10th ANNIVERSARY ISSUE

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What's Inside...

FDA NEWS

Uloric Linked to Heart-Related Deaths

The FDA has released a Drug Safety Communication regarding an increased risk of heart-related deaths with the use of Uloric (febuxostat) when compared to allopurinol, the other mainstay of gout treatment. This effect was first noted during clinical trials conducted prior to the drug's approval, resulting in a label warning and a requirement by the agency for further study. The preliminary results of that follow-up study show an increased risk of heart-related deaths and deaths from all causes, as compared with allopurinol. The FDA is recommending that prescribers consider this information before deciding to prescribe or continue patients on Uloric.

Editor's Note: Commencing with this issue, PRN will be published on a bi-monthly basis. Accordingly, our next issue, #61, will be the January/February, 2018 number.

.....RX NEWS.....RX NEWS.....RX NEWS.....RX NEWS.....

STEGLATRO (Ertugliflozin).
Category: Antidiabetic (SGLT2 inhibitor).
Initial Dose: 5 mg once daily, taken in the morning, with or without food.
MDD: 15 mg.

Merck and Pfizer have collaborated to introduce a new sodium glucose co-transporter 2 (SGLT2) inhibitor called Steglatro. This new entry is the fourth SGLT2 inhibitor to reach the U.S. market, following **Invokana**, **Farxiga**, and **Jardiance**. After an initial dose of 5 mg daily, Steglatro may be increased to 15 mg daily in those tolerating the drug and needing additional glycemic control. As with all SGLT2 inhibitors, the labeling contains warnings about hypotension, ketoacidosis, acute kidney injury, urinary tract infections, and possible increased risk of lower limb amputations.

STEGLUJAN (Ertugliflozin and Sitagliptin).
Category: Antidiabetic (SGLT2 inhibitor and DPP-IV inhibitor combination agent).
Initial Dose: 5 mg ertugliflozin/100 mg Sitagliptin once daily, taken in the morning, with or without food.
MDD: 15 mg ertugliflozin/100 mg sitagliptin.

Steglujan is a combination agent containing **Steglatro** and **Januvia**. Due to the inclusion of a DPP-IV inhibitor, additional label warnings include pancreatitis, heart failure, severe and disabling arthralgia, and pemphigoid.

SEGLUROMET (Ertugliflozin and Metformin).
Category: Antidiabetic (SGLT2 inhibitor and Biguanide combination agent).
Initial Dose: Individualized based on the patient's current regimen.
MDD: 7.5 mg ertugliflozin/1000 mg metformin twice daily with meals.

Segluromet is a combination agent containing **Steglatro** and **Metformin**, and will be available in strengths of 2.5/500, 5/1000, 7.5/500 and 7.5/1000 mg. Due to the inclusion of metformin, the labeling will contain a **black box warning** regarding the risk of metformin-associated cases of lactic acidosis, which have resulted in death, hypothermia, hypotension, and arrhythmias.

LUMIFY (Brimonidine tartrate ophthalmic solution 0.025%).
Category: OTC redness reliever.
Initial Dose: 1 drop in the affected eye every 6 to 8 hours.
MDD: Do not use more than 4 times daily.

Bausch and Lomb will introduce the first and only over-the-counter eye drop containing brimonidine. Lumify is a 0.025% solution of brimonidine tartrate, and is indicated for use in the treatment of ocular redness in adults and children 5 years of age and older. The manufacturer states that Lumify works within one minute and lasts for up to 8 hours to relieve redness due to minor eye irritations. Lumify is expected to be available in the second quarter of 2018.

FDA Approves Second "Follow-On" Insulin

On December 11, 2017, the FDA granted approval for Sanofi-Aventis to market **Admelog** (insulin lispro injection), a "follow-on" version of Lilly's **Humalog**. Admelog is the second "follow-on" insulin to be approved, the first being **Basaglar** (insulin glargine solution), which, ironically, is Lilly's version of Sanofi's **Lantus**. Like biosimilars (see ***PRN*** #57 for a complete discussion of this topic), "follow-on" drugs are ***not*** considered generics, and can not be substituted for the original product without the prescriber's authorization. The FDA refers to these insulin products as "follow-ons" rather than biosimilars only because insulin is regulated under the Food, Drug, and Cosmetic Act, as opposed to biologics, which are regulated by the Public Health Service Act. Admelog will be available in both 10 mL vials and 3 mL Solostar pens. The Solostar pen in use should be kept at room temperature, and discarded 28 days after opening. Unused pens should be always be kept refrigerated.

A Cause for Celebration

With this issue, we celebrate the tenth anniversary of *PRN*, the newsletter for community pharmacists. First and foremost, we'd like to thank our loyal readers, the pharmacists and pharmacy technicians of New York State. And I, personally, would like to say thanks to the people who were there at the very beginning, the original staff of *PRN*: the amazing Irving sisters, Marghi, Lori, and Kerry, and Lilian Bejarano; pharmacists all, and good friends, too. Here's to another 10 years, at least!

James Murphy,
Founder and Editor of *PRN*

MEDICAID UPDATE

Information Regarding the New York State Medicaid Program

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

There have recently been several updates to the Dispense Brand Name Drug when Less Expensive than Generic Program, including 4 additions and 1 deletion:

Additions (effective 12/14/2017)
Efudex cream
Emend Tripack
Lexiva tablets
Transderm-Scop

Deletion (effective 12/14/2017)
Patanase

Prescriptions for drugs in the program **do not require** *"DAW"* or *"Brand Medically Necessary"* on the prescription, and have a generic copayment. If a drug is removed from the program, a new prescription is not required. The current list of drugs in the program is as follows:

Adderall XR	**Aggrenox**
Alphagan P 0.15	**Benzaclin gel pump**
Butrans	**Catapres-TTS**
Cellcept Susp	**Copaxone**
Diastat	**Edecrin**
Efudex cream	**Emend Tripack**
Exelon patch	**Focalin**
Focalin XR	**Fosrenol chew**
Gleevec	**Hepsera**
Kapvay	**Lexiva tablets**
Myfortic	**Pataday**
Protopic	**Pulmicort Resp**
Retin-A crm, gel	**Tegretol Susp**
Tegretol XR	**Tobradex Susp**
Transderm-Scop	**Trizivir**
Valcyte tablet, solution	**Voltaren Gel**
Vigamox	**Xeloda**
Xenazine	**Zyflo CR**

LAW REVIEW

Regulatory Issues Affecting Pharmacy in New York State

News from the 8th Annual Arthur Goldberg Law Day

We recently attended the annual law seminar sponsored by the Arnold and Marie Schwartz College of Pharmacy. Speakers included Lisa Lee Anderson from the Department of Health and Human Services, and Kimberly Leonard, Executive Secretary of the New York State Board of Pharmacy. A wide range of topics were covered, including HIPAA, business law, and third party and regulatory audits. Some issues of particular interest to community pharmacists are discussed below.

Update on Transferring of New Electronic Prescriptions

In November, 2016, Governor Cuomo signed into law Assembly bill A10448, which authorizes pharmacies to immediately transfer or forward an undispensed electronic prescription to another pharmacy at the request of the patient. Ms. Leonard of the Board of Pharmacy discussed the fact that there is currently no approved process for electronically transferring a prescription from one pharmacy to another. In addition, it is the opinion of the Board, as well as of the Bureau of Narcotic Enforcement, that specific regulations based on this legislation will need to be promulgated. In the meantime, therefore, in the case of new, undispensed electronic prescriptions, pharmacies should follow the current refill transfer regulations, transferring only one fill at a time.

90-Day Refill from 30-Day Rx Bill Vetoed

On October 23, 2017, Governor Cuomo vetoed Assembly bill A6371, legislation which would have allowed pharmacists to refill 30-day prescriptions for up to a 90-day supply if there were sufficient refills available to support the increase. This has become a significant issue in pharmacy due to the insistence of third parties and insurers on dispensing 90-day supplies. The Education Law, which prohibits changing the quantity on a prescription, was written long before pharmacy benefit managers starting dictating how pharmacy should be practiced. This legislation, which passed both the Assembly and Senate, was designed to eliminate the delay many patients experience while their pharmacy attempts to obtain a new, 90-day, prescription from the physician.

New York Addresses Biologic Drug Substitution

In September, 2014, the FDA published the first edition of the Purple Book, officially known as the List of Licensed Biological Products (see the July/August, 2017 edition of ***PRN*** for more information). The Purple Book lists biologic drugs (e.g., Neupogen) and any approved biosimilar versions (e.g., Zarxio). If and when the FDA decides a biosimilar is substitutable for the original product, that biosimilar would be rated "I" for interchangeable. To date, no products in the Purple Book are rated "I," but New York has amended the Education Law to prepare for such an eventuality. Substitution of an interchangeable biologic product for the original will be permitted under the following conditions:

- **Prescriber does not indicate that substitution is prohibited.**
- **Substituted product must be listed as interchangeable (I) in the FDA Purple Book**
- **Label must indicate the name and strength of the product, and the name of the manufacturer.**
- **Within 5 business days following substitution, the dispensing pharmacist must report to the prescriber the name, strength of product, and manufacturer dispensed to the patient.**
- **Reporting can be done by entering in accessible EMR, fax, electronic transmission, electronic means, or telephone.**
- **Reporting not required if no interchangeable product is listed, or when the refill does not differ from the original product dispensed.**

Review of Concentrated Insulin Products

Insulin resistance has become an increasingly common problem in the treatment of type 2 diabetes mellitus (T2DM). For many decades, the only option for treating patients requiring high doses of insulin was the U-500 version of regular insulin (Humulin R U-500), which, unfortunately, was associated with numerous administration errors leading to both underdoses and overdoses (see discussion below). Today, practitioners have several new high-dose insulin products to choose from; below is a review and comparison of the currently available agents.

Regular U-500: The Granddaddy of Concentrated Insulins

Eli Lilly first introduced U-500 insulin in 1952 (insulin beef regular, followed by pork regular in 1980). With the advent of recombinant DNA technology came Humulin R U-500 in 1994. While once a rarely utilized product, U-500 has gained wider use in recent years due to a dramatic increase in type 2 diabetic patients who exhibit insulin resistance, requiring higher doses of insulin to maintain glycemic control. Another reason for the rise in popularity of U-500 insulin among clinicians is its unique pharmacokinetic profile. Unlike U-100 regular insulin, U-500 acts as both a bolus and basal insulin, with an onset of action of 30 to 45 minutes and a duration of action between 10 and 21 hours.

The Units Problem and the Introduction of the U-500 Syringe

Since it was first introduced, concentrated U-500 insulin has been the subject of safety concerns, not simply because it is 5 times more concentrated than other insulins, but because the syringes most commonly used to administer it were calibrated for U-100 insulin. So, for example, if a patient were told to use 50 units of U-500 insulin, and drew up the dose in a standard insulin syringe, that patient would receive 250 units of insulin. Fortunately, two recent developments have ameliorated this problem: the introduction of the Humulin KwikPen delivery device, and the new BD U-500 syringe (NDC # 08290-3267-30), which should ***always*** be dispensed when providing U-500 insulin in vials.

Tresiba: the First True Ultra-long-Acting Insulin

Those pharmacist who have been around for a while may remember insulins with letters like L (for Lente) and U (for Ultralente). These were insulins formulated with added zinc to delay absorption and extend duration of action (up to 36 hours in the case of Ultralente). They were both discontinued in 2005, and the search for a true basal insulin continued, leading to products like **Lantus** and **Levemir**. But when it comes to truly ultra long-acting insulin, the title goes to Novo Nordisk's **Tresiba**, in which one of the amino acids is replaced by a 16-carbon fatty acid, leading to the formation of multi-hexamers which act as a insulin depot. The result is an insulin with a duration of action of 42 hours[1].

Insulin	Products Available	Dosing	Duration of Action	Stability at Room Temperature
Humulin R U-500 (Insulin human injection)	**Vial:** 20 mL Multiple Dose Vial **Pen:** 2 x 3 mL and 5 x 3 mL KwikPen (can deliver up to 300 units per injection)	Administer subcutaneously two or three times daily 30 minutes before a meal. If using vials, ALWAYS use a U-500 syringe (see discussion above).	10 to 21 hours	**Vial:** 40 days **Pen:** 28 days
Humalog U-200 (Insulin lispro injection)	**Pen:** 2 x 3 mL KwikPen (can deliver up to 60 units per injection)	Administer subcutaneously within 15 minutes before meals or immediately after meals.	3 to 5 hours	**Pen:** 28 days
Toujeo U-300 (Insulin glargine injection)	**Pen:** 3 x 1.5 mL and 5 x 1.5 mL SoloStar pen (can deliver up to 80 units per injec-	Administer subcutaneously once daily at any time during the day, at he same time each day.	24 to 36 hours	**Pen:** 42 days
Tresiba U-200 (Insulin degludec injection)	**Pen:** 3 x 3 mL FlexTouch pen (can deliver up to 160 units per injection)	Administer subcutaneously once daily at any time of the day.	42 hours	**Pen:** 56 days

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ASK PRN...

Our pharmacy is still occasionally receiving prescriptions by fax from some prescribers. Is this permitted under New York State regulations?

Yes, but with certain specific requirements which must be met. Firstly, a faxed prescription is ***not*** an electronic prescription, as stated in section 6802 of the Education Law. When receiving a prescription by fax, a pharmacist must ensure that it conforms to the regulations. In order to be acceptable for dispensing, a prescription sent by fax **must**:

- **Be an original hard copy prescription transmitted by facsimile directly from the prescriber to the pharmacy**
- **Be manually, not electronically, signed by the prescriber**
- **Be on an official New York State prescription form, if issued by a prescriber on New York**

We sometimes receive "e-prescriptions" through the fax machine when the original electronic submission failed. Are these prescriptions acceptable for dispensing?

No. The New York State Board of Pharmacy has published a detailed answer to this question in the FAQs section of its website (www.op.nysed.gov/prof/pharm):

A document that originated as an electronic prescription, but due to a temporary network outage or because your pharmacy is not able to receive prescriptions electronically, was converted to a computer-generated fax is NOT a valid prescription. A pharmacist receiving this order must call the prescriber, obtain confirmation of the prescription information, and document said confirmation as a telephoned prescription.

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.

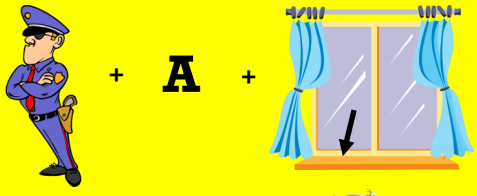
DID YOU KNOW?

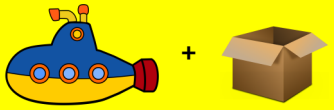
DID YOU KNOW that all three of the gifts of the Magi— gold, frankincense, and myrrh— have pharmacological properties and are still used today for medicinal purposes? In fact, one of them even requires a prescription! The Three Kings, most often identified as Caspar, Melchior, and Balthasar, dispensed a topical antiseptic and astringent (myrrh), an anti-inflammatory (frankincense), and an anti-rheumatic agent (gold). Gold salts are available by prescription under the brand name Ridaura (auranofin), which is indicated for the management of active classical or definite rheumatoid arthritis in patients who have not benefited from, or are intolerant of, an adequate trial of full doses of one or more nonsteroidal anti-inflammatory drugs (NSAIDs)

PHARMACY FUN

Back by popular demand, it's rebus time again! Name the drugs represented by the picture puzzles below. The first reader to forward the correct answers to *puzzle@prnnewsletter.com* will receive a *PRN* combination pen and touchscreen stylus.

1. 

2. 

3. 

4. END-
DANGER-
TWILIGHT-


Answers to last month's ***PHARMACY FUN***:
1. Jardiance 2. Welchol 3. Tudorza 4. Movantik

References:
1. Tresiba® [package insert]. Plainsboro, NJ: Novo Nordisk; 2016.