P.R.N.

ISSN # 1941-9481

www.prnnewsletter.com

No. 57 | **The Newsletter for Community Pharmacists** | **July/August, 2017**

What's Inside…

FDA NEWS

Opana ER to be Removed from Market

On June 8, 2017, the Food and Drug Administration (FDA) requested that Endo Pharmaceuticals remove its opioid pain medication, **Opana ER** (oxymorphone hydrochloride), from the market. The agency based its decision on a review of all available postmarketing data, which indicated a shift in the route of abuse of Opana ER from nasal to injection since the product was reformulated in 2012. Injection abuse of reformulated Opana ER has been associated with a serious outbreak of HIV and hepatitis C, as well as cases of a serious blood disorder called thrombotic microangiopathy. On July, 6, 2017, Endo Pharmaceuticals announced its decision to voluntarily withdraw Opana ER from the market. Endo stated that it plans to work with the FDA to coordinate the orderly removal of Opana ER in a manner that looks to minimize treatment disruption for patients.

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BAXDELA (Delafloxacin).
Category: Fluoroquinolone antibiotic.
Initial Dose: 450 mg every 12 hours.
MDD: 450 mg every 12 hours for 5 to 14 days total duration.

Melinta Therapeutics has been granted FDA approval for Baxdela (delafloxacin), a new fluoroquinolone antibiotic. Baxdela is indicated in adults for the treatment of acute bacterial skin and skin structure infections (ABSSSI), including those caused by MRSA (methicillin-resistant *Staphylococcus aureus*). As with all fluoroquinolones, Baxdela will carry a **black box warning** regarding serious adverse reactions, including tendonitis, tendon rupture, peripheral neuropathy, central nervous system effects, and exacerbation of myasthenia gravis. Baxdela can be administered orally or via IV infusion (the intravenous dose being 300 mg q12h). Baxdela tablets should be administered at least 2 hours before or 6 hours after antacids containing magnesium, or aluminum, with sucralfate, with metal cations such as iron, or with multivitamin preparations containing zinc or iron, or with didanosine buffered tablets for oral suspension or the pediatric powder for oral solution. Tablets can be taken with or without food.

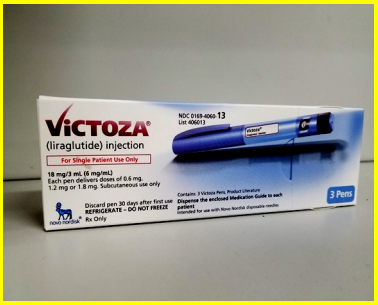
SYMJEPI (Epinephrine injection).
Category: Emergency anaphylaxis treatment.
Initial Dose: 0.3 mg (one prefilled syringe).
MDD: Do not give more than 2 sequential doses without direct medical supervision.

Adamis Pharmaceuticals will introduce Symjepi, the latest entry into the expanding epinephrine injection market. Symjepi is indicated in the emergency treatment of allergic reactions (Type I) including anaphylaxis. Initially, only the adult strength, for use in patients weighing 30 kg or more, will be available, and is expected to cost less than the **EpiPen** brand. Symjepi will be available in a single-use prefilled syringe, not in the auto-injector many patients are familiar with, and as a result will have a different method of injection. Patients should be instructed to inject Symjepi downwards into the thigh, while sitting, through clothes if necessary. After the needle is in the thigh, the plunger should be pushed all the way down until it clicks, and held for 2 seconds. Then remove the syringe and massage the injection area for 10 seconds.

EDITOR'S NOTE: You may notice that this month's issue does not include one of our regular features, the Medicaid Update, usually found on page 2 of each edition. We have removed this feature in order to allow more space for this month's Law Review. We will, however, continue to cover any news of note regarding the New York State Medicaid program in future issues.

FDA Approves New Cardiovascular Indication for Victoza

The FDA has authorized a new indication for Novo Nordisk's diabetes medication **Victoza** (liraglutide). The injectable glucagon-like peptide 1 (GLP-1) receptor agonist was originally approved in 2010 as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. The label will be revised to reflect that Victoza is also indicated to reduce the risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke) in adults with type 2 diabetes and established cardiovascular disease. Victoza is the second diabetes medication to receive an additional cardiovascular indication as a result of the FDA's 2008 recommendation that all new antidiabetic drugs be evaluated for cardiovascular safety (the first was **Jardiance**). The approval of the new indication was based upon the results of the **LEADER** (Liraglutide Effect and Action in Diabetes: Evaluation of Cardiovascular Outcome Results) trial. The trial included more than 9,000 patients with type 2 diabetes from 32 countries. The results of LEADER showed a 13% reduction in major cardiovascular events and a 22% reduction in cardiovascular morbidity in patients treated with Victoza. The added indication is particularly important in light of the fact that adults with diabetes are two to four times more likely to die from heart disease than are adults without diabetes. (Novo Nordisk also markets liraglutide injection under the brand name **Saxenda**, which is indicated for chronic weight management in patients with an initial body mass index (BMI) of 30 or greater, or 27 or greater in the presence of at least one weight-related comorbidity.)



LAW REVIEW

Regulatory Issues Affecting Pharmacy in New York State

Expanded Pharmacist-Administered Immunizations in New York

In December, 2008, pharmacists practicing in New York were given authority to administer influenza and pneumococcal vaccines to adults aged 18 years and older. Since then, the number of vaccines which New York pharmacists may give has grown to five: **Influenza, Pneumococcal, Herpes Zoster, Meningococcal, and Tetanus/Diphtheria/Pertussis**. Any of these vaccines may be administered pursuant to a patient specific order (prescription) or non-patient specific order (protocol) issued by a physician or certified nurse practitioner. Below is a review of the vaccines pharmacists are currently authorized to administer, with the exception of influenza, which will be fully covered in the September issue of ***PRN***.

Vaccine	Preparation and Administration	Adult Indications and Eligible Candidates	Notes, etc.
Prevnar 13 (pneumococcal 13-valent conjugate vaccine)	**Shake well** to obtain a homogenous, white suspension Inject 0.5 mL IM into deltoid muscle	• Persons 65 years of age and older with no or unknown previous history of vaccination, or with a previous history of Pneumovax vaccination • Persons 18 years of age or older with certain chronic medical conditions (might not be covered by non-patient specific protocol)	Give Prevnar first, followed by Pneumovax at least 12 months later. If Pneumovax already given, wait 12 months, then give Prevnar
Pneumovax 23 (pneumococcal vaccine polyvalent)	Inject 0.5 mL IM or SC into deltoid muscle or lateral mid-thigh	• Persons 65 years of age and older with no or unknown previous history of vaccination, or with a previous history of Prevnar vaccination at least 12 months prior • Persons 18 years of age or older with certain chronic medical conditions (might not be covered by non-patient specific protocol)	Give Prevnar first, followed by Pneumovax at least 12 months later. If Pneumovax already given, wait 12 months, then give Prevnar
Boostrix *or* **Adacel** (tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis)	**Shake well** to obtain a homogenous, white suspension Inject 0.5 mL IM into deltoid muscle	• Pregnant women with ***every*** pregnancy, preferable during 27 through 36 weeks gestation • Persons with a deep, contaminated, or puncture wound with no evidence of tetanus vaccine in the previous 5 years • Persons who have not received a previous dose or if vaccination status is unknown or if 3-dose primary series was completed at least 10 years prior	When possible, administer ***Boostrix*** to patients 65 years of age and older (***Adacel*** is approved for use in patients up to age 64)
Menactra *or* **Menveo** (meningococcal group A, C, Y and W-135 conjugate, ***MCV4***)	Inject 0.5 mL IM into deltoid muscle	• First year college students living in a residence hall • High-risk groups, including HIV patients, and those with functional or anatomic aspelnia • Military recruits and people travelling to areas where the disease is common, and microbiologists routinely exposed to meningococcal bacteria • Persons who are identified as at risk because of a meningitis A, C, W, or Y outbreak	May revaccinate every 5 years if high risk still exists Menactra is supplied in single dose vials. Menveo is supplied in 2 separate vials that must be combined before use
Bexsero *or* **Trumenba** (meningococcal group B vaccine)	**Shake well** to obtain a homogenous, white suspension Inject 0.5 mL IM into deltoid muscle	• Persons with functional or anatomic aspelnia • Microbiologists routinely exposed to meningococcal bacteria • Persons who are identified as at risk because of a serogroup B meningitis outbreak	***Bexsero*** is administered as a 2 dose series, with doses at least 1 month apart ***Trumenba*** is administered as either a 2 dose or 3 dose
Zostavax (zoster vaccine live)	Keep frozen. Reconstitute with supplied diluent and administer immediately. Discard if not used within 30 minutes Inject 0.65 mL SC to posterolateral upper arm	• Persons 60 years of age or older with no previous history of zoster vaccine (Advisory Committee on Immunization Practices [ACIP] recommendation) • Zostavax is FDA indicated for patients 50 years of age and older, but non-patient specific protocols generally cover only patients 60 and older. Patients between 50 and 59 years of age should obtain a prescription if they wish to receive Zostavax administration by their pharmacist	**CONTRAINDICATIONS:** • **Pregnancy or possibility of pregnancy within 4 weeks of vaccination** • **Immunosuppression (HIV/AIDS, leukemia, lymphoma, radiation or chemotherapy, immunosuppressive drugs, e.g., steroids)**

FEATURE ARTICLE...

INTRODUCTION TO THE FDA PURPLE BOOK

In October, 1980, the FDA published the first edition of the Orange Book, officially known as Approved Drug Products with Therapeutic Equivalence Evaluations. This is the publication which informs pharmacists which generics are legally substitutable for brand name drugs. Almost exactly 34 years later, in September, 2014, the agency produced the inaugural copy of the Purple Book, which is to biologic drugs what the Orange Book is to ordinary, so-called "small molecule," drugs. Below we review the history, purpose, and use of the Purple Book.

Biologics and the Affordable Care Act

The genesis of the Purple Book can be traced to the enactment of the Affordable Care Act (ACA or "Obamacare"). Before the ACA there was no regulatory framework in place for manufacturers to compete by producing their own versions of already licensed biologic products. Biologics are defined as "any virus, therapeutic serum, toxin, antitoxin, or analogous product," and are most often produced by living organisms through recombinant DNA technology. The 351(k) pathway created by the ACA requires applicants to demonstrate ***biosimilarity*** to the reference drug, defined as being "highly similar with no clinically meaningful differences." This is in contrast to small-molecule drugs, where generics must demonstrate ***bioequivalence***.

The Strange Case of Insulin, and the Stranger Case of the Naming of Biosimilars

Synthetic insulin is a large, complex molecule produced by living organisms through recombinant DNA technology. Sounds like a biologic, right? Not exactly, according to the FDA, due to the fact that insulins have always been regulated under the Food, Drug, and Cosmetic Act, whereas biologics fall under the Public Health Service Act. Therefore, when the FDA approved **Basaglar** (Lilly's version of **Lantus**), it referred to it as a "follow-on," not a biosimilar. And when it comes to naming biosimilars, the agency has discarded its original policy of using the company name as a modifier (Sandoz's version of **Neupogen** was named **filgrastim-sndz**) in favor of a random, four letter suffix (e.g., **infliximab-dyyb**).

No, they're not Generics (yet). The Pharmacists Perspective on Biosimilars

Of especial interest to the practicing pharmacist is the question of whether biosimilars are substitutable, like AB-rated generics for brands. The short answer is: no, they are not. So, for example, Basaglar can not be substituted for Lantus without contacting the prescriber. However, this may change, as the FDA has left open the door for biosimilars to be rated as ***interchangeable***, a status that would allow for pharmacist substitution. The FDA defines an interchangeable biologic as a product which "may be substituted for the reference product by a pharmacist without the intervention of the health care provider who prescribed the reference product." As indicated below, however, no biologic has yet been rated "I."

FDA Purple Book for Biosimilars (updated August 17, 2017)

Product name	Proprietary name	Date of licensure	Biosimilar (B)/ Interchangeable (I)
adalimumab	**Humira**	12/31/2002	
adalimumab-atto	**Amjevita**	09/23/2016	**B**
etanercept	**Enbrel**	11/02/1998	
etanercept-szzs	**Erelzi**	08/30/2016	**B**
filgrastim	**Neupogen**	12/20/1991	
filgrastim-sndz	**Zarxio**	03/06/15	**B**
infliximab	**Remicade**	08/24/1998	
infliximab-abda	**Renflexis**	04/21/2017	**B**
infliximab-dyyb	**Inflectra**	04/05/2016	**B**

P.R.N.

P.R.N. (ISSN # 1941-9481) is published monthly, except for two combined issues (April/May and July/August) by:
PRN Publishing LLC
7636 113th Street
Suite 6C
Forest Hills, New York 11375
Phone & Fax (718) 263-4632

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ASK PRN...

Influenza vaccination season is upon us. What is required of New York immunizing pharmacists to maintain their certification?

In order to become certified to administer vaccinations in New York State, licensed and registered pharmacists are required to complete an approved immunization course and be able show proof of current certification in Cardio Pulmonary Resuscitation (CPR) or Basic Life Support (BLS). Upon meeting these requirements the registrant's license will be updated to include the "I" modifier. In order to maintain this certification, pharmacists must renew their CPR/BLS training every 2 years ("on-line" or "virtual" courses will not be accepted). The immunization course does not need to be repeated, and no specific continuing education credits related to immunization are required. For recent graduates of pharmacy college, immunization training given as part of the school's curriculum will meet the requirement for approved immunization training.

What are the requirements pharmacies must meet in order to provide immunizations to their patients?

In addition to being staffed with certified immunizer pharmacists, pharmacies must meet the following requirements:

- **Obtain a non-patient specific protocol from a physician or nurse practitioner.**
- **Report immunizations to the New York State Immunization Information System (NYIIS).**
- **Designate an immunization area that provides for the patient's privacy.**
- **Post the most current "Recommended Adult Immunization Schedule" published by ACIP in the designated immunization area.**

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 recent research indicates that the mosquito repellant DEET doesn't actually work the way we have always thought it did? *N,N*-Diethyl-3-methylbenzamide (DEET) was developed by the U.S. army and has been marketed for over 50 years. For most of that time it was believed that the chemical worked by blocking the mosquito's ability to detect volatile substances in human sweat, essentially hiding the victim from its prey. Recent studies[1], however, have demonstrated that the insects have a specific receptor on their antennae that reacts strongly to the chemical. In other words, DEET works because mosquitos think it stinks!

PHARMACY FUN

Dies Caniculares! **The Roman phrase describing the most oppressive time of the year, weather-wise — the dog days! In honor of this sizzling season, we present a quiz on all things thermometric. Put your smartphones down and see how many of these important digits you know by heart. The first reader to submit the correct answers to *puzzle@prnnewsletter.com* will receive a custom-printed *PRN* binder.**

1. **USP controlled room temperature**
2. **USP "refrigerator" temperature**
3. **USP "freezer" temperature**
4. **USP "cold" temperature**
5. **USP "cool" temperature**
6. **USP "warm" temperature**
7. **The temperature at which Celsius and Fahrenheit thermometers read the same**
8. **Bonus question: The temperature at which paper burns, according to one of our leading science fiction authors**

Answers to last month's **PHARMACY FUN**:
1. Ethanol 2. Acetone 3. Urea 4. Glycerin

References:
1. Fox, Maggie. For mosquitos, DEET just plain stinks. *Reuters*. August 18, 2008. Retrieved from Reuters.com on July 22, 2017.