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What's Inside…

FDA NEWS

TNF Blocker Update: The FDA has issued a follow-up to a previous communication regarding the safety of tumor necrosis factor (TNF) blockers (**Cimzia**, **Enbrel**, **Humira**, **Remicade**, and **Simponi**). As a result of their analysis, the agency is requiring manufacturers of TNF blockers to update the **black box** warning in their prescribing information to reflect an increased risk of lymphoma and other malignancies in children and adolescents treated with TNF blockers. In addition, the warnings section for each agent will be updated to include reported cases of leukemia in adults, adolescents, and children using TNF blockers. The FDA recommends that healthcare professionals discuss with patients and families the increased risk of developing cancer in children and adolescents, while explaining the benefits of therapy and the risks associated with untreated illness. Practitioners and patients are urged to be aware of the possibility of malignancies and to monitor for the emergence of unusual signs or symptoms, including unexplained weight loss or fatigue, swollen lymph nodes in the neck, underarms, or groin, or easy bruising or bleeding.

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Effient: As reported here last month, Daiichi Sankyo and Eli Lilly have received approval to market **Effient** (prasugrel). Effient is a platelet inhibitor, similar to **Plavix** (clopidogrel), and is indicated for the reduction of thrombotic cardiovascular events in patients with acute coronary syndrome managed with percutaneous coronary intervention (PCI). In a comparative study, Effient proved more effective than Plavix, but was also shown to cause more major (and fatal) bleeding episodes. Effient will carry a **black box warning** regarding bleeding risk and should not be used in patients with a history of transient ischemic attack or stroke. Avoid use in patients 75 years of age or older. If possible, discontinue Effient at least 7 days prior to any surgery. The recommended dose of Effient is 10 mg once daily, with or without food. Patients treated with Effient should also take a daily aspirin (75 to 325 mg).

New Atrial Fibrillation Drug: The FDA has approved Sanofi-Aventis' **Multaq** (dronedarone) to reduce the risk of hospitalization in patients with paroxysmal or persistent atrial fibrillation (AF) or atrial flutter. Multaq is contraindicated in severe heart failure and in heart failure with a recent decompensation requiring hospitalization. Multaq, although similar to **Amiodarone**, does not cause some of that drug's more troublesome side effects, such as pulmonary fibrosis, hypo– or hyperthyroidism, and blue skin discoloration. The most common adverse reactions seen in clinical trials were diarrhea, nausea, abdominal pain, vomiting, and asthenia. Drug interactions include **digoxin**, **calcium channel blockers**, **beta blockers**, **grapefruit juice**, and **statins**. The recommended dose of Multaq is 400 mg twice a day with morning and evening meals.

New Diabetes Drug: Bristol-Myers Squibb and AstraZeneca have announced FDA approval of **Onglyza** (saxagliptin), a new dipeptidyl peptidase-4 (DPP4) inhibitor. Onglyza is indicated to improve glycemic control in adults with type 2 diabetes, either as monotherapy or in combination with metformin, sulfonylureas, or thiazolidinediones (TZD). When used with a sulfonylurea, hypoglycemia may occur; a lower dose of the sulfonylurea may be required. When used with a TZD, there is an increased risk of peripheral edema. Unlike **Januvia**, another DPP4 inhibitor, Onglyza undergoes significant metabolism via CYP3A4/5. When used with strong inhibitors of this enzyme (**ketoconazole**, **clarithromycin**, **protease inhibitors**, etc.), Onglyza dosage should be limited to 2.5 mg daily. Onglyza should not be used for Type 1 diabetes or diabetic ketoacidosis, and has not been studied in combination with insulin. The recommended dose of Onglyza is 2.5 mg or 5 mg once daily with or without food.

Glucose Test Strip Warning: The FDA has issued a public health notification regarding the potential for erroneous blood glucose readings in patients receiving drugs or biologic formulations containing non-glucose sugars, such as maltose, xylose, and galactose. The presence of these sugars in the blood can lead to falsely elevated blood glucose levels when testing with strips using the GDH-PQQ methodology (**Accu-Chek Active, Avivia, Comfort Curve, Compact, and Go strips, Freestyle and Freestyle Lite strips, and TRUEtest strips**). Products containing non-glucose sugars include: **Adept adhesion reduction solution**, **Bexxar**, **Extraneal peritoneal dialysis solution**, **Orencia**, and certain immunoglobulins, including **Octagam, WinRho SDF Liquid**, **HepaGamB,** and **Vaccinia IG (Human)**.

Court Papers Reveal Practice of Ghostwriting in Medical Literature

Recently released court documents highlight problems with a little-known but common practice in medical literature, namely the ghostwriting of widely read medical articles by advertising firms in the pay of pharmaceutical manufacturers. Wyeth pharmaceuticals is facing numerous lawsuits brought by patients who claim illnesses caused by the company's hormone replacement drugs, **Premarin** and **Prempro**. Court papers show that Wyeth contracted with a medical communications firm, DesignWrite, to prepare articles favorable to their drugs and downplaying any potential risks of hormone therapy.[1] Wyeth would then approach leading physicians in the field and compensate them for attaching their names to the articles, even when these physicians had little or nothing to do with the actual writing of the articles. This practice continued even after a major federal study was halted in 2002 when it was determined that hormone replacement therapy actually increased rates of cancer, heart disease, and stroke in menopausal women.

MEDICAID UPDATE

Information Regarding the New York State Medicaid Program

Preferred Drug Program Update

The New York State Department of Health has announced upcoming changes to the Medicaid Preferred Drug Program (PDP). Effective August 19, 2009, the following drugs will require prior authorization:

Non-Preferred Agents

Altace (capsules)
Fenofibrate
Fosamax (tablets)

The following drugs will be covered without prior authorization:

Preferred Agents

Symbicort
Trilipix

For a complete list of all preferred and non-preferred drugs, go to:
https://newyork.fhsc.com

Prior Authorization Process

In order to obtain coverage for a non-preferred drug, the prescriber, or an agent of the prescriber, must call the prior authorization phone line at: **1-877-309-9493**. After entering the provider's NPI, the patient's ID number, and the drug name, the prescriber will be asked a series of questions. If authorization is granted, an 11-digit prior authorization number, ending in "W", will be issued. This number should be written on the patient's prescription. Pharmacists receiving such prescriptions must also call the prior authorization phone line to validate the authorization. Once validated, the authorization number is valid for all refills available on the prescription. After completing this process, the prescription may be submitted to Medicaid. When entering the authorization number in the prior authorization field, the letter "W" should be omitted. The same procedure is used by pharmacists to dispense brand-name drugs through the Mandatory Generic Program, and drugs authorized through the Clinical Drug Review Program.

LAW REVIEW

Regulatory Issues Affecting Pharmacy in New York State

Prescription Drug Diversion

Newspapers, broadcast and cable news programs, and other media sources have recently highlighted a national problem that pharmacists are already all too familiar with, that of prescription drug diversion and abuse. A report released in May by the White House Office of National Drug Control Policy found that opioids are the most commonly diverted prescription drugs, and documented a 114% increase in opioid-related deaths between 2001 and 2005. Pharmacist's awareness of the problem is not only a key to stopping diversion, but is also legally required. Section 1306.04(a) of the Federal Controlled Substance Act states:

> **A prescription for a controlled substance to be effective must be issued for a legitimate medical purpose by an individual practitioner acting in the usual course of his professional practice. The responsibility for the proper prescribing and dispensing of controlled substances is upon the prescribing practitioner, but a *corresponding responsibility rests with the pharmacist who fills the prescription*.**

The Drug Enforcement Administration has issued guidance for pharmacists which includes the following criteria which *may* indicate that a purported prescription was not issued for a legitimate medical purpose:

- **A prescriber writes significantly more prescriptions (or in larger quantities) compared to other practitioners in your area**
- **The prescriber writes for antagonistic drugs, such as depressants and stimulants, at the same time. Drug abusers often request prescriptions for "uppers and downers" at the same time**
- **Patient appears presenting prescriptions written in the names of other people**
- **A number of people appear simultaneously, or within a short time, all bearing similar prescriptions from the same physician**
- **Numerous "strangers," people who are not regular patrons, suddenly show up with prescriptions from the same prescriber**

The New York State Bureau of Narcotic Enforcement has also issued a pamphlet, entitles "A Pharmacist's Guide to Controlled Substance Diversion," which includes the following list of characteristics of forged prescriptions:

- **Prescribing practitioner is not from your local area**
- **Patient is unfamiliar to you or is from out of town**
- **Patient exhibits suspicious behavior**
- **Patient is picking up prescription for someone else**
- **Prescription is presented or phoned in near closing time**
- **Prescription is phoned in by practitioner covering after hours or on the weekend**
- **Prescription appears too perfect**
- **Prescription contains errors in spelling or prescribing symbols**
- **Prescription appears to be copied or scanned. It is not of proper size or does not appear to have been torn from an official prescription pad or official EMR paper**

The Bureau of Narcotic Enforcement also points out that the law (*Rules and Regulations on Controlled Substances,* section 80.73[e]) requires a person picking up **any** controlled substance prescription to present appropriate identification if the person is unknown to the pharmacy.

Feature Article..

REVIEW OF PROTON PUMP INHIBITORS

Since The Approval of **Prilosec** (then known as *Losec*) in September, 1989, proton pump inhibitors (PPIs) have become a mainstay of therapy, revolutionized the treatment of ulcers and other gastrointestinal disorders, and generated annual sales in excess of 10 billion dollars in the United States alone. PPIs are known to be highly effective and well tolerated by most patients. However, as the 20th anniversary of their debut approaches, some practitioners are rethinking the widespread use of these agents in light of recent evidence of problems associated with their use in some patient populations. Below is a discussion of some of these issues, as well as a chart comparing the currently available agents.

PPIs and Plavix

Patients on antiplatelet therapy, such as Plavix combined with aspirin, are often prescribed PPIs to protect against the possibility of GI bleeding. Recent studies, however, have indicated that PPI use may decrease the efficacy of Plavix, leading to a higher rate of cardiovascular events. At first, the evidence seemed to point specifically towards Prilosec, a strong inhibitor of the enzyme (CYP2C19) needed to convert Plavix to its active metabolite. More recent reports point to a "class effect," leading some experts to warn against the use of any PPIs in patients taking Plavix, unless there is a compelling indication. There is no evidence that H2 antagonists interfere with the efficacy of Plavix, though they are not as effective as PPIs in preventing bleeding. At this time, the clinical importance of this interaction is still an evolving question.

PPIs and Infections

Overuse of PPIs in hospitalized patients may lead to increased rates of certain types of infections. Recent studies have demonstrated that patients on PPIs had greater rates of infection with hospital-acquired pneumonia and *clostridium difficile*. It has been postulated that gastric acidity plays a role in defense against the organisms causing these infections. Both PPIs and H2 antagonists significantly reduce gastric acidity.

PPIs and Fractures

Long-term acid suppression with PPI use has been shown to decrease calcium absorption. A 2006 study linked PPI use of greater than 1 year duration to an increased rate of hip fracture, possibly due to decreased calcium levels. Patients on chronic PPI therapy should be advised to increase their calcium and vitamin D intake through diet or supplements.

Brand Name (active ingredient)	Dosage Forms and Strengths	Generic Available?	Initial Dose for GERD	Notable Drug Interactions*	Most Common Adverse Reactions
Aciphex (rabeprazole)	**Tablet** (20 mg)	No	20 mg QD	Cyclosporine, Plavix, Reyataz, Viracept, Warfarin	Headache, diarrhea, nausea
Kapidex (dexlansoprazole)	**Capsule** (30, 60 mg)	No	30 mg QD	Plavix, Reyataz, Viracept, Warfarin	Diarrhea, abdominal pain, nausea
Nexium (esomeprazole)	**Capsule** (20. 40 mg) **Powder packet** (10, 20, 40 mg) **IV** (20, 40 mg)	No	20 mg QD	Plavix, Reyataz, Viracept, Warfarin	Headache, abdominal pain, diarrhea
Prevacid (lansoprazole)	**Capsule** (15, 30 mg) **SoluTab** (15, 30 mg) **Powder packet** (15, 30 mg) **IV** (30 mg)	No	15 mg QD	Plavix, Prograf, Reyataz, Viracept, Warfarin	Diarrhea, nausea, abdominal pain, constipation
Prilosec (omeprazole)	**Capsule** (10, 20, 40 mg) **Powder packet** (2.5, 10 mg)	Yes	20 mg QD	Cyclosporine, Plavix, Prograf, Reyataz, Viracept, Warfarin	Headache, abdominal pain, nausea
Protonix (pantoprazole)	**Tablets** (20, 40 mg) **Powder packet** (40 mg) **IV** (40 mg)	Yes	40 mg QD**	Plavix, Reyataz, Viracept, Warfarin	Headache, diarrhea, flatulence
Zegerid (omeprazole and sodium bicarbonate)	**Capsule** (20, 40 mg) **Powder packet** (20, 40 mg)	No	20 mg QD	Cyclosporine, Plavix, Prograf, Reyataz, Viracept, Warfarin	Headache, abdominal pain, nausea

* Drug interactions based on manufacturer's package inserts and current literature
** Protonix lacks an FDA indication for GERD; dose based on erosive esophagitis treatment

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ASK PRN...

Now that Plan B One-Step is on the market, will the original Plan B still be available?

The original Plan B has been discontinued. Once supplies are exhausted, it will no longer be available.

Is the single dose regimen as effective as the original two-dose product?

Plan B One-Step contains levonorgestrel 1.5 mg taken as a single dose instead of the two doses of 0.75 mg taken 12 hours apart in the original Plan B. In a comparative study of 2,381 healthy woman, Plan B One-Step was found to be 84% effective in preventing pregnancy, while the two-dose Plan B was 79% effective. Although the original study of two-dose Plan B showed 89% effectiveness, the results of the head-to-head comparison study confirm that the single dose regimen is just as effective.

A generic for the original Plan B called Next Choice is now on the market. Currently, it is available by prescription only. Will it be going over-the-counter?

Next Choice, a two-dose regimen, was approved for women 17 and younger and by prescription only. A spokesperson for Watson, the manufacturer, confirmed that the company has applied to the FDA for over-the-counter use, which could take effect as early as August 24, 2009, the date when OTC exclusivity rights for Plan B expire.

Can patients take both Next Choice tablets at once instead of waiting 12 hours to take the second dose?

Taking two 0.75 mg tablets is equivalent to taking one 1.5 mg tablet.

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 six of the most important drugs developed in the 20th century all stemmed from the work of one researcher? Gertrude B. Elion, born in New York City to immigrant parents in 1918, never completed her doctorate degree and yet was awarded the Nobel Prize in Medicine in 1988. Working with George H. Hitchings at Burroughs-Wellcome, Elion was involved in development of **Purinethol** (6-mercaptopurine), **Imuran** (azathioprine), **Zyloprim** (allopurinol), **Daraprim** (pyrimethamine), **Proloprim** (trimethoprim), and **Zovirax** (acyclovir). She was later awarded several honorary doctorate degrees, including one from Polytechnic University in Brooklyn, and was the first woman inducted into the National Inventor's Hall of Fame.

PHARMACY FUN

This month's puzzle is from our weights and measures department. You're given 300 mg of a drug in powder form. Your mission is to separate the powder into 3 separate portions of 150 mg, 100 mg, and 50 mg. An easy enough task using a modern, digital scale, but you don't have one! All you get to accomplish this task is a classic double-pan pharmacy balance and 2 weights, one 30 mg and one 5 mg. The first reader to send the correct answer, *in the fewest number of steps,* to *puzzle@prnnewsletter.com* will receive a custom-printed *PRN* binder.

Answers to last month's **PHARMACY FUN**:
Take 3 tablets from bottle A, 2 tablets from bottle B, and 1 tablet from bottle C. Weigh all 6 tablets at once on the scale. If the scale reads 3,030 mg, then bottle A holds the real antidote. If the scale reads 3,020 mg, then bottle B holds the real antidote, If the scale reads 3,010 mg, then bottle C holds the real antidote.

References:
1. Natasha Singer, "Medical papers by Ghostwriters Pushed Therapy," *New York Times*, August 5, 2009.