P.R.N.

ISSN # 1941-9481

www.prnnewsletter.com

Volume 4, Number 10 | A Monthly Newsletter for Community Pharmacists | October, 2010

What's Inside…

FDA NEWS

FDA Reminds Public of Plavix-Prilosec Interaction

This month the Food and Drug Administration (FDA) is reminding the public that it continues to warn against the use of any products containing **omeprazole** in patients who are currently taking **Plavix** (clopidogrel). The announcement is a follow-up to previous announcements and label changes regarding the reduced effectiveness of Plavix when taken with omeprazole, which is believed to inhibit the conversion of clopidogrel to its active metabolite. Products containing omeprazole include: **Prilosec**, **Prilosec OTC**, **Zegerid**, **Zegerid OTC**, and generic **omeprazole**). The FDA wishes to emphasize the following facts to avoid confusion over this issue:

- **This recommendation applies only to omeprazole, and not to all Proton Pump Inhibitors (PPIs). Not all PPIs have the same inhibitory effect on the conversion, via CYP2C19, of clopidogrel to its active form**
- **Protonix (pantoprazole) may be an alternative PPI for consideration. It is a weak inhibitor of CYP2C19**

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New A-Fib Agent: The FDA has approved Boehringer Ingelheim's **Pradaxa** (dabigatran etexilate) for the prevention of stroke and systemic embolism in patients with non-valvular atrial fibrillation (A-Fib). Pradaxa is a direct thrombin inhibitor, which prevents the conversion of fibrinogen into fibrin, thereby reducing the formation of thrombi. Pradaxa is contraindicated in the presence of active pathological bleeding. In clinical trials, the most common adverse reactions were gastritis-like symptoms and bleeding. While the overall risk of bleeding with Pradaxa was similar to that of warfarin, the risk of major gastrointestinal bleeds was higher in patients treated with Pradaxa. Patients aged 75 years and older also had a greater risk of bleeding with Pradaxa. In a study comparing the new agent with warfarin, Pradaxa was more effective in preventing stroke. When converting patients from warfarin to Pradaxa, discontinue warfarin and start Pradaxa when the international normalized ratio (INR) is below 2. The recommended dose of Pradaxa is 150 mg twice daily, with or without food, for patients with a CrCl >30mL/min. Patients with a CrCl between 15 and 30 mL/min should be given 75 mg twice daily. Lapses in therapy should be avoided, as they may increase the risk of stroke. If Pradaxa must be discontinued due to surgical or invasive procedures, therapy should be restarted as soon as possible. Patients should be advised to swallow the capsule whole. Breaking, chewing, or emptying the contents of the capsule can result in increased exposure. The manufacturer states that Pradaxa should be dispensed and stored in the original container and, once opened, must be used within 30 days.

Oral MS Treatment: Novartis has been granted FDA approval to market **Gilenya** (fingolimod), the first oral treatment indicated for the treatment of patients with relapsing forms of multiple sclerosis (MS). Gilenya reduces the frequency of clinical exacerbations and delays the accumulation of physical disability. Gilenya is a sphingosine 1-phosphate receptor modulator, which is thought to work by causing lymphocytes to be retained in the lymph nodes, preventing them from reaching the central nervous system where they may cause damage to nerve cells. In clinical trials, the most common adverse reactions were headache, influenza, diarrhea, back pain, liver transaminases elevations, and cough. After the initial dose of Gilenya, given at the physician's office or clinic, patients must be observed for 6 hours for signs and symptoms of bradycardia. Gilenya may increase the risk of infections and should not be started in patients with active acute or chronic infections and patients should avoid live vaccines during, and for 2 months following, treatment with Gilenya. An ophthalmic exam should performed before starting treatment, as Gilenya may cause macular edema. Liver and pulmonary function should also be assessed before starting treatment. Women of childbearing potential should use effective contraception during and for 2 months after stopping Gilenya treatment (pregnancy category C). A registry has been established to collect information about the effect of Gilenya use during pregnancy. Physicians are encouraged to enroll pregnant patients, or pregnant women may enroll themselves in the Gilenya pregnancy registry by calling 1-877-598-7237. The recommended dose of Gilenya capsules is 0.5 mg once daily, with or without food.

FDA to Restrict Access to Avandia

Dr. Jane Woodcock, the director of the Food and Drug Administration's (FDA) Center for Drug Evaluation and Research, has announced the agency's decision concerning the continued marketing of **Avandia** (rosiglitazone). The decision comes in response to a number of studies which indicate increased cardiovascular events in patients taking the drug. The FDA will allow products containing rosiglitazone (**Avandia**, **Avandamet**, and **Avandaryl**) to remain on the market, but only as restricted access drugs under a Risk Evaluation and Mitigation Strategy (REMS) to be developed by the manufacturer, GlaxoSmithKline (GKS). It is expected to take several months to put the REMS in place and until such time, patients already taking rosiglitazone products may continue to receive them. Once the REMS is in effect, current users of rosiglitazone will only be able to continue using the medication if they acknowledge and document that they understand the risks associated with the drug. Patients not previously treated with rosiglitazone will only be allowed to be prescribed the drug if they are unable to achieve glycemic control on other medications and decide not to take **Actos** (pioglitazone) for medical reasons. The agency also ordered GSK to commission an independent re-adjudication of the RECORD study, evaluating the cardiovascular risk of Avandia.

MEDICAID UPDATE

Information Regarding the New York State Medicaid Program

Preferred Drug Program Update

The following changes to the Preferred Drug Program will become effective November 10, 2010:

Non-Steroidal Anti-Inflammatory Drugs (NSAIDS)

Preferred: Voltaren Gel

Narcotics - Long Acting

Non-Preferred: Fentanyl Patch

Alzheimer's Agents

Non-Preferred: Exelon (capsule)

Brand Less Expensive Than Generic Program Update

The list of drugs in this program, in which Medicaid covers the brand name drug rather than the generic, has changed. As of October 16, 2010, the following drugs remain in the program:

Adderall XR

Astelin Nasal Spray

Lovenox

Valtrex

Medicaid will cover the brand name version of these drugs, even where the prescriber has *not* indicated "Dispense as Written" (DAW) or "Brand Medically Necessary" on the prescription.

National Provider Identifier (NPI) Update

Effective December 2, 2010, all pharmacy claims *must* include the prescriber's NPI number. Prescription claims submitted using a prescriber's MMIS provider ID or profession code and state license number will be denied as of that date. The NPI number is currently being imprinted on New York State Official Prescription pads for those prescribers who have provided their NPI number to New York State. The NPI may also be written on the Rx.

LAW REVIEW

Regulatory Issues Affecting Pharmacy in New York State

DEA Issues Policy Statement on Role of Authorized Agents in Communicating Controlled Substance Prescriptions to Pharmacists

In the October 6, 2010 edition of the Federal Register, the Drug Enforcement Agency (DEA) released a statement of policy clarifying the regulations regarding the communication of oral prescriptions for controlled substances. Under existing federal regulations, oral prescriptions for Schedule III, IV, and V drugs may be communicated to a pharmacist by an employee or agent of the prescriber *[21 CFR 1306.03(b)]*. While it is clear which persons are employees of a prescriber, the definition of "agent" was not always clear prior to the issuance of the policy statement. In fact, a recent New York Times article[1] discussed the problem of patients in nursing homes enduring long waits for pain medications because nurses who are not employees of prescribing physicians have not been allowed to transmit orders to pharmacists. The DEA has now stated that prescribers may designate non-employees as agents who may communicate oral prescriptions for controlled substances on the prescriber's behalf.

Stricter New York Regulation Overrides Federal Policy

It should be noted that the federal policy stated above ***does not apply in New York State***. Section 80.70 of the Rules and Regulations on Controlled Substances in New York State reads: "...a *practitioner* may orally prescribe and a pharmacist may dispense, to an ultimate user, controlled substances in schedule III, IV, or V." The Bureau of Narcotic Enforcement has verified that this requires that the prescriber him or herself must communicate oral prescriptions for controlled substances to pharmacists, but the Bureau also stated that they are currently reviewing this policy.

Who is an Agent of an Individual Practitioner?

The federal Controlled Substance Act (CSA) defines an "agent" as "an authorized person who acts on behalf or at the direction of a manufacturer, distributer, or dispenser." Under the CSA, the term "dispense" includes "prescribing." The policy statement further defines an "agency" as a "relationship that arises when one person (a "principal") manifests assent to another person (an "agent") that the agent shall act on the principal's behalf and subject to the principal's control, and the agent manifests assent or otherwise consents so to act."

DEA Recommends Written Agreement for Agents

Due to the legal responsibilities of prescribers and pharmacists under the CSA, the DEA believes it is in the best interests of prescribers, agents, and pharmacists that the designation of those persons authorized to act on behalf of prescribers be reduced to writing and include the following list of activities which may be performed by the agent:

1. **To prepare, for my signature, written prescriptions for controlled substances in those instances where I have expressly directed the agent to do so and where I have specified to the agent the required elements of the prescription.**
2. **To convey to a pharmacist by telephone oral prescriptions for controlled substances in Schedules III. IV, and V in those instances where I have expressly directed the agent to do so and where I have specified to the agent the required elements of the prescription.**
3. **To transmit by facsimile to a pharmacy prescriptions for controlled substances in those instances where I have expressly directed the agent to do so and where I have specified to the agent the required elements of the prescription and I have signed the prescription.**

Feature Article..

RX TOPICAL NSAIDS: A NOVEL APPROACH

Nonsteroidal Anti-inflammatory Drugs (NSAIDs) are among the most effective, and popular, treatments available for osteoarthritis and acute musculoskeletal conditions. In recent years however, this class of drugs, long known to have the potential for G.I. and renal toxicity, has been shown to increase cardiovascular risk as well. A possible solution to this problem is offered by the relatively recent appearance on the market of topical versions these agents, which have proven to be highly effective and have lower rates of systemic adverse events. Long available in Europe, the first prescription topical NSAIDs for pain were approved in the U.S. in 2007 (**Solaraze** was approved for the treatment of actinic keratoses in 2000). Below is a review of the currently available products, including instructions for proper use of each individual dosage form.

VOLTAREN GEL

Active: Diclofenac Sodium 1%

Indication: Relief of the pain of osteoarthritis of joints amenable to topical treatment, such as the knees and those of the hands.

Dosage: Upper extremities - Apply 2 gm to the affected area 4 times a day (no more than 8 grams daily to any one joint). **Lower extremities -** Apply 4 gm to the affected area (no more than 16 grams daily to any one joint).

Counseling points:

- **Do not use more than a total of 32 grams daily**
- **Use the dosing card to measure and apply gel and discard after use**
- **Do not shower or bathe for at least 1 hour after use**
- **Wait 10 minutes before covering the treated skin with clothing**

PENNSAID SOLUTION

Active: Diclofenac Sodium 1.5 %

Indication: Treatment of the signs and symptoms of osteoarthritis of the knee(s).

Dosage: 40 drops on each painful knee 4 times a day.

Counseling points:

- **Apply to clean, dry skin**
- **Dispense 10 drops at a time either directly onto knee or first into the hand and then onto the knee. Spread evenly around front, back, and sides of knee and repeat until 40 drops have been applied**
- **Wash hands after administering product**
- **Wait until the area is completely dry before covering with clothing or applying sunscreen, insect repellent, cosmetics, topical medications, or other substances**

FLECTOR PATCH

Active: Diclofenac Epolamine 1.3%

Indication: Topical treatment of acute pain due to minor strains, sprains, and contusions.

Dosage: Apply 1 patch to the most painful area twice a day.

Counseling points:

- **Do not apply patch to damaged or broken skin**
- **Do not wear patch while bathing or showering**
- **Do not take oral NSAIDs while using Flector patch**
- **If the edges of the patch begin to peel off, they may be taped down with medical tape**
- **Always wash hands after handling patch**
- **Discard unused patches 3 months after opening envelope**

SOLARAZE GEL

Active: Diclofenac Sodium 3 %

Indication: Topical treatment of actinic keratoses (AK)

Dosage: Apply to lesion areas twice daily

Counseling points:

- **Do not apply to open skin wounds, infections, and red, scaly skin**
- **Gently smooth a small amount of Solaraze gel on affected skin, covering it completely**
- **Do not cover treated areas with dressings or bandages**
- **Wash hands after applying gel**
- **Avoid sun exposure during treatment**
- **The recommended duration of therapy is from 60 to 90 days**

P.R.N.

P.R.N. (ISSN # 1941-9481)
is published monthly by:
PRN Publishing LLC
68-37 Yellowstone Boulevard
Suite C-22
Forest Hills, New York 11375
Phone & Fax (718) 263-4632

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ASK PRN...

New York State law prohibits prescribers from writing for more than one drug per prescription blank. Does this restriction apply to oral prescriptions reduced to writing by a pharmacist?

Section 6810(7)(a) of the education law states that "no prescription for a drug *written* in this state….shall be on a prescription form which authorizes the dispensing or compounding of any other drug." As our italics indicate, this regulation refers specifically to written prescriptions, not to telephone Rxs transcribed by pharmacists. There is no specific requirement regarding the form used to record oral Rxs, and therefore such forms may contain more than one drug. Since there is no requirement for a "DAW" box in the case of oral prescriptions, section 6816-a(1)(a) mandates that the prescriber must "expressly state whether substitution is to be permitted or prohibited. Any oral prescription that does not include such an express statement shall not be filled."

The label on each package of Effient tablets states that the product must be dispensed in the *original container*. What is the reason for this restriction?

According to the manufacturer, Eli Lilly and Company, Effient tablets are susceptible to both hydrolytic and oxidative degradation. In addition, a partial conversion of the active ingredient from prasugrel hydrochloride to prasugrel free base may occur during manufacture and storage of the tablets. As a result, the manufacturer recommends the following:

- **Dispense and keep Effient in the original, manufacturer-supplied container.**
- **Keep the container closed when not in use and do not remove the desiccant canister from the bottle.**

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 the famous Boehringer Ingelheim (BI) logo, which appears on all their pharmaceutical products, is actually a stylized depiction of the central section of the Imperial palace of Charlemagne, King of the Franks and Roman Emperor? The company was founded in 1885 in the village of Ingelheim in Germany, where the Emperor stayed in the late 8th century and built the palace that served as the inspiration for the BI logo.

Boehringer Ingelheim

PHARMACY FUN

This month's puzzle involves a topic near and dear to many a heart - cholesterol! This once obscure laboratory value has become so entrenched in the popular imagination that people now compare HDLs and LDLs the way they once discussed their golf handicap! After answering for each lipid-related clue below, take the first letter of each answer to spell the name of a certain style of a piece of equipment that every pharmacist uses every day. The first reader to submit the correct answers, including the hidden word, to *puzzle@prnnewsletter.com* will receive a custom-printed *PRN* binder.

1. Bile acid sequestrant available in "light" form (brand name)

2. Bile acid sequestrant also indicated for type 2 diabetes (brand name)

3. Inhibits absorption of cholesterol at brush border of intestine (generic name)

4. The second most potent statin, based on mg to mg comparison (generic name)

5. An ester containing glycerol and 3 fatty acids (try to keep it under 150!)

6. A natural product which contains a statin-like chemical, red _____ rice

Answers to last month's **PHARMACY FUN**:
1. c. carboxylic acid 2. a. ether 3. b. ester 4. e. alcohol 5. d. ketone

References:
1. John Leland, "A Battle Against Prescription Drugs Causes Pain," *New York Times*, October 2, 2010.