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.....NEW DRUGS.....NEW DRUGS.....NEW DRUGS.....

DALIRESP (Roflumilast).
Category: COPD treatment (Phosphodiesterase type 4 [PDE-4] Inhibitor).
Initial Dose: 500 mg once daily, with or without food.
MDD: 500 mg.

Forest Laboratories has received FDA approval to market Daliresp, the first PDE-4 Inhibitor approved to reduce the risk of COPD exacerbations in patients with severe COPD associated with chronic bronchitis and a history of exacerbations. Daliresp is not a bronchodilator and is not indicated for relief of bronchospasm. Daliresp should be used with caution in patients with a history of depression and/or suicidal thoughts. Patient's weight should be monitored regularly; consider discontinuation of Daliresp if unexplained or significant weight loss occurs.

AMTURNIDE (Aliskiren/Amlodipine/HCTZ).
Category: Antihypertensive (Renin Inhibitor/CCB/Thiazide Diuretic).
Initial Dose: Individualized based on patient's current regimen. Take once daily.
MDD: 300/10/25 mg.

Novartis has introduced the third triple therapy antihypertensive to reach the market. Amturnide combines the direct renin inhibitor aliskiren, the calcium channel blocker amlodipine, and the thiazide diuretic hydrochlorothiazide. Amturnide may be used as add-on/switch therapy for patients not adequately controlled on any 2 of the component drugs. Patients should establish a routine pattern for taking Amturnide, either with or without a meal. High-fat meals decrease absorption of aliskiren substantially.

FDA NEWS

FDA Intends to Remove Unapproved Prescription Cough, Cold, and Allergy Products from Market

The FDA has announced a plan to remove from the U.S. marketplace any prescription cough, cold, and allergy product which has not gone through the FDA approval process. This represents the 17th action on a drug class as part of the agency's *Unapproved Drugs Initiative*, which began in June, 2006 (see this month's Feature Article on page 3 for a detailed discussion of the program). In taking this action, the FDA noted that there are currently many drugs for cough, cold, and allergy that do meet FDA standards, both in prescription and OTC form. Consumers currently taking one of the unapproved products are urged to speak with their healthcare professional about FDA approved alternatives. Some of the more popular products to be removed include the **Allerx** line of allergy formulas and **Sildec PE** and **Sildec PE DM** cold and cough syrups. Manufacturers of the affected products must stop producing them within 90 days and stop shipments within 180 days. The complete list of unapproved drugs is available at www.fda.gov.

AXIRON (Testosterone topical solution).
Category: Hormone replacement (Androgen).
Initial Dose: 60 mg applied once daily at the same time each morning (1 pump actuation of 30 mg to each axilla).
MDD: 120 mg.

The latest addition to the growing number of testosterone products is Eli Lilly's Axiron, which boasts a unique application site and method. The solution is applied to the underarms with a special applicator, which minimizes the exposure risk to people in close contact with the patient after application. Dosage adjustments based on serum testosterone concentrations can be made after 14 days of treatment.

HORIZANT (Gabapentin enacarbil).
Category: RLS treatment (GABA-like agent).
Initial Dose: 600 mg once daily taken with food at about 5 PM.
MDD: 1200 mg (this dose provided no additional benefit compared with the 600 mg dose, but caused an increase in adverse reactions).

The FDA has approved GlaxoSmithKline's Horizant, the first drug in its class to be approved for the treatment of moderate-to-severe primary Restless Leg Syndrome in adults. Horizant is an extended release tablet containing a prodrug of the anticonvulsant gabapentin. Horizant is not recommended for people who are required to sleep during the day and remain awake at night. Instruct patients not to cut, crush, or chew tablets.

FDA Safety Communication: Pradaxa Good for 60 Days After Opening

As previously reported in *PRN*, the anticoagulant **Pradaxa** (dabigatran) requires special handling and storage. Specifically, the label states that the product must be dispensed and stored in the original container and any remaining capsules be discarded 30 days after the bottle is opened. In a safety communication from the FDA intended to highlight these requirements, the agency has stated that they are reviewing data that indicate the product actually maintains its potency up to 60 days after bottle opening. In addition, the manufacturer is gathering more information to determine whether the product can be used after 60 days. The current recommendations for pharmacists regarding the dispensing and storage of Pradaxa are as follows:

- **Dispense Pradaxa in the original container with the original desiccant cap. Do not repackage.**
- **Pharmacists should not open the bottle when dispensing. When more than one bottle is dispensed, number each bottle and tell the patient to open only one bottle at a time.**
- **Pharmacists should place an auxiliary expiration label on the bottle and instruct the patient to date the bottle to expire 60 days after opening.**

MEDICAID UPDATE

Information Regarding the New York State Medicaid Program

New York Medicaid Pharmacy Home Delivery Policy

The Department of Health has issued a statement clarifying their policies regarding home deliveries to Medicaid recipients by pharmacies. Some of the key points covered in the policy statement included:

1. **All shipping and delivery costs are the responsibility of the pharmacy.**
2. **Medicaid beneficiaries can not be charged for delivery if Medicaid reimburses for all or any portion of the item being delivered.**
3. **The pharmacy should inform the recipient of the pharmacy's deliver schedule and explain that a signature will be required at the time of delivery.**
4. **The pharmacy must advise the recipient, either verbally or in writing, of the correct handling and storage of the delivered prescriptions.**
5. **The pharmacy is accountable for proper delivery and will obtain a signature from the beneficiary or their designee confirming the delivery. A waiver signature form is not an acceptable practice and such forms will not serve as confirmation of delivery. Delivery industry tracking receipts that contain a signature qualify as a signature for receipt of delivery, as do electronic signatures. Delivery confirmation must be maintained by the pharmacy for 6 years from the date of payment and must be retrievable upon audit.**
6. **The pharmacy is liable for the cost of any prescription damaged or lost through distribution and delivery.**

LAW REVIEW

Regulatory Issues Affecting Pharmacy in New York State Update from the New York State Board of Pharmacy

The New York State Board of Pharmacy held a meeting on March 23, 2011 at St. John's University in Queens, New York. Some of the topic discussed are outlined below:

• Changes to the Official New York State Prescription

The board has approved mandating that the prescriber's NPI number appear on all prescriptions.

The 8 organ diagnosis system will be removed from the back of prescriptions.

The board has approved a diagnosis spot to be added to the front of the prescription, below the directions and above the prescriber's signature, where an ICD-9 code or actual diagnosis can be indicated

• Proposal of Change in Prescription Requirement

The board is considering a proposal to require that all prescriptions written for patients 18 years of age and younger include the patient's weight in addition to name, address, and age.

The board is also considering a motion to include allergies on prescriptions and the elimination of the words teaspoon and tablespoon.

• Collaborative Drug Therapy Management (CDTM)

On the question of whether only a PharmD can perform CDTM, the board opposes two different standards (BS and PharmD are both licensed pharmacists)

Proposal to require pharmacists to complete 5 CE credits on CDTM every 3 years (see Legislative Update below)

• Immunization

Proposal to expand immunization to all adult vaccines (see Legislative Update below).

Legislative Update: Current Bills of Interest to Pharmacists

There are a number of bills currently under consideration by the New York State legislature which would affect the practice of pharmacy. Several deal with the business side of pharmacy, addressing grievances pharmacists have with the Medicaid program, PBMs, and mail order programs. Others, including the following, address the professional aspects of practice.

A6301/S3808: Immunization Expansion and Reform seeks to expand pharmacist immunizations to include all adult vaccines (currently pharmacists are only authorized to administer influenza and pneumococcal vaccines). This bill also allows certified pharmacy interns to administer vaccinations under the direct supervision of a certified pharmacist, and does away with the triennial re-registration fee for a certificate of administration.

A4579/S2985: Collaborative Drug Therapy Management would add collaborative drug therapy management to the definition of the profession of pharmacy. CDTM to require a written agreement between a pharmacist and a physician or nurse practitioner in the context of a teaching hospital or its affiliated clinics. Such written agreements may authorize the pharmacist to adjust a drug dosage, frequency or route of administration, order clinical laboratory tests, and monitor the patient with regard to medication therapy. In addition, any pharmacist participating in CDTM would need to complete at least 5 hours of continuing education in the area or areas of practice related to any CDTM protocols to which they are subject.

FDA'S UNAPPROVED DRUGS INITIATIVE

Most pharmacists, doctors, and patients are well aware of the rigorous process new drugs must undergo in order to gain FDA approval and enter the marketplace. What many do not realize is that there are literally thousands of unapproved products on the market, both prescription and OTC, which sit on pharmacy shelves right next to their FDA-approved counterparts. The FDA has serious concerns that drugs marketed without required approval may not meet modern standards for safety, effectiveness, quality, and labeling. In order to address this concern, the agency launched the Unapproved Drugs Initiative in June, 2006. Since the program's inception, the FDA has taken action on 17 drug classes, most recently targeting unapproved prescription cough, cold and allergy products (see FDA News on page 1). Here's a look at some of the reasons why so many unapproved drugs are still marketed, and a review of some of the major actions taken as a result of the initiative.

The "Unapproved Universe": Why Are There So Many Unapproved Drugs On The Market?

To answer this question, one has first to look at the legal and regulatory framework in place when many of these unapproved drugs were first marketed. Three landmark pieces of federal drug legislation are most relevant to this discussion:

The **Pure Food and Drug Act of 1906** prohibited the sale of adulterated or misbranded drugs.

The **Food, Drug, and Cosmetic Act of 1938 (FDCA)** mandated that new drugs must be proven safe before they could be marketed.

The **Kefauver-Harris Amendment to the FDCA of 1962** further required that all new drugs be shown to be not only safe, but also effective.

The aggregate of marketed unapproved drugs, sometimes referred to as the "unapproved universe," consists mainly of three categories of drugs: drugs which were marketed without approval before passage of the Acts ("grandfathered drugs"), so-called DESI (Drug Efficacy Study Implementation) drugs marketed between the 1938 and 1962 Acts, and drugs marketed without approval after 1962. However, in order to be marketed legally without approval, a drug must qualify for one of the following three categories:

Grandfathered: although many drugs are marketed on the belief that they are pre-1938 or 1962 "grandfathered" products, the FDA believes that very few are entitled to that status due to changes in formulation, dosage or strength, route of administration, or labeling.

DESI pending: according to the FDA, only a small number of drugs are still DESI pending, and in most of those cases the agency has made an initial determination that the products lack effectiveness. Even those DESI drugs which were determined to be safe and effective were required to apply for and be granted FDA approval as a condition of continued marketing.

GRASE: drugs generally recognized as safe and effective (GRASE) are not considered "new drugs" and therefore not subject to approval, but since a designation of GRASE requires a consensus among experts based on published scientific literature, the agency believes that it is unlikely that any currently marketed unapproved drug is GRASE.

FDA Enforcement Priorities

Due to the large number of unapproved drugs on the market, the FDA has identified the following categories which will receive the highest enforcement priority:

- **Drugs with potential safety risks**
- **Drugs that lack evidence of effectiveness**
- **Fraudulent drugs**
- **Drugs that present challenges to the new drug approval and OTC monograph system**
- **Unapproved new drugs that also violate the FDCA in other ways**
- **Drugs that are reformulated to avoid an FDA enforcement action**
- **Unapproved drugs that directly compete with an approved drug**

Major Enforcement Actions

- ◆ **Balanced Salt Solution (ophth) products (2008)**
- ◆ **Carbinoxamine-containing products (2006)**
- ◆ **Codeine Sulfate tablets (2009)**
- ◆ **Colchicine products (2010)**
- ◆ **Cough, Cold, and Allergy products (2011)**
- ◆ **Epinephrine 0.3 mg prefilled single dose syringe (2010)**
- ◆ **Ergotamine-containing products (2007)**
- ◆ **Time-Release Guaifenesin products (2007)**
- ◆ **Unapproved Hydrocodone products (2007)**
- ◆ **Unapproved Narcotics containing Morphine Sulfate, Hydromorphone, or Oxycodone (2009)**
- ◆ **Unapproved Nitroglycerin Sublingual tablets (2010)**
- ◆ **Topical Papain-containing products (2008)**
- ◆ **Quinine Sulfate products (2006)**
- ◆ **Trimethobenzamide HCL suppositories (2007)**



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Phone & Fax (718) 263-4632

Founder and Editor:

James Murphy, RPh

Medical Liaison:

Deborah Blenner, MD

Contributors to this Issue:

Giacomo Colarullo, CPhT

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Is there an established formula for preparing an oral suspension of Plavix for pediatric use?

Yes. Skillman and colleagues¹ recently published a formula for an extemporaneously prepared suspension of Plavix 5 mg/mL:

⇒ **Crush 4 Plavix 75 mg tablets and reduce to a fine powder.**

⇒ **Add a small amount of a 1:1 mixture of Ora-Sweet® and Ora-Plus® and mix to a uniform paste.**

⇒ **Mix while adding vehicle in geometric proportions to almost 60 mL; transfer to a calibrated bottle.**

⇒ **Rinse mortar with vehicle and qs to 60 mL.**

⇒ **Label "shake well." Product is stable for 60 days at room temperature or under refrigeration.**

I just became certified as an immunizing pharmacist in New York State. Do I have to re-register every 3 years and, if so, is there any requirement for CE credits related to immunization?

Currently, the regulations require that a \$100.00 fee for certificate of administration be paid on a triennial basis. At this time, there is no requirement that specific continuing education credits be completed beyond the original courses needed for certification, but pharmacists, of course, have a duty to maintain competence. A bill currently in the New York State legislature (see Law Update on page 2) would eliminate the triennial renewal fee and would broaden the scope of practice to allow pharmacists to administer all immunizations and vaccines formulated in adult dosage.

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 study of phosphodiesterase inhibitors for pharmacologic purposes was inspired by the effects of a good hot cup of coffee? Henry Hyde Salter (1823-1871), a physician and asthma sufferer, noticed that both he and his patients breathed more freely after a dose of coffee, preferably served black and hot. In his landmark book, *On Asthma: Its Pathology and Treatment* (1860), he further described the effects of coffee as follows: "It produces rapidity of thought, vivacity of spirit, clearness of apprehension, greatly increases the working powers, and altogether intensifies mental processes." A hundred years would pass before the science caught up with Dr. Salter's observations, when caffeine and its chemical cousin theophylline were shown to be non-selective inhibitors of phosphodiesterase, an enzyme predominant in cells implicated in inflammatory airway disease

PHARMACY FUN

Well it's tax season once again, and that got us thinking about how many drugs contain the word "tax" in their name. In between filling out our state and federal returns, we managed to come up with six drugs that fit the bill. How many can you name? (for hints, see below) The first reader to submit the correct answers to puzzle@prnnewsletter.com will receive a custom-printed PRN binder.

- | | |
|------------------------------------|--------------------------------------|
| 1. Topical antifungal (brand name) | 4. Antineoplastic agent (brand name) |
| 2. Beta blocker (generic name) | 5. Muscle relaxant (generic name) |
| 3. Cephalosporin (generic name) | 6. PDE-5 ODT (brand name) |

Answers to last month's **PHARMACY FUN**:

1. Tamiflu 2. Flumadine 3. Sudafed 4. Theraflu 5. Amantadine 6. Relenza

References:

1. Skillman KL, Caruthers RL, and Johnson CE, "Stability of an Extemporaneously Prepared Clopidogrel Oral Suspension," *Am J Health Syst Pharm*, 2010, 67(7):559-61.