NEW DRUGS

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**Generic Approvals**

**Generic Xanax (Alprazolam)**

Barr Laboratories has received final approval from the U.S. Food and Drug Administration (FDA) for its application to manufacture and market a generic version of Pfizer’s Xanax XR (alprazolam extended-release) tablets, 0.5 mg, 1 mg, 2 mg, and 3 mg. The company intends to launch its product immediately.

Xanax XR Tablets are indicated for the treatment of panic disorder, with or without agoraphobia.

(Source: Barr, August 1, 2006.)

**Generic Effexor (Venlafaxine)**

The first generic version of Wyeth’s antidepressant drug, Effexor (venlafaxine), has been approved. Venlafaxine is indicated for the treatment of major depressive disorder. The tablets, in strengths of 25 mg, 37.5 mg, 50 mg, 75 mg, and 100 mg, are made by Teva Pharmaceuticals. This product will carry the same labeling as the originator drug, including the boxed warning.

(Source: FDA, August 9, 2006.)

**Pioglitazone/Glimepiride For Glucose Control in Diabetes**

The FDA has approved Takeda’s New Drug Application (NDA) for a combination of pioglitazone HCl (Actos) and glimepiride for the treatment of type-2 diabetes. The combination drug is called Duetact.

Actos directly targets insulin resistance, and glimepiride, a sulfonylurea, acts primarily by increasing the amount of insulin produced by the pancreas.

Duetact will be available in two commonly used dosages of pioglitazone/glimepiride, to be taken once daily: 30 mg/2 mg and 30 mg/4 mg. The medication will be on the market this year.

(Sources: Takeda, July 31, 2006; www.actos.com.)

**NEW INDICATIONS**

**Risedronate for Men With Osteoporosis**

On August 11, 2006, the FDA approved risedronate sodium tablets (Actonel, Procter & Gamble) 35 mg to increase bone mass in men with osteoporosis.

Actonel 5 mg was approved in 2000 for use in men and women to prevent and treat steroid-induced osteoporosis. Actonel 35 mg is also approved to prevent and treat osteoporosis in post-menopausal women.

The approval of Actonel for men with osteoporosis was based on a two-year, placebo-controlled, double-blind multicenter clinical trial. Patients treated with once-a-week Actonel 35 mg experienced statistically significant improvements in lumbar spine bone mineral density at six, 12, and 24 months.

Statistically significant reductions in bone turnover markers were also achieved at three, six, 12, and 24 months.

According to the National Osteoporosis Foundation, osteoporosis affects 2 million men in the U.S., and another 12 million are at risk for developing the disease. About 50% of osteoporosis cases in men are associated with aging; the other 50% of cases are secondary to oral steroid use, low testosterone levels, and heavy alcohol use. Men with age-related osteoporosis usually develop the disease later in life than women do.

(Sources: Alliance for Better Bone Health, August 14, 2006; www.actonel.com.)

**Adalimumab for Ankylosing Spondylitis**

Abbott Laboratories has announced the approval of adalimumab (Humira) for reducing signs and symptoms of active ankylosing spondylitis (AS). An autoimmune disease, AS affects the spine and large peripheral joints and causes inflammatory back pain and stiffness. It can also be associated with other inflammatory diseases of the skin, eyes and intestines. Over time, severe AS can result in complete spinal fusion.

The recommended dose is 40 mg every other week by subcutaneous injection, the usual dose recommended for patients with moderate-to-severe rheumatoid arthritis and psoriatic arthritis.

Adalimumab is available in the U.S. in a pre-filled syringe.

The approval for this new indication was based on data from the Adalimumab Trial Evaluating Long-Term Efficacy and Safety in AS (ATLAS).

(Source: Abbott Labs, July 31, 2006.)

**Clopidogrel and Prevention Of Heart Attacks**

Clopidogrel bisulfate (Plavix, Bristol-Myers Squibb/Sanoﬁ-Aventis) has been approved for patients who have had a type of heart attack called acute ST-segment elevation myocardial infarction (STEMI) and who are not scheduled for angioplasty (coronary artery repair).

A STEMI is a severe heart attack caused by the sudden, total blockage of an artery. The drug prevents subsequent blockage in the damaged heart vessel.

Clopidogrel was approved in November 1997 to decrease platelet function in people with acute coronary syndrome. Platelets help to form clots, and they can contribute to blocked coronary arteries.

The Clopidogrel and Metoprolol in Myocardial Infarction Trial (COMMIT) showed that Plavix, when combined with other standard treatments, reduced mortality and the combined number of recurrent heart attacks, strokes, and deaths. The COMMIT findings were supported by the results of another study, Clopidogrel as Adjunctive Reperfusion Therapy (CLARITY). In this study, coronary artery blood flow was better with clopidogrel than with placebo.

(Source: FDA, August 17, 2006.)

**When Will Actos be Available?**

Takeda’s application will be on the market this year.

**30 mg/2 mg and 30 mg/4 mg. The med-**

**ication will be on the market this year.**

(Abbott Laboratories, July 31, 2006.)
NEW FORMULATIONS
Topical Ketoconazole For Seborrheic Dermatitis
One-daily ketoconazole gel 2% (Xolegel, Barrier Therapeutics) is now approved for the topical treatment of seborrheic dermatitis in immunocompetent adults and children 12 years of age and older. Previously known as Sebazole, the formulation contains 2% ketoconazole, an antifungal agent, in a waterless gel for once-daily application.

Seborrheic dermatitis, a common skin inflammation, usually occurs on the face, scalp, hairline, eyebrows, and trunk.

Xolegel is the first prescription gel formulation of ketoconazole approved in the U.S. Until this approval, prescription therapies consisted primarily of shampoos, topical antifungal creams, and topical steroids.

Patients apply the gel once a day for two weeks. They need 75% fewer applications compared with some traditional therapies. The steroid-free gel is effective with minimal skin irritation.

(Source: Barrier, July 28, 2006.)

Oral Aripiprazole For Psychotic Disorders
Bristol-Myers Squibb and Otsuka Pharmaceuticals have launched aripiprazole orally disintegrating tablets (Discmelt). The tablets are are bioequivalent to the antipsychotic medication Abilify. Discmelt was approved on June 7, 2006.

The tablets offer a convenient alternative for adults with schizophrenia or manic episodes associated with Bipolar I Disorder. They disintegrate rapidly upon contact with saliva. No liquids are needed.

The vanilla-flavored 10- and 15-mg tablets are available in blister packs.

Adults with phenylketonuria should be advised that this product contains phenylalanine. A boxed warning states that Discmelt is not approved for patients with dementia-related psychosis.


IV Levetiracetam in Epilepsy
The FDA has approved an IV formulation of levetiracetam (Keppra, UCB) solution as an infusion for the adjunctive use in the treatment of partial-onset seizures in adults with epilepsy. The 100-mg/ml injection is intended as an alternative when oral administration of levetiracetam is temporarily not feasible.

When patients are switched from the oral to the IV form, the initial total daily dose should be equivalent to the total daily dosage and frequency of oral levetiracetam.

Levetiracetam should be administered as a 15-minute infusion following dilution of the dose with 100 ml of 0.9% sodium chloride, lactated Ringer’s solution, or 5% dextrose injection. Levetiracetam is compatible with lorazepam, diazepam, and valproate sodium injections for concomitant use.

Previously approved formulations include 250-, 500-, and 750-mg tablets and a 100-mg/ml oral solution for patients four years of age and older.

(Source: Medscape Medical News, July 31, 2006.)

DRUG NEWS
Combination Cancer Treatment Benefits Some Older Patients
Elderly patients with metastatic colorectal cancer responded well to a combination of two Roche agents, capecitabine (Xeloda) and oxaliplatin (Xelox).

In the Southern Italy Cooperative Oncology Group Trial, about 75% of the group achieved some disease control. Surprisingly, patients 75 years of age and older had an even better response rate than those aged 75 or younger.

Starting patients at low doses and increasing the doses only if they were well tolerated helped avoid unwanted and unpredictable toxicity. The combination regimen was well tolerated, in part because capecitabine and oxaliplatin do not have overlapping toxicities. The conservative step-up dosage schedule, combined with a limited number of delivered cycles also meant that patients received a relatively low cumulative dosage of oxaliplatin.

Ongoing trials will help determine whether capecitabine can replace 5-fluorouracil/leucovorin (5-FU/LV) in combination with oxaliplatin in patients with metastatic colorectal cancer. The switch would eliminate the need for a central venous catheter and the risks of catheter-related infection and thromboembolism, and patients would need only one clinic visit during each cycle for the infusion—a benefit that many patients, particularly the elderly, would appreciate.

(Source: Cancer 2006;104:282–289.)

Spironolactone Raises Risk of Gastrointestinal Problems
Spironolactone (e.g., Aldactone, Pfizer), a diuretic and aldosterone antagonist, may nearly triple the risk of upper gastrointestinal (GI) events such as bleeding and ulcers, according to a study from Erasmus Medical Center in Rotterdam, The Netherlands. Researchers studied data from 306,645 patients, of whom 523 had definite gastric or duodenal ulcer or upper GI bleeding. Those patients were matched with 5,230 controls. Most patients used spironolactone for heart failure, but some used it for hypertension, and one used it for liver cirrhosis.

The current use of spironolactone was associated with a 2.7-fold increased risk of a GI event. Patients taking higher doses had a five-fold increased risk. The risk was most pronounced when spironolactone was started at low doses and increasing the doses only if they were well tolerated helped avoid unwanted and unpredictable toxicity. The combination regimen was well tolerated, in part because capecitabine and oxaliplatin do not have overlapping toxicities. The conservative step-up dosage schedule, combined with a limited number of delivered cycles also meant that patients received a relatively low cumulative dosage of oxaliplatin.

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(Source: Cancer 2006;104:282–289.)
lactone was combined with ulcerogenic drugs.

(Source: BMJ, July 13, 2006.)

**Influenza Vaccines for Next Season**

The FDA has announced its approvals of this year’s seasonal influenza vaccines, which include the new strains of virus judged likely to cause flu in the Northern Hemisphere in 2006 and 2007. This season’s formulation includes one strain from last year’s vaccine and two new strains.

Four vaccine manufacturers will be able to market their vaccines in the U.S.: Chiron, GlaxoSmithKline, MedImmune, and Sanofi Pasteur. The manufacturers plan to make about 100 million doses of influenza vaccine for 2006–2007, but these projections might change.

See the Drug Forecast column on Flu-axir (page 505) and “P&T Around the World” for an article about the measles–mumps–rubella vaccine (page 522).

(Source: FDA, August 3, 2006.)

**Isotretinoin for Acne May Raise Blood Fats and Liver Enzymes**

An effective treatment for acne has been linked with potentially harmful changes in the blood and damage to the liver. Almost 90% of patients who used isotretinoin tablets (Accutane, Roche) were found to be at an increased risk for high triglyceride and cholesterol levels. Liver function tests showed the presence of enzymes that normally signal liver damage.

The prescribing information mentions that 25% of patients may sustain higher levels of triglycerides while taking the drug and that higher liver enzyme levels will affect 15%.

Researchers at the University of California in San Francisco monitored almost 14,000 patients between 13 and 50 years of age between 1995 and 2002. Forty-four percent of patients who had normal triglyceride levels before therapy developed high levels after taking the drug. High cholesterol levels developed in 31% of patients, and elevated liver enzymes developed in 11%. When patients stopped taking the drug, liver enzymes and cholesterol generally returned to normal levels.

In Britain, isotretinoin (Roaccutane) is more commonly given as a cream. The study does not indicate whether that form has the same effects.

Accutane was first approved in 1982. In 2005, the FDA announced stricter regulations in an effort to reduce an increased risk of miscarriage and birth defects associated with the drug.

(Source: Arch Dermatol 2006;142;1016–1022; London Times online, August 22, 2006, www.timesonline.co.uk.)

**Stronger Warning for ADHD Drug**

The FDA has asked GlaxoSmithKline to add a label warning about the risk of heart problems for patients taking the prescription drug dextroamphetamine sulfate (Dexedrine), a stimulant used to treat attention-deficit/hyperactivity disorder (ADHD).

The FDA has received reports of sudden death among children and teenagers who had heart problems and who took Dexedrine.

In May 2006, the FDA had asked the makers of similar stimulant ADHD drugs to add the warnings. In March, an FDA advisory committee had recommended that ADHD drugs not carry the more severe boxed warnings but that simpler language be used and more information be included about heart risks. However, a month earlier, a different committee had called for a boxed warning on ADHD drugs because of possible cardiac risks. The FDA has apparently settled for the less severe advisory.

The warnings issued since last spring also cite possible suppression of growth and a heightened risk for psychosis, bipolar illness, and aggression. It is unclear whether other ADHD drugs might be affected by this new warning.

The new warning, it is hoped, should remind clinicians to review the side-effect profiles of medications. Dexedrine is in an older class of stimulants. Whether other ADHD drugs must also add new labeling remains to be seen.

(Source: Forbes online and Medical News Today, August 22, 2006.)

**“Plan B” Emergency Contraception**

The FDA has approved a contraceptive drug, known as Plan B, as an over-the-counter (OTC) option for women 18 years of age and older. Plan B is also known as the “morning-after pill.”

Two levonorgestrel pills (0.75 mg in each pill) are taken by mouth after unprotected sexual intercourse. Plan B will be available behind the counter at the pharmacy in order to manage both prescription (for those 17 years and under) and OTC (18 years and over) dispensing.

Duramed, a subsidiary of Barr Pharmaceuticals, will make Plan B available with a rigorous labeling, packaging, education, distribution, and monitoring program.

(Source: FDA, August 24, 2006.)

**NEW MEDICAL DEVICES**

Marvin M. Goldenberg, PhD, RPh, MS

Name: Cell-Dyn Ruby
Manufacturer: Abbott Labs, Chicago
Approval Date: July 19, 2006
Use Classification: With its advanced laser optics, this hematology instrument offers enhanced cellular analysis and greater efficiency for laboratories performing a complete blood count, a routine test to assess a patient’s overall
health.

**Description:** A key facet of Cell-Dyn Ruby is its use of laser light to differentiate cellular components. Multi-Angle Polarized Scatter Separation (MAPSS), an all-optical technology, provides detailed results in easy-to-view diagrams, visually depicting changes in blood cells and platelets.

**Purpose:** This instrument is considered a premium, mid-volume analyzer that will support the needs of small to medium-sized hospital laboratories and clinics. Only four reagents are required. Intuitive software and online tutorials to facilitate training are included.

**Benefit:** A multicenter medical evaluation showed clinically equivalent results with Cell-Dyn Sapphire, a higher-volume, automated analyzer introduced last year.

**Sources:** www.pharmacyonesource.com; www.abbottdiagnostics.com

**Name:** i-Stat Brain Natriuretic Peptide (BNP) Cartridge

**Manufacturer:** Abbott Labs, East Windsor, NJ

**Approval Date:** July 26, 2006

**Use Classification:** This new point-of-care diagnostic test is used to quickly assess brain natriuretic peptide (BNP) levels in patients in emergency rooms, cardiac-care clinics, and observation units, laboratories, and other critical-care settings.

**Description:** The cartridge is used with the i-Stat System, an automated hand-held blood analyzer that performs a comprehensive panel of critical tests at the patient’s bedside in only a few minutes. Laboratory-quality results enable health care professionals to make rapid diagnoses and treatment decisions.

**Purpose:** BNP is a protein secreted into the bloodstream by heart tissue during congestive heart failure, a disease in which the heart loses its ability to adequately pump blood throughout the body and which results in a build-up of fluid pressure inside the heart. The cartridge is a single-use, *in vitro* diagnostic test to be used by licensed practitioners to measure the BNP level with only one drop of blood. The results can be delivered in just 10 minutes. Currently, the turnaround time for BNP results should be less than 60 minutes.

**Benefit:** Congestive heart failure is often challenging to diagnose because its key signs and symptoms (shortness of breath and fatigue) are relatively non-specific and are often associated with other conditions. Determining the level of BNP in the blood, an objective marker of the presence of heart failure, can help physicians quickly and more accurately assess disease severity. BNP testing at the patient’s bedside accelerates triage, diagnosis, treatment, and disposition of patients, all of which help to clear overcrowded emergency departments.

**Sources:** www.pharmacyonesource.com; www.abbott.com

**Name:** Adept Adhesion Reduction Solution

**Manufacturer:** Innovata Plc/Baxter Healthcare Corporation, Nottingham, UK, and Deerfield, Ill

**Approval Date:** August 1, 2006

**Use Classification:** The solution is used intraperitoneally as an adjunct to good surgical technique to reduce postsurgical adhesions in patients undergoing gynecological laparoscopic adhesiolysis. Adhesions are abnormal attachments between tissues or organs. Gynecological adhesions may cause pain, secondary infertility, or other complications in women.

**Description:** Adept was evaluated in three clinical trials involving 548 patients undergoing gynecological laparoscopic surgery with follow-up laparoscopy after the initial procedure. In the pivotal study, for the patients in the treatment group, 45.4% were defined as a “clinical success,” compared with 35.6% of those in the control group. Clinical success was measured as a reduction in the number of adhesions between the first and second laparoscopies.

**Benefit:** Patients in the Adept group had significantly fewer sites with adhesions at a second-look evaluation compared with first-look adhesiolysis laparoscopy (*P* = .016). This is the first approved fluid-based approach for adhesion reduction in gynecological laparoscopic adhesiolysis in the U.S. Because the solution is a liquid, it can be delivered directly and rapidly to the site through a laparoscopic port during surgery.

**Precautions:** Adept is contraindicated in patients with known or suspected allergy to icodextrin and similar polymers. It is not used in laparotomy, in cases involving bowel resection or repair, in appendectomy, or in surgical cases with frank abdominal–pelvic infection.

**Sources:** www.pharmacyonesource.com; www.baxter.com

**FDA Device Initiative**

The FDA is looking for information on how the use of a unique identifier system for medical devices might reduce medical errors, facilitate device recalls, and improve adverse event reporting about the devices. Similar to the bar-code rule for drugs and biologic products, unique identifiers for medical devices might have potential benefits for improving the quality of care for patients. The Agency is seeking public comments, and a meeting is planned for the fall.

**Sources:** www.fda.gov/cdrh/ocd/mdii.html; www.pharmacyonesource.com