PRN

ISSN # 1941-9481

www.prnnewsletter.com

Volume 2, Number 12 | A Monthly Newsletter for Community Pharmacists | December, 2008

What's Inside…

FDA NEWS

Recent FDA actions and approvals include:

Tapentadol is a new analgesic approved for treatment of moderate to severe acute pain in adults. Tapentadol is related to an active metabolite of **tramadol**, and works by activation of mu-opiate receptors and by inhibiting norepinephrine reuptake. The manufacturer, Johnson and Johnson, has not yet designated a brand name for the product, and is still awaiting scheduling by the DEA.

Banzel (rufinamide) has been approved for adjunctive treatment of seizures associated with Lennox-Gastaut Syndrome in children 4 years and older and adults. Banzel will be available from Esai in 200 mg and 400 mg scored tablets which should be taken with food.

Apriso (mesalamine), by Salix Pharmaceuticals, is the first FDA-approved once-daily mesalamine treatment for the maintenance of remission of ulcerative colitis. The recommended dose is four 0.375g capsules (1.5 g total) once daily in the morning with or without food. Apriso should not be taken with antacids due to its pH-sensitive delayed release formulation. Apriso will become available early in 2009.

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Oral Agent for Chronic ITP: The FDA has approved GlaxoSmithKline's **Promacta** (eltrombopag), the first oral thrombopoietin (TPO) agonist for the treatment of chronic idiopathic thrombocytopenia purpura (ITP). ITP is sometimes referred to as immunologic thrombocytopenia since many cases involve the development of platelet antibodies. Standard treatment consists of corticosteroids, spleenectomy, or administration of immunoglobulins. Promacta is for ITP patients who have not responded sufficiently to these therapies. Because use of Promacta requires extensive monitoring, including regular CBCs, platelet and WBC counts, as well as liver function tests, the FDA has restricted its use to physicians, pharmacies, and patients who have joined the PROMACTA *CARES* registry (pharmacists call 1-800-9-PROMACTA or visit ***www.promactacares.com***). For a review of some of the other restricted access drug programs you're likely to encounter in your practice, see this month's feature article on page 3.

Study Compares Brands and Generics: A meta analysis published in the Journal of the American Medical Association reviewed studies comparing brand vs. generic versions of drugs in 9 subclasses of cardiovascular medications.[1] The overwhelming majority of studies reported clinical equivalence, even in the case of narrow therapeutic index drugs. The authors surmise that continuing resistance to generics among some physicians and editorialists may be based on anecdotal experience and/or the effect of financial relationships with drug companies.

New Overactive Bladder Agent: Pfizer has been granted FDA approval to market **Toviaz** (fesoterodine fumarate) for the treatment of overactive bladder in adults. Toviaz is an extended-release formulation of fesoterodine, which is rapidly converted to the antimuscarinic 5-hydroxymethyl tolterodine, an active metabolite of **Detrol**. The most common adverse effects reported in clinical trials were dry mouth (18 - 34%), constipation (4.2 - 6%), and dry eyes (1.4 - 3.7%). Toviaz is contraindicated in patients with urinary or gastric retention, or uncontrolled narrow-angle glaucoma. The recommended starting dose of Toviaz is 4 mg once daily, with or without food. The dose may be increased as needed and tolerated to 8 mg once daily, except in patients with severe renal insufficiency (CL_{CR} <30 mL/min) and those taking potent CYP3A4 inhibitors, such as ketoconazole, itraconazole, or clarithromycin.

Pharmacist-Nurse Team Improves Outcomes: A study published in the Archives of Internal Medicine concluded that a pharmacist and nurse team-based intervention resulted in a clinically important improvement in blood pressure, even in patients who have diabetes and hypertension that are relatively well controlled.[2] In this randomized trial conducted in Canada, patients who received cardiovascular risk reduction counseling by a nurse-pharmacist team showed a reduction in systolic blood pressure twice that of patients in the control arm (10.1 vs. 5.0 mm Hg). This study is in agreement with an earlier trial (see July, 2008 ***PRN***) which demonstrated the value of pharmacist counseling in improving outcomes.

Reaction to the JUPITER Study: A Case of 'Irrational Exuberance'?

The results of the Justification for the Use of Statins in Prevention: an Intervention Trial Evaluating Rosuvastatin (JUPITER) study made headlines last month.[3] The study, funded by AstraZeneca, maker of **Crestor** (rosuvastatin), evaluated the use of a statin in apparently healthy patients with normal cholesterol levels in the presence of elevated C-reactive protein (CRP). CRP is a measure of inflammation associated with increased cardiovascular risk. The study's primary result, a 50% reduction in cardiovascular events, has lead some to renew the call to "put statins in the drinking water." However, it should be noted that the 50% figure represents a reduction in *relative risk* (1.8% of control subjects had an event vs. 0.9% of Crestor subjects). The reduction in *absolute risk*, considered by many to be more important in evaluating whether to treat, was only 0.9% (1.8 - 0.9). Another finding of the study, the fact that 3% of the Crestor group developed diabetes during the study vs. only 2.4% of the control subjects, may, as the authors assert, be due to chance, but if couched in terms of *relative risk* would represent a statistically significant *25% increase in diabetes incidence* in patients taking Crestor. Again, the increase in *absolute risk* is much less dramatic: 0.6%. JUPITER is an important milestone, suggesting another route for prevention of cardiovascular events in a select subset of patients, but more evidence of long-term efficacy and safety should be obtained before committing large numbers of otherwise healthy patients to a lifetime of statin therapy.

MEDICAID UPDATE

Information Regarding the New York State Medicaid Program

Medicaid Rules on Filling and Refilling of Prescriptions

The New York State Medicaid program sets rules regarding filling of prescriptions that are, in many cases, stricter than those of the Board of Pharmacy. These rules are delineated in the Provider Manual, which is available online at ***www.emedny.org***.

Filling Prescriptions

Prescriptions for non-controlled substances ***must be filled within 60 days of the date written*****.** The 60-day rule also applies to fiscal orders for OTC drugs and medical/surgical supplies. Prescriptions for controlled substances must be filled within 30 days of the date written, in agreement with state law.

Refilling Prescriptions

Prescriptions for both controlled and non-controlled substances may be refilled, if authorized by the prescriber, ***up to 5 times within 180 days of the date written***. In accordance with state and federal regulations, prescriptions for schedule II drugs and benzodiazepines may not be refilled.

Unauthorized Practices

A number of common practices regarding the refilling of prescriptions, while allowed under state law, are prohibited under Medicaid rules. They include:

- **Automatic refilling of prescriptions is not allowed. This restriction also applies to fiscal orders for OTCs, medical/surgical supplies, and enteral products**
- **Refill transfers between pharmacies are not allowed. This applies to both controlled and non-controlled substances**
- **Faxed refill authorization requests are not allowed**

LAW REVIEW

Regulatory Issues Affecting Pharmacy in New York State

Filling Out-of-State and Foreign Prescriptions

As a major destination for both tourists and immigrants, New York sees more than its share of out-of-state and foreign prescriptions. This month, ***PRN*** reviews the rules and regulations that apply to the filling of these prescriptions.

Non-Controlled Substances: Out-of-State

An out-of-state prescription for a non-controlled substance may be filled in New York State as long as the prescription contains all the information required by section 29.7(a)(1) of the Rules of the Board of Regents, including name, address, and age of the patient, name, address, telephone number, profession, and signature of prescriber, date written, and name, strength, quantity, and directions for use of the drug prescribed. Additionally, if the prescription is being filled for a Medicaid recipient, the pharmacist must ensure that the prescription blank is in compliance with the Federal Tamper-Resistant Prescription Pad Law (see April, 2008 issue of ***PRN*** for details). When billing Medicaid, use serial number ZZZZZZZZ to indicate an out-of-state prescription.

Non-Controlled Substances: Foreign

A prescription for a non-controlled substance written in a foreign country may be filled in New York State provided that the drug requested is available in *exactly the same strength and dosage form* as written. It would not be appropriate to substitute a product similar to one available only in the country of origin. Professional judgment should be used to assess whether the prescription was written by an authorized prescriber, and if the drug is one that requires close medical supervision, it should be determined that the patient has access to a local physician.

Controlled Substances: Out-of-State

An out-of-state prescription for a Schedule II, III, IV, or V substance may be filled in New York State according to the specifications set forth in section 80.78 of the Rules and Regulations on Controlled Substances. These include the following:

- **The prescription must contain all the information required for a controlled substance in New York, including:**
  - **Patient name, sex, address, and age**
  - **Printed name, address, DEA number, telephone number, and handwritten signature of prescribing practitioner**
  - **Specific directions for use, including, but not limited to, the dosage and frequency of dose**
  - **Date upon which the prescription was prepared and actually signed. The prescription shall have been dated as of, and signed on, the date it is issued**
- **The prescription must be filled within 30 days of the date it was signed. While federal law gives no time limit regarding when a prescription may be filled, New York regulations prohibit filling a prescription for a controlled substance more than 30 days after it has been issued (signed).**
- **Where federal and state schedules conflict, pharmacists must follow the New York State schedule. Anabolic steroids, schedule III federally (and therefore refillable), are schedule II in New York and *may not* be refilled. Document that the prescriber has been contacted to authorize any changes in quantity or refills allowed. Similarly, benzodiazepines, though schedule IV, are *not* refillable in New York State.**

Controlled Substances: Foreign

Foreign prescriptions for controlled substances may only be filled in New York State if the prescriber has a valid United States DEA number. In addition, all other restrictions listed above for non-controlled foreign prescriptions, as well as those for out-of-state controlled substance prescriptions, apply to foreign controlled substance prescriptions.

Feature Article..

RESTRICTED ACCESS DRUG PROGRAMS

All Drugs have side effects, precautions, warnings, and contraindications. For a select few agents, however, the nature of the associated risks has led the FDA to restrict access to their use. Restricted access drug programs involve informed consent of patients, and adherence to established protocols by prescribers and dispensers. In some cases, the drug is distributed directly from the manufacturer to the physician or patient (**Tracleer**, **Iressa**, **Mifeprex**, **Xyrem**). Other programs allow for distribution through registered pharmacies; these include the four drugs discussed below: **Clozapine**, **Isotretinoin**, **Lotronex**, and **Thalomid**. Two restricted drugs not reviewed here are **Tikosyn** and the newly approved **Promacta**. For information on Tikosyn call 1-877-TIKOSYN. For information on Promacta call 1-877-9-PROMACTA.

CLOZAPINE

Brand Names: Clozaril, FazaClo ODT.

Indications: Refractory schizophrenia; reduction in risk of recurrent suicidal behavior in schizophrenic or schizoaffective disorder.

Monitored Adverse Effect: Significant risk of potentially life-threatening agranulocytosis.

Program Protocols: Regular monitoring of White Blood Cell (WBC) count and Absolute Neutrophil Count (ANC). To initiate therapy, WBC must be at least 3500/mm^3 and ANC must be at least 2000/mm^3.

Key Points for Pharmacists:

- **Must verify patient is eligible and registered, and fax current lab results to appropriate patient registry**
- **Initially, 7-day supply maximum, after 6 months, 14-day supply allowed, and after 1 year, 28-day supply allowed**
- **Refills allowed, but require new blood work for each refill**
- **Phone, fax, and e-prescriptions are allowed**

Contact: 1-800-448-5938 (Clozaril)
1-877-FAZACLO (FazaClo ODT)
1-800-843-9915 (Mylan)
1-800-507-8334 (Teva)

LOTRONEX

Generic name: Alosetron.

Indication: Diarrhea-predominant Irritable Bowel Syndrome (D-IBS) in women.

Monitored Adverse Effect: Serious gastrointestinal adverse reactions, including ischemic colitis, have been reported with the use of Lotronex.

Program Protocols: Patients must meet specific criteria and sign informed consent.

Key Points for Pharmacists:

- **Dispense only prescriptions that have a Prescribing Program for Lotronex (PPL) sticker**
- **Patients using Lotronex should follow up with their physicians 4 weeks after the initial dose to evaluate their treatment**
- **Refills are permitted on written prescriptions**
- **Phone, fax, and e-prescriptions are NOT allowed**

Contact: 1-888-423-5227

ISOTRETINOIN

Brand Names: Accutane, Amnesteem, Claravis, Sotret.

Indication: Treatment of severe recalcitrant nodular acne unresponsive to conventional therapy.

Monitored Adverse Effect: There is an extremely high risk that severe birth defects will result if pregnancy occurs while taking Isotretinoin in any amount, even for a short period of time

Program Protocols: All patients must sign informed consent and agree not to donate blood during and for 1 month after treatment. Females of childbearing potential must have initial and monthly pregnancy tests and agree to use 2 forms of contraception for 1 month before, during, and for 1 month after treatment.

Key Points for Pharmacists:

- **Must obtain authorization and a Risk Management Authorization (RMA) number before filling prescription**
- **Maximum of 30-day supply may be dispensed**
- **No refills allowed**
- **Phone, fax, and e-prescriptions are allowed**

Contact: 1-866-495-0654

THALOMID

Generic Name: Thalidomide.

Indications: Treatment of multiple myeloma; treatment of cutaneous manifestations of erythema nodosum leprosum.

Monitored Adverse Effect: Thalidomide is a known teratogen which has cause phocomelia, amelia, and death.

Program Protocols: All patients must sign informed consent. Females of childbearing potential must have a pregnancy test and agree to use 2 forms of contraception for 1 month before, during, and for 1 month after treatment. Males agree to use latex condoms during sexual activity with women of childbearing age.

Key Points for Pharmacists:

- **Before dispensing Thalomid, pharmacists must activate the authorization number on every prescription and record the confirmation number on the prescription**
- **Prescriptions must be filled within 7 days of issuance**
- **Maximum of 28-day supply may be dispensed**
- **No refills allowed**
- **Phone, fax, and e-prescriptions are NOT allowed**

Contact: 1-888-423-5436

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...

We have recently seen a number of prescriptions for non-controlled substances with stickers containing the drug name, strength, and directions affixed to the face of the prescription. Is this practice acceptable?

No. For non-controlled substance prescriptions, only 2 types of stickers or labels affixed to the official prescription are acceptable:

1. **Labels containing only patient information (patient name, address, and date of birth)**
2. **Labels indicating a change in the address of the prescriber's practice.**

For controlled substance prescriptions, ONLY change of practice address labels are allowed. Labels containing patient information are NOT acceptable. *Labels containing drug information are not valid for use on any official prescriptions, whether for controlled or non-controlled substances.*

Are there any important differences between the solution and suspension forms of Cortisporin Otic drops? Prescribers often neglect to specify the form on the prescription.

Yes, there are important differences. Cortisporin otic *solution* is ONLY indicated for treatment of superficial bacterial infections of the external auditory canal. The *suspension* is indicated for infections of mastoidectomy and fenestration cavities, as well as for superficial bacterial infections. In addition, the *suspension* is less acidic, and therefore less likely to cause irritation, especially if the tympanic membrane is perforated (although neither form is recommended for tympanic rupture due to neomycin ototoxicity). For these reasons, the *suspension* is the preferred preparation for otic use.

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 United States avoided the tragic effects of Thalidomide given to pregnant woman in the 1960s due to the efforts of one person, Frances Oldham Kelly? Kelly was the FDA reviewer who, despite pressure from the manufacturer, refused to approve Thalidomide for use in the U.S. The drug was later discovered to be highly teratogenic, having caused severe birth defects in thousands of children born in Europe and Canada.

PHARMACY FUN

This month's puzzle: *Name That Prodrug!* A prodrug is generally defined as an inactive, or less active, agent that is metabolized, partially or completely, into an active drug. Loratadine (Claritin), for example, is metabolized *in vivo* to Desloratadine (Clarinex). Each of the following drugs has a prodrug, or precursor, which is itself a currently marketed drug. How many can you name? The first reader to send the correct answers to *puzzle@prnnewsletter.com* will receive a custom-printed *PRN* binder.

1. **Acyclovir**
2. **Amprenavir**
3. **Cetirizine**
4. **Desipramine**
5. **Dopamine**
6. **Gancyclovir**
7. **Hydrocortisone**
8. **Meprobamate**
9. **Morphine**
10. **Nortriptyline**
11. **Paliperidone**
12. **Phenobarbital**
13. **Phenytoin**
14. **Prednisolone**
15. **Theophylline**

Answers to last month's ***PHARMACY FUN***:
1. (N)-Acetyl-Para-Amino-Phenol 2. Acetyl Salicylic Acid 3. 5-Amino Salicylic Acid 4. Cyclophosphamide Hydroxydaunorubicin Oncovin Prednisone 5. Carbamazepine 6. 5-Fluorouracil 7. Iso Nicotinly Hydrazine 8.Mechlorethamine Oncovin Procarbazine Prednisone 9. 6-Mercaptopurine 10. Methotrexate 11. Normal Saline Solution 12. Sodium Polystyrene Sulfonate 13. Saturated Solution of Potassium Iodide 14. Troleandomycin 15. Tetracycline

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