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What's Inside…

FDA NEWS

FDA to Require Color Changes on Duragesic

In a drug safety communication, the FDA announced that it will require color changes to the writing on Duragesic and fentanyl patches to avoid accidental exposure to the patches, which can cause serious harm and death in children, pets, and others. The agency continues to receive reports of deaths from accidental exposure to fentanyl patches, including 2 recent cases involving children. The change involves printing the name and strength of the drug on the patch itself in long-lasting ink, in a color that is clearly visible to patients and caregivers. The FDA also wants patients to be aware of the following:

- **Patches may accidently fall off and stick to someone in close contact, such as a child. To prevent this, patients should check periodically, by sight or touch, to make sure the patch is still sticking to the skin properly.**
- **Used fentanyl patches require proper disposal after use – fold patch, sticky sides together, and flush it down the toilet immediately.**

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

BREO ELLIPTA (Fluticasone furoate and Vilanterol inhalation powder).
Category: ICS/LABA for COPD.
Initial dose: One inhalation (100mcg/25mcg) once daily.
MDD: One inhalation (100mcg/25mcg) once daily.

GlaxoSmithKline has announced FDA approval of Breo Ellipta, the first once-daily inhaled corticosteroid (ICS)/long-acting beta$_2$ agonist (LABA) combination for the treatment of chronic obstructive pulmonary disease (COPD), which includes chronic bronchitis and emphysema. Breo Ellipta is *not* indicated for the relief of acute bronchospasm or for the treatment of asthma. Because the formulation includes lactose, Breo Ellipta should not be used in patients who have hypersensitivity to milk proteins.

BRISDELLE (Paroxetine).
Category: SSRI for the treatment of symptoms of menopause.
Initial dose: 7.5 mg once daily at bedtime.
MDD: 7.5 mg once daily at bedtime.

Noven Therapeutics will introduce Brisdelle, the first non-hormonal treatment for moderate to severe vasomotor symptoms (e.g., hot flashes) associated with menopause. Brisdelle contains the selective serotonin reuptake inhibitor (SSRI) paroxetine in a low dose formulation (7.5 mg) to be taken once daily at bedtime. In addition to warning against the use of **MAOIs** with Brisdelle, the labeling will also recommend avoiding concomitant use with **tamoxifen**, which may be less effective when taken with Brisdelle.

EPANED (Enalapril for oral suspension).
Category: Antihypertensive (ACE Inhibitor).
Initial dose: Adult: 5 mg once daily.
Pediatric: 0.08 mg/kg (up to 5 mg) once daily.
MDD: 40 mg (adults).

Silvergate Pharmaceuticals has received FDA approval to market Epaned, the first commercially available oral liquid preparation of the antihypertensive enalapril maleate. Developed with children in mind, Epaned is an option for any patient with difficulty swallowing tablets. Epaned will be available as a kit containing one bottle of enalapril maleate powder and one bottle of Ora-Sweet SF diluent for reconstitution, which yields a 1mg/mL enalapril oral solution. Instructions for preparation are as follows: tap the powder bottle on a hard surface 5 times. Add approximately half the Ora-Sweet SF diluent (75 mL) to the powder bottle and shake for 30 seconds. Add remaining diluent, shake for an additional 30 seconds, and label the bottle with a 60 day expiration date (Epaned solution should be stored at room temperature).

LIPTRUZET (Atorvastatin and Ezetimibe).
Category: Antihyperlipidemic (Statin/Cholesterol Absorption Inhibitor combination).
Initial dose: 10/10 mg/day or 10/20 mg/day.
MDD: 10/80 mg/day.

Merck (MSD) will market Liptruzet, a combination of the statin **Lipitor** and the cholesterol absorption inhibitor **Zetia**, for the treatment of elevated low-density lipoprotein (LDL) in patients with primary or mixed hyperlipidemia. Liptruzet will be available in 10/10, 10/20, 10/40, and 10/80 mg.

FDA Questions Safety, As Well As Legal Status, Of Asthmanefrin

The FDA has released a statement warning patients and health care professionals of the potential harm of using the over-the-counter product **Asthmanefrin** (racepinephrine) for the treatment of symptoms of bronchial asthma. Asthmanefrin became the only OTC inhaler for asthma after **Primatene Mist** was taken off the market in 2012. In the statement, the agency cites multiple adverse events reports, including complaints of chest pain, nausea/vomiting, increased blood pressure, increased heart rate, and hemoptysis. In addition, the statement questions whether the product can be legally marketed in the United States, since Asthmanefrin has not been evaluated by FDA for safety and effectiveness under the new drug application process. As we go to press, the maker of Asthmanefrin, Nephron Pharmaceuticals, has yet to respond publicly to the agency's assertions. Meanwhile, Armstrong Pharmaceuticals has submitted an NDA for a reformulated version of Primatene Mist and is awaiting a decision from the FDA.

MEDICAID UPDATE

Information Regarding the New York State Medicaid Program

OPRA Implementation Delayed Until January 1, 2014

In July, the New York State Medicaid program announced the implementation of the new Ordering/Prescribing/Referring/Attending (OPRA) claims edit, which would automatically reject any prescription claim which includes they NPI of a non-enrolled provider. The implementation, originally scheduled for October 1, 2013, has been delayed until January 1, 2014 in order to allow more time for providers to request and obtain enrollment. The OPRA restriction, mandated by the Affordable Care Act, does *not* apply to Medicaid Managed Care plans. The Department of Health has provided answers to the following questions regarding OPRA:

What professions must enroll in fee-for-service Medicaid?

Physicians and other healthcare professionals who order or refer services under the state plan must enroll in Medicaid.

Do out of state ordering/referring professionals need to be enrolled in NYS Medicaid?

Yes, out of state professionals ordering/referring for services paid by fee-for-service Medicaid must enroll.

What rejection will pharmacists receive if the prescriber is not enrolled?

Reject Code "56" - Non-matched Prescriber ID.

Can a pharmacist override a rejected transaction if the prescriber is not enrolled?

No.

What should a pharmacist do once a transaction is rejected?

Pharmacists can either contact the prescriber or return the prescription to the member to contact the prescriber.

LAW REVIEW

Regulatory Issues Affecting Pharmacy in New York State

Pharmacist Immunization Expanded to Include Meningitis

Effective October 29, 2013, pharmacists in New York State will be authorized to administer meningococcal vaccine to patients 18 years of age and older, pursuant to a patient specific order or non-patient specific regimen prescribed or ordered by a physician or certified nurse practitioner. The legislation approving the expansion of pharmacist's immunizing privileges, signed into law by the governor in July, was prompted by a recent outbreak of deadly bacterial meningitis among gay and bisexual men in New York City. A novel strain of the bacteria found in this community has led to 22 known cases and seven deaths since 2010. There are currently three licensed quadrivalent meningococcal vaccines available for adults.

Meningococcal Vaccines Approved for Use in Adults

Vaccine (manufacturer)	Type	Approved Age Group	Dose	Route of Administration
Menactra (Sanofi)	Conjugate vaccine	9 months to 55 years	0.5 ml	IM
Menveo (Novartis)	Conjugate vaccine	2 years to 55 years	0.5 ml	IM
Menomune (Sanofi)	Polysaccharide vaccine	≥2 years	0.5 ml	SC

The New York City Department of Health has issued the following Frequently Asked Questions for meningococcal vaccine providers:

Who should receive meningococcal vaccine as part of the response to the current outbreak?

Meningococcal vaccine should be administered to the following New York City residents:

1. HIV-infected men who have sex with men (MSM)
2. MSM, regardless of HIV status, who regularly have close or intimate contact with other men met through an online website, digital application ("app"), or at a bar or party

Which vaccine should I use to vaccinate patients meeting the outbreak criteria?

For adults 55 years of age or younger, meningococcal conjugate vaccines (MCV4) should be used. For patients 56 years of age or older, meningococcal polysaccharide vaccine (MPSV4) should be used.

How many doses of vaccine should be administered?

HIV infected patients should receive two doses of MCV4; the second dose should ideally be administered eight weeks after the first dose but no less than six weeks. In addition, patients with other conditions that put them at increased risk of invasive meningococcal disease, including anatomic or functional asplenia (i.e., sickle cell disease) or persistent complement component deficiencies, should also receive two doses of vaccine, administered at least 8 weeks apart. Patients who are not HIV positive, or who do not have one of the aforementioned co-morbidities, require only one dose. Only one dose is needed for any patient who receives MPSV4.

Feature Article..

REVIEW OF THE NEW ORAL ANTICOAGULANTS

Warfarin was first approved for human use in 1954, and for the next 60 plus years reigned supreme as the oral anticoagulant of choice, specifically in the prevention of thromboembolism in nonvalvular atrial fibrillation (A-fib). That domination came to an end with the introduction of **Pradaxa** in 2010, which was quickly followed by **Xarelto** in 2011 and **Eliquis** in 2012. All three have the advantage of not requiring frequent blood draws to check the international normalized ratio (INR), which is necessary with warfarin use, but also share the drawback of having no antidote available, unlike warfarin, which can be reversed with Vitamin K. The newcomers also have in common a **black box warning** about the increased risk of stroke upon discontinuation of therapy. We have put together the following chart comparing the three agents and also provided manufacturer's recommendations for switching patients from and to warfarin therapy.

Brand Name (active ingredient) *strengths*	**Mechanism of Action**	**Dosage and Administration for Nonvalvular A-fib**	**Discontinuation for Surgery and Other Interventions**
Pradaxa (dabigatran) *75 mg, 150 mg*	Pradaxa is a direct thrombin inhibitor which prevents the conversion of fibrinogen to fibrin. Both free and clot-bound thrombin, and thrombin-induced platelet aggregation are inhibited.	For patients with CrCl <30mL/min: **150 mg twice daily** For patients with CrCl 15-30 mL/min: **75 mg twice daily**	If possible, discontinue Pradaxa 1 to 2 days (CrCl ≥50mL.min) or 3 to 5 days (CrCl <50 mL/min) before invasive or surgical procedures.
Xarelto (rivaroxaban) *10 mg, 15 mg, 20 mg*	Xarelto is a direct inhibitor of factor Xa, which catalyzes the conversion of prothrombin to thrombin; thrombin is responsible for platelet activation and the conversion of fibrinogen to fibrin.	For patients with CrCl <50mL/min: **20 mg once daily with the evening meal** For patients with CrCl 15-50 mL/min: **15 mg once daily with the evening meal**	If anticoagulation must be discontinued to reduce the risk of bleeding with surgical or other procedures, Xarelto should be stopped at least 24 hours before the procedure.
Eliquis (apixaban) *2.5 mg, 5 mg*	Eliquis is a direct inhibitor of factor Xa, which catalyzes the conversion of prothrombin to thrombin; thrombin is responsible for platelet activation and the conversion of fibrinogen to fibrin.	**5 mg twice daily** For patients with at least two of the following characteristics: age ≥80 years, body weight ≤60 kg, or serum creatinine ≥1.5 mg/dL: **2.5 mg twice daily**	Eliquis should be discontinued at least 48 hours prior to elective surgery or invasive procedures with a moderate or high risk of bleeding.

Pradaxa: Converting From or To Warfarin

When converting patients from warfarin to Pradaxa, discontinue warfarin and start Pradaxa when the INR is below 2.0.

When converting patients from Pradaxa to warfarin:

- For CrCl ≥50 mL/min, start warfarin 3 days before discontinuing Pradaxa
- For CrCl 30-50 mL/min, start warfarin 2 days before discontinuing Pradaxa
- For CrCl 15-30 mL/min, start warfarin 1 day before discontinuing Pradaxa

Xarelto: Converting From or To Warfarin

When converting patients from warfarin to Xarelto, discontinue warfarin and start Xarelto as soon as the INR is below 3.0 to avoid periods of inadequate anticoagulation.

No clinical trial data are available to guide converting patients from Xarelto to warfarin. Xarelto affects INR, so INR measurements made during coadministration with warfarin may not be useful. One approach is to discontinue Xarelto and begin both a parenteral anticoagulant and warfarin at the time the next dose of Xarelto would have been taken.

Eliquis: Converting From or To Warfarin

When converting patients from warfarin to Eliquis, warfarin should be discontinued and Eliquis started when the INR is below 2.0.

Converting patients from Eliquis to warfarin: Eliquis affects INR, so INR measurements made during coadministration with warfarin may not be useful. If continuous anticoagulation is necessary, discontinue Eliquis and begin both a parenteral anticoagulant and warfarin at the time the next dose of Eliquis would have been taken, discontinuing the parenteral anticoagulant when INR reaches an acceptable range.

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ASK PRN...

When refilling a prescription for a controlled substance in New York State, are pharmacists still required to pull the original hard-copy prescription and endorse it with the amount and date dispensed and pharmacist's signature?

No. When using an electronic recordkeeping system it is no longer required that the pharmacist refilling a controlled substance prescription pull and sign the original hard-copy prescription. The regulations regarding refilling Schedule III, IV, and V prescriptions were amended and became effective on March 27, 2013. The pertinent section now reads as follows:

Part 80 Rules and Regulations on Controlled Substances

Section 80.69 - Schedule III, IV and V substances (i):

When refills are recorded in an electronic recordkeeping system:
(1) the pharmacist shall ensure that the computer application used for such recordkeeping shall: (i) provide online retrieval of original prescription information; and (ii) provide online retrieval of the current refill history for Schedule III, IV, and V controlled substance prescriptions.
(2) each time an official New York State prescription or an out-of-state written prescription for a Schedule III, IV, or V controlled substance is refilled, the dispensing pharmacist shall document that the refill information entered into the computer has been reviewed and is correct by manually signing: (i) a hard-copy printout of each day's controlled substance refill data, or; (ii) a bound log book containing a statement that the refill information entered into the computer that day has been reviewed and is correct as shown.

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 anticoagulant warfarin was discovered as a result of a series of mysterious cattle deaths in 1921? It was during the winter of that year that farmers in the U.S. and Canada began reporting loss of livestock due to hemorrhages of unknown cause, and a Canadian veterinarian, Frank Schofield, determined the cause to be ingestion of spoiled clover, naming the disorder "sweet clover disease." Years later, the chemist Karl Paul Link identified the offending compound in the clover as dicoumarol, and his lab then synthesized a more potent and long-acting derivative. Since Dr. Link's work was supported by the Wisconsin Alumni Research Foundation (WARF), the new compound was named warfarin.

PHARMACY FUN

It's September, and that can mean only one thing...time for our sixth annual back-to-school quiz! Whether you graduated this year, or back in the days when dinosaurs roamed the Earth, here's your chance to prove you were paying attention! This edition of the quiz focuses on the USP. The first reader to submit the correct answers to *puzzle@prnnewsletter.com* will receive a custom-printed *PRN* binder.

1. **What temperature range is considered USP "controlled room temperature"?**
2. **What temperature range is considered USP "refrigerator"?**
3. **According to USP, an expiration date which states only month and year indicates expiration on the first or last day of that month?**
4. **Which alcohol is "USP alcohol"?**
5. **According to USP, what contains 4.93 (± 0.24) mL?**
6. **In past editions, USP defined the official dropper as delivering how many drops per mL?**

Answers to last month's **PHARMACY FUN**:
1. Graduate 2. Mortar 3. Balance 4. Tablet 5. Script 6. Log 7. Capsule 8. Doughnut Hole