P.R.N.

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What's Inside…

FDA NEWS

Proton Pump Inhibitors May Increase Risk of *C. difficile*-related Diarrhea

The FDA has released a Drug Safety Communication regarding the association between the use of proton pump inhibitors (PPIs) and the development of *C. difficile*-associated diarrhea (CDAD). An FDA review of the medical literature revealed a higher risk of *C. difficile* infection or disease, including CDAD, associated with PPI exposure compared to no PPI exposure. The agency has provided the following advice for healthcare professionals:

- **A diagnosis of CDAD should be considered for PPI users with diarrhea that does not improve.**
- **Advise patients to seek immediate care from a healthcare professional if they experience watery stool that does not go away, abdominal pain, or fever while taking PPIs.**
- **Patients should use the lowest dose and shortest duration of PPI therapy appropriate to the condition for which they are being treated.**

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

JENTADUETO (Linagliptin and Metformin).
Category: Antidiabetic (DPP-IV Inhibitor and Biguanide combination agent).
Initial Dose: Individualize based on patient's current regimen. Take twice daily with meals.
MDD: 5 mg Linagliptin/ 2000 mg Metformin.

Boehringer Ingelheim and Eli Lilly will introduce a new antidiabetic product called Jentadueto, which is a combination of Tradjenta and metformin, indicated for the treatment of type 2 diabetes. Jentadueto is not intended for the treatment of type 1 diabetes or diabetic ketoacidosis, and has not been studied in combination with insulin. Jentadueto is contraindicated in renal impairment and should be temporarily discontinued in patients undergoing radiological studies using iodinated contrast materials.

EDARBYCLOR (Azilsartan and Chlorthalidone).
Category: Antihypertensive (ARB/Thiazide Diuretic combination).
Initial Dose: 40 mg Azilsartan/ 12.5 mg Chlorthalidone once daily with or without food.
MDD: 40 mg Azilsartan/ 25 mg Chlorthalidone.

Takeda Pharmaceuticals has been granted FDA approval to market Edarbyclor, a combination antihypertensive containing the angiotensin II receptor blocker Edarbi and the thiazide-like diuretic chlorthalidone, the first such combination available in the U.S. As with all drugs acting directly on the renin-angiotensin system, Edarbyclor carries a **black box warning** against use in pregnancy. The initial dose of 40/12.5 once daily may be increased to the maximal dose of 40/25 after 2 to 4 weeks as needed.

BYDUREON (Exenatide extended-release for injectable suspension).
Category: Antidiabetic (GLP-1 Receptor Agonist).
Initial Dose: 2 mg by subcutaneous injection once weekly at any time of day and with or without meals.
MDD: 2 mg weekly.

Amylin Pharmaceuticals has announced approval of Bydureon, a once-weekly form of the injectable glucagon-like peptide-1 (GLP-1) receptor agonist Byetta. Bydureon is indicated for the improvement of glycemic control in adults with type 2 diabetes. Bydureon is not indicated for use in type 1 diabetics or for treatment of diabetic ketoacidosis and is not recommended for use with insulin. This extended release form of exenatide carries a **black box warning** related to the finding of thyroid C-cell tumors at clinically relevant exposures in rats. Bydureon will be available in cartons of 4 single-dose trays containing powder for reconstitution, diluents, syringe and needle for preparation and injection by the patient.

ZIOPTAN (Tafluprost Ophthalmic Solution)
Category: Antiglaucoma agent (Prostaglandin Analogue)
Initial Dose: One drop in affected eye(s) once daily in the evening.
MDD: One drop in affected eye(s) once daily.

Merck has received FDA approval to market Zioptan, the first preservative-free prostaglandin analogue for the treatment of open-angle glaucoma or ocular hypertension. Zioptan may cause permanent pigmentation of the iris, and temporarily increase length, thickness, and number of eyelashes.

Novartis Halts Tekturna Trial Early Due To Increased Adverse Events

Novartis has announced the early termination of its trial of **Tekturna** (aliskiren) in combination with an ACE inhibitor or angiotensin receptor blocker (ARB) in patients with type 2 diabetes and renal impairment. The trial, know as ALTITUDE (Aliskiren Trial in Type 2 Diabetes Using Cardiovascular and Renal Disease Endpoints), was a placebo-controlled Phase III study to determine if adding Tekturna to an ACE or ARB would reduce the risk of cardiovascular or renal events in diabetic patients. The trial was halted after data analysis revealed a higher incidence of nonfatal stroke, renal complications, hyperkalemia, and hypotension in the Tekturna-treated patients. The manufacturer now states that Tekturna or Tekturna-containing combination products (**Tekturna HCT**, **Valturna**, **Tekamlo**, **Amturnide**) *should not be used* in combination with ACE inhibitors or ARBs in patients with diabetes. While the FDA has not yet commented on these results, their European counterpart, the European Medicines Agency, went further than the drug maker in recommending that Tekturna should not be combined with an ACE or ARB in any patients, diabetic or not.[1] This would call into question the continued viability of at least one Novartis product, Valturna, which contains both Tekturna and the angiotensin receptor blocker valsartan.

MEDICAID UPDATE

Information Regarding the New York State Medicaid Program

Changes to Pharmacy Prior Authorization Process

At the end of December, 2011, the Department of Health announced changes to the prior authorization system designed to streamline the often cumbersome process. Beginning on December 29, 2011, the system will perform editing at the point of sale to allow claims to pay without prior authorization if certain clinical criteria are met, for example when filling a prescription for a patient already stabilized on a non-preferred atypical antipsychotic. If clinical criteria are not met, a prior authorization will still be required, but the process will be a simpler one for pharmacists:

- **Pharmacy providers will no longer have to validate prior authorizations**
- **Prior authorization numbers will be generated systemically and will no longer need to be written on the prescription or submitted on the claim**

Update on Brand Less than Generic Program

Since April, 2010, the New York State Medicaid program has promoted the use of some brand-name prescription drugs which cost the program less than their generic equivalents. For these drugs, the brand may be dispensed even if the prescription does not contain a "DAW" or "Brand Medically Necessary." Effective April 1, 2012, the program covers the following drugs:

Adderall XR	**Kadian**
Arixtra	**Lexapro**
Astelin	**Lovenox**
Carbatrol	**Nasacort AQ**
Concerta	**Uroxatral**
Diastat	**Valtrex**
Epivir	**Zyprexa tablets**
Geodon	

LAW REVIEW

Regulatory Issues Affecting Pharmacy in New York State

Review of Regulatory Changes of 2011

A number of important regulatory initiatives affecting the practice of pharmacy became law in 2011 on both the state and federal levels. In New York, perhaps the most talked about piece of legislation was the so-called AMMO bill, which prohibits mandatory mail order prescriptions in the state. This bill, and a related one mandating coverage of fertility drugs in community pharmacies if a plan covers such drugs through mail order, was signed into law by governor Andrew Cuomo on December 12, 2011 (see ***PRN # 41*** for details). Some of the less well-known new rules and regulations are covered below.

Extension of Pharmacists as Immunizers Law

In 2008, New York State passed legislation authorizing pharmacists to administer influenza and pneumococcal vaccines to adults. That bill contained a "sunset clause" which would automatically repeal the law on March 31, 2012. Assembly bill 8030 (S.3807), signed by the governor in August, 2011, extends the authorization of the pharmacists as immunizers act another 4 years, to March 31, 2016. Another pharmacists as immunizers-related bill, A.6301/S.3808, seeks to expand pharmacist immunizations to include all adult vaccines, and would allow certified pharmacy interns to administer vaccines under the direct supervision of a certified pharmacist. This legislation would also do away with the triennial re-registration fee for a certificate of administration, making it a one-time fee only. As of this writing, the bill has not reached a vote in either house of the state legislature.

Soma Reclassified as a Controlled Substance

In December of 2011, the Drug Enforcement Agency (DEA) published a final rule making Soma (carisoprodol) a federal controlled substance. Previously, the muscle relaxant was not a scheduled drug federally, although at least 18 states had already classified it as such due to widespread reports of abuse. Carisoprodol officially became a schedule IV controlled substance on January 11, 2012. Registrants who possess any quantity of carisoprodol must take an initial inventory of all stocks on-hand on or before January 11, 2012 and then include carisoprodol in their biennial inventory thereafter.

Collaborative Drug Therapy Management

New York State Senate bill 2985 (A.4579) authorizes pharmacists to perform collaborative drug therapy management (CDTM) in certain settings. Specifically, the law permits pharmacists in teaching hospitals to adjust a patient's drug dosage, frequency or route of administration, order clinical laboratory tests, and monitor the patient with regard to medication therapy. CDTM requires a written agreement between the pharmacist and a physician or nurse practitioner, as well as the completion of at least 5 hours of continuing education in the area or areas of practice related to any CDTM protocol to which the pharmacist is subject.

Early Refills for Ophthalmic Drops

New York Assembly bill 1219 (S.1430) requires insurance companies to cover the authorized refill of any prescription eye drop medication when such refill is requested prior to the expiration of the period of usage. This law is intended to address the problem of patients running out of their eye drops before the expected days supply has elapsed due to additional drops spilling from the container during use.

Coverage of Orally Administered Chemotherapy Agents

Effective January 1, 2012, insurance companies which cover infusion chemotherapy for cancer treatment must also cover orally administered chemotherapy treatments and may not penalize patients financially with higher co-pays, coinsurance, or deductibles than would be charged for infusion treatments.

Feature Article..

RECENT FDA SAFETY ADVICE ON STATIN USE

In Recent Months, the Food and Drug Administration (FDA) has announced a number of updated recommendations regarding the safe use of HMG-CoA Reductase Inhibitors, commonly known as statins. These alerts have included information about drug interactions, post-marketing reports of adverse events, and laboratory monitoring protocols. In this article we summarize the key points covered by these recent FDA communications.

Periodic Liver Enzyme Checks Ineffective

Statin labels have been revised to remove the need for routine periodic monitoring of liver enzymes in patients taking the cholesterol-lowering drugs. The new recommendations state that liver enzyme tests should be performed before initiating statin therapy in patients and as clinically indicated thereafter. The change was based on the FDA's conclusion that serious liver injury with statins is rare and unpredictable in individual patients and that routine monitoring does not appear to be effective in preventing injury.

Memory Loss and Increased Blood Glucose Reported with Statin Use

The FDA has added two new warnings to statin labels based upon post-marketing reports of cognitive impairment and increased fasting serum glucose levels. The reports of cognitive impairment included memory loss, forgetfulness, amnesia, memory impairment, and confusion, which were generally reversible upon statin discontinuation. Time to onset was variable (1 day to years), as was time to symptom resolution (median of 3 weeks).

Lovastatin Label Revised

Following the June, 2011 label revisions to simvastatin (see ***PRN* #38**), a review of drug-drug interactions with the chemically similar agent lovastatin was undertaken, resulting in the following changes to the lovastatin label:

Previous lovastatin label	New lovastatin label
Avoid lovastatin with: • Itraconazole • Ketoconazole • Erythromycin • Clarithromycin • Telithromycin • HIV protease inhibitors • Nefazodone	**Contraindicated with lovastatin:** • Itraconazole • Ketoconazole • Posaconazole • Erythromycin • Clarithromycin • Telithromycin • HIV protease inhibitors • Boceprevir • Telaprevir • Nefazodone
Do not exceed 20 mg lovastatin daily with: • Gemfibrozil • Other fibrates • Lipid-lowering doses (≥1 g/day) of niacin • Cyclosporine • Danazol	**Avoid with lovastatin:** • Cyclosporine • Gemfibrozil **Do not exceed 20 mg lovastatin daily with:** • Danazol • Diltiazem • Verapamil
Do not exceed 40 mg lovastatin daily with: • Amiodarone • Verapamil	**Do not exceed 40 mg lovastatin daily with:** • Amiodarone
Avoid large quantities of grapefruit juice (>1 quart daily)	**Avoid large quantities of grapefruit juice (>1 quart daily)**

Statin - HIV Drug Interaction Update

The FDA has made changes to the labels of statins and protease inhibitors, used to treat HIV and Hepatitis C, to reflect the latest recommendations on prescribing these drugs. Co-administration of certain statins and protease inhibitors can increase the risk of serious side effects, including myopathy and rhabdomyolysis.

Statin	Interacting protease inhibitor(s)	Prescribing recommendation
Atorvastatin	• Tipranavir + ritonavir • Telaprevir	Avoid atorvastatin
	• Lopinavir + ritonavir	Use with caution and use with the lowest atorvastatin dose necessary
	• Darunavir + ritonavir • Fosamprenavir • Fosamprenavir + ritonavir • Saquinavir + ritonavir	Do not exceed 20 mg atorvastatin daily
	• Nelfinavir	Do not exceed 40 mg atorvas-
Fluvastatin		No data available
Lovastatin	• HIV protease inhibitors • Boceprevir • Telaprevir	Contraindicated
Pitavastatin	• Atazanavir ± ritonavir • Darunavir + ritonavir • Lopinavir + ritonavir	No dose limitations
Pravastatin	• Darunavir + ritonavir • Lopinavir + ritonavir	No dose limitations
Rosuvastatin	• Atazanavir ± ritonavir • Lopinavir + ritonavir	Limit rosuvastatin dose to 10 mg once daily
Simvastatin	• HIV protease inhibitors • Boceprevir • Telaprevir	Contraindicated

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ASK PRN...

Most pharmacies limit refills of prescriptions to one year from the date the prescription was written. Is there any basis in state or federal pharmacy law for this restriction?

With regard to non-controlled substances, the answer is no; there are no provisions in federal or state regulations regarding a time limit on the refilling of such prescriptions. The one year limit on refills is simply a common practice, and it makes sense if you consider that when a prescription is refilled, it is assumed that the patient is still under the prescribing physician's care. If more than a year has elapsed since the prescription was issued, there is room for doubt as to whether that doctor-patient relationship still exists. There may also be insurance-related restrictions as to how long or for how many refills a prescription may be covered. There are, however, two situations where the law puts time restrictions on refills: controlled substances and syringes and/or needles. Both federal (21 CFR 1306.22) and New York State (80.69(g)) regulations limit the refilling of Schedule III and IV (and in New York, V) controlled substances to six months from the day the prescription was issued (signed), up to a maximum of 5 times if authorized by the prescriber. Schedule II controlled substances (and, in New York, benzodiazepines and anabolic steroids) may never be refilled. As for syringes and/or needles, although the regulations are now being revised, current New York State law (80.131(f)) states that refill authorization shall be effective for a period of two years from the date the prescription is signed.

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?

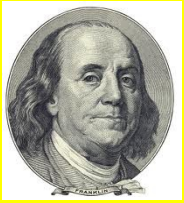
DID YOU KNOW that the pain relieving cream Bengay was named after the French pharmacist who invented the product? Dr. Jules Bengué combined menthol and methyl salicylate with lanolin and first marketed it in France in 1896 under the trade name *Balme Analgésique Bengué*. Two years later, the product came to the United States, sold by Thomas Leeming and Company under the original French name. Years later, the name was anglicized to Ben-Gay, and eventually streamlined to its current form, Bengay.

PHARMACY FUN

***Non verbis, sed rebus* is a Latin phrase meaning "not with words, but with things," and the source of the name of this month's puzzle, the rebus (celebrity edition!). The first reader to submit the correct answers (all brand-name drugs) to *puzzle@prnnewsletter.com* will receive a custom-printed *PRN* binder.**

1.  + "N"

2. "C" + 

3.  + "E" + 

Answers to last month's ***PHARMACY FUN***:
1. Doral 2. Muse 3. Sonata 4. Murine 5. Soma

References:
1. European Medicines Agency Recommendations, accessed 2/17/12 at *http://www.ema.europa.eu*