NEW DRUGS

Effient, an Anticoagulant For Heart Patients

The FDA has approved prasugrel tablets (Effient, Eli Lilly/Daiichi Sankyo) to lower the risk of blood clots from forming in patients who undergo angioplasty to unblock a clogged coronary artery. If blood platelets clump around the procedure site, clots can form and can lead to heart attack, stroke, and death.

The drug’s labeling will include a boxed warning alerting physicians that the drug can cause significant, sometimes fatal, bleeding. Prasugrel should not be used in patients with active pathological bleeding, a history of transient ischemic attacks, stroke, or an urgent need for surgery, including coronary artery bypass graft surgery.

For more information on prasugrel, please see this month’s Drug Forecast column on page 417.

Source: FDA, July 10, 2009

Onsolis, a Fentanyl Opioid For Breakthrough Cancer Pain

A form of fentanyl (Onsolis, Aveva/BioDelivery Sciences International/Meda) is now approved to manage breakthrough pain in cancer patients. This drug is indicated for opioid-tolerant patients with cancer who are 18 years of age and older and who already use around-the-clock opioids and who need high doses of an additional opioid drug.

Fentanyl, a potent opioid, is delivered through the oral mucous membranes. The absorbable film sticks to the inside of the cheek. Onsolis can provide strong pain relief to patients who are opioid-tolerant. For those who are not opioid-tolerant, however, it can lead to overdose, sudden serious breathing difficulties, and death.

Because fentanyl is subject to abuse and misuse, Onsolis was approved with a Risk Evaluation and Mitigation Strategy (REMS). This REMS is specific for Onsolis and is not intended to be viewed as a model REMS for other long-acting and extended-release opioids. Only participating pharmacies that send the product directly to the patient’s home may fill prescription orders.

A boxed warning states that Onsolis is not indicated for migraine, dental pain, or postoperative pain, intermittent use, or as-needed pain relief. Onsolis should not be substituted for other fentanyl products.

Source: FDA, July 16, 2009

Multaq for Heart Arrhythmias

Dronedarone tablets (Multaq, Sanofi-Aventis) have been approved to help maintain normal heart rhythm in patients with a history of atrial fibrillation or atrial flutter. This drug is indicated for patients whose hearts have returned to normal rhythm or for those who need drug therapy or electric shock to restore a normal heartbeat.

Dronedarone may cause critical adverse reactions, including death, in patients with recent severe heart failure. A boxed warning cautions that the drug should not be used in patients with severe heart failure.

In a clinical trial involving more than 4,600 patients, dronedarone reduced rates of cardiovascular hospitalization or death from any cause by 24% compared with placebo.

Common adverse reactions in clinical trials included diarrhea, nausea, vomiting, fatigue, and loss of strength.

Source: FDA, July 2, 2009

Generic Plan B Contraceptive for Teens

The first generic version of Duramed’s emergency contraceptive Plan B (levonorgestrel) tablets, 0.75 mg, has been approved. The generic product, made by Watson, will be available by prescription only for girls 17 years of age and younger.

Plan B was first approved in 1999 only as a prescription agent for females of all ages. In 2006, Plan B was approved for nonprescription use for women 18 years of age and older. Plan B remained available as a prescription-only product for girls 17 years of age and younger. On August 24, 2009, the marketing exclusivity held by Duramed expired for nonprescription use.

Levonorgestrel is not effective in terminating an existing pregnancy, and it does not protect against sexually transmitted diseases or HIV infection.

Source: FDA, June 24, 2009

Vaccine for 2009–2010 Seasonal Influenza

The FDA has approved a vaccine for 2009–2010 seasonal influenza in the U.S. This vaccine does not protect against the 2009 H1N1 influenza virus that resulted in the declaration of a pandemic by the World Health Organization on June 11, 2009.

The products are Afluria (CSL Ltd); Fluarix (GlaxoSmithKline) Flu-Laval (ID Biomedical); Fluvirin (Novartis); Fluzone (Sanofi Pasteur); and FluMist (MedImmune). The vaccine contains an A/Brisbane/59/2007 (H1N1)-like virus, an A/Brisbane/10/2007 (H3N2)-like virus, and a B/Brisbane/60/2008-like virus.

Source: FDA, July 23, 2009

NEW INDICATIONS

Alimta Maintenance Therapy For Advanced Lung Cancer

Pemetrexed (Alimta, Eli Lilly) is now indicated as maintenance therapy for patients with advanced or metastatic lung cancer. The drug disrupts metabolic processes that depend on folate, a B vitamin, which is necessary for cell replication.

In a clinical trial, patients with pre-
dominantly squamous cell cancer did not benefit from pemetrexed, but those with other subtypes survived an average 15.5 months following treatment compared with 10.3 months for patients who received a placebo. Each patient received standard medical care. Adverse events included damage to blood cells, fatigue, nausea, loss of appetite, tingling or numbness in the hands and feet, and skin rash.

Initially approved in 2004 to treat mesothelioma, pemetrexed was later indicated for patients with non–small-cell lung cancer whose disease had worsened with prior chemotherapy. Pemetrexed is also indicated as an initial therapy for patients with advanced non–small-cell lung cancer.

Source: FDA, July 6, 2009

**Forteo for Glucocorticoid-Induced Osteoporosis**

Eli Lilly’s teriparatide (rDNA origin) injection (Forteo) has been approved to treat osteoporosis associated with sustained, systemic glucocorticoid therapy in men and women at high risk of fractures. Glucocorticoid therapy, often prescribed for inflammatory conditions such as rheumatoid arthritis, is the most common cause of secondary osteoporosis.

The use of glucocorticoids can lead to reduced bone formation. Teriparatide can counteract this effect by stimulating bone formation.

The company has updated the language in the existing boxed warning regarding the risk of osteosarcoma to re-emphasize that teriparatide should not be used in young patients whose bones are still growing. A voluntary patient registry is also being established.

Source: Eli Lilly, July 23, 2009

**DRUG NEWS**

**Pharmacists Must Dispense Plan B Contraceptive**

Regardless of their personal opinions or religious beliefs about the morning-after contraceptive, pharmacists are now required to dispense the Plan B tablet, a federal appeals court ruled Wednesday. The case could affect policy across the U.S. A supermarket pharmacy in Olympia, Washington, failed in its challenge of changes made to the 2007 regulations requiring all Washington pharmacists to have and dispense the product. Ralph’s Thriftyway and two pharmacists employed elsewhere had sued Washington state officials over the regulation.

The plaintiffs claimed that their religious beliefs prevented them from dispensing the medication and said that the new regulations were unfair, forcing them to choose between their jobs and their religion.

The plaintiffs, who had sought protection under the First Amendment right to free exercise of religion, won a temporary injunction from the U.S. District Court in Seattle pending trial. The order stopped state officials from penalizing pharmacists who refused to dispense Plan B, but the U.S. 9th Circuit Court of Appeals has lifted the injunction.

Source: Drug Topics, July 16, 2009

**Labeling Changes**

**Chantix and Zyban**

The FDA is adding a boxed warning on the prescribing information for the smoking-cessation drugs varenclidine (Chantix, Pfizer) and bupropion (Zyban, GlaxoSmithKline) to highlight the risk of serious mental health events, such as behavioral changes, depressed mood, hostility, and suicidal thoughts.

Bupropion is also sold as the antidepressant Wellbutrin. Varenclidine and bupropion already carry a boxed warning for suicidal behavior in patients with psychiatric disorders.

Some patients taking the drugs experienced unusual changes in behavior, became depressed, or had worsening depression and thoughts of suicide or dying. The problems often began shortly after they started taking the drug and ended when they stopped taking it; however, some patients continued to have symptoms after stopping the medication.

Neither agent contains nicotine, and some of the symptoms might be a response to nicotine withdrawal.

The FDA also is requesting more information in the warnings section of the prescribing information and an updated medication guide.

Source: FDA, July 1, 2009

**Antirejection Drugs**

Manufacturers of some drugs used as immunosuppressants in renal transplantation will be required to update the labeling to reflect an increased risk of opportunistic infections and activation of latent viral infections. The label changes affect sirolimus (Rapamune, Wyeth); cyclosporine (Sandimmune) as well as generic brands and modified cyclosporine (Neoral, Sandoz/Novartis) and generic brands; mycophenolate mofetil (CellCept, Roche) and generic brands; and mycophenolic acid (Myfortic, Novartis).

These infections can lead to serious outcomes, including kidney graft loss. Information about the increased risk of opportunistic infections is already included in the labeling for tacrolimus (Prograf, Astellas US).

Source: FDA, July 14, 2009

**Erbilutix and Vectibix**

Bristol-Myers Squibb, Eli Lilly, and Amgen are now able to state that colon cancer patients with a mutation to the KRAS gene do not respond to two of their drugs. The FDA has approved revised labeling for cetuximab (Erbilutix, Bristol-Myers Squibb/ImClone) and panitumumab (Vectibix, Eli Lilly and Amgen), which is in the same drug class. Merck
Accutane Pulled from Market

Roche has discontinued the manufacture and distribution of isotretinoin (Accutane, Roche), a medication for severe acne, in the U.S. The company said that the withdrawal was based on business reasons. Isotretinoin will continue to be available as a generic agent.

First developed as a chemotherapy agent, the capsules were approved in 1982 and became Roche’s second-largest selling drug before its patent expired in 2002 and other companies began marketing generic versions.


Catheter Ablation Or Antiarrhythmic Drugs?

Which treatment helps patients with atrial fibrillation survive longer—catheter ablation or antiarrhythmic drugs? There was no difference, according to researchers from Greece and Germany. In a meta-analysis of eight trials involving 930 patients, mortality and rates of stroke and transient ischemic attacks (TIAs) were similar; seven patients died, three in the ablation arm and four in the drug-therapy arm.

This finding appears to contradict results from nonrandomized studies indicating improved survival after ablation, compared with pharmacotherapy, and also contradicts the expected effect of a method of providing potentially curative treatment of a disease associated with increased mortality.

However, a main characteristic of the randomized trials was the low-risk population, consisting of younger patients (mean age, 51 to 65 years), with a low prevalence of structural heart disease and thus a good prognosis. By contrast, the nonrandomized trials had involved older, sicker patients. The researchers cited one study that followed patients for a median of 2.5 years, showing a mortality rate of 6.5% in the ablation arm and 14.3% in the drug therapy group.

Another factor might be the study’s duration. The studies in the meta-analysis tended to be relatively short (12 months). In the nonrandomized trials, the described survival benefits seemed to become evident after the first year of follow-up. Moreover, the researchers added, the regimen of oral anticoagulation after the catheter ablation was not uniform. Regimens ranged from continuous anticoagulation after ablation to discontinuation at six weeks in the absence of arrhythmia recurrences, thereby limiting the interpretation regarding the occurrence of stroke and TIAs.

Source: Am Heart J 2009;158:15–20

Hormone Replacement Therapy: Less Precise Mammography

Density in breast tissue is affected by exogenous and endogenous reproductive hormones. As breast density increases, the sensitivity and specificity of mammography decrease. Women receiving hormone replacement therapy (HRT) are more likely to need additional mammograms. Women who discontinue HRT between mammographic screenings have had reduced tissue density to a level similar to that in nonusers of HRT. In fact, some reports have encouraged women to consider suspending HRT in the short term, with the idea that cancer will be more easily detected.

University of Washington researchers sought to test whether stopping HRT for one to two months before screening could improve mammographic accuracy.

In a randomized trial, 1,704 women 45 to 80 years of age who were using HRT were scheduled for screening. One group did not suspend HRT, and the other two groups stopped therapy for one or two months.

Just over 10% of the women needed...
further imaging. Recall rates were 11.3% for the women who did not suspend HRT (61 of 542 women), 12.3% in the women who stopped therapy for one month (50 of 478 women), and 9.8% in the women who suspended HRT for two months (44 of 451 women).

Suspending HRT did result in less breast density. Although the reductions in tissue density and in the number of recalls were small, they might have a meaningful effect in larger groups. Despite the benefit of reduced breast density, suspending HRT was also linked to increases in menopausal symptoms.


**Statins Might Not Help Patients with Pneumonia**

Thanks to their anti-inflammatory and immunomodulatory effects, statins have been linked to reduced morbidity and mortality caused by infection, including pneumonia. But in a study of older adults, researchers from the University of Washington found no reduced risk of pneumonia among those taking statins.

Compared with controls, patients with pneumonia were more likely to have severe chronic lung and heart disease and functional or cognitive impairment. Approximately 15% of both groups were using statins. Among patients admitted to the hospital, 17% of those with pneumonia and 14% of controls were using statins.

The researchers urge caution in interpreting the results. Statin use is less common in people with certain comorbidities, so the dramatic negative associations reported in the earlier studies could reflect “healthy user bias.” More work is needed to learn how to improve the content of large databases by incorporating more detailed data, such as comorbidities.

Source: *BMJ*, June 16, 2009

**Could Clozapine Have Saved Lives of Patients With Schizophrenia?**

According to a new study, thousands of patients with schizophrenia might not have died if they had received the antipsychotic agent clozapine (e.g., Clozaril, Novartis).

Approved in the 1970s, clozapine was banned for about 10 years because of a rare but potentially deadly side effect: up to 2% of patients lose white blood cells while taking the drug. The drug was brought back to the market in the 1980s with warnings about its use. In most developed countries, clozapine is recommended only as a last resort if patients have already tried two other drugs but have not improved.

In a study comparing death rates of about 67,000 patients in Finland with those of the general population between 1996 and 2006, researchers found that patients taking clozapine had the lowest risk of dying compared with other patients with schizophrenia.

With these surprising findings, there might now be a reason to revise the guidelines to make clozapine available to more patients. Even though the use of antipsychotic agents has increased in the last decade, patients with schizophrenia in Finland die about two decades earlier than other people.

The researchers of this study concluded that newer drugs, such as quetiapine (Seroquel), haloperidol (Haldol), and risperidone (Risperdal) increase the risk of death by 41%, 37%, and 34%, respectively, compared with older drugs. In contrast, clozapine was associated with a 26% lower risk of death.

Clozapine appears to be particularly effective in reducing suicidal tendencies in schizophrenic patients (suicide accounts for about 40% of unexpected deaths). One expert suggested that clozapine has been overlooked in part because its patent expired long ago, and not much money can be made from marketing it.

Sources: *Lancet* online, July 13, 2009; Associated Press, July 12, 2009

**Antibiotic Resistance and Urinary Tract Infections**

Antibiotic resistance is making it more difficult to treat common urinary tract infections (UTIs). Resistance to beta-lactam antibiotics prompted a switch to trimethoprim/sulfamethoxazole (TMP/SMX, Bactrim); however, this agent was also susceptible to resistance, and fluoroquinolones became the new first-line choice.

Researchers from Istanbul say that fluoroquinolone overuse, leading to resistance, is similar to that against TMP/SMX. In a retrospective study, fluoroquinolones were the most frequently prescribed antibiotics at their institution, with ofloxacin (Floxin, PriCara) the most popular choice. The resistance rate for TMP/SMX was 34%. All of the antibiotic-resistant microorganisms were *Escherichia coli*. The resistance rate for the fluoroquinolone group was 16.4%; again, the resistant microorganisms were *E. coli*. The high resistance rates for both drugs led the researchers to caution against the empirical use of fluoroquinolones.


**RESEARCH NEWS**

**Genetics and Blood Pressure In African-Americans**

Researchers from the National Institutes of Health (NIH) have discovered five genetic variants related to blood pressure (BP) in African-Americans. This genome-wide association study may provide new clues to treating and preventing hypertension in this population.

About one-third of adults in the U.S. have chronic high BP. In African-Ameri-
Researchers analyzed DNA samples from 1,017 participants in the Howard University Family Study who identified themselves as African-American. Five genetic variants were found significantly more often in people with hypertension than in those without it. The variants were associated with high systolic BP but not with diastolic BP or combined systolic/diastolic BP.

Although the effect of each genetic variant was modest, the findings extended the scope of what was known about genetics and hypertension. Calcium-channel blockers already target one of the genes, CACNA1H.

Source: *PLoS Genetics*, July 17 online

**NIH and Wikimedia To Develop Online Health Information**

The National Institutes of Health and the Wikimedia Foundation (the nonprofit organization that operates the Wikipedia online encyclopedia) plan to collaborate to make health and science information more accessible and reliable.

Wikipedia contains nearly 13.5 million articles written in more than 250 languages. On average, more than 14 million pages are viewed per hour.

Experts at the NIH will be able to contribute to Wikipedia to help develop best practices. Instructions about how to contribute will be available on the NIH and the Wikipedia Web sites for scientists throughout the U.S.


**NEW MEDICAL DEVICES**

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

**Name:** Architect Core Reagent Kit, Calibrator, and Controls

**Manufacturer:** Abbott Laboratories, Diagnostic Division, Abbott Park, Ill.

**Premarket Approval Date:** April 10, 2009

**Use Classification:** This immunoassay is used to detect immunoglobulin G and M (IgG and IgM) antibodies to hepatitis B core antigen (anti-HBC). Along with other laboratory results, the kit is intended as an aid in the diagnosis of acute, chronic, or resolved hepatitis B virus (HBV) infection in adults, children, and newborns.

**Description:** A sample of the patient’s blood is combined with recombinant HBc antigen (rHBcAg)-coated paramagnetic microparticles. If anti-HBc antibodies are present in the blood, they bind to the microparticles. A labeled anti-human conjugate is added, producing a chemiluminescent reaction with the antibodies bound to the microparticles. The system can measure the amount of light produced. Comparing an active calibration determines the presence or absence of anti-HBc.

**Purpose:** The laboratory test is used to detect antibodies associated with HBV core antigen. The presence of anti-HBc antibodies can indicate current or previous infection with HBV.

**Benefit:** The test results, in addition to other clinical findings, help to identify the stage of HBV infection and an appropriate course of treatment.

Source: www.ida.gov

**Name:** Microcyn Skin and Wound Gel

**Manufacturer:** Oculus Innovative Sciences, Inc., Petaluma, Calif.

**Approval (510k) Date:** May 27, 2009

**Use Classification:** The gel has been approved as both a prescription and over-the-counter formulation. The prescription product, under the supervision of a health care professional, is indicated for patients with exuding wounds (ulcers of the leg, pressure ulcers, and diabetic ulcers) and for managing mechanically or surgically debrided wounds.

**Description:** The clear, amorphous, isotonic hydrogel helps to maintain a moist environment that helps speed wound healing. A biocompatible, shelf-stable solution is currently sold in the U.S., Europe, India, China, Mexico, and some Middle East countries. Several of the solutions are used to treat a wide range of pathogens, including antibiotic-resistant strains of bacteria (such as methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant enterococci), viruses, fungi, and spores. These solutions also help to increase blood flow to the wound site, reduce inflammation and pain, and facilitate rapid wound closure.

**Purpose:** An antimicrobial agent is delivered to the wound bed. Several products based upon the Microcyn Technology include new formulations that help to reduce the need for antibiotics during infection care.

**Benefit:** This is the first hydrogel product that is reimbursable by both Medicare and Medicaid. The nonadherent gel keeps wounds moist without the need for gauze or adhesive strips. The product can be removed without trauma to the wound bed.

Sources: www.medicalnewstoday.com; www.streetinsider.com; http://ir.oculusis.com

**Name:** Scandinavian Total Ankle Replacement System (STAR)

**Manufacturer:** Small Bone Innovations, Inc., Morrisville, Pa.

**Premarket Approval Date:** May 28, 2009

**Use Classification:** A non-cemented implant is used to replace a painful arthritic ankle joint caused by osteoarthritis, post-traumatic arthritis, or rheumatoid arthritis.

**Description:** STAR is the only FDA-approved total ankle replacement system for uncemented use, which allows
for better in-growth, stabilization, and preservation of bone. The mobile-bearing system moves across a flexible polyethylene surface and does not restrict the ankle joint from rotating.

**Purpose:** As an alternative to fusion surgery, the implant is used to replace an arthritic or deformed ankle while preserving some range of motion in the joint.

**Benefit:** STAR has been found to be superior in effectiveness and safety when compared with ankle fusion. STAR was less invasive than the fusion technique, resulting in less blood loss, a shorter operating time, better pain relief, and more mobility of the foot.

**Sources:** www.fda.gov; wwwtotalsmallbone.com; www.medicalnewstoday.com

**Device Recall**

In June 2009, Medtronic Neurologic Technologies recalled its Bioglide Ventricular Snap Shunt Catheter, a component of a shunt system that is used to treat hydrocephalus. The catheters had the potential to become detached from the snap base assembly, increasing the need for emergency corrective surgery.

Medtronic has requested that its customers stop having the device implanted and asked them to return all unused catheters to the company. Patients who already have the shunt system implanted but who are not experiencing symptoms of shunt malfunction should continue to follow standard protocols.

If a disconnection does occur, symptoms of hydrocephalus (e.g., nausea, vomiting, headache, lethargy, change in mental status, and seizures) may return. Patients with these symptoms should be assessed for shunt malfunction.

Source: FDA, www.accessdata.fda.gov