P.R.N.

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FDA NEWS

New Contraindication for IBS-D Drug

The FDA has announced that the use of **Viberzi** (eluxadoline) is now contraindicated in patients without a gallbladder. Previously, a reduced dosage was recommended for such patients. Viberzi is one of 3 prescription drugs currently indicated for use in patients with diarrhea-predominant irritable bowel syndrome (IBS-D). Since 2015, when the drug was first introduced, the FDA has received 120 reports of serious cases of pancreatitis or death, the majority of which occurred in patients without a gallbladder. The agency is recommending that physicians consider using alternative treatments for their IBS-D patients without a gallbladder, including OTC medications, such as Kaopectate, Pepto-Bismol, simethicone, and Imodium. The two other prescription medications currently indicated for use in IBS-D are **Lotronex** (alosetron) and **Xifaxan** (rifaximin).

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

QTERN (Dapagliflozin and Saxagliptin).
Category: Antidiabetic (SGLT2 Inhibitor and DPP-IV Inhibitor combination agent).
Initial Dose: 10 mg dapagliflozin/5 mg saxagliptin once daily in the morning, with or without food.
MDD: 10 mg dapagliflozin/5 mg saxagliptin.

AstraZeneca has received FDA approval to market Qtern, a fixed-dose combination agent containing two of their previously marketed antidiabetic agents: the SGLT2 inhibitor dapagliflozin (**Farxiga**) and the DPP-IV inhibitor saxagliptin (**Onglyza**). This is the second such combination drug to be marketed, the first being **Glyxambi**. Qtern is indicated as an adjunct to diet an exercise to improve glycemic control in adults with type 2 diabetes mellitus who have inadequate control with dapagliflozin or who are already treated with dapagliflozin and saxagliptin. Qtern should not be used in patients with an eGFR below 60 mL/min/1.73 m^2. Tablets should be swallowed whole and not split or cut. As with all agents containing a DPP-IV inhibitor, Qtern should be promptly discontinued if pancreatitis is suspected.

TRULANCE (Plecanatide).
Category: Guanylate cyclase-C agonist for chronic idiopathic constipation.
Initial Dose: 3 mg once daily, with or without food.
MDD: 3 mg once daily.

The FDA has approved Synergy Pharmaceuticals' Trulance (plecanatide) for the treatment of chronic idiopathic constipation in adults. Trulance is the second guanylate cyclase-C agonist approved for this indication (the first was **Linzess**). Although the product is only approved for adults, it contains a **black box warning** contraindication against its use in children due to the risk of serious dehydration. For adult patients with difficulty swallowing, Trulance can be crushed and administered orally either in applesauce or with water. To administer in applesauce, place tablet in a clean container, crush, and mix with one teaspoonful of room temperature applesauce. Consume the entire mixture immediately. To administer in water, place tablet in a clean cup and add approximately 30 mL of room temperature water. Mix gently by swirling the tablet and water mixture for at least 10 seconds. The tablet will fall apart in the water. Swallow the entire contents of the tablet-water mixture immediately.

FDA: Codeine and Tramadol Now Contraindicated in Children

The FDA is adding new warnings to the labels of all prescription medications which contain **codeine** or **tramadol**, restricting the use of these drugs in children. The action is a result of the agency's review of several decades of adverse event reports, which identified numerous cases of serious breathing problems, including deaths, in children treated with these medications. The new labels will contain the following:

- The FDA's strongest warning, a ***contraindication***, alerting that codeine should not be used to treat pain or cough, and tramadol should not be used to treat pain, in children younger than 12 years of age.
- A new ***contraindication*** will be added to the tramadol label warning against its use in children younger than 18 years of age to treat pain after surgery to remove the tonsils and/or adenoids (this warning was already added to codeine labels in 2013).
- A new ***warning*** will be added to codeine and tramadol drug labels to recommend against their use in adolescents between 12 and 18 years of age who are obese or have conditions such as obstructive sleep apnea or severe lung disease, which may increase the risk of serious breathing problems.
- A strengthened ***warning*** will be added to codeine and tramadol labels stating that breastfeeding is not recommended when taking codeine or tramadol due to the risk of serious adverse reactions in breastfed infants. These can include excess sleepiness, difficulty breastfeeding, or serious breathing problems that could result in death.

MEDICAID UPDATE

Information Regarding the New York State Medicaid Program

Update on Emergency Contraceptive Coverage

Both prescription and over-the-counter (OTC) emergency contraception is a covered benefit for all Medicaid Fee-for-Service ("straight" Medicaid) and Managed Care enrollees. Non-prescription (OTC) emergency contraceptive drugs can be obtained without a written order from a practitioner. Effective March 1, 2017, New York State Medicaid has **eliminated age restrictions when dispensing non-prescription emergency contraceptive drugs without a written order**, following FDA guidelines. When dispensing these products on Medicaid without a written/electronic/oral order, the prescriber identification field for pharmacy claims may be left blank and the claim will still be processed. For Medicaid eligible females, a fiscal order or prescription is not required for non-prescription (OTC) emergency contraception, but individuals are limited to 6 courses of therapy in a 12-month period. For Managed Care billing, refer to the individual plan for instructions (information for all New York Managed Care plans is available at ***http://mmcdruginformation.nysdoh.suny.edu/***).

Additions to the Dispense Brand Name Drug when Less Expensive than Generic Program

Effective June 22, 2017, three new drugs have been added to the Dispense Brand Name Drug when Less Expensive than Generic Program:

- **Focalin**
- **Tazorac cream**
- **Zyflo CR**

In conformance with State Education Law, which intends that patients receive the lower cost alternative, brand name drugs included in this program:

- **Do not require 'Dispense as Written' (DAW) or 'Brand Medically Necessary' on the prescription.**
- **Have a generic copayment**
- **Are paid at the Brand name Drug reimbursement rate or usual and customary price, whichever is lower (SMAC/FUL are not applied).**
- **Do not require a new prescription if the drug is removed from this program.**

LAW REVIEW

Regulatory Issues Affecting Pharmacy in New York State

New Law on Transferring Electronic Prescriptions Takes Effect

On February 26, 2017, New York State Assembly bill A10448 became law. The bill, signed by Governor Cuomo in November, 2016, seeks to address the problem which arises when a patient wishes to fill a new electronic prescription in a pharmacy other than the one which actually received the prescription from the prescriber. The memo attached to the legislation explains the issue well:

> **The majority of medical prescriptions in New York are now required to be done electronically. While electronic prescriptions (e-scripts) have tremendous advantages, including certain securities and efficiencies, there are certain circumstances where e-scripts are problematic. Specifically, regarding initial prescriptions where the pharmacy receiving the initial e-script is unable to immediately fill the script, patients have to go back to their health care provider for the e-script to be sent to another pharmacy, rather than being able to direct the pharmacy itself to transfer the e-script to another pharmacy that is able to fill the script.**

The new law amends section 6810 of the Education Law by adding a new subdivision 10-a to read as follows:

> **10-a. A Pharmacy that receives an electronic prescription from the person issuing the prescription may, if the prescription has not been dispensed and at the request of the patient or a person authorized to make the request on behalf of the patient, immediately transfer or forward such prescription to an alternative pharmacy designated by the requesting party.**

Note that although the text of the legislation uses the terms "transfer" and "forward," the title of the bill is "An act to amend the public health and education law, in relation to allowing pharmacies to *electronically* transfer prescriptions to other pharmacies." Since the protocols and procedures for such electronic transfers are not yet established, it is more than likely that the Board of Pharmacy will need to promulgate specific regulations governing such transfers. In our discussions with the Board, they have indicated their opinion that, for the time being, pharmacists should continue to transfer only one fill at a time of new, undispensed electronic prescriptions according to the existing refill transfer regulations. We will keep our readers updated as to the publication of any future rules and regulations allowing for the transfer of the entirety of a new, undispensed electronic prescription.

Deadline Approaching for Mandatory Prescriber Education

Changes to the Public Health Law (§3309-a [3]) enacted last year require all prescribers licensed in New York who treat people and have a DEA registration to complete at least 3 hours of course work in pain management, palliative care and addiction. The deadline for completing the training is July 1, 2017. The requirement also applies to medical residents who prescribe controlled substances under a facility's DEA registration number. The Department of Health offers a free online course that meets the minimum three hour requirement and is available at: ***http://pharmacy.buffalo.edu/opioid-training***. For any course to fulfill the requirement it must cover the following eight topics:

NY State and federal requirements for prescribing controlled substances
Prevention, screening and signs of addiction
Pain management
Managing acute pain
Responses to abuse and addiction
Appropriate prescribing
Palliative medicine
End of life care

Feature Article..

REVIEW OF SGLT2 INHIBITORS FOR DIABETES

The Latest Addition to the arsenal of oral antidiabetic medications is the class known as "gliflozins," the Sodium-Glucose Cotransporter 2, or SGLT2, Inhibitors. The first agent to market was **Invokana**, approved by the FDA in March, 2013. **Farxiga** followed in January, 2014, and the latest, **Jardiance**, was approved in August, 2014. The class quickly gained acceptance by prescribing physicians, but just as rapidly drew scrutiny, and a number of Safety Alerts, from the FDA. Below is a review of the currently available agents.

Mechanism of Action

Sodium glucose cotransporters (SGLT) are a group of proteins responsible for the reabsorption of renal glucose. SGLT2 works in the S1 segment of the proximal convoluted tubule of the nephron and accounts for 90 percent of glucose reabsorption. By blocking the function of this protein, SGLT2 inhibitors cause glucose to be excreted in the urine, thereby reducing blood glucose and HbA1c. Collateral benefits include weight loss (approximately 2 to 3% of body weight, on average) and lowering of blood pressure. In addition, in December, 2016 the FDA approved a new indication for **Jardiance** to reduce cardiovascular deaths in adults with type 2 diabetes.

Timeline of FDA Safety Warnings

May, 2015: FDA warns that SGLT2 inhibitors may cause ketoacidosis.

September, 2015: FDA strengthens the warning label for **Invokana** regarding increased risk for bone fractures and adds a warning about risk of decreased bone mineral density.

December, 2015: SGLT2 labels are revised to include warnings about the risk of ketoacidosis and serious urinary tract infections in patients using these drugs.

June, 2016: FDA strengthens the warning labels on **Invokana** and **Farxiga** regarding the risk of acute kidney injury in patients using these drugs.

May, 2017 FDA Safety Warning

Last month, the FDA issued a Drug Safety Communication to confirm that there exists an increased risk of leg and foot amputations in patients taking **Invokana**. A **black box warning** will be added to the label regarding this risk. The final results of two clinical trials showed that leg and foot amputations occurred about twice as often in patients treated with Invokana compared to patients treated with placebo. The agency recommends that, before prescribing the drug, practitioners consider factors in a patients history that may predispose them to the need for amputations, such as peripheral vascular disease, neuropathy, foot ulcers, and prior amputations.

SODIUM-GLUCOSE COTRANSPORTER 2 INHIBITORS (SGLT2 Inhibitors)

Brand Name (active ingredient)	Dosage Forms and Strengths	Dosage and Administration	Renal Disease Dosing	Warnings and Precautions	Fixed-Dose Combinations Available
Invokana (canagliflozin)	Tablets: **100 mg** **300 mg**	100 mg once daily, taken before the first meal of the day. Dose may be increased to 300 mg daily.	Limit the dose to 100 mg in patients who have an eGFR of 45 to 60 mL/min/1.73 m^2. Do not use if below 45.	**Black box warning** of increased risk of leg and foot amputations. May cause hypotension, ketoacidosis, acute kidney injury, hyperkalemia, urinary tract infections, genital mycotic infections, increased hemoglobin, increased LDL-C and increased risk of bone fractures.	**Invokamet, Invokamet XR** (canagliflozin and metformin)
Farxiga (dapagliflozin)	Tablets: **5 mg** **10 mg**	5 mg once daily, taken in the morning, with or without food. Dose may be increased to 10 mg daily.	Not recommended in patients with an eGFR between 30 and less than 60 mL/min/1.73 m^2. Do not use if below 30.	May cause hypotension, ketoacidosis, acute kidney injury, urinary tract infections, genital mycotic infections, increased hematocrit, increased LDL-C and increased risk of bone fractures*. Do not use in patients with active bladder cancer. Use with caution in patients with a prior history of bladder cancer.	**Xigduo XR** (dapagliflozin and metformin) **Qtern** (dapagliflozin and saxagliptin)
Jardiance (empagliflozin)	Tablets: **10 mg** **25 mg**	10 mg once daily, taken in the morning, with or without food. Dose may be increased to 25 mg daily	Not recommended for patients who have an eGFR less than 45 mL/min/1.73 m^2. Do not use if below 30.	May cause hypotension, ketoacidosis, acute kidney injury, urinary tract infections, genital mycotic infections, increased hematocrit, increased LDL-C and increased risk of bone fractures*.	**Synjardy, Synjardy XR** (empagliflozin and metformin) **Glyxambi** (empagliflozin and linagliptin)

* Increased risk of bone fracture is listed by the FDA for Invokana only, but is considered a class effect by the American Diabetes Association.

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ASK PRN...

Pharmacists in New York are now required to provide educational materials to patients when dispensing controlled substances. What information must this material contain, and is an approved version available from the state?

Effective October 22, 2016, pharmacies in New York State are required to distribute educational materials at the time of dispensing any controlled substance prescription, whether new or refill. The materials must cover the following:

- **The risks of using or consuming such controlled substances**
- **The physical, behavioral, and advanced warning signs of addiction to such controlled substances**
- **Available alcohol and drug treatment resources**
- **Procedures for safe disposal of unused controlled substances**
- **Such other information that the commissioner shall deem to be necessary**

Pharmacies may choose to offer additional information as well, and, at the patient's option, the pharmacy may distribute the materials electronically. The Department of Health has prepared a one-sheet document which meets all of the requirements for pharmacies. This document is available in pdf form at the following website:

https://combatheroin.ny.gov/sites/default/files/resources/12022_ImportantFacts_RxPainMeds_101816.pdf

For convenience, the form may be ordered, in quantities up to 200 sheets, in English, Spanish, or Russian, from the following link:

https://combatheroin.ny.gov/sites/default/files/resources/CH-OrderForm.pdf

GOT QUESTIONS? WE HAVE ANSWERS!
Send your questions to us at:
askprn@prnnewsletter.com

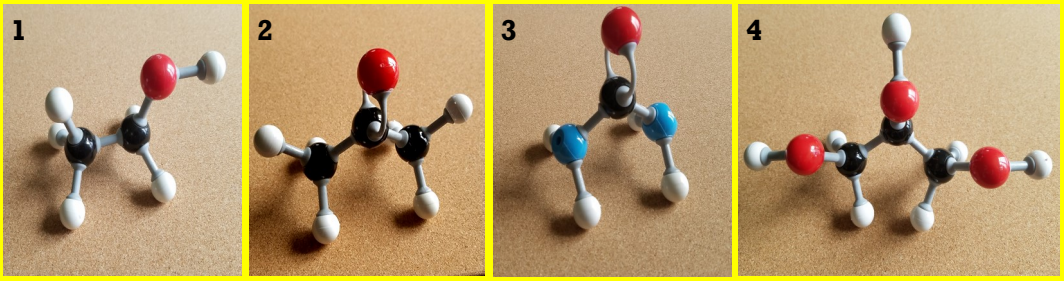
PRN welcomes your questions on any topics relating to the practice of pharmacy. All answers are researched by our staff and, when necessary, discussed with the appropriate regulatory agencies. The information provided is not intended as legal advice, nor is it a substitute for professional judgment in clinical practice.

DID YOU KNOW?

DID YOU KNOW that the white coat, so emblematic of the health care professional, is a relatively recent invention? And that prior to the late 19th century, most physicians actually wore black?[1] Prior to the acceptance of the "germ theory," encounters with physicians were considered formal and somber events, calling for formal (black) attire, and little thought was given to the importance of cleanliness or sterility. Once the theories of Lord Lister and others took hold, white became the symbol of the healer. The white coat may, however, be headed for the same fate as its dark predecessor, as it is now seen, along with neckties, as a possible source of the spread of infections in hospitals.

PHARMACY FUN

It's time for Fun with Chemistry! Have a look at the Molymod[tm] structures we have created below. Can you name the chemicals, commonly used in pharmacy, that they represent? In case you've forgotten, black is carbon, white is hydrogen, red is oxygen and blue is nitrogen. The first reader to submit the correct answers to *puzzle@prnnewsletter.com* will receive a custom-printed PRN binder.



Answers to last month's ***PHARMACY FUN***:
1. Spironolactone 2. Cimetidine 3. Thorazine 4. Indomethacin 5. Eflornithine 6. Metformin
7. Propranolol 8. Demeclocycline

References:
1. Hochberg, Mark S. The Doctor's White Coat—An Historical Perspective. *AMA Journal of Ethics.* 2007; Vol. 9 No. 4: 310-314.