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What's Inside…

FDA NEWS

FDA Proposes Withdrawal of ProAmantine

The Food and Drug Administration signaled that it will move to withdraw **ProAmantine** (midodrine) from the market. ProAmantine, indicated for the treatment of orthostatic hypotension, was approved in 1996 under the agency's accelerated approval regulations for drugs to treat serious or life-threatening diseases. Such approvals mandate that the drug manufacturer verify clinical benefit through post-approval studies. To date, neither the original manufacturer, Shire, nor any of the generic manufacturers have demonstrated the drug's clinical benefit. The FDA will consider written comments from the manufacturers before making a final decision on withdrawing the drug. Approximately 100,000 patients in the United States filled prescriptions for brand or generic forms of midodrine in 2009. The agency is currently working with manufacturers to develop an expanded-access program for patients now using the drug. Patients who currently take midodrine should not stop taking it, and should consult their physician about other treatment options

……RX NEWS……RX NEWS……RX NEWS……RX NEWS……

New Emergency Contraceptive: The FDA has approved a new prescription-only emergency contraceptive (EC) called **Ella**, which will be distributed in the United States by Watson Pharma, Inc. Ella (ulipristal acetate) is a progesterone agonist/antagonist and is effective in preventing pregnancy when taken orally within 120 hours (5 days) after a contraceptive failure or unprotected intercourse. Ella is contraindicated in known or suspected pregnancy (Pregnancy Category X); pregnancy should be excluded before prescribing Ella. In clinical trials, the most common adverse reactions were headache, abdominal pain, nausea, dysmenorrhea, fatigue, and dizziness. Women who become pregnant or complain of lower abdominal pain after taking Ella should be evaluated for ectopic pregnancy. Ella may alter the next expected menses; if menses is delayed beyond 1 week, pregnancy should be ruled out. Ella will be available as a single 30 mg tablet, which can be taken with or without food.

New Conjunctivitis Treatment: Vistakon Pharmaceuticals has received FDA approval to market **Lastacaft** (alcaftadine) ophthalmic solution for the prevention of itching associated with allergic conjunctivitis. Lastacaft is an H1 histamine receptor antagonist which also inhibits the release of histamine from mast cells. The most common adverse reactions are irritation, burning, and/or stinging on instillation, eye redness and eye pruritis. Lastacaft should not be used to treat contact lens-related irritation. Contact lenses should be removed before use and may be reinserted after 10 minutes if eyes are not red. The recommended dose for adults and children aged 2 years and older is one drop in each eye once daily.

New Triple Therapy for HTN: Daiichi Sankyo, Inc. has been granted FDA approval to market a new fixed-dose combination treatment for hypertension called **Tribenzor**. Tribenzor is a combination of an angiotensin receptor blocker (**olmesartan**), a calcium channel blocker (**amlodipine**), and a thiazide diuretic (**hydrochlorothiazide**). Tribenzor should not be used in pregnancy or by nursing mothers. In clinical trials, the most common adverse reactions were dizziness, peripheral edema, headache, fatigue, nasopharyngitis, muscle spasm, upper respiratory tract infection, diarrhea, urinary tract infection, and joint swelling. Tribenzor is not indicated for initial therapy, but may be substituted for its individually titrated components or used as add-on/switch therapy. Dosage may be increased after 2 weeks to a maximum of 40/10/25 mg once a day. Tribenzor will be available in the following strengths (dosage expressed as olmesartan/amlodipine/hydrochlorothiazide): **20/5/12.5**, **40/5/12.5**, **40/5/25**, **40/10/12.5**, and **40/10/25** mg.

Another HTN Combo: The FDA has also recently approved yet another antihypertensive combo, Novartis' **Tekamlo**, which combines the direct renin inhibitor **aliskiren** with the calcium channel blocker **amlodipine**. Tekamlo is indicated for the treatment of hypertension as initial therapy in patients likely to need multiple drugs to achieve their blood pressure goals, in patients not adequately controlled on monotherapy, or as a substitute for its titrated components. Tekamlo will be available in the following strengths (dosage expressed as aliskiren/amlodipine): **150/5**, **150/10**, **300/5**, and **300/10** mg. For more information on fixed-dose combinations for the treatment of hypertension, see our feature article on page 3 of this issue.

FDA Approves a Risk Management Plan for Qualaquin

In response to continued reports of serious side effects related to the "off-label" use of **Qualaquin** (quinine sulfate), the FDA has approved a Risk Evaluation and Mitigation Strategy (REMS) and patient medication guide for the drug. Qualaquin is only approved for the treatment of uncomplicated malaria caused by *Plasmodium falciparum*, but it is commonly prescribed "off-label" for nocturnal leg cramps. Quinine sulfate may cause serious and life-threatening hematological reactions, including serous bleeding due to thrombocytopenia, and hemolytic-uremic syndrome/thrombotic thrombocytopenic purpura. In the absence of evidence of the effectiveness of quinine sulfate in the treatment of nocturnal leg cramps, the risks clearly outweigh the benefits. The agency's states that Qualaquin should not be used for the treatment or prevention of nocturnal leg cramps. In addition, those patients who are prescribed Qualaquin for its approved use should be educated about the warning signs of thrombocytopenia, such as easy bruising, severe nose bleeds, blood in the urine or stool, bleeding gums, and the appearance of unusual purple, brown or red spots on the skin.[1]

MEDICAID UPDATE

Information Regarding the New York State Medicaid Program

.Preferred Drug Program Update

The following additions to the New York State Medicaid Preferred Drug Program became effective on July 28, 2010. As of that date, all non-preferred drugs listed below will require prior authorization. Prescribers may obtain prior authorization by calling the Clinical Call Center at **(800) 309-9493**. Pharmacists filling prescriptions with prior authorizations must also call the Clinical Call Center to validate the prescription.

Biguanides

Preferred: Metformin, Metformin ER

Non-Preferred: Fortamet, Glucophage, Glucophage XR, Glumetza, Riomet Solution

Corticosteroids - Intranasal

Preferred: Fluticasone, Nasacort AQ

Non-Preferred: Beconase AQ, Flonase, Flunisolide, Nasonex, Omnaris, Rhinocort Aqua, Veramyst

NSAIDS - Ophthalmic

Preferred: Diclofenac, Flurbiprofen, Ketorolac

Non-Preferred: Acular, Acular LS, Acular PF, Acuvail, Nevanac, Ocufen, Voltaren, Xibrom

Platelet Inhibitors

Preferred: Aggrenox, Dipyridamole, Effient, Plavix

Non-Preferred: Persantine, Ticlopidine

Serotonin Agonists (Triptans)

Preferred: Maxalt-MLT, Relpax, Sumatriptan

Non-Preferred: Amerge, Axert, Frova, Imitrex, Maxalt, Treximet, Zomig

Xanthine Oxidase Inhibitors

Preferred: Allopurinol

Non-Preferred: Uloric, Zyloprim

LAW REVIEW

Regulatory Issues Affecting Pharmacy in New York State

DEA Holds National "Take Back Day" for Rx Drugs

In an effort to prevent diversion of prescription drugs, the Drug Enforcement Agency (DEA) held a nationwide event designed to collect expired, unused, or unwanted drugs from consumers for destruction. On Saturday, September 25, the agency accepted medications dropped off at approximately 4,094 collection sites. While the main focus of the drive was to stem the rising tide of prescription drug abuse, there were also environmental benefits to the effort. The Environmental Protection Agency (EPA) continues to investigate the negative impact of prescription drugs on the nation's water supply due to the common, but now discouraged, practice of flushing unwanted drugs down the toilet.

Proper Disposal of Prescription Drugs

The drugs collected by the DEA on "Take Back Day" were destroyed by incineration, which may be the ideal method to get rid of potentially dangerous unwanted medications. However, since this method is not an option for the average consumer, it is important for pharmacists to be able to instruct their patients on the best ways to dispose of their unused prescription medications. In fact, New York State requires that all pharmacies post a sign that contains information on the proper storage and disposal of drugs. The White House Office of National Drug Control Policy has issued the following guidelines for drug disposal:

1. **Take prescription drugs out of their original containers**
2. **Mix drugs with an undesirable substance, such as cat litter or used coffee grounds**
3. **Put the mixture into a disposable container with a lid, such as an empty margarine tub, or into a sealable bag**
4. **Conceal or remove any personal information, including Rx number, on the empty containers by covering it with black permanent marker or duct tape, or by scratching it off**
5. **Place the sealed container with the mixture, and the empty drug containers, in the trash**

The Food and Drug Administration (FDA) has published a list of drugs for which they do still recommend disposal by flushing down the sink or toilet to avoid immediate danger to people and pets in the home. To access the current list, visit our website at ***www.prnnewsletter.com*** and click on "FDA Flushable List."

Bureau of Narcotics Statement on Returned Controlled Substances

The New York State Bureau of Narcotic Enforcement (BNE) has issued a statement regarding the return of unused controlled substances to pharmacies by patients, which is prohibited. The following appeared in the Summer, 2009 edition of the BNE Pharmacy Update:

> *In accord with New York State Public Health Law, Section 3320, all entities that possess a DEA registration shall only procure controlled substances from a distributer (wholesaler) or manufacturer licensed as such with the State Department of Health's Bureau of Narcotic Enforcement. This law prohibits any DEA registrant from accepting a patient's own controlled substance medication. Community pharmacies may not take back any controlled substances once dispensed. Similarly, hospital pharmacies are prohibited from accepting a patient's own controlled substance either for safeguarding or for future administration.*

The BNE encourages communities to sponsor pharmaceutical collection events such as "Take Back Day," and pharmacies can help by either sponsoring an event or passing on information about scheduled events to their patients.

Feature Article..

FIXED-DOSE COMBINATIONS FOR HYPERTENSION

The JNC 7 (Joint National Committee on the Prevention, Detection, Evaluation, and Treatment of High Blood Pressure) states that the majority of patients with hypertension will require two or more medications to reach their blood pressure goals. Fixed-dose combination therapy has the advantage of increasing patient compliance and, in some cases, reducing costs. And while combination drugs combining thiazide diuretics with a number of other agents have been marketed for many years, recently there has been increasing interest in non-diuretic fixed-dose combinations of two drugs from complimentary antihypertensive drug classes. In the review below, we will focus on the most popular of these newer, non-diuretic fixed dose combination products.

CCB plus ACE

These agents combine a Calcium Channel Blocker (CCB) with an Angiotensin Converting Enzyme Inhibitor (ACE).

LOTREL (Amlodipine + Benazapril)

Strengths Available: **2.5 mg/10 mg**
5 mg/10 mg
5 mg/20 mg
5 mg/40 mg
10 mg/20 mg
10 mg/40 mg

Maximum Daily Dose: **10 mg/80 mg**

Indicated for initial therapy of HTN? **NO**

TARKA (Trandolapril + Verapamil)

Strengths Available: **1 mg/240 mg**
2 mg/180 mg
2 mg/240 mg
4 mg/240 mg

Maximum Daily Dose: **8 mg/480 mg**

Indicated for initial therapy of HTN? **NO**

Note: LEXXEL, which contained Enalapril and Felodipine, was discontinued by AstraZeneca in July, 2008. There is no generic formulation of this product on the market at this time.

Renin Inhibitor plus CCB

This agent combines the Direct Renin Inhibitor Aliskiren with a Calcium Channel Blocker (CCB).

TEKAMLO (Aliskiren + Amlodipine)

Strengths Available: **150 mg/5 mg**
150 mg/10 mg
300 mg/5 mg
300 mg/10 mg

Maximum Daily Dose: **300 mg/10 mg**

Indicated for initial therapy of HTN? **YES**

CCB plus ARB

These agents combine a Calcium Channel Blocker (CCB) with an Angiotensin II Receptor Blocker (ARB).

AZOR (Amlodipine + Olmesartan)

Strengths Available: **5 mg/20 mg**
5 mg/40 mg
10 mg/20 mg
10 mg/40 mg

Maximum Daily Dose: **10 mg/40 mg**

Indicated for initial therapy of HTN? **YES**

EXFORGE (Amlodipine + Valsartan)

Strengths Available: **5 mg/160 mg**
5 mg/320 mg
10 mg/160 mg
10 mg/320 mg

Maximum Daily Dose: **10 mg/320 mg**

Indicated for initial therapy of HTN? **YES**

TWYNSTA (Telmisartan + Amlodipine)

Strengths Available: **40 mg/5 mg**
40 mg/10 mg
80 mg/5 mg
80 mg/10 mg

Maximum Daily Dose: **80 mg/10 mg**

Indicated for initial therapy of HTN? **YES**

Renin Inhibitor plus ARB

This agent combines the Direct Renin Inhibitor Aliskiren with an Angiotensin II Receptor Blocker (ARB).

VALTURNA (Aliskiren + Valsartan)

Strengths Available: **150 mg/160 mg**
300 mg/320 mg

Maximum Daily Dose: **300 mg/320 mg**

Indicated for initial therapy of HTN? **YES**

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ASK PRN...

We have begun to receive shipments of the new, reformulated OxyContin. What's different about the new formulation, and why was the change made?

In April, 2010, the FDA approved Purdue Pharma's New Drug Application for a reformulation of OxyContin. The reformulated tablet is harder, even somewhat plastic-like, which will make it more difficult to break or crush the tablet, a practice favored by those who abuse the medication. In addition, when mixed with water, the contents form a gelatinous substance which would be difficult if not impossible to inject through a syringe. Beside these alterations, intended to prevent abuse of OxyContin, there are also some changes to the appearance of the product. The reformulated tablets are marked "OP" rather than "OC" and the 60 mg and 80 mg tablets are slightly larger in size than the currently marketed tablets. On April 5, 2010, Purdue Pharma released a statement about the reformulation of OxyContin, which read, in part:

The U.S. Food and Drug Administration (FDA) approved Purdue Pharma L.P.'s New Drug Application for a reformulation of OxyContin (oxycodone HCl controlled-release) Tablets.

The Reformulation has met FDA criteria for bioequivalence to the original formula, which means there is no significant difference in the rate and extent of absorption of the therapeutic ingredient.

Purdue elected to reformulate OxyContin to be bioequivalent to the original formulation and in an effort to make the tablet more difficult to manipulate for the purpose of intentional misuse and abuse, however, there is no evidence that the reformulation of OxyContin is less subject to misuse, abuse, diversion, overdose, or addiction.

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 1199, the healthcare workers union, was originally formed to represent pharmacists and drug store workers? In 1932, Leon J. Davis, a drug store clerk who had dropped out of Columbia University's School of Pharmacy, founded the union in New York City. Over the years, the organization expanded to cover workers in hospitals, nursing homes, clinics, and home health aides. Ironically, most pharmacists now working in New York are not members of this "pharmacist's union."

PHARMACY FUN

It's September once again, and around here that means only one thing: time for our third annual back-to-school quiz! This year we ask that you cast your mind back - way back - to those pre-pharmacy years, when your mind was filled with chemical structures, formulas, and reactions. See if you can match the general formulas below to their corresponding common names. The first reader to submit the correct answers to *puzzle@prnnewsletter.com* will receive a custom-printed *PRN* binder.

1. RCOOH	**a. ether**
2. ROR	**b. ester**
3. RCOOR	**c. carboxylic acid**
4. ROH	**d. ketone**
5. RCOR	**e. alcohol**

Answers to last month's **PHARMACY FUN**:
1. Cardura 2. Catapres 3. Isordil

References:
1. FDA Drug Safety Communication: New Risk management plan and patient Medication Guide for Qualaquin (quinine sulfate). Accessed 8/25/2010 at *www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm218202.htm*