# P.R.N.

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**What's Inside…**



## FDA NEWS

### FDA Warns of Intestinal Problems Associated with Use of Benicar

The U.S. Food and Drug Administration (FDA) is warning that the angiotensin II receptor blocker Benicar (olmesartan), used in the treatment of hypertension, can cause an intestinal condition known as sprue-like enteropathy. Symptoms include severe, chronic diarrhea with substantial weight loss. The condition may take months or even years to develop after starting therapy with olmesartan, which is also a component of **Benicar HCT**, **Azor**, and **Tribenzor**. This does not seem to be a class effect of ARBs, and all affected patients have shown improvement after discontinuation of the drug. While the mechanism for this enteropathy is unclear, evidence suggests that it may represent a delayed hypersensitivity reaction. Patients taking any olmesartan-containing product who develop severe, chronic diarrhea with weight loss should be advised to contact their physician for further evaluation. If no other etiology for the symptoms can be found, olmesartan should be discontinued and an alternative antihypertensive should be started.

## ……RX NEWS……RX NEWS……RX NEWS……RX NEWS……

**INVOKANA** (Canagliflozin).
**Category:** Antidiabetic (SGLT2 Inhibitor).
**Initial dose:** 100 mg once daily, taken before the first meal of the day.
**MDD:** 300 mg once daily.

The FDA has approved Janssen Pharmaceuticals' Invokana, the first in a new class of oral antidiabetic agents. Invokana inhibits sodium-glucose cotransporter 2 (SGLT2) in the proximal renal tubules, leading to increased urinary excretion of glucose and lower plasma glucose levels. Invokana is indicated for the treatment of type 2 diabetes mellitus as monotherapy or in combination with other antidiabetic agents. The starting dose is 100 mg once daily, taken before the first meal of the day. Dosage may be increased to 300 mg once daily in patients who have an eGFR of 60mL/min/1.73 $m^2$ or greater. Invokana can cause increased urination, thirst, and genitourinary infection, including candidiasis.

**ELIQUIS** (Apixaban).
**Category:** Anticoagulant (Factor Xa Inhibitor).
**Initial dose:** 5 mg twice daily.
**MDD:** 5 mg twice daily.

The FDA has approved yet another warfarin alternative, adding to the competition between ***Pradaxa*** and ***Xarelto***. Eliquis, co-marketed by Bristol-Myers Squibb and Pfizer, is a factor Xa inhibitor indicated to reduce the risk of stroke and systemic embolism in patients with nonvalvular atrial fibrillation. All three of the new anticoagulants carry a **black box warning** stating that discontinuation of anticoagulants increases the risk of stroke. The recommended dose of Eliquis is 5 mg twice daily; use 2.5 mg twice daily in patients with at least 2 of the following characteristics: age ≥ 80 years, weight ≤ 60 kg, or serum creatinine ≥ 1.5 mg/dL.

**NESINA** (Alogliptin).
**Category:** Antidiabetic (DPP-IV Inhibitor).
**Initial dose:** 25 mg once daily, with or without food.
**MDD:** 25 mg once daily

Takeda Pharmaceuticals has introduced Nesina, the fourth and latest dipeptidyl peptidase-4 (DPP-IV) inhibitor to reach the market, following Januvia, Onglyza, and Tradjenta. DPP-IV inhibitors work by increasing incretin levels and insulin synthesis while decreasing hepatic glucose production. As with all incretin mimetics, there is an increased risk of pancreatitis associated with the use of Nesina. The FDA is currently investigating unpublished reports of pancreatic toxicity, including pre-cancerous findings, involving this class of drugs. Nesina is also available in lower dosage tablets (6.25 mg and 12.5 mg) for use in patients with renal impairment. Takeda is simultaneously releasing two fixed-dose combination products containing Nesina, which are discussed below.

**KAZANO** (Alogliptin and Metformin).
**Category:** Antidiabetic (DPP-IV Inhibitor and Biguanide combination agent).
**Initial dose:** Initial dose should be based on current dose of alogliptin and metformin, given twice daily with meals.
**MDD:** Alogliptin 25 mg/metformin 2000 mg daily.

**OSENI** (Alogliptin and Pioglitazone).
**Category:** Antidiabetic (DPP-IV Inhibitor and Thiazolidinedione).
**Initial dose:** Initial dose should be based on current dose of alogliptin and pioglitazone
**MDD:** Alogliptin 25 mg/pioglitazone 45 mg daily.

Patients currently receiving an adjusted dose of Alogliptin for severe renal impairment or end-stage renal disease should not be switched to a combination product.

## Lesson *Not* Learned: Glaxo Accused Again

Last year, British pharmaceutical giant GlaxoSmithKline (GSK) was fined 3 billion dollars, the largest health care fraud settlement in U.S. history. That case involved unlawful promotion of certain drugs and failure to report drug safety data. Now GSK is under investigation by the Chinese government, which claims that the company has been bribing doctors, hospitals, and government officials for years in order to increase sales of their drug products in the world's most populous nation. China has detained four top GSK officials, all Chinese nationals, and has prohibited the company's British finance executive from leaving the country during the investigation.[1]

## Editor's Note

Following the publication of our last issue (PRN #47, Nov/Dec, 2012), we had to temporarily suspend publication due to unexpected production difficulties. We are pleased to announce that we are back, and that we will now be publishing ***PRN*** on a monthly basis, (12 issues per year) rather than bi-monthly. All current subscriptions will be automatically extended until the end of 2013.

# MEDICAID UPDATE

*Information Regarding the New York State Medicaid Program*

### Brand Less Than Generic Program Update

The New York State Medicaid Dispense Brand Name Drug When Less Than Generic (BLTG) Program has been updated to include an additional 12 brand name drugs. The program, which began in April, 2010, mandates the dispensing of brand name drugs over generics when the cost to Medicaid would be less due to manufacturer's rebates. The dispensing of a lower cost drug is in compliance with New York State Education law, therefore prescriptions for drugs in this program *do not require* "Dispense as Written" (DAW) or "Brand Medically Necessary" to be written on the prescription. Prescriptions for drugs in the program will be assigned a generic copayment and will be paid at the brand name drug reimbursement rate or usual and customary price, whichever is lower. Patients will not need to obtain a new prescription if a drug is removed from the program. The current list of drugs in the BLTG program follows (program updates are available online at ***https://newyork.fhsc.com***):

| | |
|---|---|
| **Accolate** | **Lovenox** |
| **Adderall*** | **Maxalt MLT** |
| **Alphagan P 0.15%** | **Nasacort AQ** |
| **Astelin** | **Pulmicort Resp.** |
| **Bactroban Cream** | **Sanctura XR** |
| **Carbatrol** | **Singulair Granule** |
| **Catapres - TTS** | **Symbyax** |
| **Combivir** | **Tegretol Susp.** |
| **Diastat** | **Tegretol XR** |
| **Diovan HCT** | **Tobradex** |
| **Duetact** | **Tricor** |
| **Epivir** | **Trileptal Susp.** |
| **Felbatol** | **Vancocin** |
| **Gabitril 2mg, 4mg** | **Valtrex** |
| **Gris-PEG** | **Ziagen Tablet** |
| **Kadian** | **Zovirax Ointment** |

* Both regular and XR are include in program

# LAW REVIEW

*Regulatory Issues Affecting Pharmacy in New York State*

## News from the N.Y. State Bureau of Narcotic Enforcement

Recently, there have been a number of major changes to the regulations governing the prescribing and dispensing of controlled substances in New York State. Some of these changes are already in effect, while others will take effect in the very near future. Among the most important revisions are the authorization of electronic prescribing of controlled substances, the initiation of pharmacist accessibility to the Prescription Monitoring Program, and the long-awaited update to the regulations covering hypodermic needles and syringes.

### Electronic Prescribing and Dispensing of Controlled Substances

As of March 27, 2013, the electronic prescribing and dispensing of controlled substances is permissible in New York State. Public Health Law 3302(37) and the Rules and Regulations on Controlled Substances (Part 80) now authorize practitioners to issue electronic prescriptions for controlled substances in Schedules II through V and permit pharmacists to annotate, dispense, and electronically archive such prescriptions. All such electronic prescriptions must be issued in accordance with state and federal security requirements, and computer applications used in the prescribing and dispensing of controlled substances must be registered with the Bureau of narcotic Enforcement. In addition, section 6810(10) of the Education Law now mandates that by March 27, 2015, ALL prescriptions issued in New York State must be electronic prescriptions, with certain limited exceptions.

### Pharmacist Access to the Prescription Monitoring Program

Effective August 27, 2013, pharmacists in New York State will be able to access the Prescription Monitoring Program (PMP) registry. The PMP is an online database of controlled substance prescriptions prescribed and dispensed in New York State, with mandatory real-time reporting by prescribers and pharmacists. Prescribers will be required to consult the PMP prior to prescribing any Schedule II, III, or IV controlled substance. Pharmacists may consult the PMP before dispensing a controlled substance, but are not required to do so. In order to access the PMP starting August 27, pharmacists must establish a Health Commerce System (HCS) account. Pharmacist can apply for an HCS account online by visiting ***https://hcsteamwork1.health.state.ny.us/pub/top.html*** and following the instructions. Pharmacist should apply as soon as possible, as it can take up to two weeks to establish a new account.

### Updated Regulations on Hypodermic Needles and Syringes Published

In New York State, the laws governing hypodermic needles and syringes are found in Article 33, the Controlled Substance Act. As such, prescriptions for needles, syringes, and pre-filled syringe products such as insulin pens, EpiPen, and Byetta, have been subject to many of the same restrictions as controlled substances. Legislation passed in 2010 lifted those restrictions, but pharmacists were advised to continue to enforce those restrictions until new regulations could be promulgated. Those new regulations have now been published in the New York State Register for June 5, 2013, and are expected to take effect after the 45-day public comment period has elapsed. This will result in the following changes to the prescribing and dispensing of needles and syringes and related products:

- **Electronic prescriptions for needles and syringes will be permitted.**
- **The restriction of 100 needles or syringes on an oral prescription will be removed. As with other non-controlled prescriptions, there will be no quantity limit.**
- **Refill transfers for needle/syringe prescriptions will be permitted.**
- **Pharmacists will no longer be required to pull and sign the original hard copy when refilling prescriptions for needles/syringes.**

*Feature Article..*

# REVIEW OF INCRETIN MIMETICS

**Since** their introduction in 2005, the antihyperglycemic drugs known as incretin mimetics have become an important part of the pharmacological armamentarium in the fight against diabetes mellitus. The introduction of a fourth DPP-IV inhibitor (see this month's ***RX NEWS*** on page 1) signals the fact that drug manufacturers believe this category will continue to play an major role in the treatment of diabetes, despite some troubling reports of serious side effects. A review of currently available incretin mimetics, and a discussion of the adverse effects which may be associated with their use, appears below.

## Incretin Mimetics: 2 Mechanisms: 1 Goal

The drug class that has come to be known as incretin mimetics actually consists of two unique types of medications, with different mechanisms of action. The injectable forms (Byetta, etc.) are glucagon-like peptide-1 (GLP-1) receptor agonists which act like incretin to increase insulin secretion and decrease hepatic glucose production. The oral forms (Januvia, etc.) are dipeptidyl peptidase-4 (DPP-IV) inhibitors, which prolong the effects of endogenous incretin hormones by inhibiting the enzyme that inactivates GLP-1 and glucose-dependent insulinotropic polypeptide (GIP).

## FDA Comment on Reports of Pancreatitis

In March of this year, the FDA released a drug safety communication regarding the possible increased risk of pancreatitis and pre-cancerous findings of the pancreas following the use of incretin mimetics. The findings come from an unpublished report by academic researchers who studied a small number of post-mortem pancreatic tissue samples. The FDA has not yet reached any conclusions regarding this study and recommends patients continue taking their medications as directed until speaking with the their health care professionals.

**Oral Incretin Mimetics (DPP-IV Inhibitors)**

| Brand Name (active ingredient) | Dosage Forms and Strengths | Dosage and Administration | Renal Disease Dosing | Warnings and Precautions | Fixed-Dose Combinations Available |
|---|---|---|---|---|---|
| **Januvia** (sitagliptin) | Tablets: **25 mg** **50 mg** **100 mg** | 100 mg once daily, with or without food. | *Moderate*: 50 mg daily *Severe*: 25 mg daily | Postmarketing reports of pancreatitis and acute renal failure. Risk of hypoglycemia when used with insulin or sulfonylurea. | **Janumet, Janumet XR** (sitagliptin and metformin) **Juvisync** (sitagliptin and simvastatin) |
| **Nesina** (alogliptin) | Tablets: **6.25 mg** **12.5 mg** **25 mg** | 25 mg once daily, with or without food. | *Moderate*: 12.5 mg daily *Severe*: 6.25 mg daily | Postmarketing reports of pancreatitis and hepatic failure. Risk of hypoglycemia when used with insulin or sulfonylurea. | **Kazano** (alogliptin and metformin) **Oseni** (alogliptin and pioglitazone) |
| **Onglyza** (saxagliptin) | Tablets: **2.5 mg** **5 mg** | 2.5 or 5 mg once daily, with or without food. | *Moderate or severe:* 2.5 mg daily | Postmarketing reports of pancreatitis. Risk of hypoglycemia when used with insulin or sulfonylurea. | **Kombiglyze XR** (saxagliptin and metformin) |
| **Tradjenta** (linagliptin) | Tablets: **5 mg** | 5 mg once daily, with or without food. | No dosage adjustment necessary | Postmarketing reports of pancreatitis. Risk of hypoglycemia when used with insulin or sulfonylurea. | **Jentadueto** (linagliptin and metformin) |

**Injectable Incretin Mimetics (GLP-1 Receptor Agonists)**

| Brand Name (active ingredient) | Dosage Forms and Strengths | Dosage and Administration | Warnings and Precautions |
|---|---|---|---|
| **Bydureon** (exenatide extended release ) | Injection: **2 mg** vial for reconstitution | 2 mg SQ once every 7 days, at any time of the day and with or without meals. | Possible risk of thyroid C-cell tumors. Postmarketing reports of pancreatitis. Risk of hypoglycemia when used with sulfonylurea. |
| **Byetta** (exenatide) | Injection: **5 mcg/dose** (60 dose pen) **10 mcg/dose** (60 dose pen) | Start at 5 mcg SQ twice daily within 60 minutes prior to morning and evening meals. Increase to 10 mcg twice daily after 1 month based on response. | Postmarketing reports of pancreatitis and renal impairment. Risk of hypoglycemia when used with insulin or sulfonylurea. |
| **Victoza** (liraglutide) | Injection: **6 mg/mL** pen which delivers doses of **0.6**, **1.2** and **1.8** mg | Start at 0.6 mg SQ once daily at any time of day with or without food for 1 week, then increase to 1.2 mg daily. May increase to 1.8 mg based on response. | Possible risk of thyroid C-cell tumors. Postmarketing reports of pancreatitis and renal impairment.. Risk of hypoglycemia when used with insulin or sulfonylurea. |

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# ASK PRN...

**As a result of the I-STOP legislation, pharmacists will soon be able to review patients' controlled substance history. How will pharmacies access this information?**

Starting on August 27, 2013, pharmacists in New York State will be able to view patients' controlled substance prescription history by accessing the Prescription Monitoring Program (PMP) registry. In order to access the registry, pharmacists must first obtain an individual Health Commerce System (HCS) account using the online application found at: ***https://hcsteamwork1.health.state.ny.us/pub/top.html***. When asked to select the main reason for access, pharmacists should click on "Controlled Substance Information (CSI) on Dispensed Prescriptions." Within 3 days after completing the application, applicants will receive an email containing an HCS document, which must be notarized and mailed to the Department of Health. Within 2 weeks after mailing in the notarized HCS document, applicants will receive a letter in the mail containing a PIN number and instructions on how to activate the HCS account. Once the account is activated, use the following steps to access the PMP registry:

1. Navigate to the HCS website at: ***https://commerce.health.state.ny.us***.
2. Log on with user ID and password.
3. Select "applications" at the top of the page and click on the letter 'P.'
4. Scroll down to "Prescription Monitoring Program Registry."
5. Click the green plus sign under the Add/Remove column to add this application to your favorites.
6. Click to open the program, and enter all the required information.

**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 first birth control pill produced in the United States was supposed to contain only a synthetic progesterone, but was found to be accidentally contaminated with a synthetic estrogen, which reduced breakthrough bleeding and was therefore kept in the final product? ***Enovid***, developed by the G.D Searle company, was approved for treating menstrual disorders in 1957, and later (May, 1960) for use as a contraceptive. At the time, some states outlawed the use of oral contraceptives, and in Massachusetts, unmarried women were prohibited from purchasing birth control pills until a Supreme Court decision struck down the ban in 1972.

## PHARMACY FUN

**It's rebus time once again, ultra-short edition. Name the drugs represented in the following 2-character rebuses (or is that rebi?!) The first reader to submit the correct answers to *puzzle@prnnewsletter.com* will receive a custom-printed *PRN* binder.**

1.  + 

2.  + 6

3.  + 

4.  + 

Answers to last month's ***PHARMACY FUN***:
1. Sprix 2. Tudorza 3. Aubagio 4. Myrbetriq 5. Picato 6. Stendra (Put them all together, and they spell….STAMPS!)

**References:**
1. Barboza, David. "Glaxo Used Travel Firms for Bribery, China Says." *New York Times* July 15, 2013