

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
New CDC recommendations for the management of the H1N1/09 virus



What's New at UMMS?
Clinical services expand to the Montana Association of Health Care Purchasers

New Generics

- **Aspirin/dipyridamole extended release (Aggrenox®)**
Approved: 8/14/09
Launched: TBD
- **Clindamycin/benzoyl peroxide gel (Benzaclin®)**
Launched: 8/27/09
- **Clonidine transdermal system (Catapres TTS®)**
Launched: 8/20/09
- **Levalbuterol Inhalation Solution (Xopenex®)**
1.25 mg/0.5 ml solution
Launched: 8/28/09
- **Levonorgestrel [Next Choice™ (Plan B®)]**
Launched: 8/28/09
- **Nateglinide (Starlix®)**
Launched: 9/10/09
- **Tacrolimus (Prograf®)**
Launched: 8/11/09

Drug Watch

New To Market

Effient™ (prasugrel)

Approved: 7/10/2009
Mfr: Daiichi Sankyo/Eli Lilly
Formulation: Tablet
Cost (AWP): \$6.54/tablet

Effient™ (prasugrel) is a new thienopyridine adenosine diphosphate (ADP) receptor antagonist indicated to reduce thrombotic cardiovascular (CV) events in patients with acute coronary syndrome (ACS) managed with percutaneous coronary intervention (PCI). Prasugrel inhibits platelet activation and aggregation by irreversibly binding to the P2Y₁₂ class of ADP receptors on platelets. Dosing is initiated as a single 60 mg loading dose followed by a 10 mg once-daily maintenance dose in patients over 60 kg, while a 5 mg once-daily dose should be considered in patients less than 60 kg.

In the TRITON-TIMI 38 study (N=13,608), prasugrel significantly decreased the composite endpoint which was defined as death from CV causes, nonfatal myocardial infarction (MI), or nonfatal stroke when compared to Plavix® (clopidogrel) (P<0.001). When analyzed separately, only the reduction in nonfatal MI was significant.

Prasugrel carries a black box warning for significant, sometimes fatal bleeding. It is contraindicated in any patient with an active bleed or history of stroke and it is not recommended in patients ages 75 and older. Prasugrel represents a new alternative to clopidogrel for patients with ACS in need of PCI. Unlike clopidogrel, it does not interact with potent CYP3A4 inhibitors.

New To Market

Multaq® (dronedarone)

Approved: 7/1/2009
Mfr: Sanofi-aventis
Formulation: Tablet
Cost (AWP): \$4.32/tablet

Dronedarone (Multaq®) is a new anti-arrhythmic that is indicated to reduce the risk of cardiovascular hospitalization in patients with paroxysmal or persistent atrial fibrillation or atrial flutter. The exact mechanism of dronedarone is unknown; however, it appears to block the same ion channels as amiodarone.

FDA approval of dronedarone was based on four trials encompassing 5,867 patients. In the ATHENA trial (N=4,628), administration of dronedarone 400 mg twice-daily reduced the risk of first cardiovascular hospitalization or death by 24 percent (P<0.001) over 21 months, as compared to placebo. Of note, the ANDROMEDA trial was terminated early due to excess mortality from worsening heart failure (HR=2.13, P=0.027) in the dronedarone group.

Dronedarone has a black box warning that contraindicates its use in patients with New York Heart Association class IV heart failure or class II-III heart failure with recent decompensation. Common adverse reactions to dronedarone include diarrhea, nausea, abdominal pain, vomiting, and asthenia.

Dronedarone is currently the only anti-arrhythmic that has shown a significant reduction in morbidity and mortality in clinical trials. Unlike amiodarone, it does not require monitoring of thyroid or pulmonary function when initiating.

New FDA-Approved Indications

- **Risperdal® Consta® (risperidone long-acting injection)**
Approved on 5/15/09. Risperidone long-acting injection is indicated as monotherapy or as adjunctive therapy to lithium or valproate for the maintenance treatment of bipolar I disorder.
- **Avastin® (bevacizumab)**
Approved on 7/31/09. Bevacizumab is indicated for the treatment of metastatic renal cell carcinoma in conjunction with interferon alpha.
- **Forteo® (teriparatide [rDNA origin] injection)**
Approved on 7/22/09. Teriparatide is indicated for treatment of men and women at high risk of fracture due to osteoporosis associated with sustained systemic glucocorticoid therapy.
- **Tracleer® (bosentan)**
Approved on 8/7/09. Bosentan is indicated for treatment of pulmonary arterial hypertension (World Health Organization [WHO] Group I) with WHO Class II symptoms to improve exercise capacity and decrease clinical worsening.

New Formulations and Dosages

- **Plan B® One-Step (levonorgestrel)**
1.5 mg tablet
Approved: 7/10/09
- **Invega® Sustenna™ (extended release paliperidone palmitate)**
39 mg/0.25 ml, 78 mg/0.5 ml, 117 mg/0.75 ml, 156 mg/ml, 234 mg/1.5 ml for IM injection
Approved: 7/31/09
- **Renvela® (sevelamer carbonate)**
0.8 g, 2.4 g soluble powder in single-dose packets
Approved: 8/12/09

Information available at www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm



Clinical Notes

Use of Synagis® (palivizumab) for Prevention of Respiratory Syncytial Virus Infections

2009 Recommendations from the American Academy of Pediatrics: Selected Key Points

- The American Academy of Pediatrics (AAP) updated their recommendations for immunoprophylaxis with palivizumab for respiratory syncytial virus (RSV) infections using evidence-based medicine to ensure the most favorable balance of benefit and cost of the intervention. This policy statement was released in August 2009 and replaces the 2003 AAP statement and the 2006 Red Book recommendations.
- According to the Centers for Disease Control, peak RSV activity in most areas of the United States typically occurs between November and March.
- The AAP's definition of gestational age is used throughout this section. For example, 32 to 35 weeks gestation is defined as 32 weeks, zero days through 34 weeks, 6 days. The previous definition was 32 weeks, 1 day through 35 weeks, zero days.
- According to the revised AAP recommendations, a maximum of five monthly doses of palivizumab prophylaxis is recommended in the following high-risk groups:
 - Children younger than 24 months with hemodynamically significant congenital heart disease (CHD) which requires medical therapy
 - Children younger than 24 months with chronic lung disease of prematurity (CLD, formerly called bronchopulmonary dysplasia) that requires medical therapy
 - Infants younger than 6 months and born prematurely between 29 and 32 weeks of gestation at the start of the RSV season
 - Infants younger than 12 months and born prematurely at or before 28 weeks of gestation at the start of the RSV season
 - Infants younger than 12 months and born prematurely before 35 weeks of gestation at the start of the RSV season with either congenital abnormality of the airways or neuromuscular disease compromising handling of respiratory tract secretions
- The fifth palivizumab dose administered in March should provide immunologic protection through April due to a cumulative effect on serum concentration.
- The 2009 AAP recommendations have been updated to target children at highest risk of severe RSV infection within the category of premature infants born between 32 and 35 weeks of gestation. The risk factors have been modified to include child care attendance or living with siblings/children younger than 5 years. This is different from the previous recommendation that required two of five risk factors for this high-risk group to qualify for immunoprophylaxis with palivizumab.
- According to the revised AAP recommendations, a maximum of three monthly doses of palivizumab prophylaxis is recommended for infants who have not reached 3 months of age during the start of RSV season and were born prematurely between 32 and 35 weeks of gestation, with at least one of the two risk factors mentioned above. This is different from the previous recommendation for five monthly doses of palivizumab for this high-risk group.

Advisories

Risk of Pediatric Malignancies with Tumor Necrosis Factor Blockers

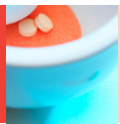
On 8/4/09, the FDA mandated an updated boxed warning for tumor necrosis factor (TNF) blockers, including Remicade® (infliximab), Enbrel® (etanercept), Humira® (adalimumab), Cimzia® (certolizumab pegol), and Simponi® (golimumab). The warning describes the increased risk of cancer, particularly lymphomas, in children and adolescents treated with TNF blockers for various inflammatory diseases. Based on the 48 cases of pediatric malignancies reported between 2001 and 2008, the cancer often developed after 30 months of treatment and may be fatal. There is no evidence to suggest that this risk is dose-related. New safety concerns and resulting label changes for TNF blockers have also been made relative to new-onset psoriasis and associated risk for leukemia.

Labeling Changes for Immunosuppressant Drugs

On 7/14/09, the FDA announced that it will require manufacturers of certain immunosuppressant drugs used to prevent rejection of kidney transplants to update their labeling. As a result of the FDA's review of reported adverse events, the new labeling must reflect the increased risk for opportunistic infections. Opportunistic infections include the activation of latent viral infections as well as BK virus-associated nephropathy, which primarily affects kidney transplant recipients. Currently, Prograf® (tacrolimus) carries this warning. Rapamune® (sirolimus), Sandimmune® (cyclosporine), Neoral® (cyclosporine modified), Cellcept® (mycophenolate mofetil), Myfortic® (mycophenolic acid), and all available generic formulations of these drugs will now require updated labeling.

Suicidal Ideation and Behavioral Changes with Varenicline and Bupropion

On 7/1/09, a boxed warning was added to the product label and medication guide of the smoking cessation products Chantix® (varenicline) and bupropion. The warning describes reports of changes in behavior such as hostility, agitation, depressed mood, and suicidal thoughts/actions. Based on a review of the FDA's Adverse Event Reporting System from the approval dates of these agents to November 2007, there were 153 reports of suicidal adverse events for varenicline and 75 for bupropion. These events occurred at recommended doses and within two weeks of starting the medication, regardless of whether there were pre-existing psychiatric conditions. No clear association was identified between nicotine replacement patches and suicidal ideation/behavior.



From The Hill

Federal

Comparative Effectiveness Research

Comparative effectiveness research (CER) is defined as the evaluation of one treatment modality versus another. This research focuses on areas in which treatment guidelines are unclear or lacking. Clinicians use the information obtained from CER to make informed decisions when delivering patient-centered care. To facilitate this research, the federal government has allocated \$1.1 billion from the American Recovery and Reinvestment Act of 2009. The Act mandates that these funds are not utilized to support research that could potentially mandate health care coverage or reimbursement for any public or private payer.

A report published by the Congressional Budget Office described the possibility that CER could lead to an increase in health care spending if data shows that the benefits of an expensive treatment outweigh the cost. On the other hand, CER may demonstrate that a less costly alternative treatment could be a better option. CER's effect on health care spending may not be significant if there is no incentive for changing prescribing habits to comply with the outcomes of this research.

State

Emergency Authorization to immunize Against H1N1/09 Virus

On 8/12/09, Massachusetts Public Health Council deputized pharmacists, dentists, paramedics, and medical/nursing students to help vaccinate the public against the H1N1/09 virus. Effective 9/14/09, an emergency amendment to 105 CMR 700.000 allows the Commissioner of the Massachusetts Department of Public Health (DPH) to authorize these additional vaccinators in case of such a public need. A "Guideline for Designated Vaccinators" published by the Massachusetts DPH, describes the qualifications necessary for these additional vaccinators, including training and supervision requirements. This move could add about 21,000 volunteer health care professionals to help immunize the public during vaccination campaigns throughout the state. These additional health care workers will help relieve practitioners so that they may focus on other urgent patient care needs. With availability beginning in early October, over nine million doses of both seasonal and H1N1/09 flu vaccine will likely be administered in Massachusetts this season.

Pipeline

Belysta™ (belimumab)

Belimumab is a human monoclonal antibody being developed for the treatment of systemic lupus erythematosus (SLE). In SLE, elevated levels of B-lymphocyte stimulators contribute to the production of autoantibodies that attack the body's own tissue. Belimumab works by inhibiting B-lymphocyte stimulators.

In July 2009, belimumab met the primary endpoint in BLISS-52, the first of its two Phase III trials; results for the second trial is due in November 2009. Results from BLISS-52 showed that belimumab 10 mg/kg led to a statistically significant improvement in patient response compared to placebo (57.6% versus 43.6%, $P=0.0006$). Belimumab has the potential to become the first new drug approved for SLE in more than 50 years.

Traficet-EN™ (CCX282)

CCX282 works by selectively blocking the CCR9 chemokine receptor to inhibit the migration of T-cells to the digestive tract and prevent the inflammation associated with Crohn's disease.

Results from the induction phase of the Phase II/III PROTECT-1 trial demonstrated that patients treated with CCX282 had a statistically significant response rate compared to placebo (55% versus 40%, $P=0.029$). Response rate was defined as ≥ 100 points improvement on the Crohn's Disease Activity Index at week 12. As a first-in-class agent, CCX282 is available orally as opposed to injectable agents typically used for Crohn's. CCX282 is also being investigated for treatment of ulcerative colitis and celiac disease.

Noteworthy

New Centers for Disease Control (CDC) Recommendations for the Management of the H1N1/09 Virus

In addition to the seasonal flu vaccine, high risk patients are advised to get a separate vaccine against the new H1N1/09 influenza strain. Patients who should receive the H1N1/09 vaccine include pregnant women, individuals living with or caring for children 6 months or younger, health care and emergency medical service employees with direct patient contact, children and young adults from ages 6 months to 24 years, and adults ages 25 to 64 years who are at a higher risk for influenza-related complications due to chronic health disorders or compromised immune systems.

The H1N1/09 vaccine will require one dose for individuals ages 10 and older and two doses for individuals ages 9 and younger. The seasonal flu vaccine and the H1N1/09 vaccine can be administered on the same day.

Patients younger than 2 years or ages 65 and older, pregnant women, patients with chronic health disorders/compromised immune systems, and children younger than 19 years receiving long-term aspirin therapy are considered to be high-risk individuals for influenza-related complications and should be treated with an antiviral medication.

Tamiflu® (oseltamivir) and Relenza® (zanamivir) are indicated for both, treatment and prophylaxis of H1N1/09 virus. Twice-daily dosing for five days is recommended for treatment and once-daily dosing for 10 days is recommended for prophylaxis for both antiviral medications.

What's New at UMMS?

In April 2009, Clinical Pharmacy Services (CPS), as subcontracted through MedMetrics Health Partners, assumed clinical support responsibilities for our newest client, the Montana Association of Health Care Purchasers (MAHCP). MAHCP is an independent, not-for-profit partnership of public and private self-insured employers serving more than 80,000 employees and their dependents. The two largest employer groups of MAHCP are the Montana University System and the State of Montana. MAHCP's goal is to provide purchasing power, data aggregation from various claims administrators/health screenings/payroll/etc., and risk-based reporting analytics in obtaining cost-efficient, quality health care for its member groups.

In support of MAHCP, CPS provides various clinical pharmacy support services including evidence-based therapeutic class and new drug reviews, draft drug coverage guidelines, formulary and utilization management recommendations, and other support to the MAHCP Pharmacy and Therapeutics Advisory Committee.

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, high quality information to our clients. We hope that you find this resource of value and welcome your suggestions for improvement.

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