

MedMetrics Rx-Pulse



MedMetrics Rx-Pulse is produced by the University of Massachusetts Medical School's Clinical Pharmacy Services division and distributed quarterly.

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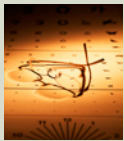
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At a Glance



Noteworthy
Tamsulosin associated with serious ophthalmic adverse events



What's New at UMMS?
Clinical initiatives expand in partnering with the State University of New York

New Generics

- **Topamax[®] (topiramate) 15 mg and 25 mg capsules**
Approved: 4/15/2009
Launched: 4/15/2009
- **Tegretol XR[®] (carbamazepine ER) 200 mg and 400 mg tablets**
Approved: 3/31/2009
Launched: 5/22/2009
- **Urso 250[®] (ursodiol) 250 mg and Urso Forte[®] (ursodiol) 500 mg tablets**
Approved: 5/13/2009
Launched: 5/18/2009
- **Cellcept[®] (mycophenolate) 250 mg capsules and 500 mg tablets**
Approved: 7/29/2008
Launched: 5/4/2009

Drug Watch



Simponi[™] (golimumab)
Approved: 4/24/2009
Mfr.: Centor Ortho Biotech, Inc.
Formulation: SC Injection
Cost (AWP): \$3,937.50/syringe

Simponi[™] (golimumab) is a new-to-market human monoclonal antibody that is indicated for the treatment of ankylosing spondylitis, psoriasis with arthropathy, and moderate to severe rheumatoid arthritis (RA). Golimumab exerts its effects by inhibiting the activity of tumor necrosis factor (TNF)-alpha. The medication is administered as a once-monthly 50 mg subcutaneous (SC) injection by either a 50 mg/0.5 ml single dose prefilled syringe or SmartJect[™] autoinjector device.

In the GOLimumab After Former anti-TNF Therapy Evaluated in RA (GO-AFTER) study, 39 percent of patients (N=461) treated with golimumab who had previously failed other anti-TNF agents due to lack of efficacy achieved at least a 20 percent improvement in arthritis symptoms at week 14 compared to 18 percent with placebo (P<0.001).

Common adverse reactions include upper respiratory tract infection and nasopharyngitis. Golimumab has a black box warning highlighting the increased risk of developing infections that can lead to hospitalization or death. Unlike Humira[®] and Enbrel[®], which are given every two weeks and once weekly, respectively, golimumab is the first approved once-monthly anti-TNF-alpha therapy available on the market.



Cycloset[™] (bromocriptine)
Approved: 5/5/2009
Manufacturer: VeroScience
Formulation: Oral tablet
Cost (AWP): Unavailable

Bromocriptine, a centrally-acting dopamine-D₂ receptor agonist, is FDA approved as monotherapy or in conjunction with antidiabetic therapies to improve glycemic control in adults with type 2 diabetes. Increasing dopamine activity during the day is thought to reduce plasma glucose, triglyceride, and free fatty acid levels in the fasting and postprandial states in insulin-resistant adults.

Relative to placebo in two separate 24-week Phase III clinical trials, bromocriptine reduced HbA_{1c} by 0.56 points as monotherapy (P<0.02) and 0.55 points in combination with a sulfonylurea (P<0.0001). In a 52-week safety trial (N=3,000), bromocriptine did not increase the risk of myocardial infarction, stroke, congestive heart failure, hospitalization for unstable angina, or revascularization surgery.

The recommended starting dose, 0.8 mg once daily with food within two hours of waking in the morning, is increased by 0.8 mg weekly until the target range of 1.6-4.8 mg is reached. Bromocriptine, a first-in-class agent, is not associated with the increased cardiovascular risk noted with other antidiabetic agents. Bromocriptine, dosed at higher strengths, is also FDA approved for treating Parkinson's disease and pituitary tumors.

New FDA-Approved Indications

- **Azor® (amlodipine/olmesartan medoxomil)**
Approved on 5/11/2009. Amlodipine/olmesartan medoxomil is indicated for initial therapy in patients likely to need multiple antihypertensive agents to achieve their blood pressure goals.
- **Cimzia® (certolizumab pegol)**
Approved on 5/13/2009. Certolizumab pegol is indicated for adults with moderately or severely active rheumatoid arthritis.
- **Reclast® (zoledronic acid)**
Approved on 5/29/2009. Zoledronic acid is indicated for the prevention of osteoporosis for two years with a single dose.
- **Axert® (almotriptan)**
Approved on 6/3/2009. Almotriptan is indicated for the acute treatment of migraine in adolescents (ages 12 to 17).

New Formulations and Dosages

- **Exforge HCT® (amlodipine/hydrochlorothiazide/valsartan)**
5/12.5/160 mg, 5/25/160 mg, 10/12.5/160 mg, 10/25/160 mg, 10/25/320 mg tablets
Approved: 4/30/2009
- **Lamictal® ODT™ (lamotrigine)**
25 mg, 50 mg, 100 mg, 200 mg orally disintegrating tablets
Approved: 5/8/2009
- **Lamictal® XR™ (lamotrigine)**
25 mg, 50mg, 100 mg, 200 mg extended-release tablets
Approved: 5/29/2009

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



Clinical Notes

Clinical Practice Guidelines for the Management of Candidiasis - March 2009

2009 Recommendations from the Infectious Diseases Society of America: Selected Key Points

- The Infectious Diseases Society of America released clinical practice guidelines for the management of invasive and mucosal candidiasis. These updated guidelines replace the guidelines published in 2004. Since 2004, several new antifungal agents have become available, including anidulafungin, micafungin, and posaconazole. Additionally, new literature has been published relating to the management of candidemia, other forms of invasive candidiasis, and mucosal disease.
- Fluconazole or an echinocandin (caspofungin, micafungin, or anidulafungin) is recommended as initial therapy for most non-neutropenic patients with candidemia. For moderate to severe illness, or in patients with a recent azole exposure, an echinocandin is the preferred therapy. Specifically, an echinocandin is preferred for infection due to *Candida glabrata* while fluconazole is recommended for infection due to *Candida parapsilosis*. The recommended duration of therapy for candidemia without obvious metastatic complications is two weeks after blood clearance of *Candida* and resolution of candidemia-related symptoms.
- In non-neutropenic patients with suspected candidiasis, empirical therapy is similar to that for proven candidiasis. Critically ill patients with risk factors for invasive candidiasis and no other known cause of fever should receive empirical therapy. The choice of therapy should be based on assessment of risk factors, serologic markers for invasive candidiasis, and/or culture data from nonsterile sites.
- An echinocandin is recommended for most neutropenic patients with candidemia. Less critically ill patients with no recent azole exposure can use fluconazole as an alternative. When additional mold coverage is needed, voriconazole may be used. Specifically for infection due to *Candida parapsilosis*, initial therapy with fluconazole or a lipid formulation of Amphotericin B (LFAmB) is preferred.
- LFAmB, caspofungin, or voriconazole are recommended for empirical treatment for suspected invasive candidiasis in neutropenic patients. Fluconazole and itraconazole are reasonable alternatives. Azoles should be avoided as empirical therapy in patients who have previously received an azole for prophylaxis.
- Amphotericin B (AmB) deoxycholate is recommended for neonates with disseminated candidiasis. Fluconazole is a reasonable alternative and LFAmB can be used if there is no involvement of the urinary tract. The recommended length of therapy is three weeks.
- Fluconazole or liposomal AmB is recommended as postoperative antifungals of choice for prophylaxis for liver, pancreas, and small bowel transplant recipients at high risk for candidiasis.
- Fluconazole, posaconazole, or caspofungin is recommended for patients with chemotherapy-induced neutropenia. Therapy should be administered during induction chemotherapy for the duration of neutropenia. An effective alternative is oral itraconazole; however, this agent is less well tolerated and offers little advantage over other agents.

Advisories

Boxed Warning for Botulinum Toxin Type A and Type B

On 4/30/09, the FDA issued an update to a previous 2007 alert regarding serious adverse reactions associated with botulinum toxin including respiratory compromise and muscle weakness. These reactions, which are suggestive of botulism, occurred mostly in children and have led to hospitalization and/or death. In addition to requesting additional safety data, the FDA has required Allergan® to add a boxed warning regarding these risks. Allergan® must also develop and implement a Risk Evaluation and Mitigation Strategy (REMS). This initiative will include a communication plan to educate providers and patients on the risks associated with the use of botulinum toxin and the lack of bioequivalence between currently-marketed products.

Boxed Warning for Topical Testosterone

On 5/7/2009, the FDA required the addition of a boxed warning on the label of the topical testosterone products AndroGel® and Testim®, regarding the risk of secondary exposure. As of December 2008, the FDA was notified of eight cases of secondary exposure to testosterone in children ages 9 months to 5 years resulting in inappropriate enlargement of the genitalia, premature development of pubic hair, advanced bone age, increased libido, and aggressive behavior. In most cases, symptoms regressed when the product was removed from the skin. However, several children required invasive diagnostic procedures, and one child required surgery. The FDA is now requiring the development of a REMS to ensure the benefits of these products continue to outweigh the potential risks.

New Safety Information for Tarceva®

On 5/8/2009, the FDA announced that new safety information would be added to the warning and precaution section of Tarceva® (erlotinib) labeling. Erlotinib is indicated for the treatment of patients with locally advanced metastatic non-small cell lung cancer after failure of at least one prior chemotherapy regimen. The newly reported risks include gastrointestinal perforation (GIP), ocular disorders, and bullous, blistering, and exfoliative skin conditions. If GIP develops, therapy should be permanently discontinued. Interruption or discontinuation of erlotinib is recommended in patients who develop severe bullous, blistering, or exfoliating skin conditions, and ocular disorders. Additionally, the dosage and administration section of the labeling has been updated to reflect the dose interruptions and discontinuation.

From The Hill

Federal

Recession May Cause an Increase in Rx-to-OTC Switches

According to the results of a new analysis from Kalorama Information, an independent market research firm specializing in life sciences, over-the-counter (OTC) marketing of prescription products may become more prevalent due to economic conditions and cost-control measures. Opposing generic competition through the courts can be costly. In response, drug manufacturers may need to agree more often to allow equivalent generic formulations to come to the market before patent expiration. An OTC switch is a viable alternative to extend the patent, and consequently, a product's lifecycle. Several OTC gastrointestinal products, for example, have demonstrated success in the market. Kalorama Information believes that OTC status will expand to include hyperlipidemia, osteoporosis, overactive bladder, sexual dysfunction, and contraceptive agents. This could result in continued growth of the Rx-to-OTC market, which was valued at \$6.7 billion in 2008, with annual growth estimated at 8 percent between 2009 and 2013.

Senators Advocate For E-Prescribing of Controlled Drugs

On 5/7/2009, a bipartisan group of 11 U.S. senators requested that the Obama administration broaden and accelerate the adoption of electronic prescribing. Although it is currently used in 18 percent of doctors' offices, widespread adoption of this practice has been limited by Drug Enforcement Administration (DEA) regulations. These statutes prohibit the use of this technology for controlled medications due to the risks of abuse and diversion.

Previous studies have shown that electronic prescribing could save \$20 billion a year by increasing patient adherence and decreasing adverse reactions. In June 2008, the DEA issued a draft rule that would lift the prohibition on paperless prescribing of controlled substances. However, the rule has not yet been finalized. The senators urge cooperation between the Department of Justice and the Department of Health and Human Services in expediting the creation of a rule that advances health care efficiency while minimizing the risk of diversion.

Pipeline

Embeda™ (morphine sulfate/naltrexone hydrochloride)

Embeda™ is an extended-release formulation of morphine sulfate with a sequestered core of naltrexone designed to be resistant to common forms of abuse. If the capsules are chewed or crushed, the naltrexone is rapidly absorbed and reduces the euphoric effects of the morphine component, decreasing likeability and abuse potential.

In a Phase III study (N=344), Embeda™ significantly reduced pain, as measured by the change in Brief Pain Inventory from baseline to week 12, when compared to placebo (P=0.045). An NDA was submitted to the FDA in June 2008 and was granted priority review. An FDA response is anticipated in early 2010.

Fablyn® (Lasofoxifene)

Lasofoxifene, a new selective estrogen receptor modulator, is currently under review for the treatment of postmenopausal osteoporosis. In a pivotal Phase III study, postmenopausal women (N=8,554) demonstrated that both 0.25 mg and 0.5 mg daily doses reduced the risk of a new or worsening radiographic vertebral fracture by 31 and 42 percent, respectively, when compared to placebo (P=0.002 and P<0.001). Prior to issuing a complete response in January 2009, the FDA had expressed concern over higher rates of death, blood clots, and gynecological problems in patients treated with lasofoxifene. Pfizer, Inc., is currently reviewing this complete response to determine the next steps for this product.

Noteworthy

Association Between Tamsulosin and Serious Ophthalmic Adverse Events in Older Men Following Cataract Surgery

A recent study in the *Journal of the American Medical Association* found that men ages 66 and older who were exposed to tamsulosin within the 14 days before undergoing cataract surgery were 2.3 times more likely to experience serious ophthalmic adverse events.

The study evaluated postoperative events in men who were prescribed tamsulosin or other alpha blockers at the time of cataract surgery, using a nested case-control analysis of a population-based retrospective cohort study. Patient data was derived from a Canadian Health care database. The primary endpoint was a composite of serious ophthalmic procedures that occurred within 14 days post-cataract surgery, including retinal detachment, lost lens or lens fragment, or endophthalmitis.

The results of the study indicated that 3,550 patients had a recent exposure to tamsulosin, and 7,426 had been exposed to another alpha blocker. In total, 284 patients had an adverse event in the 14 days after surgery. The number of events was significantly greater in the patients who had recent exposure to tamsulosin compared to the control group (7.5 percent versus 2.7 percent; adjusted odds ratio, 2.33; 95 percent confidence interval, 1.22-4.43). No significant associations were found with pre-surgery exposure to other alpha blockers or to tamsulosin exposure occurring between 15 to 365 days prior to surgery.

Bell CM, et al. JAMA. 2009;301(19):1991-1996.

What's New at UMMS?

Clinical initiatives through the partnership with the State University of New York (SUNY) have continued to expand. The Synagis® prescriber education program is now operational and initial feedback from prescribers has been positive. The New York Department of Health has asked the SUNY, in partnership with CPS, to develop a hypertension module focused on drug therapy in African Americans for launch in the summer. The development of the medication therapy management (MTM) program has also continued and an official launch is slated for the summer. The MTM program will utilize community pharmacists to provide education directly to patients on general disease management strategies, the importance of medication adherence, and proper medication administration. In addition, pharmacists will also interact directly with prescribers to recommend changes to current medication therapy regimens in order to improve patient outcomes.



A PARTNERSHIP IN CLINICAL EXCELLENCE

In an effort to deliver the highest possible level of quality and innovation in our clinical programming for our clients, MedMetrics has partnered with the University of Massachusetts Medical School's Clinical Pharmacy Services division. They bring exceptional depth and experience in the development and implementation of unique 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. *MedMetrics Rx-Pulse* is an educational resource produced quarterly to highlight this unique relationship. We hope that you find this resource of value and welcome your suggestions for improvement.

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