Idursulfase for Hunter Syndrome

The U.S. Food and Drug Administration (FDA) has approved idursulfase (Elaprase, Shire), the first product for the treatment of Hunter syndrome, also known as mucopolysaccharidosis II.

This rare, inherited disease usually becomes apparent in children one to three years of age. The disease is characterized by a defect in the production of the chemical iduronate-2-sulfatase, which is needed to break down complex sugars produced in the body. In severe cases, patients experience respiratory and cardiac problems, an enlarged liver and spleen, neurological deficits, and premature death.

Hunter syndrome affects about one out of 65,000 to 132,000 births. Designated as an orphan product, idursulfase was approved after a randomized, double-blind, placebo-controlled study of 96 patients. At the end of the 53-week trial, patients who received infusions of the study drug experienced, on average, a 38-yard greater increase in the distance walked in six minutes compared with the patients receiving placebo.

Because of the potential for severe hypersensitivity reactions, medical support should be available when idursulfase is administered. Patients and their physicians are encouraged to participate in a voluntary Hunter Outcome Survey, which has been established to monitor and evaluate the agent’s safety and long-term effects.

(Source: FDA, July 24, 2006.)

Therapies for HIV Infection
Triple-Combination Regimen: Atripla

Bristol-Myers Squibb and Gilead Sciences have announced the FDA’s approval of Atripla for the treatment of HIV-1 infection in adults.

Atripla is the first once-daily, single-tablet regimen for HIV intended as a stand-alone therapy or in combination with other antiretrovirals. It combines Sustiva (efavirenz) plus Truvada (emtricitabine and tenofovir disoproxil fumarate). Truvada is a fixed-dose product that contains Gilead’s Viread (tenofovir disoproxil fumarate) and Emtriva (emtricitabine).

Atripla can also be combined with other HIV/AIDS therapies. It was approved in less than three months.

The collaboration among the three companies is the first of its kind in the HIV/AIDS field. The new combination simplifies treatment and has the potential to reduce the emergence of drug-resistant HIV strains that develop more rapidly when patients forget to take some doses of their medications.

(Source: FDA, Market Watch; Dow Jones, July 12, 2006.)

Generic Approvals
Meloxicam (Mobic)

The FDA has approved several first generic versions of Boehringer Ingelheim’s Mobic tablets (meloxicam), which are indicated for the treatment of osteoarthritis.

The approval of meloxicam was the result of a “cluster” review approach, a process instituted by the FDA to facilitate the review of generic drug applications.

(Sources: FDA, July 20, 2006.)

Sertraline (Zoloft)

The first generic version of Zoloft tablets (sertraline, Ivax), as well as a liquid concentrate (sertraline HCl, Roxane), has been approved.

The tablet is indicated for adults with Major Depressive Disorder (MDD). The liquid is approved for MDD and some anxiety-related disorders.

(Source: FDA, June 30, 2006.)

Etonogestrel, an Implantable Contraceptive

A 68-mg progestin (etonogestrel) implant (Implanon, Organon) has been approved as the first single-rod contraceptive for women.

About the size of a matchstick, the implant is made of a soft medical polymer. A health care provider inserts it just beneath the skin on the inner side of a woman’s upper arm.

A low, steady dose of etonogestrel is continually released for a period of up to three years. After insertion, the implant is not usually visible. It can be removed at any time, after which the woman’s fertility returns to her pre-existing level.

Implanon has been used worldwide by approximately 2.5 million women in more than 30 countries since 1998. Organon USA will be sponsoring a national clinical training program to educate health care providers in insertion and removal of the implant. Only health care providers trained through the Organon-sponsored programs will be able to order Implanon. As the training program progresses, Implanon will
become more widely available in 2007. The implant does not protect against HIV infection or other sexually transmitted diseases.

(Source: Organon, July 18, 2006; www.implanon-usa.com.)

**Rituximab for Rheumatoid Arthritis Approved in Europe**

MabThera (rituximab, Roche) has been approved by the European Commission for the treatment of rheumatoid arthritis (RA) in Europe. In combination with methotrexate, rituximab is indicated for adults with severe active RA who have had an inadequate response to or are intolerant of current treatment options, including one or more tumor necrosis factor inhibitors.

The drug’s approval was based on the results of the multicenter, randomized, double-blind, placebo-controlled phase 3 REFLEX trial.

Rituximab is marketed in the U.S. by Genentech and Biogen Idec as Rituxan.

(Source: Roche, July 11, 2006.)

**Aprepitant as Antiemetic Therapy**

The FDA has approved aprepitant (Emend, Merck) for the prevention of postoperative nausea and vomiting (PONV). A single, oral 40-mg dose is administered within three hours before the induction of anesthesia.

Aprepitant belongs to a class of medications called substance P/neurokinin 1 (NK-1) receptor antagonists. It is thought to work by blocking nausea and vomiting signals to the brain.

The FDA’s approval was based on two multicenter, randomized, double-blind, active comparator-controlled, parallel-group studies of 1,658 patients undergoing open abdominal surgery.

Aprepitant is used only to help prevent nausea and vomiting after surgery. It is not used if patients have already begun to experience these symptoms.

(Source: Merck, July 11, 2006.)

**Combination Inhaler for Asthma Approved in U.S.**

AstraZeneca plans to launch a new budesonide/formoterol inhaler (Symbicort) for the maintenance treatment of asthma in patients 12 years of age and younger.

This twice-daily therapy combines budesonide, an inhaled corticosteroid, and formoterol, a rapid and long-acting beta2-agonist, into one inhaler.

The product will be available in a pressurized metered-dose inhaler. Two dosage strengths of budesonide/formoterol have been approved: 80/4.5 mcg and 160/4.5 mcg, respectively.

Symbicort is currently approved in more than 90 countries. The inhaler is scheduled to be available in the U.S. in mid-2007.

(Source: AstraZeneca, July 22, 2006.)

**NEW INDICATIONS**

**Lenalidomide/Dexamethasone for Multiple Myeloma**

The FDA has approved Celgene Corporation’s supplemental New Drug Application (sNDA) for lenalidomide (Revlimid) to be used in combination with dexamethasone (Decadron, Merck) for patients with multiple myeloma (MM) who have received at least one prior therapy.

Lenalidomide is also approved for patients with transfusion-dependent anemia caused by low-risk or intermediate-1-risk myelodysplastic syndromes associated with a deletion 5q cytogenetic abnormality with or without additional cytogenetic abnormalities.

MM is the second most common blood cancer in the U.S. It affects approximately 50,000 people, and 14,600 new cases of MM are diagnosed each year.

For more information, see the supplement on this product in Section Two.

(Source: Celgene, June 29, 2006.)

**Pegaspargase for Acute Lymphoblastic Leukemia**

Pegaspargase (Oncaspar, Enzon) is now approved for the treatment of children and adults with newly diagnosed acute lymphoblastic leukemia (ALL) as part of a multiple-drug chemotherapy regimen. Pegaspargase had originally been approved in 1994 only for patients with ALL who were unable to receive L-asparaginase (Elspar, Merck) because they were allergic to that drug.

This is one of the first products that will come with prescription information in a new format designed to provide clear and concise information to health professionals.

The use of pegaspargase as a replacement for L-asparaginase reduces the number of drug injections required, from 21 injections with Elspar to three with Oncaspar over the 20-week course of treatment.

The approval was based on a randomized, multicenter trial conducted by the Children’s Cancer Group.

(Source: FDA, July 24, 2006.)

**Gemcitabine for Recurrent Ovarian Cancer**

Gemcitabine (Gemzar, Eli Lilly) has been approved for women with recurrent ovarian cancer. This marks the fourth FDA indication for this anti-cancer agent.

The FDA specifies that gemcitabine should be used in combination with carboplatin for women with advanced ovarian cancer who have relapsed at least six months after initial therapy.

Patients who were given a gemcitabine/carboplatin combination experienced a significant improvement in progression-free survival and response continued on page 439
rates, compared with carboplatin alone.

Progression-free survival is particularly important in ovarian cancer. As the eighth most common cancer among women, it recurs in approximately 90% of women who are treated for the first time. The American Cancer Society has predicted that almost 21,000 new cases of ovarian cancer will be diagnosed in the U.S. in 2006.

Gemzar has been used in the U.S. for 10 years and is approved in more than 90 countries.

(Source: Eli Lilly, www.gemzar.com, July 17, 2006.)

**Rosiglitazone/Metformin as First-Line Therapy For Type-2 Diabetes**

A combination of rosiglitazone maleate and metformin HCl (Avandamet, GlaxoSmithKline) has been approved for use as initial treatment of type-2 diabetes as an adjunct to diet and exercise.

Avandamet was originally approved in the U.S. in 2002 as a second-line therapy for patients with uncontrolled blood glucose levels with metformin monotherapy. The drug is available in four tablet strengths of rosiglitazone/metformin: 2 mg/500 mg, 4 mg/500 mg, 2 mg/1,000 mg, and 4 mg/1,000 mg, respectively.

Rosiglitazone is marketed separately as Avandia.

Source: GlaxoSmithKline, July 11, 2006.)

**DRUG NEWS**

**FDA Advisory: Serotonin Syndrome**

The FDA has published safety information about taking triptans to treat migraine headaches together with some antidepressant medications, namely selective serotonin reuptake inhibitors (SSRIs) and selective serotonin/norepinephrine reuptake inhibitors (SNRIs).

A life-threatening condition called serotonin syndrome may occur when triptans are used together with SSRIs or SNRIs. It occurs when the body has too much serotonin. Symptoms may include restlessness, hallucinations, loss of coordination, fast heartbeat, rapid blood pressure changes, increased body temperature, overactive reflexes, nausea, vomiting, and diarrhea. The syndrome is more likely to affect patients who are starting or increasing the dose of a triptan, SSRI, or SNRI.

The FDA requests that all manufacturers of triptans, SSRIs, and SNRIs update their prescribing information to warn of the possibility of serotonin syndrome when triptans are taken with SSRIs or SNRIs.

(Source: FDA, July 20, 2006.)

**Tamoxifen: Breast Cancer Risk-Reduction Benefit Less Than Expected**

Most women at high risk for breast cancer do not experience an increased life expectancy by taking the anti-estrogen drug tamoxifen, according to researchers from the University of California, Davis, the University of San Francisco, the University of Pittsburgh, and McMaster University in Ontario, Canada. The use of tamoxifen to reduce the risk of developing breast cancer appears to help survival only for women at very high risk. Tamoxifen (Nolvadex, AstraZeneca) is an expensive cancer-prevention strategy, costing as much as $1.3 million per year of life saved.

Most breast cancers are estrogen receptor (ER)–positive. Among high-risk postmenopausal women (with a five-year risk of 1.67% or higher), the preventive use of tamoxifen has been found to cut the risk of developing breast cancer by almost half. This lowered risk, however, is accompanied by an increased risk of endometrial cancer, blood clots, cataracts, deep vein thrombosis, endometrial cancer, and stroke.

A history of hysterectomy is also an important consideration. Tamoxifen increases the risk of uterine cancer, but this risk does not apply to women who have had a hysterectomy.

Tamoxifen does not reduce the likelihood of ER-negative breast cancer. Failure to consider the probability of ER-negative breast cancer can lead to an overestimation of tamoxifen’s benefits. A benefit in survival did not appear until the women reached a five-year risk of 3% or higher.

Women taking tamoxifen for risk reduction, and who do develop breast cancer, are also more likely to develop an ER-negative tumor, which carries a worse prognosis.


**Telithromycin Warning Label**

The FDA has advised health practitioners and patients to be aware of rare but potentially serious health risks associated with telithromycin (Ketek, Sanofi-Aventis). As the first FDA-approved antibiotic of the ketolide class, it is indicated for the treatment of acute exacerbation of chronic bronchitis; acute bacterial sinusitis; and community-acquired pneumonia of mild to moderate severity, including pneumonia caused by resistant streptococcal infections.

The drug has been associated with rare cases of serious liver injury and liver failure, with four reported deaths and one liver transplant procedure after the administration of the drug. (More than 30% of the dose is metabolized by the liver.)

Sanofi-Aventis had stopped enrolling children in some studies because of reports that the drug might cause liver failure in adults.
At Carolinas Medical Center in Charlotte, North Carolina, three patients developed severe hepatotoxicity a few days after taking telithromycin. One of the three patients needed a liver transplant, and one patient died. Although two livers revealed massive tissue death, those two patients reported alcohol use.

In premarketing studies, liver problems were infrequent and usually reversible. On May 16, the FDA recommended the addition of a black-box warning mentioning liver problems.

The new warning results from the FDA’s vigilant monitoring of all drugs after their introduction to the market. When the agency approved telithromycin in 2004, the risk of liver injury was similar to that of other marketed antibiotics. As the product entered into wider use, the FDA received reports of serious liver problems, including some cases of acute liver failure leading to death or requiring liver transplantation.


**Are Antibiotics a Factor In Childhood Asthma?**

Exposure to at least one course of antibiotics in an infant’s first year of life may be a risk factor for childhood asthma, according to a meta-analysis from the University of British Columbia.

Researchers reviewed four prospective and four retrospective studies. Studies of exposure to at least one antibiotic were compared to studies of no exposure. Of 12,082 children, 1,817 had asthma. For the dose–response analysis, the researchers included data from 27,167 children, 3,392 of whom had asthma.

The pooled odds ratio for all eight studies was 2.05; the association was significantly stronger in the retrospective studies, possibly because of recall bias, the researchers acknowledge. The overall odds ratio for the dose–response analysis was 1.16 for each additional course of antibiotic.

(Source: Chest 2006; 129:610–618.)

**NEW MEDICAL DEVICES**

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

**Name:** Humira Pen

**Manufacturer:** Abbott Labs, Chicago

**Approval Date:** June 26, 2006

**Use Classification:** A pen is used to administer adalimumab (Humira), an inhibitor of tumor necrosis factor. Adalimumab is approved for the treatment of moderate-to-severe rheumatoid arthritis (RA) and psoriatic arthritis (PsA).

**Description:** Activated by one touch, the pen is easy to grasp for patients, many of whom may have swelling or stiffness in the hands. The pen has a needle that is not visible during the injection process, thereby producing a less painful experience for some patients. Patients place the pen against the skin, press a button, and wait for the medication to be injected.

**Purpose:** Adalimumab is delivered via a pen instead of the current method, a subcutaneous injection with a prefilled syringe.

**Benefit:** Injectable medications are among the most effective treatments available for RA and PsA. The pen represents an important advance because it offers people a more comfortable option than the syringe.

In the Trial of Usability in Clinical Settings of Humira Autoinjector vs. Prefilled Syringe (TOUCH), 90% of patients preferred the pen, rating it more convenient and easier to use; 80% found it to be less painful than other pens. Patients also found the pen preferable in terms of the time needed to complete the injection.

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

**Name:** Evicel Fibrin Sealant

**Manufacturer:** Omrix Biopharmaceuticals, Inc., New York, NY

**Approval Date:** July 10, 2006

**Use Classification:** This second-generation sealant is used to control bleeding during hepatic surgery.

**Description:** The sealant provides hemostasis support when conventional surgical techniques (sutures, ligatures, cautery) are inefficient or impractical.

**Purpose:** Surgeons can use the sealant in cases of severe, uncontrolled bleeding during procedures.

**Benefit:** Evicel contains no bovine-derived products, and there is no neurosurgical contraindication; unlike Crossseal, Omrix’s first-generation fibrin

**Name:** Vashe Wound Cleansing System

**Manufacturer:** PuriCore PLC, Malvern, PA/Stafford, England

**Approval Date:** July 7, 2006

**Use Classification:** The solution is indicated for wound cleaning, irrigating, moistening, and debriding acute and chronic dermal lesions.

**Description:** The Vashe System is based on products that create hypochlorous acid from the electrolysis of a saline solution from a tabletop or a floor-mounted system. This is the first wound-cleaning system of its kind that can produce a solution on-site at the point of use by the clinician.

**Purpose:** The solution is indicated for various ulcers (stage I–IV pressure ulcers, stasis ulcers, and diabetic ulcers), postsurgical wounds, first-degree and second-degree burns, abrasions, and minor skin irritations.

**Benefit:** This system is safe and mimics the body’s natural antimicrobial agent, hypochlorous acid.

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

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**NEW DRUGS**

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continued on page 479
sealant, Evicel does not need to contain a stabilizer. Evicel is immediately available to the surgeon.

Sources: www.biospace.com; www.pharmalive.com

Medical Device News Alerts

Infusion Pumps. Baxter Healthcare Corporation and two of its executives have agreed to stop manufacturing and distributing all models of the Colleague Volumetric Infusion Pump and the Syndeco Patient Controlled Analgesic Syringe Pump within the U.S. until it can correct manufacturing deficiencies and until the electronic devices comply with the FDA’s current Good Manufacturing Practice (CGMP) requirements and Quality System (QS) regulations for devices.

The pumps control the delivery of life-saving medications and nutrition to critically ill patients. They are used when a drug must be administered intravenously or through other routes, continuously or intermittently, for a prolonged period of time.


Power Packs. Disetronic Medical Systems and the FDA have announced a voluntary nationwide recall of the company’s D-TRONplus Power Packs, which supply power to the D-TRONplus Insulin Pump. There is the possibility that the power pack might shut down the insulin pump without any warning. If a shutdown occurs, insulin delivery is interrupted, possibly leading to uncontrolled diabetes mellitus, resulting in hyperglycemia, which may lead to serious patient injury and/or death.

Patients should replace the power pack every two weeks to prevent the pump from turning off unexpectedly. It is important that this two-week period not be extended. The company and its distributors will supply power packs with instructions free of charge by United Parcel Service for next-day shipment to all users until corrective actions have been implemented.