

INSIGHTSM

SUMMER 2009

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Influenza prevention: gearing up for next season Part I

Diane Karpelis, PharmD

Influenza (the flu) is a contagious respiratory disease caused by a variety of influenza viruses. The severity of the illness ranges from mild to severe with the greatest risk of complications in those with existing heart or lung conditions, the elderly, and young children. Every year, an estimated 226,000 hospitalizations and 36,000 deaths in the United States are due to influenza complications.¹

Typically, the flu causes the following symptoms in adults: fever, chills, muscle aches, headache, cough, sore throat, and fatigue. Children usually have additional gastrointestinal symptoms not experienced by adults; those symptoms can include nausea, vomiting, and diarrhea.

The peak of the flu season in the U.S. is usually between November and March. This correlates to the cold season and is the time of year when contagious respiratory diseases are more easily spread, as people tend to spend a lot of time indoors and in close proximity to each other.

According to the Centers for Disease Control and Prevention (CDC), spread of the flu can be prevented in several ways. The most important step against prevention is getting an annual flu vaccine. Flu vaccines are of two types: inactivated vaccine (flu shot) and live, attenuated vaccine (nasal spray). Because influenza viruses are constantly mutating, new vaccines are created every year and the specific types of viral strains within the vaccines can vary year to year. After a vaccine is administered, it can take up to two weeks for the body to build immunity to the flu and, generally, protection lasts up to a year.²

Patients should speak with their doctors to determine whether they should be vaccinated against

influenza. The CDC recommends vaccination for:²

- all children between ages 6 months and 18 years;
- adults 50 years and older;
- anyone at risk for complications from influenza or more likely to require medical care;
- anyone who lives with or cares for people at high risk for influenza-related complications.



Health care providers may make recommendations on case-by-case basis, as deemed appropriate for those who want to reduce the likelihood of becoming ill with influenza or spreading influenza to others.

In addition to the influenza vaccine, the CDC recommends reinforcement of daily preventive measures, some of which include:¹

- washing your hands often with soap and water;
- avoiding touching your eyes, nose, and mouth;

(continued on page 3)

Consumer safety warning: New package labeling aimed at stemming unintentional overdoses

Natalie Habiyaremye, PharmD

Over-the-counter (OTC) medications are the cause of continued safety concerns regarding inappropriate usage. An estimated 500 deaths and more than 50,000 emergency room visits are blamed each year on acetaminophen overdose (commonly marketed with the brand name Tylenol®).⁴ Acetaminophen is the most commonly used medication in the United States, with nearly 70 million American adults taking the drug each week.⁵ The danger of acetaminophen comes when it is used at doses greater than 4 grams (4,000 mg) daily. At these dosage levels, acetaminophen is a leading cause of acute liver failure.⁴ “Because acetaminophen is so commonly used and prescribed, it is important to ensure that American consumers are aware that acetaminophen misuse or overdose can have serious health risks, including the risk of liver damage,” according to a statement by Linday A. Suydam, president of the Consumer Healthcare Products Association.⁵

One of the most common reasons for unintentional overdose is that patients unknowingly take multiple products containing acetaminophen at the same time. In response to this problem, the U.S. Food and Drug

Administration, recently issued a ruling requiring manufacturers of OTC pain relievers and fever reducers to prominently display the active ingredients on the drug labels. For additional consumer safety, the labeling must also warn of the risks of severe liver damage for acetaminophen. The new rule gives the manufacturers of the affected drugs one year to relabel their products.

What is the recommended safe dosage?

The manufacturer has set a maximum dose of 4 grams (4,000 mg) of acetaminophen per day:

- 8 extra-strength tablets or capsules (500 mg each) per day;
- 12 regular-strength tablets or capsules (325 mg each) per day.

For those regularly consuming three or more alcoholic beverages a day:

- a number of authors recommend a maximum of 2 – 3 grams (2,000 – 3,000 mg) per 24 hours;
- 4 – 6 extra-strength tablets or capsules (500 mg each) per day;
- 6 – 9 regular-strength tablets or capsules (325 mg) per day.

acetaminophen (not all-inclusive):

Anacin® aspirin free maximum strength tablets®
Excedrin PM® caplets
Excedrin PM® geltabs
Excedrin PM® tablets
Excedrin® extra-strength caplets
Excedrin® extra-strength tablets
Excedrin® migraine caplets
Excedrin® migraine geltabs
Excedrin® migraine tablets
Feverall® children’s
Feverall® infant’s
Feverall® junior strength
Gelpirin®
Genapap
Genapap® children’s
Genapap® drops infant’s
Genapap® extra-strength caplets
Genapap® extra-strength tablets

Genapap® gel-coat caplets
Genebs®
Genebs® extra-strength caplets
Genebs® extra-strength tablets
Goody’s® extra-strength tablets
Goody’s® fast pain relief tablets
Goody’s® headache powders
Tylenol®
Tylenol® arthritis pain extended relief caplets
Tylenol® meltaways children’s
Tylenol® concentrated drops infant’s
Tylenol® extra-strength adult
Tylenol® extra-strength caplets
Tylenol® extra-strength gelcaps
Tylenol® extra-strength geltabs
Tylenol® extra-strength tablets
Tylenol® meltaways junior strength
Tylenol® suspension children’s

First-time generic drug approvals

March 2009

Apraclonidine Ophthalmic Solution USP 0.5% (base)

Approved: March 12, 2009, Akorn, Inc.

Generic for: Iopidine® Ophthalmic Solution, 0.5%

Carbamazepine Extended-Release Tablets USP 100 mg, 200 mg and 400 mg

Approved: March 31, 2009, Taro Pharmaceuticals USA, Inc.

Generic for: Tegretol® XR Tablets

Drospirenone and Ethinyl Estradiol Tablets 3 mg/0.02 mg (28-Day Regimen)

Approved: March 30, 2009, Barr Laboratories, Inc.

Generic for: Yaz® Tablets

Levalbuterol Inhalation Solution USP, (Concentrate) 0.25% (1.25 mg/0.5mL)

Approved: March 20, 2009, Dey LP

Generic for: Xopenex® Inhalation Solution (Concentrate)

Liothyronine Sodium Tablets USP 5 mcg, 25 mcg, and 50 mcg

Approved: March 20, 2009, Coastal Pharmaceuticals

Generic for: Cytomel® Tablets

Malathion Lotion USP 0.5%

Approved: March 6, 2009, Synerx Pharma, LLC

Generic for: Ovide® Lotion, 0.5%

April 2009

Azelastine Hydrochloride Nasal Solution (Nasal Spray)

0.1% [125 mcg (base)/spray]

Approved: April 30, 2009, Apotex Inc.

Generic for: Astelin® Nasal Spray

Topiramate Capsules (Sprinkle) 15 mg and 25 mg

Approved: April 15, 2009, Cobalt Laboratories, Inc.; Barr Laboratories, Inc.

Generic for: Topamax® Sprinkle Capsules

Mycophenolate Mofetil 250 mg and 500 mg

Approved: April 22, 2009, Apotex Corporation

Generic for: Cellcept®

May 2009

Galantamine Hydrobromide 4 mg, 8 mg, 12 mg

Approved: May 29, 2009, Mylan Pharmaceuticals

Generic for: Razadyne®

Galantamine Hydrobromide 8 mg, 16 mg, 24 mg

Approved: May 27, 2009, Impax Labs

Generic for: Razadyne® ER

Influenza prevention (cont. from page 1)

- covering your nose and mouth with a tissue when you sneeze;
- avoiding close contact with sick people.

So what is in store for the future? Researchers have identified new human antibodies that inactivate influenza viruses. Typically, drugs and vaccines target the head of the influenza virus, which is the part of the virus that mutates and makes itself resistant to

medications and vaccines. These newly identified antibodies attack the viral stem, which is consistent among the different strains and less susceptible to resistance. The major implication of this finding is the identification of a mechanism by which a universal influenza vaccine could potentially be created. Although it is still early in the research phase, this is a promising future development.³

Look for Part 2 in the fall edition of InSight which will focus on the developments surrounding the H1N1 Influenza virus and its potential impact.

FDA acts against unapproved narcotic drugs

Jomy Joseph, PharmD

Some two percent of all prescriptions in the U.S. are for unapproved drugs. These drugs have received neither the Food and Drug Administration's (FDA) approval nor over-the-counter (OTC) drug review. The FDA is taking steps to either persuade manufacturers of unapproved drugs to comply with the approval provisions of the Federal Food, Drug, and Cosmetic Act, or to pull their noncompliant products from the market. New drug approval and OTC drug monograph processes play an important role in certifying that all drugs are both safe and effective for their intended uses.



In June 2006, the FDA declared a new drug safety initiative entitled “Marketed Unapproved Drugs — Compliance Policy Guide,” aimed at efficiently moving all such drugs into the approval process. The FDA uses a risk-based enforcement program to focus on products that create the highest risk to public health, without inflicting undue burdens on consumers or unreasonably disrupting the market. The compliance initiative grants official notice that any illegally marketed product is subject to FDA enforcement at any time and explains that the FDA intends to use a risk-based approach to enforcement. After the risk-based evaluation, the FDA can take any number of enforcement actions, including, but not limited to, “requesting voluntary compliance, presenting notice of action in a federal register notice, issuing untitled and or warning letters, or starting a seizure, injunction, or other proceeding.”¹²

In March 2009, the FDA ordered 14 unapproved narcotic painkillers off the market, including prescription versions of potent morphine, hydromorphone, and oxycodone, declaring that ample authorized versions of the painkillers are available for patients who need relief. The active pharmaceutical ingredients morphine sulfate, hydromorphone, and oxycodone are strong drugs of the opioid class, a family of related drugs that relieve pain. This FDA move was the latest step since 2006 in cleaning up drugs that fall through cracks in the approval process. Among the drugs affected by the enforcement action are two branded products containing morphine sulfate and oxycodone (Roxanol™ and Roxicodone®, respectively) as well as generic versions of the three painkillers. All the affected products are tablets or oral solutions. Oxycodone capsules and extended-release opioids were unaffected by these actions. This action will have the most impact on consumers who use high-concentrate unapproved morphine sulfate oral solutions and unapproved immediate-release tablets containing morphine sulfate, hydromorphone, or oxycodone.

The FDA asked nine of these drug manufacturers to suspend distribution of the drugs within 90 days. Previously manufactured products may still be found on pharmacy shelves for a short time. The companies told to pull their products are Mallinckrodt, Boehringer Ingelheim Roxane, Inc.; Roxane Laboratories, Inc.; Glenmark Generics Inc.; Lannett Company, Inc.; Lehigh Valley Technologies, Inc.; Physicians Total Care, Inc.; Xanodyne Pharmaceuticals, Inc; and Cody Laboratories, Inc. Deborah M. Autor, J.D., director of CDER's Office of Compliance said that the companies must submit responses to the warning letters within 15 days or face sanctions. Autor also stated that the companies may seek approval for the products, but, in the meantime, unapproved drugs must be pulled from the market. Patients who have been taking the unapproved medications are urged to seek prescriptions for equivalent or similar approved products.

“Consumers have a right to expect that their drugs meet the FDA's safety and effectiveness standards,” said Janet Woodcock, director of the FDA's Center for Drug Evaluation and Research. “Doctors and patients are often unaware that not all drugs on the market are backed by FDA approval. It is a high priority for the FDA to remove these products from the market because they may be unsafe, ineffective, inappropriately labeled, or of poor quality.”¹⁵

New indications

Avastin[®]

Genentech, Inc. announced that the FDA granted accelerated approval of Avastin[®] (bevacizumab) for people with glioblastoma with progressive disease following prior therapy. The effectiveness of Avastin[®] in this aggressive form of brain cancer is based on an improvement in objective response rate. The new indication for Avastin[®] was granted under the FDA's accelerated approval program that allows provisional approval of medicines for cancer or other life-threatening diseases.

Axert[®]

Almirall announced that the FDA has approved a new indication for the use of Axert[®] (almotriptan) for the acute treatment of migraine headache in adolescent patients (age 12 to 17 years). Almotriptan, a product coming from Almirall R&D, obtained the initial approval in USA in 2001 for the same indication in adults. Axert[®] (almotriptan) is the first triptan to be approved for treatment of migraine in adolescents by the FDA.

Azor[®]

Daiichi Sankyo, Inc. announced that the FDA has approved the combination treatment Azor[®] (amlodipine and olmesartan medoxomil) as initial or 'first-line' therapy in patients likely to need multiple antihypertensive agents to achieve their blood pressure (BP) goals. The FDA approval of Azor for first-line use reinforces current U.S. guidelines to prescribe combination drugs as initial therapy for patients likely to need more than one drug.

Lexapro[®]

Forest Laboratories, Inc. announced that the FDA has approved Lexapro[®] (escitalopram oxalate) for the acute and maintenance treatment of Major Depressive Disorder (MDD) in adolescents, 12 – 17 years of age. Lexapro[®] is only the second antidepressant to be approved for the treatment of MDD in adolescents, a medical condition that affects approximately 2 million adolescents in the U.S.

Prograf[®]

The FDA has granted Astellas Pharma US, Inc. approval for the use of Prograf[®] (tacrolimus) in conjunction with mycophenolate mofetil (MMF) for the prevention of organ rejection in kidney transplant recipients. Prograf[®] is a cornerstone therapy for preventing transplant rejection in liver, kidney and heart transplant recipients. The FDA approved Prograf[®] combination use with MMF for heart transplant recipients in March 2006.

Reclast[®]

A single infusion of Reclast[®] increases bone mass for two years in postmenopausal women with osteopenia, a condition that can lead to osteoporosis. Reclast[®] already approved as once-yearly infusion for treatment of postmenopausal osteoporosis.

Risperdal[®] *Consta*[®]

Alkermes, Inc. announced that Johnson & Johnson Pharmaceutical Research & Development, L.L.C. (J&JPRD) has received approval from the FDA for the use of Risperdal[®] Consta[®] (risperidone) Long-Acting Injection as both a monotherapy and adjunctive therapy to lithium or valproate in the maintenance treatment of bipolar I disorder.

Symbicort[®]

AstraZeneca Pharmaceuticals announced that the FDA has approved Symbicort[®] (budesonide/formoterol fumarate dihydrate) 160/4.5 mcg for the twice daily maintenance treatment of airflow obstruction in patients with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and emphysema. Symbicort[®] has been available in the U.S. since June 2007 for the long-term maintenance treatment of asthma in patients 12 years of age and older.

Symbyax[®]

Eli Lilly and Company has announced that the FDA has approved a new indication for Symbyax[®] (olanzapine and fluoxetine HCl capsules). Symbyax[®] is now the first drug approved by the FDA for the acute treatment of treatment-resistant depression (TRD).

New Drugs

ACTOplus met[®] XR

Takeda Pharmaceutical Company Limited announced that the FDA approved an extended-release version of the combination medication ACTOplus met[®] XR (pioglitazone HCl and metformin HCl) as an adjunct to diet and exercise for the treatment of type 2 diabetes. ACTOplus met[®] XR is the first prescription oral antidiabetic fixed-dose combination medication available with the extended-release form of metformin to help improve glycemic control in a convenient, once-daily dosing option.

Adcirca[™]

United Therapeutics Corporation announced that the FDA has approved Adcirca[™] (tadalafil) tablets, with a recommended dose of 40 mg, as the first once-daily phosphodiesterase type 5 (PDE5) inhibitor for the treatment of pulmonary arterial hypertension (PAH).

Besivance[™]

Bausch & Lomb announced that the FDA approved Besivance[™] (besifloxacin ophthalmic suspension) 0.6% for the treatment of bacterial conjunctivitis.

Cambia[™]

Kowa Pharmaceuticals America, Inc. (KPA), announced that the FDA has approved Cambia[™], a diclofenac-based, non-steroidal anti-inflammatory drug combined with potassium bicarbonate, for the treatment of acute migraine with or without aura in adults.

Coartem[®]

Coartem[®] (artemether 20 mg/lumefantrine 120 mg), the leading artemisinin-based combination treatment (ACT) for malaria worldwide, has been approved by the FDA. Coartem[®] is a fixed-dose combination of two novel antimalarials. It is a highly effective three-day malaria treatment with cure rates of over 96% even in areas of multi-drug resistance.

Cetraxal[®]

The FDA has approved Cetraxal[®] (ciprofloxacin otic solution) 0.2% manufactured by Salvat for the treatment of acute otitis externa due to susceptible isolates of *Pseudomonas aeruginosa* or *Staphylococcus aureus*.

Creon[®]

Solvay Pharmaceuticals, Inc. announced that the FDA approved Creon[®] (pancrelipase) Delayed-Release Capsules for the treatment of exocrine pancreatic insufficiency (EPI) due to cystic fibrosis (CF) or other conditions. Creon[®] is the first and only pancreatic enzyme product (PEP) to receive FDA approval under new guidelines for the class.

Cycloset[®]

VeroScience, in collaboration with S2 Therapeutics, Inc. (S2), announced that the FDA approved its first-in-class drug Cycloset[®] for the treatment of Type 2 diabetes. Cycloset[®] improves glycemic control across a broad patient population as a monotherapy or as an adjunctive therapy to sulfonylurea, metformin plus sulfonylurea, and single or dual oral hypoglycemic agent therapies. Cycloset[®] is the first drug to be approved subsequent to the FDA's new guidelines that require studies demonstrating that diabetes drugs do not increase cardiovascular risk.

DYSPORT[™]

Medicis and Ipsen today announced the FDA approval of the Biologics License Application (BLA) for DYSPORT[™] (abobotulinumtoxinA), an acetylcholine release inhibitor and a neuromuscular blocking agent. The approval includes two separate indications, the treatment of cervical dystonia in adults to reduce the severity of abnormal head position and neck pain, and the temporary improvement in the appearance of moderate to severe glabellar lines in adults younger than 65 years of age. Additionally, DYSPORT[™] is differentiated from other marketed botulinum toxin products with the unique established name abobotulinumtoxinA.

Exforge HCT[®]

The FDA has approved Novartis' Exforge HCT[®], the only single pill to combine the three most prescribed high blood pressure treatments in their classes in the US: amlodipine, a calcium channel blocker, valsartan, an angiotensin receptor blocker, and hydrochlorothiazide, a diuretic.

FANAPT[™]

The FDA has approved FANAPT[™] tablets (iloperidone) to treat adults with schizophrenia, a chronic, severe and disabling brain disorder. It is a mixed dopamine and serotonin receptor antagonist manufactured by Vanda Pharmaceuticals Inc., and belongs to the class of atypical antipsychotics.

Ilaris[®]

The FDA has approved Ilaris[®] (canakinumab) for the treatment of children and adults with cryopyrin-associated periodic syndrome (CAPS), which includes a number of rare but life-long auto-inflammatory disorders with debilitating symptoms and limited treatment options.

Lamictal® ODT™

GlaxoSmithKline announced today that the FDA has approved Lamictal® ODT™ (lamotrigine) Orally Disintegrating Tablets. Lamictal® ODT™ uses a novel drug-delivery formulation to provide Lamictal in a tablet that has a pleasant taste and disintegrates on the tongue.

Lamictal® XR™

GlaxoSmithKline announced that the FDA has approved Lamictal® XR™ (lamotrigine) Extended-Release Tablets as once-a-day add-on therapy for epilepsy patients 13 years of age or older with partial onset seizures.

Ozurdex™

The FDA has approved Ozurdex™ (dexamethasone intravitreal implant) 0.7 mg as the first drug therapy indicated for the treatment of macular edema following branch retinal vein occlusion (BRVO) or central retinal vein occlusion (CRVO). Ozurdex™ is a first-of-its kind therapy administered via intravitreal injection delivering dexamethasone, a highly potent corticosteroid, via Allergan's proprietary and innovative NOVADUR solid polymer delivery system.

Prevacid® 24HR

Novartis announced that Prevacid® 24HR (lansoprazole delayed-release capsules 15 mg) has been approved by the FDA as the first over-the-counter (OTC) Proton Pump Inhibitor (PPI) for the treatment of frequent heartburn since 2003. Prevacid® 24HR is expected to be available over the counter in 2009. Once-daily Prevacid® 24HR is the first OTC PPI approved in its original prescription formulation.

SAMSCA™

Otsuka Pharmaceutical Co., Ltd. (OPC) announced that the FDA has approved SAMSCA™ (tolvaptan) as the only oral selective vasopressin antagonist for the treatment of patients with clinically significant hypervolemic and euvolemic hyponatremia including patients with heart failure, cirrhosis, and the syndrome of inappropriate anti-diuretic hormone (SIADH).

SIMPONI™

Centocor Ortho Biotech® Inc. announced that the FDA has approved SIMPONI™ (golimumab) for the treatment of moderately to severely active rheumatoid arthritis, active psoriatic arthritis and active ankylosing spondylitis. SIMPONI™ is the first patient-administered anti-tumor necrosis factor (TNF)-alpha therapy that offers an effective once-monthly treatment option.

Zipsor™

The FDA has approved Zipsor™ (diclofenac potassium) Liquid Filled Capsules manufactured by Xanodyne Pharmaceuticals, Inc. for the relief of mild to moderate acute pain in adults (18 years of age or older).

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