# P.R.N.

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**What's Inside…**



## FDA NEWS

**Propoxyphene Warning:** On July 7, the FDA announced several actions regarding drugs containing the opioid **propoxyphene** (**Darvon**, **Darvocet**). The agency noted the fact that propoxyphene has been implicated in fatal overdoses, both intentional and accidental. Recent evidence from European studies suggests that propoxyphene may be more lethal in overdose than other pain medications. The actions taken by the FDA include:

- **Manufacturers will be required to strengthen their label, including the black box warning, to emphasize the potential for overdose when using propoxyphene**
- **A Medication Guide for patients must be developed, stressing the importance of taking propoxyphene only as directed**
- **The FDA will require a new safety study to assess the effects of propoxyphene on the heart at higher than recommended doses**

## ……RX NEWS……RX NEWS……RX NEWS……RX NEWS……

**New Opioid Analgesic:** PriCara, a division of Ortho-McNeil-Janssen Pharmaceuticals, has been granted approval for **Nucynta**, a centrally-acting opioid analgesic. Nucynta, a Schedule II drug, is chemically similar to tramadol (**Ultram**), and, like tramadol, is also an inhibitor of norepinephrine reuptake. Nucynta is indicated for the relief of moderate to severe acute pain in patients 18 years of age or older. Contraindications include impaired pulmonary function (significant respiratory depression, acute or severe bronchial asthma, or hypercapnia in unmonitored settings), paralytic ileus, and concomitant use of MAOIs or use within 14 days. Nucynta should be used with caution in patients with a history of seizures and those taking serotonergic drugs (SSRIs, SNRIs, TCAs, MAOIs, and triptans). Patients should be advised to avoid use of alcohol. Nucynta has been rated Pregnancy Category C, and should not be used during breast-feeding. The most common adverse effects seen in clinical trials were nausea, dizziness, vomiting and somnolence. The recommended initial dose of Nucynta is 50, 75, or 100 mg, with or without food, every 4 to 6 hours depending upon pain intensity. On the first day of use, a second dose may be administered as soon as 1 hour after the first dose if adequate pain relief is not attained with the first dose. The maximum recommended dose per day is 700 mg on the first day and 600 mg on subsequent days.

**Plan B One-Step:** Teva Pharmaceuticals has announced FDA approval of a new, one-dose version of the emergency contraceptive (EC) **Plan B**, which contains one tablet of levonorgestrel 1.5 mg, and will be marketed as **Plan B One-Step**. The single dose should be taken orally as soon as possible within 72 hours after unprotected intercourse or a known or suspected contraceptive failure. In accordance with a District Court ruling in March, 2009, Plan B One-Step will be available *without* a prescription to women aged *17 years or older*. A prescription will be required for women younger that 17 years old. Plan B One-Step is expected to reach pharmacy shelves by the end of July, 2009. In other EC news, a generic for the original Plan B has been approved. Watson Pharmaceuticals' **Next Choice** is currently available by prescription only, but the manufacturer has applied for OTC status, which may take effect after Plan B's OTC exclusivity rights expire on August 24, 2009.

**New ACS Agent:** The FDA has approved the controversial antiplatelet drug **Effient** (prasugrel) for use in patients with Acute Coronary Syndrome (ACS). In a comparative study with **Plavix,** called TRITON-TIMI 38, Effient was shown to be more effective than Plavix, but critics claim this result was due to a too high dose of Effient, which led to increased major (and fatal) bleeding events. Unlike Plavix, Effient will carry a **black box warning** regarding the risk of serious bleeding.

## FTC Issues Interim Report on "Authorized Generics"

In 2005, a number of U.S. legislators requested that the Federal Trade Commission (FTC) undertake a study of the effects of so-called "authorized generics" on competition in the prescription drug marketplace. Authorized generics (AGs) are brand-name drugs, repackaged or relabeled by the brand-name manufacturer, and sold as "generics" in direct competition with first-to-market AB-rated generic drugs. AGs essentially nullify the 180-day exclusivity granted to the first generic under the Hatch-Waxman Act, which was intended to encourage the development of lower cost generic drugs. The interim report found that retail drug prices were 4.2% lower when AGs competed with first-to-market generics than when AGs did not enter them market. In contrast to this small price decrease, the report revealed that revenues of generic drug companies drop between 47 and 51% when AGs enter the market. The FTC notes that, to prevent this loss of revenue, generic firms may be willing to delay entry of their drug into the market in exchange for cash ("pay for delay" deals) or a promise not to introduce AGs in the future. The data show that such deals defer introduction of generics by an average of 34.7 months, greatly increasing overall prescription drug costs to consumers. As reported in last month's ***PRN***, a bill now in Congress, the Protecting Consumer Access to Generic Drugs Act of 2009 (H.R. 1706), would, if passed, prohibit brand-name drug manufacturers from compensating generic drug companies to delay the entry of generic drugs into the market.

# MEDICAID UPDATE

*Information Regarding the New York State Medicaid Program*

### Medicaid Audits

In 2006, the Office of the Medicaid Inspector General (OMIG) was established in an effort to combat fraud, waste, and abuse in the New York State Medicaid program. In recent years, however, many pharmacists, and their professional societies, have complained that OMIG audits have resulted in exorbitant fines based upon minor technical errors which do not in any way represent fraudulent practices. ***PRN*** has analyzed the results of 37 OMIG pharmacy audits conducted between March and June of 2009. The average repayment requested by OMIG was $70,219.00 (median= $37,935.00), based on a statistical extrapolation of the actual flagged claims. For example, in a recent audit, OMIG requested repayment of $68,147.00 based on actual flagged claims totaling only $457.71. Our analysis revealed the 5 most common issues identified in OMIG pharmacy audits:

**Ordering Provider Conflicts with Claim Provider:** claims billed with incorrect license numbers have become a significant problem since Medicaid stopped accepting facility MMIS numbers for interns and residents, who generate many Medicaid prescriptions

**Prescription Missing Required Information:** most commonly this involves prescriptions missing the date written

**Missing Prescription or Fiscal Order:** Medicaid prescriptions must be kept on file for 6 years from date of payment

**Prescription or Fiscal Order Refilled Beyond 180 Days of Issuance:** no prescription or fiscal order for a drug or supply may be refilled more than 180 days from the date of issuance

**Imprinted or Stamped Name of Prescriber Missing on Prescription:** every prescription written in New York State must be imprinted or stamped legibly and conspicuously with the name of the prescriber who has signed the prescription

# LAW REVIEW

*Regulatory Issues Affecting Pharmacy in New York State*

### FDA Rule on Side Effect Labeling Takes Effect

Effective July 1, 2009, every new and refill prescription dispensed by pharmacies must contain the following statement:

***Call your doctor for medical advice about side effects.***
***You may report side effects to the FDA at 1-800-FDA-1088***

The rule, promulgated by the Food and Drug Administration (FDA), may be complied with in a number of ways:

- A sticker containing the statement may be applied to the package, vial, or container
- The statement may appear on a preprinted prescription vial cap
- The statement may be distributed on a separate piece of paper
- The statement may be included in consumer medical information
- The statement may appear in the FDA-approved Medication Guide

### FDA Panel Recommends Ban on Vicodin and Percocet

On June 29, 2009, an FDA panel consisting of three advisory committees met to address the public health problem of liver injury related to the use of acetaminophen. The panel made a number of recommendations, the most newsworthy being a narrow vote (20 to 17) to remove Vicodin and Percocet from the market. Though it seems unlikely that the FDA will act on this recommendation, it does highlight a serious concern: fixed dose combinations of opioids and acetaminophen which can lead to overdoses of acetaminophen, the leading cause of acute liver failure in the United States. Unintentional overdoses, which account for 50% of cases, can occur when opioid tolerance causes patients to need higher amounts of the narcotic component of a combination product, leading to doses in excess of 4000 mg of acetaminophen, the current maximum recommended daily dose. Pharmacists have been dealing with this issue for years, and routinely call physicians to correct blatant overdoses of acetaminophen on prescriptions for products like Vicodin ES, which contains 750 mg of acetaminophen per tablet and is often prescribed as "Take 1 to 2 tablets every 4 hours" (which could lead a patient to ingest 9000 mg of acetaminophen!). Below is a quick-reference chart of the maximum daily doses, based on acetaminophen content, of some popular combination drugs.

| Name of Combination Product | Acetaminophen dose per tablet | Maximum Daily Dose |
|---|---|---|
| Darvocet N-100 | 650 mg | **6** |
| Percocet 5/325 | 325 mg | **12** |
| Percocet 7.5/500 | 500 mg | **8** |
| Percocet 10/650 | 650 mg | **6** |
| Vicodin | 500 mg | **8** |
| Vicodin HP | 660 mg | **6** |
| Vicodin ES | 750 mg | **5** |

*Feature Article..*

# REVIEW OF FDA PREGNANCY RATINGS

**The Food And Drug Administration** (FDA) announced last year that it planned to make major revisions to the physician labeling of prescription drugs regarding the effects of medications used during pregnancy. The agency said it would replace the familiar letter ratings, A,B,C,D, and X, with a more detailed pregnancy label consisting of three principle components: Risk Summary, Clinical Considerations, and Data. These label revisions are expected to be implemented over a period of years; in the meantime, prescribers, pharmacists, and patients will still need to be familiar with the current letter category system, however imprecise it may be. Below is a description of each of the 5 letter categories and a look at the ratings of some popular drugs for conditions most likely to affect women in pregnancy.

## FDA Use-In-Pregnancy Ratings*

**A** **Controlled Studies Show No Risk:** Adequate, well-controlled studies in pregnant women have failed to demonstrate a risk to the fetus in any trimester of pregnancy

**B** **No Evidence Of Risk In Humans:** Adequate, well-controlled studies in pregnant women have not shown increased risk despite adverse findings in animals, or, in the absence of adequate human studies, animal studies show no risk. The chance of fetal harm is remote, but remains a possibility

**C** **Risk Cannot Be Ruled Out:** Adequate, well-controlled human studies are lacking, and animal studies have shown a risk to the fetus or are lacking as well. There is a chance of fetal harm if the drug is administered during pregnancy, but the potential benefits may outweigh the potential risks

**D** **Positive Evidence Of Risk:** Studies in humans, or investigational or post-marketing data, have demonstrated fetal risk. Nevertheless, potential benefits may outweigh potential risks, for example in a life-threatening situation or serious disease for which safer drugs cannot be used or are ineffective

**X** **Contraindicated In Pregnancy:** Studies in animals or humans, or investigational or post-marketing data, have demonstrated positive evidence of fetal abnormalities or risk which clearly outweighs any possible benefit to the patient

* Adapted from 2009 PDR Supplement A

| PAIN | ALLERGY/COLD | ANTIBIOTICS | NAUSEA/VOMITING |
|---|---|---|---|
| **B**<br>Acetaminophen | **B**<br>Cetirizine<br>Chlorpheniramine<br>Diphenhydramine<br>Levocetirizine<br>Loratadine<br>Budesonide Nasal | **B**<br>Azithromycin<br>Cephalosporins<br>Clindamycin<br>Erythromycin<br>Nitrofurantoin***<br>Penicillins<br>Vancomycin (oral)<br>***Contraindicated at term | **A**<br>Pyridoxine |
| **C**<br>APAP with Codeine<br>Diclofenac**<br>Hydrocodone/APAP<br>Ibuprofen**<br>Meloxicam**<br>Nabumetone**<br>Naproxen**<br>Oxaprozin**<br>Oxycodone/APAP<br>Tramadol<br>Tapentadol | **C**<br>Brompheniramine<br>Ciclesonide Nasal<br>Desloratadine<br>Dextromethorphan<br>Fexofenadine<br>Fluticasone Nasal<br>Guaifenesin<br>Mometasone Nasal<br>Phenylephrine<br>Pseudoephedrine<br>Triamcinolone Nasal | **C**<br>Clarithromycin<br>Fluoroquinolones<br>SMZ/TMP<br>Vancomycin (injection) | **B**<br>Dimenhydrinate<br>Doxylamine<br>Meclizine<br>Metoclopramide<br>Ondansetron |
| **D**<br>Aspirin<br>**NSAIDs are rated D in the 3rd trimester | | **D**<br>Doxycycline<br>Minocycline<br>Tetracycline | **C**<br>Chlorpromazine<br>Methylprednisolone<br>Prochlorperazine<br>Promethazine<br>Trimethobenzamide |

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# ASK PRN...

**Other than controlled substance prescriptions, are there any other situations in which pharmacists in New York State are *required* to obtain follow-up hard copies to oral orders?**

Yes. There are a number of instances where hard copy prescriptions are required:

- **Syringes and/or needles:** Emergency oral prescription for syringes/needles are allowed up to a maximum quantity of 100 units. A follow-up hard copy must be sent to the pharmacy within 72 hours. This regulation would also apply to any product dispensed in a pre-filled syringe, such as **EpiPen**, **Byetta**, and pre-filled insulin pen devices, such as **Lantus Solostar**, **Novolog FlexPen**, and **Humalog Pen**.
- **Medicaid/Medicare DMEs:** Hard copy prescriptions are required for medical/surgical supplies and durable medical equipment (DME) prescriptions billed to either New York State Medicaid or Medicare Part B. If a pharmacy accepts an oral order for any of these items, including **blood glucose strips**, **lancets**, and **enteral formulas**, that pharmacy is responsible for obtaining a follow-up hard copy from the prescriber. Recent OMIG audits (see **Medicaid Update** on page 2 of this issue) have sought recovery of thousands of dollars from pharmacies that did not produce hard copy prescriptions for these items.

In addition to those products that *require* follow-up prescriptions, there are several cases where it may be wise for pharmacists to request hard copies for their own protection. Examples include any unusual or very expensive prescription billed to a third-party payer, and certain non-controlled drugs which may be subject to abuse, such as **carisoprodol**.

**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 Apollo lunar missions each carried on board a medical kit replete with all the leading pharmaceuticals of the day? Since July 20, 2009 is the 40th anniversary of the first moon landing, we thought we'd have a look inside Apollo 11's flying pharmacy[1]; here's what it contained: 72 Aspirin, 60 Actifed, 60 Ampicillin, 40 Mylicon, 24 Lomotil, 21 Seconal, 18 Darvon Compound, 12 Dexedrine, 3 Marezine Injectors, 3 Demerol Injectors, and 2 tubes if antibiotic ointment. Those astronauts were truly ready for anything!

## PHARMACY FUN

**This month we have a classic riddle, told with a pharmaceutical twist. On a visit to a pharmaceutical lab, you are examining three bottles of identical-looking tablets marked only as "A," "B," and "C." The lab director informs you that two of the bottles contain placebo tablets and the remaining bottle contains a new life-saving oral anti-venom tablet, which, if taken immediately, will avert the sudden death caused by the bite of a spider endemic to the area. As you pick up one of the bottles, you realize that one of the lab's residents, the deadly spider itself, has just bitten you! There's no time to check the protocols to see which bottle holds the anti-venom, and the only information the lab director can remember is that the real tablets weigh 510 mg each, while the placebos weigh only 500 mg each. Oh, and, by the way, the placebos *inactivate* the anti-venom, so you can't just take one of each! With time running out, you grab a scale from the benchtop, but you only have enough time for one weighing! Exactly what should you put on the scale in order to be 100% sure that you will be able to determine, with just one reading, which bottle contains the life-saving tablets? The first reader to answer correctly at *puzzle@prnnewsletter.com* will receive a custom-printed *PRN* binder.**


Answers to last month's ***PHARMACY FUN***:
1. Colace 2. Dimetapp 3. Mylicon 4. Benadryl

**References:**
1. http://history.nasa.gov/SP-4029/Apollo_18-42_Apollo_Medical_Kits.htm *accessed July , 2009.*