**NEW DRUGS**

**Generic Zithromax Approved**

The U.S. Food and Drug Administration (FDA) has approved an Abbreviated New Drug Application (ANDA) for Azithromycin for Injection (American Pharmaceutical Partners), the generic equivalent of Pfizer’s Zithromax.

Azithromycin is indicated for the treatment of community-acquired pneumonia and pelvic inflammatory disease when caused by susceptible microorganisms.

The product will be available in 500-mg vials. It is preservative-free and AP-rated. Each vial will include a bar code and a latex-free vial stopper.

(Source: American Pharmaceutical Partners, December 14, 2005.)

**First Subcutaneous Immune Globulin**

The first immune globulin product for subcutaneous injection to prevent serious infections in patients with primary immune deficiency diseases (PIDDs) has been approved.

Vivaglobin (ZLB Behring GmbH, Germany) is manufactured from human plasma collected at U.S. licensed plasma centers. It is given under the skin on a weekly basis via an infusion pump. Patients can self-administer the product at home. Other immune globulins are given intravenously or intramuscularly.

As with all immune globulin preparations, the plasma must be tested and found to be nonreactive for the human immunodeficiency virus (HIV) and hepatitis viruses prior to its use, and the manufacturing process includes steps that further reduce the risk of transmission of viruses.

(Source: FDA, January 10, 2006.)

**Once-Daily Psoriasis Therapy**

Warner Chilcott and Leo Pharma have announced the FDA’s approval of their New Drug Application (NDA) for a topical ointment (Taclonex) to treat psoriasis vulgaris in adults. The product is a combination of calcipotriene 0.005% and betamethasone dipropionate 0.064%. Taclonex is sold outside the U.S. as Dovobet and Daivobet.

Warner Chilcott is Leo Pharma’s exclusive licensee of Taclonex in the U.S. Taclonex is expected to be launched in the first half of 2006.

(Source: Warner Chilcott/Leo Pharma, January 10, 2006.)

**CIP-Fenofibrate for Cholesterol Disorders**

Final approval has been granted for CIP-Fenofibrate (Lipofen, Cipher Pharmaceuticals), a novel formulation of the active ingredient fenofibrate, which is used in the treatment of hyperlipidemia.

Three dosages were approved: 50, 100 and 150 mg. The 150-mg strength is equivalent to Abbott’s Tricor 160 mg (under fed, not fasting, conditions). The new agent’s absorption is increased under high-fat conditions (in relation to low-fat conditions).

CIP-Fenofibrate may be used as an adjunctive therapy to diet to reduce levels of low-density lipoprotein-cholesterol, total cholesterol, triglycerides, and apolipoprotein B. It is also indicated for raising high-density lipoprotein cholesterol levels in adults with primary hypercholesterolemia or mixed dyslipidemia and in adults with hypertriglyceridemia.

CIP-Fenofibrate is based on the Lidose delivery system (consisting of oral semi-liquid capsules).

(Source: Cipher, January 13, 2006.)

**Generic Ultracet for Pain**

Caraco Pharmaceutical Laboratories Ltd. has announced the FDA’s final approval of an ANDA for Tramadol HCl with acetaminophen tablets. This is the generic equivalent of Ortho-McNeil’s brand product, Ultracet, which is indicated for the short-term management of acute pain over a period of five days or less.

(Source: Caraco, December 19, 2005.)

**Tentative Approval for Generic Pediatric AIDS Drug**

The FDA has tentatively approved Stavudine for Oral Solution, 1 mg/ml (Aurobindo Pharma Ltd., India). This antiretroviral agent is the first generic version of Zerit Oral Solution (Bristol-Myers Squibb). This child-friendly agent is indicated for pediatric patients with HIV infection, from birth through adolescence.

Stavudine (d4T) helps to prevent the AIDS virus from reproducing. It is used in combination with other antiretroviral agents to treat HIV-1 infection.

(Sources: FDA, December 21, 2005, www.fda.gov/oashi/aids/hiv.html.)

**Sorafenib Tosylate Improves Survival in Kidney Cancer**

Sorafenib tosylate (Nexavar, Bayer), a new anti-cancer medication for adults with advanced renal cell carcinoma, has been approved. In the U.S., kidney cancer accounts for approximately 3% of all adult cancers.

In two studies, patients who were treated with sorafenib had more time before tumor progression or death. In the larger study, most patients had received interleukin-2 or interferon. The median time to tumor progression or death was 167 days for sorafenib patients and 84 days for controls.

(Sources: FDA, December 21, 2005; American Cancer Society.)

**IV Conivaptan Helps Correct Sodium/Water Imbalance**

The FDA has approved conivaptan HCl injection (YM087, Vaprisol, Astellas Pharma), an arginine vasopressin (AVP) antagonist for hospitalized patients with...
euvoletic hyponatremia.

Euvolemic hyponatremia is a potentially life-threatening condition that occurs when the body’s blood sodium level falls significantly below normal. Hyponatremia affects almost 4% of hospitalized patients in the U.S. each year. Although many patients have no symptoms, the condition can cause brain swelling, respiratory arrest, and death.

Conivaptan blocks the activity of AVP and helps to increase urine output without the loss of valuable electrolytes such as sodium and potassium. This effect, known as “aquarexia,” helps to correct serum sodium levels in patients with hyponatremia caused by increased body water (dilutional hyponatremia).

The FDA has also issued an approvable letter for conivaptan as a therapy for hypervolemic hyponatremia.

(Sources: FDA, December 30, 2005; www.astellas.com/us.)

**Inhalable Version of Insulin**

Adults with diabetes may now have an alternative to some of the insulin injections they must now take.

Exubera (Pfizer), a powder form of recombinant human insulin, represents the first new method of delivery since the hormone’s discovery in the 1920s. Pfizer developed the drug and dispenser with Sanofi-Aventis and Nektar Therapeutics.

The device, about the size of an eyeglass case, delivers insulin as a dry powder, packaged in 1- or 3-mg inhalable capsules, to the lungs through the mouth. In clinical trials, it controlled glucose levels as effectively as injected insulin. However, its use does not mean the elimination of needles, pens, or pumps. Needles allow better dosage control.

An FDA review panel expressed concern about the bulkiness of the dispenser. Some patients using the drug experienced coughing or a slight decrease in lung capacity.

Patients with type-1 and type-2 diabetes can use the rapid-acting, inhaled insulin before or after meals, but the device would not replace the longer-acting insulin injections that some patients, especially those with type-1 diabetes, need to take in the morning or before bed. Patients must continue pricking their fingers to test blood glucose levels.

Patients with poorly controlled or unstable lung disease, or who smoke or who have recently quit, should not use Exubera.

(Sources: FDA; Associated Press, January 27, 2006; www.pfizer.com.)

**Sunitinib for Two Cancers**

The FDA has approved sunitinib (Sutent, Pfizer), a targeted treatment for patients with advanced kidney cancer and gastrointestinal stromal tumors (GISTs), a rare stomach cancer. This action marks the first time that the agency has approved an oncology product for two indications simultaneously.

Sunitinib, a tyrosine kinase inhibitor, deprives tumor cells of blood and nutrients needed to grow. It was approved for patients with GISTs whose disease has progressed or who cannot tolerate imatinib mesylate (Gleevec, Novartis), the current therapy for GISTs.

Sunitinib delayed the time it took for tumors or new lesions to grow (27 weeks vs. six weeks for untreated patients).

The accelerated approval for advanced renal cell carcinoma was based on the drug’s ability to reduce tumor size.

According to the American Cancer Society, about 32,000 new cases of advanced kidney cancer and 5,000 GISTs are diagnosed each year.

(Sources: FDA, January 26, 2006.)

**NEW INDICATIONS**

**Hormone Patch May Prevent Osteoporosis after Menopause**

An estradiol/levonorgestrel transdermal system (Climara Pro, Schering) is now available for the prevention of postmenopausal osteoporosis in the U.S.

This patch was approved in 2003 to treat moderate-to-severe vasomotor symptoms such as hot flashes and night sweats associated with menopause.

The transdermal patch allows for week-long continuous delivery of the hormone estradiol (0.045 mg/day), combined with levonorgestrel (0.015 mg/day). The thin, translucent patch is easily affixed to the skin.

(Source: Schering AG, January 4, 2006.)

**Early Breast Cancer May Benefit from Letrozole**

Letrozole (Femara, Novartis), an aromatase inhibitor, has been granted FDA approval as adjuvant therapy for patients with early hormone receptor–positive breast cancer.

With the added indication, letrozole becomes the second agent in its class to gain an equal footing with tamoxifen (Nolvadex, AstraZeneca) for immediate use after surgery in postmenopausal women with early breast cancer. It joined anastrozole (Arimidex, AstraZeneca), which earned a similar green light from the FDA in September 2005. A year ago, once-daily oral letrozole was approved for the extended adjuvant treatment of early breast cancer in postmenopausal women who had received five years of adjuvant tamoxifen therapy.


**NEW FORMULATION**

**IV Ibandronate for Osteoporosis**

The FDA has approved ibandronate sodium (Boniva Injection, Roche/GlaxoSmithKline), the first quarterly IV bisphosphonate indicated for the treatment...continued on page 80
of postmenopausal osteoporosis.

IV ibandronate is administered by a health care professional once every three months. The process takes 15 to 30 seconds. This formulation offers an alternative for patients who have difficulty with oral bisphosphonate dosing requirements, including an inability to sit upright for 30 to 60 minutes or to swallow tablets.

The FDA approved the IV form based on results of the DIVA study (Dosing IntraVenous Administration). This clinical trial enrolled 1,358 postmenopausal women with osteoporosis. The average increase in lumbar spine bone mineral density at one year with the injection (3 mg once every three months) was statistically superior to that with the daily oral tablets (4.5% vs. 3.5% for the two treatments, respectively; P < .001). Patients receiving the IV form also had consistently higher bone density increases in the total hip and other sites than patients taking the oral daily form.

The FDA approved once-monthly ibandronate as the first once-a-month tablet for postmenopausal osteoporosis in March 2005. The injection will be available in early 2006.

(All: Roche, January 6, 2006.)

**DRUG NEWS**

**Effects of Beta Blockers on Albuminuria in Diabetes**

Not all beta blockers have the same effect on cardiovascular risk factors in patients with diabetes. The Glycemic Effects in Diabetes Mellitus Carvedilol—Metoprolol Comparison in Hypertensives (GEMINI) trial found that, in the presence of an angiotensin-converting enzyme (ACE) inhibitor or an angiotensin-receptor blocker (ARB), the beta blocker carvedilol (e.g., Coreg, GlaxoSmithKline) preserved glycemic control, whereas metoprolol (e.g., Toprol, AstraZeneca) did not. Carvedilol also reduced the risk of albuminuria, another marker of cardiovascular risk, by 47%.

As many as 40% of type-2 diabetic patients have microalbuminuria. Recent studies suggest that lowering both blood pressure and albuminuria levels may have better cardiovascular and renal effects than just lowering blood pressure. Of 388 patients assigned to receive carvedilol, 6.6% of those with normal albumin levels at screening developed microalbuminuria, compared with 11% of 542 patients receiving metoprolol.

In the cohort without microalbuminuria, similar numbers of patients needed a calcium antagonist to achieve blood pressure goals. More patients taking carvedilol required low-dose hydrochlorothiazide; this was also true in patients without microalbuminuria. Even with a higher rate of diuretic use, these patients still had better glycemic control.

In a separate analysis, patients with the metabolic syndrome at the baseline evaluation had a 168% increase in the odds of experiencing a worsening in albuminuria over the five months of follow-up. (Source: Hypertension 2005;46:1309–1315.)

**Black-Box Warning Added to Labels for Two Eczema Creams**

Two prescription creams used to treat eczema will now carry strong warnings about the possible risk of skin cancer, lymphoma, and other cancers associated with their use.

The packaging for pimecrolimus (Elidel, Novartis AG) and tacrolimus (Protopic, Astellas Pharma) will contain “black-box” warnings—the strongest type used in the U.S.—10 months after the agency first called for them.

FDA officials said that although a clear link between the drugs and cancer risk had not been found, there have been enough cancer reports to warrant the change. A total of 78 cases were reported for both products as of October 2005. The labels clarify that both treatments are to be used after other drugs have failed and that they should not be used in children younger than 2 years of age.

Animal research linked the creams to an increased risk of skin cancer and non-Hodgkin’s lymphoma. The risk of cancer increased as the drug doses increased.

These medications control eczema by suppressing the immune system and are viewed as an alternative to steroid-based drugs. The products should be used only for short periods of time and are not indicated for children or adults with weakened immune systems. The minimum amount should be used to control symptoms.

(All: FDA; WebMD, January 19, 2006; Reuters, www.alertnet.org/thenews/newsdesk/N19331576.htm.)

**Daily Aspirin: Benefits Differ in Men and Women**

New findings indicate that low-dose aspirin has cardiovascular benefits that differ for men and women, but it raises the risk of bleeding for both.

Although heart-attack survivors do benefit from low-dose aspirin, controversy remains as to whether anyone should take aspirin to prevent a first heart attack or stroke.

In an analysis of six large clinical trials, aspirin decreased men’s risk of a heart attack by 32% but not their risk of stroke, and it reduced women’s risk of stroke by 17% but not their risk of a heart attack.

Unfortunately, aspirin also increased the risk of major bleeding (from stomach or intestinal ulcers) by 70% for both men and women. Both men and women receive a small, but potentially life-saving, benefit from daily aspirin at the cost of a small but potentially life-threatening risk of “major bleeding events.”

People who take daily aspirin are estimated to have 0.1% to 0.2% fewer heart attacks.
attacks per year than those not taking aspirin. For people with a low to intermediate risk of a heart attack, however, it might not be advisable to take an aspirin a day.

(Sources: *JAMA* 2006;295:306–313; Web MD, January 17, 2006.)

**Improving Patient Safety: New Format for Drug Labels**

The FDA has unveiled a major revision to the format of drug labels (package inserts) to give health care professionals clearer and more concise prescribing information. The plan also includes a government database that allows people to search for information online.

The format is being revised for the first time in more than 25 years. FDA officials said that one goal was to ensure that doctors would not overlook essential safety information, which is often buried deep in the document.

The labels will include (1) the date of initial U.S. approval, (2) recent changes to information about the drug, (3) a toll-free phone number for patients or doctors to report suspected side effects to the FDA, (4) drug interactions discussed in one place, and (5) a section prompting doctors on keys facts to relay to patients. The format also includes a summary of important information at the top (“Highlights”), a “table of contents,” a section on patient counseling, and greater prominence of essential prescribing information.

These changes are to take effect by the spring for new drugs and their new approved uses. A Web site, http://daily-med.nlm.nih.gov, will provide updates.


**NEW MEDICAL DEVICES**

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

**Name:** IBI-1500T6 (Irvine Biomedical, Inc.) Cardiac Ablation Generator

**Description:** The catheter offers a single-sensor, temperature-monitoring system for the treatment of supraventricular tachycardia. The generator automatically limits radiofrequency delivery to a maximum power output of 50 watts when it is used with a 4-mm tip ablation electrode.

**Sources:** www.pharmacyonesource.com; http://biz.yahoo.com, December 1, 2005

**Name:** Procleix West Nile Virus Assay

**Manufacturer:** Gen-Probe, San Diego, CA/Chiron Corporation, Emeryville, CA

**Approval Date:** December 1, 2005

**Use Classification:** The assay is used to detect West Nile virus RNA in plasma specimens from living and cadaveric donors. It is not intended for use on cord blood specimens.

**Description:** The system incorporates state-of-the-art amplified nucleic acid testing technology to detect viral RNA and DNA in donated blood and plasma during the early stages of infection. At this stage, infectious agents are present but cannot be detected by immunodiagnostic tests.

**Purpose:** The assay has been used to screen more than 29 million units of blood on an “investigational use” only basis since June 2003, and it has intercepted more than 1,500 donations positive for the West Nile virus.

**Benefit:** This is the first fully automated nucleic acid testing system available for blood screening. Its use with the Procleix assay should allow for maximum sensitivity by enabling individual donor testing and should bring a new level of quality assurance in detecting potential transfusion-transmitted viruses.

**Sources:** www.pharmacyonesource.com; http://phx.corporate-ir.net, December 1, 2005

**Name:** VaporMax Side-Firing Laser Fiber

**Manufacturer:** Trimedyne, Inc., Irvine, CA

**Approval Date:** January 6, 2006

**Use Classification:** The device is used with its Holmium lasers to treat benign prostatic hyperplasia (BPH), an enlargement of the prostate gland.

**Description:** The system incorporates state-of-the-art amplified nucleic acid testing technology to detect viral RNA and DNA in donated blood and plasma during the early stages of infection. At this stage, infectious agents are present but cannot be detected by immunodiagnostic tests.

**Purpose:** The assay has been used to screen more than 29 million units of blood on an “investigational use” only basis since June 2003, and it has intercepted more than 1,500 donations positive for the West Nile virus.

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**Sources:** www.pharmacyonesource.com; http://phx.corporate-ir.net, December 1, 2005
faster than that provided by other laser devices.

**Purpose:** The product allows minimally invasive surgery in men with BPH.

**Benefit:** A faster vaporization rate minimizes physician and costly operating room time. These fibers are more durable than other side-firing laser fibers. One device should be sufficient to treat even very large prostate glands.

Laser vaporization is rapidly replacing surgical resection of the prostate, because it eliminates the one- to three-day hospital stay and reduces bleeding, the risk of anesthesia, and impotence and incontinence, which can occur after surgery. The higher reimbursement rate makes this procedure attractive to physicians, hospitals, and outpatient surgery centers.

**Sources:** www.pharmacyonesource.com; www.salesandmarketingnetwork.com, January 6, 2006

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**Device Alerts: Defibrillators**

This is an update of the Preliminary Public Health Notifications of July 14 and October 13, 2005, regarding the Guidant Prizm 2 and Contak Renewal implantable cardioverter defibrillators. These devices were the subjects of a Class I recall announced by the FDA on July 1, 2005. The affected models are as follows:

- Ventak Prizm, 2 DR, Model 1861, manufactured on or before April 16, 2002
- Contak Renewal, Model H135, on or before August 26, 2004
- Contak Renewal 2, Model H155, manufactured on or before August 26, 2004

Guidant has informed the FDA of 14 additional occurrences exhibiting this failure mode for the Contak Renewal and Renewal 2 devices since the October 13 notification. As of December 21, 2005, 35 clinical failures, including five patient deaths, have been reported worldwide. Guidant has also informed the FDA of four clinical failures for the Ventak Prizm 2DR since the October 13 notification, including one patient death. As of December 21, 2005, 32 clinical failures, including two patient deaths, have been reported worldwide.

Source: www.fda.gov/cdrh/safety/122805-guidant.html