



## NEW DRUGS

### Generic Zoloft Tentatively Approved

Alpharma, Inc., has announced the U.S. Food and Drug Administration's (FDA's) tentative approval of its Abbreviated New Drug Application for sertraline HCl 25-, 50-, and 100-mg tablets. These tablets are the AB-rated generic equivalent of Pfizer's antidepressant Zoloft.

In October, the company announced that it would sell its U.S. and International Generics businesses to Actavis Group.

(Source: Alpharma, Inc., December 8, 2005.)

## NEW INDICATION

### Divalproex Sodium for Acute Mania

The FDA has approved a new indication for extended-release divalproex sodium tablets (Depakote, Abbott Laboratories) for the treatment of acute manic or mixed episodes associated with bipolar disorder, with or without psychotic features.

The effectiveness of Depakote ER for this indication was confirmed in a randomized, double-blind, placebo-controlled parallel group, three-week, multicenter study.

Depakote ER is also approved for seizures, migraine prevention, and mania associated with bipolar disorder.

(Source: Abbott, December 7, 2005.)

## DRUG NEWS

### Teratogenic Drugs: Reassessing the Risks

Each year, millions of women of child-bearing age are prescribed drugs that have the potential to cause birth defects, according to a study from the University of Pittsburgh and the University of California, San Francisco. During an estimated 11 million annual office visits, 11.7

million class D or class X medications were documented. Class D drugs may have benefits in pregnancy despite a risk to the fetus; class X drugs are contraindicated in women who are or may become pregnant.

The most commonly prescribed teratogens were anxiolytic agents, anti-convulsants, antibiotics such as doxycycline (e.g., Vibramycin, Pfizer), and statins. Fewer than 5% of the prescriptions were for isotretinoin.

White women were prescribed potentially teratogenic drugs more often, in part because they were also more likely to be prescribed anxiolytic agents. Women with public insurance were also more likely to receive potentially teratogenic drugs than those with private insurance. Physicians who identified themselves as the patient's primary care provider were less likely to prescribe the drugs, according to their reporting.

The researchers advise engaging women in shared decision-making about contraception when class D or class X drugs are involved. Although approximately 20% of the visits at which a teratogenic medication was prescribed would be expected to have included concurrent counseling about contraceptives, only 6% of visits actually did. Indeed, the researchers found no significant difference in the rates of contraceptive counseling with use of low-risk drugs and the potential teratogens.

Not all teratogenic drugs are equally dangerous, they emphasize. Anticonvulsants are associated with structural deformities, and there is "growing evidence" of central nervous system anomalies with the use of statins. Tetracyclines, which can cause tooth discoloration, and benzodiazepines, which cross the placenta but are not associated with structural deformities, are lower on the scale of risk.

(Source: *Am J Med* 2005;118:1240-1249.)

### Is Inhaled Insulin Better Than Oral Diabetes Drugs?

"Surprisingly effective despite its short duration of action" is the verdict on inhaled insulin.

In a 12-week study of 309 patients at 48 outpatient centers, researchers compared inhaled insulin (alone or added to dual oral therapy) with dual-agent therapy alone. Inhaled insulin was administered within 10 minutes before meals. At the 12th week, both of the patient groups receiving inhaled insulin experienced statistically significantly greater reductions in mean glycosylated hemoglobin (HbA<sub>1c</sub>) levels, compared with the dual-agent patients. The value of inhaled insulin seems greater, the researchers say, when it is used with oral agents.

For the patients using inhaled insulin along with two oral agents, the HbA<sub>1c</sub> concentration dropped 1.9 percentage points, from 9.2%.

For the patients using inhaled insulin monotherapy, HbA<sub>1c</sub> dropped by 1.4 percentage points; for patients using the oral drugs, HbA<sub>1c</sub> fell by only 0.2 percentage point.

In addition to improving postprandial glucose control, inhaled insulin reduced fasting plasma glucose concentrations. Its glucose-lowering effect extended beyond the postprandial period. This effect has also persisted in other studies, but the reasons are not clear.

Hypoglycemia, mild weight gain, mild cough, and insulin antibodies were more common with inhaled insulin.

(Source: *Ann Intern Med* 2005;143:549-558.)

### Revised Labeling for Three Anemia Drugs

Health care professionals have been alerted to revisions of the prescribing information for darbepoietin alfa (Aranesp, Amgen), erythropoietin alfa (Epogen, Amgen), and epoetin alfa



(Procrit, Ortho Biotech).

The revised labeling provides updated safety information on reports of pure red blood cell aplasia and severe anemia, with or without other cytopenia, associated with neutralizing antibodies to erythropoietin in patients with chronic renal failure who have been treated with these products.

This observation has been most common with subcutaneous administration. (Source: FDA, December 1, 2005.)

### Counterfeit Flu Drug Seized

Customs agents intercepted more than 50 shipments of counterfeit Tamiflu (Roche), the antiviral drug being stockpiled in anticipation of a deadly bird flu pandemic.

The first package was intercepted on November 26 at an air mail facility near San Francisco International Airport. Since then, agents have seized 51 separate packages, each containing up to 50 counterfeit capsules labeled generic Tamiflu.

The fake drugs had only trace elements of the drug but none of Tamiflu's active ingredients. Initial tests indicated some vitamin C in the capsules. Information on the packages was written in Chinese, but it is unclear where the drugs originated. They were sent by Asian suppliers to individuals who placed orders over the Internet. None of the intercepted shipments has been bound for doctors or hospitals.

Agents became suspicious because because no generic version of Tamiflu is available.

The Roche Web site says the company does not advocate buying this medication from the Internet. Patients should consult with a health care professional before buying Tamiflu and should make sure that they obtain it from a "reliable source."

The FDA will seek criminal charges

if it finds any U.S. businesses were involved in the fake drug shipments.

(Source: Yahoo Business News, December 19, 2005, [news.yahoo.com/s/ap/20051219/ap\\_on\\_he\\_me/counterfeit\\_tamiflu](http://news.yahoo.com/s/ap/20051219/ap_on_he_me/counterfeit_tamiflu).)

### Paroxetine and Birth Defects

The FDA has alerted health care professionals and patients that paroxetine (Paxil, GlaxoSmithKline) might increase the risk of birth defects, particularly heart defects, for women taking it during the first trimester of pregnancy. Paroxetine is approved for the treatment of depression and other psychiatric disorders.

The FDA is advising health care professionals to discuss the potential risk of birth defects with patients who plan to become pregnant or who are in their first three months of pregnancy. Health care professionals should consider discontinuing the agent and prescribing another antidepressant if indicated.

In some patients, the benefits of continuing therapy with paroxetine may be greater than the potential risk to the fetus.

Early results of two studies showed that women who taking paroxetine during the first trimester were about 1.5 to two times as likely to have a baby with a heart defect as women taking other antidepressants or women in the general population. Most of the heart problems were atrial and ventricular septal defects.

The FDA has asked the manufacturer to change the pregnancy category from C to D, which carries a stronger warning. (Source: FDA, December 8, 2005.)

### Program Offers Help with Medicare Part D Drug Plan

"My Medicare Matters" is a new national education program to help people understand the new Medicare Prescription Drug Coverage, assess their situation, compare plans, and make

appropriate enrollment decisions. The program is sponsored by the National Council on the Aging and the Access to Benefits Coalition, with support from AstraZeneca.

Wireless laptop computers, pre-loaded software, and a Web site, "MyMedicareMatters.org" will be provided. Educators will be available to assist enrollees in completing the online process or to advise them about other methods of joining a plan. The program will remain active throughout the six-month Part D enrollment period.

(Sources: National Council on the Aging, [www.ncoa.org](http://www.ncoa.org); AstraZeneca, [www.astrazeneca-us.com](http://www.astrazeneca-us.com), November 22, 2005.)

### Imaging Agent for Diagnosis of Appendicitis Recalled

Marketing for technetium 99m fanlesomab (NeuroSpec, Palatin Technologies) is being suspended immediately because of safety concerns. NeuroSpec is an antibody radiolabeled with technetium-99m, indicated for radiological imaging of patients five years of age or older with unclear signs and symptoms of appendicitis.

The agent carries a radioactive tracer to white blood cells and binds to them. A radioactivity-spotting camera is used to determine whether the white blood cells have clustered in the appendix, a sign of infection.

The FDA received reports from Palatin of two deaths and 15 additional life-threatening adverse events in patients receiving NeuroSpec. These events occurred within minutes of administration and included shortness of breath, low blood pressure, and cardiopulmonary arrest. An additional 46 patients experienced adverse events that were similar but less severe. Most of the adverse effects occurred when NeuroSpec was used to diagnose infections



other than appendicitis.

Health care providers should discontinue their use of existing stocks and contact Palatin regarding their return.

The FDA plans to debate whether additional safety measures would allow the agent to return to the market.

Sources: FDA Medwatch, December 19, 2005; Associated Press.

### Recombinant Factor VIIa and Arterial Thromboembolism

Novo Nordisk and the FDA have notified health care professionals of changes to the prescribing information for recombinant human factor VIIa (rFVIIa) (NovoSeven) because of the occurrence of thrombotic and thromboembolic adverse events.

A clinical study of elderly, non-hemophilic patients who had experienced intracerebral hemorrhage indicated a potential increased risk of arterial thromboembolic events after the use of NovoSeven, including myocardial ischemia and infarction as well as cerebral ischemia and infarction.

(Source: FDA, December 1, 2005.)

### NEW MEDICAL DEVICES

**Marvin M. Goldenberg, PhD, RPh, MS**

**Name:** Trilogy AB (Alternate Bearing) Acetabular System

**Manufacturer:** Zimmer Holdings, Inc., Warsaw, IN

**Approval Date:** December 14, 2005

**Use Classification:** The Trilogy AB system, which is used for total hip arthroplasty, is part of the Trilogy Acetabular System, first launched in 1994.

**Description:** The femoral head and cup liner components are made of alumina ceramic and are designed to provide hard, wear-resistant articulating surfaces in either cemented or non-cemented hip arthroplasty.

**Purpose:** The device is a ceramic-on-

ceramic option for surgeons who prefer Zimmer fiber-metal backed cups and acetabular instruments.

**Benefit:** The introduction of this device is part of an overall effort to offer a comprehensive range of bearing surfaces, including the highly cross-linked polyethylene and metal-on-metal and ceramic-on-ceramic options.

**Sources:** www.pharmacyonesource.com; www.zimmer.co.uk

**Name:** GEM 21S (Growth-factor Enhanced Matrix)

**Manufacturer:** Biomimetics Pharmaceuticals Inc., Franklin, TN

**Approval Date:** November 18, 2005

**Use Classification:** This dental-filling device with its biological component may be used in patients who have bone defects caused by periodontal disease.

**Description:** The device is a combination of osteoconductive, biocompatible, and resorbable beta calcium phosphate. This sterile, porous filler is used to repair bony defects. Becaplermin is a highly purified recombinant human platelet-derived growth factor.

**Purpose:** The GEM 21S fills in bony defects, and the biological component encourages bone growth.

**Benefit:** Defects can be filled in a shorter time than products without the biological component.

**Precautions:** The GEM 21S should not be used in patients with an infection or cancerous growth in the defect area or who do not have enough gum tissue to cover the bone-filling device.

**Sources:** www.fda.gov/cdrh/mda/docs/p040013.html; www.fda.gov/cdrh/pdf4/p040013b.pdf

**Name:** SilvaGard Antimicrobial Surface Treatment

**Manufacturer:** AcryMed, Inc., Portland, OR

**Approval Date:** December 14, 2005

**Use Classification:** SilvaGard is a coating that can be used to render medical devices impervious to infection-causing bacteria. Its use does not alter the device's original properties.

**Description:** A silver nanoparticle antimicrobial coating prevents the formation of infection-causing biofilm.

**Purpose:** A unique nanotechnology design provides an easy, cost-effective method of applying a surface treatment of ionic silver to a device. The treatment is effective for days, weeks, or even months, depending upon application requirements.

**Benefit:** SilvaGard is expected to have a significant impact on the battle against hospital-related infections. Prior to the use of SilvaGard, other antimicrobial technologies were beset by least one of four problems: (1) some coatings could not be applied to certain elastic or interior surfaces of the device; (2) some coatings altered the original characteristics of the product, thus making it unsuitable for the intended use; (3) in some cases, expensive re-engineering was required; and (4) there were concerns about the length of effective sustainability relative to the cost of application.

**Sources:** www.nanotechnology.com/news/?id=7713; www.acrymed.com/techATD.htm

### Device Alert

On December 14, 2005, the FDA classified Baxter Healthcare Meridian Hemodialysis Instrument (Product Codes 5M5576 and 5M5576R) as a Class I recall. There have been reports of hemolysis related to kinks in the blood tubing sets used with this instrument. To date, one death and at least one serious injury have been documented.

**Source:** www.fda.gov/medwatch/safety/2005/safety05.htm#Meridian ■