number. This initiative is intended to ensure that prescriptions are being filled by pharmacists with a valid license. Pharmacists who do not currently have an NPI and wish to continue to fill Medicaid prescriptions must obtain an NPI by applying at: ***www.cms.hhs.gov/NationalProvIdentStand/***

How to Obtain an NPI

After navigating to the site listed above, click on ***Apply Now - National Plan and Provider Enumeration System (NPPES)***. From there, click on ***National Provider Identifier (NPI)*** to be taken to the online application form. According to the Health and Human Services (HHS) website, a provider who submits a properly completed electronic application could receive an NPI in 10 days.

New Combined Limits on Incontinence Products

As of December, 2009, the New York State Medicaid Program has instituted revised utilization limits for incontinence products. For patients using both disposable diapers *and* liners, Medicaid will now allow for ***any combination of 250 diapers and/or liners per month***. To allow for early refills, 1,750 diaper/liners are allowed in a six month period. For patients using both disposable underpads *and* reusable underpads, Medicaid will allow ***up to 2,121 of any combination of disposable underpads and reusable underpads in a 180 day period***. For patients using disposable diapers/liners and reusable diapers, Medicaid will allow ***up to 1,750 of any combination of disposable diapers/liners and reusable diapers in a 180 day period***.

LAW REVIEW

Regulatory Issues Affecting Pharmacy in New York State

HITECH Act, An Extension of HIPAA Rules

When President Obama signed the American Recovery and Reinvestment Act of 2009, also known as the stimulus bill, an important expansion of HIPAA became the law of the land. The Health Information Technology for Economic and Clinical Health (HITECH) Act includes among its provisions a requirement for HIPAA-covered entities, such as pharmacies, to notify patients in writing of any unauthorized disclosure, or "breach," of their protected health information (PHI). PHI is defined as individually identifiable health information relating to a patient's past, present, or future physical or mental health condition.

Definition of Breach and Exceptions

The HITECH Act defines a PHI "breach" as the unauthorized access, use, or disclosure of protected health information which compromises the security or privacy of such information. The Act also lists **three exceptions** to the definition of breach which are particularly relevant to the application of the HIPAA privacy rule to community pharmacies:

1. **Unauthorized acquisition, access, or use of PHI by an employee of a covered entity done in good faith in the course of employment which does not lead to further use or disclosure**
2. **Inadvertent disclosure of PHI from one person authorized to access PHI at a covered entity to another authorized person at that covered entity if the information is not further used or disclosed without authorization**
3. **Unauthorized disclosure in which the unauthorized person to whom PHI is disclosed would not reasonably have been able to retain the information**

Methods and Requirements of Notification

Should a breach of unsecured PHI be discovered, the covered entity (e.g., pharmacy) must notify the individual whose PHI has been inappropriately accessed, acquired, or disclosed. Notification must be made without unreasonable delay but in no case later than 60 calendar days after the discovery of the breach. The Act specifies the following methods of notification:

- **Written notice to the individual at the last known address of the individual by first-class mail (or by electronic mail if specified by the individual)**
- **In cases that the entity deems urgent, notification by telephone or other means is permitted in addition to the above method**

The notification is required to include:

1. **A brief description of what happened and the date of the breach and the date of discovery of the breach, if known**
2. **A description of the types of PHI involved in the breach**
3. **The steps individuals should take to protect themselves from potential harm resulting from the breach**
4. **A brief description of what the covered entity involved is doing to investigate the breach, to mitigate losses, and to protect against any further breaches**
5. **Contact procedures for individuals to ask questions or learn additional information, which shall include a toll-free telephone number, an e-mail address, Web site, or postal address**

Feature Article..

REVIEW OF HMG-CoA REDUCTASE INHIBITORS

February is American Heart Month, and we thought that would be a good time to review the latest information regarding one of the mainstays of cardiovascular pharmacotherapy, namely HMG-CoA Reductase Inhibitors, popularly known as the "statins." In addition to a chart comparing all the available agents, we have also reviewed the latest recommendations on the most commonly encountered interactions involving statins:

Statins and Warfarin
All statins, to some degree, have the potential to increase INR in patients taking warfarin. INR should be monitored whenever starting, changing, or stopping therapy with a statin.

Statins and Fibrates
Fibric acid derivatives increase the risk for rhabdomyolysis when used with statins. Gemfibrozil can also increase statin blood levels, therefore fenofibrate is the better choice if combination therapy is required.

Statins and Grapefruit
Grapefruit and grapefruit juice inhibit the activity of intestinal CYP3A4, which can increase blood levels of **Lipitor**, **Mevacor**, and **Zocor**. Mevacor and Zocor appear to be affected to a greater extent than Lipitor.

Brand (generic)	**Crestor** (rosuvastatin)	**Lescol** (fluvastatin)	**Lipitor** (atorvastatin)	**Livalo** (pitavastatin)	**Mevacor** (lovastatin)	**Pravachol** (pravastatin)	**Zocor** (simvastatin)
Strengths Available	5, 10, 20, 40 mg	20, 40, 80 (XL) mg	10, 20, 40, 80 mg	1, 2, 4 mg	10, 20, 40 mg	10, 20, 40, 80 mg	5, 10, 20, 40, 80 mg
Dosage Range	5 to 40 mg QD	20 to 80 mg QD	10 to 80 mg QD	1 to 4 mg QD	10 to 80 mg QD	10 to 80 mg QD	5 to 80 mg QD
Approximate Equivalent Dose	5 mg	80 mg	10 mg	2 mg	40 mg	40 mg	20 mg
Directions for use	Take any time of day	Take in the evening (XL any time of day)	Take any time of day	Take any time of day	Take in the evening	Take any time of day	Take in the evening
Timing with regard to meals	Take with or without food	Take with or without food	Take with or without food	Take with or without food	Must take with food	Take with or without food	Take with or without food
Renal Dosing Adjustment	CrCl < 30mL/min= Initial dose is 5 mg Max dose is 10 mg	No adjustment necessary (use caution in *severe* impairment)	No adjustment necessary	GFR 30 - 60 mL/min= Initial dose is 1 mg Max dose is 2 mg GFR < 30= Do not use	CrCl < 30 mL/min= use caution with doses greater than 20 mg/day	CrCl < 60 mL/min= Initial dose is 10 mg	No adjustment necessary (*severe* impairment start at 5 mg/day)
Primary Metabolic Pathway	CYP2C9 (minor)	CYP2C9 (major)	CYP3A4 (major)	CYP2C9 (minor)	CYP3A4 (major)	Non-CYP450 pathway	CYP3A4 (major)
Significant Drug Interactions (increased statin levels)	Cyclosporine, Gemfibrozil, Protease Inhibitors	Amiodarone, Cyclosporine, Fluconazole	Amiodarone, Azole AFs*, Cyclosporine, Dronedarone, Gemfibrozil, Macrolides, Protease Inhibitors	Cyclosporine, Erythromycin, Gemfibrozil, Protease Inhibitors, Rifampin	Amiodarone, Azole AFs*, Cyclosporine, Dronedarone, Gemfibrozil, Macrolides, Protease Inhibitors	Cyclosporine, Gemfibrozil	Amiodarone, Azole AFs*, Cyclosporine, Dronedarone, Gemfibrozil, Macrolides, Protease Inhibitors

* Azole AFs = Azole Antifungals, such as Fluconazole, Itraconazole, Ketoconazole, Posaconazole, and Voriconazole.

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ASK PRN...

When dispensing prescriptions for restricted access drugs, such as isotretinoin and clozapine, are refills permitted? Also, are telephone, fax, and e-prescriptions allowed?

The rules regarding restricted access drugs differ depending on the particular agent and program involved. We have created a quick-reference chart to answer these questions for the four restricted access drugs most commonly encountered in the community pharmacy: **Clozapine**, **Isotretinoin**, **Lotronex**, and **Thalomid**. For more information on dispensing these agents, see the December, 2008 edition of ***PRN***.

Restricted Access Drug	Phone, Fax, and e-Rx allowed?	Refills Allowed?
Clozapine	Yes	Yes*
Isotretinoin	Yes	No
Lotronex	No	Yes
Thalomid	No	No

** Current blood test required*

GOT QUESTIONS? WE HAVE ANSWERS!
Send your questions to us at:
askprn@prnnewsletter.com

PRN welcomes your questions on any topics relating to the practice of pharmacy. All answers are researched by our staff and, when necessary, discussed with the appropriate regulatory agencies. The information provided is not intended as legal advice, nor is it a substitute for professional judgment in clinical practice.

DID YOU KNOW?

DID YOU KNOW that Pfizer, the world's largest drug company, was founded in 1849 in the Williamsburg section of Brooklyn? Cousins Charles Pfizer and Charles Erhardt started the company with a $2,500 loan from Pfizer's father. A small brick building at the intersection of Harrison Avenue and Bartlett Street served as the company's first headquarters, where they manufactured the antiparasitic santonin. The company's early growth was driven by a process it developed to mass produce citric acid. Later, Pfizer would become a leader in the field of antibiotics, producing penicillin for the U.S. government during World War II, and developing tetracycline, doxycycline, azithromycin, Unasyn, and Zyvox, among others. Over the years, Pfizer has also grown through acquisitions, most notably those of Warner-Lambert, Pharmacia, and, in 2009, Wyeth. The corporation's world headquarters is now located on 42nd Street in Manhattan, near historic Grand Central Terminal.

PHARMACY FUN

February is the month for love, at least according to the good folks at Hallmark! Ever since Pope Gelasius I decreed February 14th to be St. Valentine's Day back in 496 AD, people have been expressing their affections through poetry, floristry, and more recently, the purchase of greeting cards and chocolate. Lost in a romantic state of mind, it occurred to us that there are two drugs that actually contain the word "love" within their names. Both are brand-name prescription drugs. Can you find the "love" in pharmacy? The first reader to submit the correct answers to *puzzle@prnnewsletter.com* will receive a custom-printed *PRN* binder. Need a hint or two? Ok, but they may not be that helpful!

1. **One of the two drugs should not be used in patients with hypersensitivity to pork products**
2. **The other drug gains its potency from a fluorocarbothioate ester linkage at the 17 carbon position**

Answers to last month's **PHARMACY FUN**:
1. Inderal (propranolol) 2. Tagamet (cimetidine) 3. Cozaar (losartan) 4. Retrovir (zidovudine)
5. Capoten (captopril) 6. Rezulin (troglitazone) 7. Prilosec (omeprazole) 8. Prozac (fluoxetine)

References:
1. Tachjian A, Maria V, Jahangir A. Use of herbal products and potential interactions in patients with cardiovascular disease. *Journal of the American College of Cardiology* 2010;55:515-525.