P.R.N.

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What's Inside…

FDA NEWS

.FDA Warning on Post-Tonsillectomy Use of Codeine in Children

The FDA has issued a Drug Safety Communication regarding recent reports of deaths in children given codeine for pain relief after tonsillectomy and/or adenoidectomy. The cases involved children with an inherited ability to convert codeine into life-threatening or fatal amounts of codeine. These so-called "ultra-rapid metabolizers" represent between 1 and 28 percent of populations, depending on ethnic background (the highest rates are found in people of African descent). The FDA offers the following recommendations:

- **Codeine should be used on an "as needed" basis and should not be administered more than six (6) times a day in children**.
- **If a child receiving codeine exhibits unusual sleepiness, confusion, or difficult or noisy breathing, seek medical attention immediately.**
- **Consider using alternate analgesics for children having tonsils or adenoids removed.**

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

QSYMIA (Phentermine and Topiramate).
Category: Anorexiant**.**
Initial dose: 3.75 mg/23 mg taken once daily in the morning for 14 days, then increase to 7.5 mg/46 mg.
MDD: 15 mg/92 mg.

Following a 13 year period during which the FDA did not approve any drugs for weight loss, the agency has now approved 2 diet drugs in as many months. The approval of Belviq in June is now followed by that of Qsymia. Qsymia, marketed by Vivus, Inc., is actually a combination of 2 previously marketed drugs, the anorexiant phentermine and the anti-epileptic topiramate, which has been shown to reduce weight. Qsymia is indicated for chronic weight management in adults with an initial body mass index (BMI) of 30 kg/m^2 or greater or 27 kg/m^2 or greater in the presence of at least on weight-related comorbidity (e.g., hypertension, type 2 diabetes, dyslipidemia). Qsymia will, at least initially, be distributed only by mail order through certified pharmacies in the Qsymia Home Delivery Network.

VASCEPA (Icosapent Ethyl).
Category: Antihyperlipidemic.
Initial dose: 4 grams daily taken as 2 capsules twice daily with food.
MDD: 4 grams daily.

Amarin Corporation has been granted approval to market Vascepa, the second prescription-only Omega-3 fatty acid (the first was Lovaza). Vascepa contains an ethyl ester of eicosapentaenoic acid (EPA), while Lovaza contains ethyl esters of both EPA and docosahexaenoic acid (DHA). Vascepa is indicated as an adjunct to diet to reduce triglycerides in adults with severe hypertriglyceridemia (≥500 mg/dL).

RAYOS (Prednisone Delayed-Release).
Category: Oral Corticosteroid.
Initial dose: 5 mg once daily taken with food.
MDD: Depends upon condition being treated.

The FDA has approved Rayos, a delayed-release formulation of prednisone tablets distributed by Horizon Pharma, Inc. Rayos is approved for all the usual indications for prednisone, including allergic, dermatologic, gastrointestinal, respiratory, and rheumatologic conditions, and will be available in 1, 2, and 5 mg strengths. Rayos is unique, however, in that it is a delayed-release formulation which releases the active ingredient approximately 4 hours after intake. In clinical trials, patients were administered Rayos at 10 PM to achieve therapeutic blood levels in the middle of the night, the time when both cytokine and endogenous cortisol levels start to rise. Patients currently on immediate-release prednisone, prednisolone, or methylprednisolone can be switched to Rayos at an equivalent dose based on relative potency.

TUDORZA PRESSAIR (Aclidinium Bromide).
Category: Anticholinergic (Respiratory).
Initial dose: One inhalation (400 mcg) twice daily.
MDD: One inhalation (400 mcg) twice daily.

Forest Pharmaceuticals has announced approval of Tudorza Pressair, a new twice-daily anticholinergic inhaler indicated for maintenance treatment of bronchospasm associated with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and emphysema. Tudorza Pressair will be available in a 60-dose dry powder inhaler, which includes a dose counter and a control window to verify that the dose has been inhaled correctly. The inhaler should be discarded 45 days after opening if still in use.

Mayo Clinic Study Finds Off-Label Prescribing A Common Practice

A recent analysis by the Mayo Clinic has found that off-label drug use (OLDU), the prescribing of drugs for conditions other than their FDA-approved uses, is a common practice, accounting for up to 1 in 5 prescriptions for some commonly used medications.[1] Since the practice of medicine is not regulated by the Food and Drug Administration (FDA), it is permissible for physicians to prescribe drugs for off-label use. Some common examples of OLDU seen in the community pharmacy setting include trazodone for insomnia, metformin for polycystic ovary syndrome, and tamsulosin for kidney stones. Since the dosing and duration of therapy in OLDU may differ from those for approved uses, it is important that pharmacists become familiar with the latest trends in OLDU, and have a good working knowledge of the different dosing regimens involved. To that end, we have recently begun answering some OLDU questions in our ***Ask PRN*** section, including this month's edition, where we discuss the use of erythromycin for gastroparesis.

MEDICAID UPDATE

Information Regarding the New York State Medicaid Program

EPIC Benefits to be Restored

The Department of Health has announced that, effective January 1, 2013, EPIC will once again provide secondary coverage for Medicare Part D covered drugs. The Elderly Pharmaceutical Insurance Program (EPIC) is available to New York State residents 65 years and older with low incomes. In 2012, the program stopped offering secondary coverage for Part D, and many seniors were faced with large increases in their pharmacy co-payments. For 2013, EPIC rules include:

- **EPIC members must be enrolled in a Medicare Part D plan.**
- **EPIC will reinstate its Fee and Deductible plans.**
- **EPIC will provide secondary coverage for EPIC and Medicare Part D covered drugs after any Part D and/or EPIC deductible is met.**
- **EPIC co-payments for covered drugs will continue to be $3 to $20, depending on the cost of the drug.**
- **EPIC will continue to cover many Medicare Part D excluded drugs, such as prescription vitamins and prescription cough and cold preparations.**
- **EPIC will continue to pay Medicare Part D premiums, up to the amount of a basic plan, for members in the Fee and Deductible plans with income up to $23,000 (single) or $29,000 (married).**
- **Epic will also lower the EPIC deductible, by the annual cost of a basic Medicare Part D drug plan, for members with higher incomes that are responsible for paying their own Medicare Part D premium.**

LAW REVIEW

Regulatory Issues Affecting Pharmacy in New York State

I-STOP Bill Passes New York Legislature Unanimously

On June 11, 2012, both houses of the New York State legislature unanimously passed the Internet System for Tracking Over-Prescribing Act, also known as I-STOP. The legislation, a program bill initiated jointly by Attorney General Eric Schneiderman and Governor Andrew Cuomo, seeks to address the growing problem of prescription drug abuse. The main provision of I-STOP is the establishment of an online database of controlled substance prescriptions prescribed and dispensed in New York State, with mandatory real-time reporting by both prescribers and pharmacists. Additional provisions include the rescheduling of several prescription drugs, and the development of a program allowing for safe disposal of expired or unneeded controlled drugs by consumers. The governor is expected to sign the bill into law soon.

Key Components of I-STOP

- **I-STOP will make New York the first state in the nation to mandate that physicians consult a database of a patient's prescription history before prescribing a schedule II, III, or IV controlled substance. Accurate patient histories and better training will help physicians detect doctor shoppers and better serve patients at risk of addiction. Doctors can also use this information to avoid potentially dangerous drug interactions.**
- **I-STOP will make New York the largest, and only second state in the nation, to require real-time reporting by pharmacists when schedule II, III, IV, or V prescriptions are filled.**
- **I-STOP will make New York one of the first states to schedule the universal mandate of e-prescribing for controlled substances in December of 2014. The regulations will be promulgated by December, 2012. This will nearly eliminate the problem of forged or stolen prescriptions—used by both addicts, and criminal organizations obtaining pills to resell on the street.**
- **I-STOP will reschedule HYDROCODONE to schedule II, thereby prohibiting refills for this highly abused drug.**
- **I-STOP will schedule TRAMADOL, a "drug of concern," to schedule IV (it is currently unscheduled).**
- **I-STOP will establish a safe disposal program providing a place for New Yorkers to get rid of expired and unneeded drugs to ensure that they are not left in medicine cabinets for children or addicts to access.**

Some prescribers have expressed concern over the feasibility of the proposed reporting system, based on their experience with the current prescription monitoring program (PMP), which is know to be hard to access, time consuming, and which is not accessible by pharmacists. The following table outline the differences between the old system and I-STOP.

SYSTEM	Practitioner Reviewing	Practitioner Reporting	Pharmacist Reviewing	Pharmacist Reporting
Current PMP	Optional; Access to information restricted	None	None	Mandatory reporting of controlled substances at least once every 45 days
I-STOP	Mandated review of patient history before prescribing	Report issuing prescription at time of issuance	Access to system and reviewing is mandated	Mandatory reporting of controlled substances as they are dispensed

ALZHEIMER'S DISEASE REVIEW

The Statistics Are Alarming. Currently, one in eight people age 65 or older has Alzheimer's disease, and almost half of people age 85 and older suffer from the condition. As the United States population continues to age, the problem is expected to worsen, with projections of a doubling or tripling of the number of Alzheimer's patients by 2050. Already the sixth leading cause of death in the U.S., Alzheimer's disease will continue to be a major focus of research and development in the pharmaceutical industry for the foreseeable future, and pharmacists can expect to find themselves on the front lines of the battle against this disease.

Alzheimer's: Definition

Alzheimer's Disease, named for the German physician who first described it in 1906, is the leading cause of dementia in the U.S., accounting for between 60 and 80 percent of cases. A progressive, degenerative disease, Alzheimer's attacks brain cells, leading to loss of memory, loss of cognitive and language abilities, and behavioral changes. Most cases occur in people aged 65 and older, and 2/3 of patients are women, probably due to longer life expectancy. The two characteristics brain lesions of Alzheimer's are beta-amyloid plaques and neurofibrillary tangles of tau protein. While age is the greatest risk factor for developing Alzheimer's, several genetic factors have also been identified.

Alzheimer's: Symptoms

The Alzheimer's Association has identified the following 10 early warning signs of Alzheimer's disease:

- Memory loss that disrupts daily life
- Challenges in planning or solving problems
- Difficulty in completing familiar tasks
- Confusion with time or place
- Trouble understanding visual images and spatial relationships
- New problems with words in speaking or writing
- Misplacing things and inability to retrace steps
- Decreased or poor judgment
- Withdrawal from work or social activities
- Changes in mood and personality

Alzheimer's: Diagnosis

While there is yet no definitive test for Alzheimer's disease, new guidelines point to a more accurate method to detect the disease at a very early stage. Currently, the diagnosis is based primarily on a physician's clinical judgment, utilizing patient history, cognitive and neurological testing, and brain imaging to rule out other possible causes of dementia. Under new guidelines recommended by the National Institute on Aging, physicians may one day be able to identify preclinical Alzheimer's disease in asymptomatic patients through blood and cerebrospinal fluid tests. Such test would look for biomarkers of the disease, such as beta-amyloid or tau protein accumulation and/or evidence that brain cells are actually injured or degenerating.

FDA-Approved Pharmacotherapy For Alzheimer's Disease

Brand Name (active ingredient)	Dosage Forms and Strengths	Generic Available?	Initial Dose and Maximum Dose	Mechanism of Action	FDA Approval by Alzheimer's Stage
Aricept (donepezil)	**Tablet** (5, 10, 23 mg) **ODT** (5, 10 mg)	Yes (except 23 mg)	Initial dose 5mg QD. May increase to 10 mg QD after 4 to 6 weeks and to 23 mg QD after ≥ 3 months.	Reversibly inhibits centrally-active acetylcholinesterase.	Approved for **Mild**, **Moderate**, and **Severe** Alzheimer's Disease
Exelon (rivastigmine)	**Capsule** (1.5, 3, 4.5, 6 mg) **Solution** (2 mg/mL) **Patch** (4.6 mg/24 hours, 9.5 mg/24 hours)	Yes (capsules only)	Initial dose 1.5 mg BID. May increase every 2 weeks to maximum of 6 mg BID. Patch initial dose 4.6 mg QD. May increase to 9.5 mg QD after ≥ 4 weeks.	Reversibly inhibits centrally-active acetylcholinesterase	Approved for **Mild** to **Moderate** Alzheimer's Disease
Namenda (memantine)	**Tablet** (5, 10 mg) **Solution** (2 mg/mL)	No	Initial dose 5 mg QD. Titrate by 5 mg daily at ≥ 1 week intervals to target dose of 10 mg BID (all doses above 5 mg should be given in 2 divided doses).	N-methyl-D-aspartate receptor antagonist	Approved for **Moderate** to **Severe** Alzheimer's Disease
Razadyne (galantamine)	**Tablet** (4, 8, 12 mg) **Capsule ER** (8, 16, 24 mg) **Solution** (4 mg/mL)	Yes (except solution)	Initial dose 4 mg BID or 8 mg ER QD. May increase at ≥ 4 week intervals to a maximum daily dose of 24 mg.	Reversibly inhibits centrally-active acetylcholinesterase and stimulates nicotinic receptors	Approved for **Mild** to **Moderate** Alzheimer's Disease

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ASK PRN...

We have recently received several prescriptions for low dose erythromycin for adults, usually in liquid form. Upon checking with the physician, we were informed the patient was being treated for gastroparesis. What is the rationale for this off-label use?

Gastroparesis is a disorder of the stomach in which the normal motility which serves to propel food into the small intestine is either greatly reduced or absent altogether. This results in bloating, nausea, epigastric pain, reflux, and early fullness when eating. One of the most common causes of gastroparesis is diabetes, affecting between 25 and 30 percent of patients. Erythromycin, a macrolide antibiotic approved for use in a wide range of infections, has been used with some success in the treatment of gastroparesis. It is believed to work by binding to motilin receptors in the stomach and small intestine, resulting in peristalsis and improved emptying of the stomach. Erythromycin is most effective for gastroparesis when given intravenously, but this route is usually reserved for severe cases. The oral dose most commonly used is 125 to 250 mg given 3 to 4 times a day, 30 minutes before meals. Several studies have indicated that the liquid form is more effective than tablets, due to faster absorption and earlier maximum serum concentration (tmax). Since erythromycin is known to interact with many drugs, some clinicians have tried azithromycin as an alternative, although there is not nearly as much published evidence for its effectiveness. There is currently a Phase 2 clinical trial underway at the University of Florida to compare the two drugs head-to-head for their efficacy in treating gastroparesis.

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 a number of well-know brand-name prescription drugs actually started out with different names than the ones they are known by today? To avoid confusion with sound-alike drugs, the FDA occasionally steps in and requests a name change for the newer agent. Some example include **Prilosec**, which started life as Losec, but was altered to avoid confusion with Lasix, **Lovaza**, which used to be known as Omacor (too close to Amicar), **Razadyne**, formerly answering to Reminyl, which sounded a bit too much like Amaryl, and **Altoprev**, which was originally called Altocor until it was changed to avoid being confused with Advicor.

PHARMACY FUN

The months of July and August and named after consecutive leaders of the Roman Empire, Julius Caesar and Augustus, and though by most accounts Augustus was the better ruler (Pax Romana, etc.), it is Caesar who is best remembered today. The same is often true for pharmaceuticals; we remember the first new drug in any category better than the second, even though the second may work better or have fewer side effects. For each innovator drug listed below, can you name the second drug to hit the market in the same class? The first reader to submit the correct answers to *puzzle@prnnewsletter.com* will receive a custom-printed *PRN* binder.

1. Cozaar
2. Inderal
3. Mevacor
4. Prilosec
5. Proscar
6. Prozac
7. Retrovir
8. Tagamet
9. Viagra

Answers to last month's **PHARMACY FUN**:
1. Xifaxan 2. Canasa 3. Dipentum

References:
1. Wittich CM, Burkle CM, Lanier WL. Ten common questions (and their answers) about off-label drug use. *Mayo Clinic Proceedings* Volume 87, Number 8 (published online August 8, 2012 at *www.mayoclinicproceedings.com*).