

CPS Insider is produced by the University of Massachusetts Medical School's Clinical Pharmacy Services division and distributed to our clients quarterly.

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## At a Glance



**Noteworthy**  
Shortages of oseltamivir suspension lead to pharmacy compounding



**What's New at UMMS?**  
Clinical Pharmacy Services participates in annual Health Care Pathways Conference

## New Generics

- **Azelastine HCl ophthalmic solution, 0.05 percent (Optivar®)**  
Launched: 12/1/09
- **Buprenorphine sublingual tablets (Subutex®)**  
Launched: 10/8/09
- **Fexofenadine 60 mg/ Pseudoephedrine 120 mg ER tablets (Allegra-D® 12 hour)\***  
Launched: 11/3/09
- **Lansoprazole delayed-release capsules 15 mg, 30 mg (Prevacid®)**  
Launched: 11/11/09  
OTC launched: 11/10/09 (15 mg)
- **Omeprazole 20 mg/sodium bicarbonate 1,100 mg capsule (Zegerid OTC™)**  
Approved: 12/1/09
- **Valacyclovir tablets (Valtrex®)†**  
Launched: 11/25/09

\* Teva has 180-day exclusivity

† Ranbaxy has 180-day exclusivity

## Drug Watch



### Onglyza™ (saxagliptin)

Approved: 7/31/2009  
Mfr: Bristol-Myers Squibb  
Formulation: Oral tablet  
Cost (AWP): \$6.86/tablet

Onglyza™ (saxagliptin) is a dipeptidyl peptidase-4 (DPP-4) inhibitor indicated as an adjunct to diet and exercise to improve glucose control in adults with type 2 diabetes mellitus. The recommended dose of saxagliptin is 2.5 mg or 5 mg once daily regardless of meals.

When compared to placebo, saxagliptin 2.5 mg and 5 mg showed improvements in A1C (P<0.0001), fasting plasma glucose (FPG) (P<0.05), and two-hour postprandial glucose (PPG) (P<0.05). When added to metformin, pioglitazone, rosiglitazone, or glyburide as combination therapy, saxagliptin showed improvements in A1C, FPG, and two-hour PPG when compared to placebo (P<0.05).

Saxagliptin had neutral effects on body weight and on fasting serum lipids from baseline compared to placebo.

Common adverse reactions to saxagliptin from clinical trials include upper respiratory tract infection, urinary tract infection, and headache. The incidence of peripheral edema was greater when saxagliptin 5 mg was combined with pioglitazone or rosiglitazone than either thiazolidinedione alone. As the second DPP-4 inhibitor, saxagliptin will have a place in therapy similar to Januvia® (sitagliptin) and may be used in patients at greatest risk for complications from weight gain or hypoglycemia associated with sulfonylureas.



### Stelara™ (ustekinumab)

Approved: 9/25/2009  
Mfr: Centocor Ortho Biotech  
Formulation: SC injection  
Cost (AWP): \$5,595.60/vial

Stelara™ (ustekinumab) is a human monoclonal antibody approved for the treatment of moderate to severe plaque psoriasis in adults who are candidates for phototherapy or systemic therapy. Ustekinumab blocks interleukins 12 and 23, leading to down regulation of skin cell production and inflammation associated with psoriasis. Dosing is 45 mg for patients ≤100 kg and 90 mg for patients >100 kg subcutaneously at weeks 0 and 4, followed by every 12 weeks.

In the head-to-head Phase III ACCEPT trial (N=903), ustekinumab 45 mg or 90 mg administered at weeks 0 and 4 was compared to Enbrel® (etanercept) 50 mg twice weekly for the treatment of moderate to severe psoriasis. Compared to 57 percent of patients in the etanercept group, 68 percent (P=0.012) and 74 percent (P<0.001) in the ustekinumab 45 mg and 90 mg groups, respectively, achieved a 75 percent reduction in the Psoriasis Area and Severity Index score at week 12.

Ustekinumab was approved with a Risk Evaluation and Mitigation Strategy because of a possible increased risk of serious infections and malignancy. Ustekinumab must be administered by a health care professional, but offers an advantage of infrequent administration and a novel mechanism of action compared to the current standard of care with tumor necrosis factor-alpha blockers.

## New FDA-Approved Indications

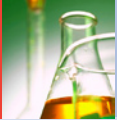
- **Abilify® (aripiprazole)**  
Approved 11/19/09 for the treatment of irritability associated with autistic disorder in pediatric patients (ages 6 to 17)
- **Byetta® (exenatide)**  
Approved 10/30/09 as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus
- **Gardasil® (Human Papillomavirus Quadrivalent [Types 6, 11, 16, and 18] Vaccine, Recombinant)**  
Approved 10/16/09 for use in boys and men ages 9 to 26 for the prevention of genital warts caused by human papillomavirus types 6 and 11
- **Isentress® (raltegravir)**  
Approved 7/8/09 for the treatment of therapy-naïve adults with HIV-1 infection in combination with other antiretrovirals
- **Selzentry™ (maraviroc)**  
Approved 11/20/09 for the treatment of therapy-naïve adults infected with CCR5-tropic HIV-1 virus in combination with other antiretrovirals
- **Seroquel® (quetiapine)**  
Approved 12/2/09 for the treatment of schizophrenia in adolescents (ages 13 to 17) and as monotherapy or as an adjunct to lithium or divalpoex for acute treatment of manic episodes associated with bipolar I disorder in children and adolescents (ages 10 to 17)

## New Formulations and Dosages

- **Metozolv™ ODT (metoclopramide)**  
5 mg, 10 mg orally disintegrating tablets  
Approved: 9/4/09
- **Qutenza™ (capsaicin)\***  
8 percent patch  
Approved: 11/16/09
- **Vagifem® (estradiol)**  
10 mcg vaginal tablet  
Approved: 11/25/09
- **Zyprexa® Relprevv™ (olanzapine, extended release powder for suspension)**  
210 mg/vial, 300 mg/vial, 405 mg/vial for IM injection  
Approved: 12/11/09

\* Rx only for post hepatic neuralgia

Information available at [www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm](http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm)



## Clinical Notes

### 2009 Guidelines for the Use of Antiretroviral Agents in HIV-1 Infected Adults and Adolescents: Selected Key Points

- The U.S. Department of Health and Human Services (DHHS) recently released updated guidelines for the use of antiretroviral agents in HIV-infected adults and adolescents. These guidelines focus on baseline assessment, treatment goals, initiation of antiretroviral therapy (ART), and recommendations for medication therapy, including preferred regimens and the management of adverse effects.
- A new section was added to the guidelines regarding the epidemiology and diagnosis of HIV-2 infection and the role of ART in the treatment of patients infected with HIV-2, as well as patients co-infected with HIV-1 and HIV-2.
- More specific recommendations for the use of genotypic and phenotypic drug resistance testing have been added:
  - Patients should undergo genotypic testing as opposed to phenotypic testing upon experiencing suboptimal virologic responses or virologic failure in response to their first or second drug regimens due to lower cost, faster turnaround time, and greater sensitivity for detecting mixtures of wild type and resistant virus.
  - Patients should undergo phenotypic and genotypic testing if they have known or suspected drug resistance, especially to protease inhibitors, to help identify which drug regimens will be active for treatment.
- The recommendations for the initiation of ART therapy have been updated to include patients with the following:
  - An AIDS-defining illness or with a CD4 count of less than 350 cells/mm<sup>3</sup>
  - HIV-associated nephropathy, hepatitis B co-infection that requires treatment, or patients who are pregnant – regardless of CD4 count
  - CD4 counts between 350 and 500 cells/mm<sup>3</sup>
  - A commitment to lifelong treatment and counseling regarding the importance of adherence and the risks and benefits of therapy
- The guidelines now include three recommended combinations of antiretroviral agents that may be used in therapy-naïve patients:
  - Non-nucleoside reverse transcriptase inhibitor and two nucleoside/nucleotide reverse transcriptase inhibitors (NRTI)
  - Protease inhibitor (boosted with ritonavir) and two NRTIs
  - Integrase inhibitor and two NRTIs

# Advisories

## New Hepatic Warnings for Products Containing Diclofenac

On 12/4/09, the FDA announced that labels for products containing diclofenac sodium, including Voltaren® (diclofenac sodium) 1 percent topical gel, would be changed to reflect potential elevation in liver function tests during treatment. In their letter to health care professionals, the manufacturers of diclofenac sodium gel report borderline or higher elevations of transaminase levels in about 15 percent of diclofenac-treated patients. Cases of drug-induced liver toxicity were reported in the first two months, but they could potentially occur at any time during treatment. Postmarketing data reports cases of severe hepatic reactions including liver necrosis, jaundice, hepatitis, and liver failure, some of which resulted in liver transplantation or fatalities.

## Revision of Exenatide Labeling to Reflect Kidney Function Problems

On 11/2/09, the FDA revised labeling requirements for Byetta® (exenatide) to include safety information about potential kidney function problems identified from postmarketing reports. The FDA has received a total of 78 reports, including 62 cases of acute renal failure and 16 cases of renal insufficiency, in patients using exenatide from April 2005 through October 2008. Some of these cases occurred in patients with one or more risk factors for developing kidney function problems or in patients with pre-existing kidney disease. Labeling changes include information from postmarketing reports of drug-induced kidney problems, recommendations to health care professionals to use caution with this medication in patients with impaired renal function, and a revised Medication Guide. The prescribing information for exenatide was updated to enable patients and health care professionals to weigh the risks and benefits of this medication.

## Clopidogrel Label Updated to Include Interactions with Proton Pump Inhibitors

On 11/17/09, the FDA announced that a new warning will be added to the labeling of Plavix® (clopidogrel) regarding its possible interaction with omeprazole (Prilosec® and Prilosec OTC®) and Nexium® (esomeprazole). This interaction is thought to be the result of omeprazole's inhibition of the CYP2C19 enzyme, which is responsible for the activation of clopidogrel into its active form. New studies have demonstrated that omeprazole reduces the active metabolite of clopidogrel by 45 percent resulting in as much as a 47 percent reduction in platelet effect. These reductions were seen whether the drug was given 12 hours apart or at the same time. Information about the interaction between clopidogrel and other proton pump inhibitors (PPIs) are unknown. The FDA recommends that providers consider all other options for acid suppression before starting PPI therapy.



## From The Hill

### Federal

#### Ban on Traveler's with HIV Lifted; 2012 International AIDS Conference to be Held in the United States

In 1987, HIV was placed on the U.S. Public Health Service's list of dangerous and contagious diseases. This led to a ban that restricted any foreign traveler with HIV or AIDS from entering the U.S. or obtaining permanent immigration status without special waivers. Due to this ban, travelers involved with past international AIDS conferences experienced difficulty gaining entry in the U.S. As a result, the conference was later held in countries without such a ban. The U.S. was one of 12 countries, including China, Russia, and Sudan, that ban foreign travelers with HIV or AIDS from entering their countries. The last International AIDS Conference held in the United States took place in 1990.

On 11/2/09, the U.S. Congress published a final rule to eliminate the 22 year old travel ban. The ban was officially eliminated on Jan. 4, 2010. Recently, it was announced that the 2012 International AIDS Conference will be held in Washington D.C. This was made possible with the lifting of the entry ban that had kept this conference away from the U.S. for over 20 years.

#### Lifting of Restrictions Allows for New Publicly Funded Stem Cell Research

The U.S. National Institutes of Health (NIH) currently has 31 research grants, worth \$21 million, on hold. These research grants are awaiting the approval of new stem cell lines so that these cell lines may potentially be used to grow heart muscle, neurological stem cells, and neurons, and to create replacement tissues to treat various conditions, including Alzheimer's disease, diabetes, Parkinson's disease, and spinal cord injuries.

When restrictions were put in place in August 2001, research was limited to about 21 stem cell lines. Due to the recent lifting of the restrictions, 13 additional stem cell lines have been added, of which 11 were created by Children's Hospital Boston and two by Rockefeller University.

About 96 more human embryonic stem cell lines are under review for NIH-funded research. Federal law prohibits using taxpayer funding to create or destroy an embryo; therefore, all stem cell lines involved were created from fertility clinic embryos that otherwise would have been disposed of.

# Pipeline

## Linaclotide

Linaclotide is an oral guanylate cyclase type-C (GC-C) receptor agonist being investigated in chronic constipation (CC) and constipation-predominant irritable bowel syndrome (IBS-C). Activation of GC-C led to reduction of abdominal pain and increased intestinal transit in preclinical models. Results from two Phase III trials (N = 1276) evaluating linaclotide in CC were released in November 2009. In one placebo-controlled trial, complete spontaneous bowel movement responder rates were increased for both doses of linaclotide (133 mcg/day,  $P \leq 0.0012$ ; 266 mcg/day,  $P < 0.0001$ ) at week 12. Results from Phase III trials examining linaclotide in IBS-C are expected to be announced in the first half of 2010. Currently, there are only adjunctive pharmacological agents available for the management of IBS-C and CC.

## Mipomersen

A once-weekly SC injection, mipomersen is being studied for the treatment of hypercholesterolemia. Mipomersen acts by decreasing the production of apolipoprotein B, which transports LDL and triglycerides. One Phase III study of mipomersen in homozygous familial hypercholesterolemia showed that 26 weeks of treatment with mipomersen resulted in a 25 percent reduction in LDL, compared to 3 percent with placebo ( $P < 0.001$ ). Patients' average LDL at baseline was greater than 400 mg/dL. Mipomersen represents a promising adjunct therapy for patients uncontrolled on current lipid-lowering medications. An NDA submission is expected in mid-2011.

# Noteworthy

## Shortages of Oseltamivir Suspension Lead to Pharmacy Compounding

Due to recent shortages of commercially available Tamiflu® (oseltamivir) oral suspension, there has been an increase in the need for compounding of the suspension for patients unable to use the capsule formulation. Emergency weight-based compounding instructions have been approved by the FDA and can be found in the oseltamivir prescribing information. Oseltamivir suspension should be compounded using Cherry Syrup (Humco®) or Ora-Sweet® SF (sugar-free) and 75 mg oseltamivir capsules. Of note, the oseltamivir compounded preparation results in a 15 mg/ml suspension while the commercially available product is 12 mg/ml. However, to avoid pharmacy compounding, oseltamivir 30 mg and 45 mg capsules may be opened and mixed with sweetened liquids.

Children ages 1 and younger or weighing less than 33 pounds are regarded as the highest priority for receiving any commercially available suspension. Additional volumes of oseltamivir suspension have been released from the CDC Strategic National Stockpile to enhance availability. Certain lots of this newly released medication may be past their expiration date but may still be used under the FDA's Emergency Use Authorization. Caution is advised when dispensing the commercial product due to the potential for dosing errors when prescriptions are written in milliliters and the product's dosing tool uses milligram graduation marks (i.e., 30 mg, 45 mg, 60 mg).

# What's New at UMMS?

On 11/19/2009, Clinical Pharmacy Services (CPS) partnered with UMass Medical School for the Massachusetts Area Health Education Center (MassAHEC) Network's annual Health Care Pathways Conference. A goal of the MassAHEC Network is to address concerns about health disparities in the commonwealth by ensuring that the diversity of the health care workforce reflects the diversity of the population it serves. The conference aims to achieve this goal by providing middle and high school teachers and counselors with career development tools for their students.

CPS pharmacists presented "Communication – Bridging the Generational Divide," which highlighted effective communication skills addressing new trends in generational and health care-related educational needs. During the conference's Health Careers Expo, CPS pharmacy residents/fellow conducted "Formulary on a Budget," which demonstrated the role of a managed care pharmacist through an interactive exercise in drug selection using a mock decision tree and play money. CPS continues to participate in other MassAHEC initiatives to further this partnership in public service.

## Who We Are and What We Do

The University of Massachusetts Medical School's Clinical Pharmacy Services is a comprehensive prescription drug management program developed in 1999 as part of the Medical School's Commonwealth Medicine division, primarily to provide drug utilization review for Massachusetts Medicaid. Today, we bring exceptional depth and experience in the development and implementation of unique, client-customized managed care-related clinical pharmacy functions including, but not limited to, evidence-based formulary support, drug utilization review, medication therapy management, clinical call center support, and provider/patient education. *CPS Insider* is an educational resource produced quarterly to deliver critical information at the highest level of quality to our clients. We hope that you find this resource of value, and we welcome your suggestions for improvement.



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