NEW DRUGS

**Everolimus (Afinitor)**  
**For Kidney Cancer**

Everolimus (Afinitor, Novartis) tablets have been approved for patients with advanced kidney cancer whose disease has progressed after they have tried other cancer therapies. In a clinical trial, patients receiving everolimus lived more than twice as long without tumor growth as those who did not receive the drug.

For more information on everolimus, please see this month’s Pharmaceutical Approval Update, page 262.

Source: FDA, March 30, 2009

**Generic Topamax To Prevent Seizures**

The FDA has approved the first generic versions of Ortho-McNeil’s Topamax tablets (topiramate) to prevent seizures. Companies receiving approval include Roxane, Par, Mylan, Barr, Teva, Ranbaxy, CIPLA, Glenmark Generics, Cobalt, Apotex, Zydis, Aurobindo, Torrent, Invagen, Unichem, Sun, and Pliva Hrvatska.

Prescribing information for the generic brands differs from that for Topamax, because some uses of Topamax continue to be protected by patents and exclusivity. The labeling for Topamax and the generic agents contains a warning about metabolic acidosis. Topiramate has been associated with a sudden decrease in vision and increased pressure in the eye.

Source: FDA, March 30, 2009

**Ixiaro Vaccine**  
**For Japanese Encephalitis**

Ixiaro, a vaccine to prevent Japanese encephalitis (JE), has been approved. The vaccine is manufactured by Intercell and distributed by Novartis.

JE is caused by a mosquito-transmitted virus found mainly in Asia. The virus that causes JE affects membranes surrounding the brain. JE usually starts as a flu-like illness but can worsen, causing high fever, neck stiffness, brain damage, coma, or even death. The disease is not spread from person to person.

In clinical studies, healthy subjects in the U.S. and Europe received either Ixiaro or Je-Vax (Sanofi-Pasteur/Biken), which has been discontinued. Ixiaro produced enough levels of antibodies in the blood to protect against JE; only two doses were needed, compared with three needed for Je-Vax.

Ixiaro will be the only available vaccine for JE in the U.S. Please see this month’s Pharmaceutical Approval Update column on page 263.

Source: FDA, March 30, 2009

**Golimumab (Simponi) For Inflammatory Diseases**

Centocor Ortho Biotech, Inc., has announced the FDA’s approval of golimumab (Simponi) for adults with moderately to severely active rheumatoid arthritis, active psoriatic arthritis, and active ankylosing spondylitis. This human monoclonal antibody can be used in combination with methotrexate for moderately to severely active rheumatoid arthritis and with methotrexate or alone for active psoriatic arthritis. This is the first patient-administered anti–tumor necrosis factor–alpha therapy offering a once-monthly treatment. In the U.S., it is available as a 50-mg once-monthly subcutaneous injection, delivered by an autoinjector or by a prefilled syringe.


**Coartem Tablets for Malaria**

The FDA has approved artemether/lumefantrine (Coartem, Novartis) to treat acute, uncomplicated malaria infections in adults and children weighing at least 11 pounds (5 kg). Coartem is not indicated for treating severe malaria or for preventing malaria.

Patients with severe malaria have altered consciousness and other metabolic and end-organ complications, and they should be given intravenous (IV) anti-malarial therapy.

Malaria is transmitted from an infected mosquito. Left untreated, the illness can cause severe complications, including death. About 90% of deaths from malaria occur in sub-Saharan Africa, but the disease is also prevalent in parts of Asia and Latin America. Coartem has been effective in geographical regions with reported resistance to chloroquine, a drug that prevents and treats malaria.

The tablets are to be taken with food, particularly fat-containing foods, for better absorption. Artemether, an active ingredient in the tablets, is derived from the leaves of the *Artemisia annua* plant.

Source: FDA, April 9, 2009

**Benzyl Alcohol Lotion for Lice**

The FDA has approved a prescription drug, Benzyl Alcohol Lotion, 5% (Sciele Pharma/Shionogi) for the treatment of head lice (*Pediculosis capitis*) in patients six months of age and older. In two studies, subjects received two 10-minute treatments of either the lotion or a topical placebo one week apart. Two weeks after the final treatment, more than 75% of those receiving the lotion were free of lice.

The lotion should be applied only to the scalp or to hair attached to the scalp. It is not approved for use in children younger than six months of age.

Source: FDA, April 9, 2009

**Psoriasis Drug Efalizumab (Raptiva) to Be Withdrawn From Market**

Genentech has begun a voluntary, phased withdrawal of its psoriasis drug efalizumab (Raptiva) from the U.S. market. Approved by the FDA in 2003,
efalizumab is a once-weekly injection for adults with moderate-to-severe plaque psoriasis.

The company is taking this action because of a potential risk of progressive multifocal leukoencephalopathy (PML), a rare, serious progressive neurological disease caused by a virus that affects the central nervous system. By June 8, 2009, this medication will no longer be available in the U.S. Prescribers are being requested not to begin prescribing efalizumab for new patients.

The risk of PML is generally associated with long-term use. PML usually affects people with weakened immune systems. There is no known effective therapy for PML.

In October 2008, the drug’s label was updated to warn of the risk of life-threatening infections, including PML. In February 2009, the FDA informed patients and prescribers of the risk of PML in those taking efalizumab after receiving reports of four patients with PML, three of whom died. In March 2009, the FDA approved a medication guide for efalizumab and included additional information in the labeling regarding PML.


FDA Cracks Down On Unapproved Drugs Cough and Cold Products …

Neilgen Pharma and Advent Pharmaceuticals are recalling all prescription cough and cold drug products sold on or after March 5, 2008, because they have not been approved by the FDA process.

Consumers should stop using and should return these products to the place of purchase and contact their health care professional to obtain a replacement medication or prescription. Although the FDA has not established the safety and effectiveness of the products, patient exposure to them is not likely to cause adverse health consequences. Both companies have stopped producing these agents, and no injuries have been reported to date.

These products are being removed at the retail level only. All of the agents were distributed to wholesalers located in Alabama and North Carolina.

This recall includes RY-Tann and D-Tann CT caplets; D-Tann CT, AT, CD, and DM suspensions; Ben-Tann suspension; B-Vex and B-Vex D suspensions; Brom-Tann, 8-mg/DM Tann, 60-mg/ PSE Tann, 90-mg suspension; DM-Tann, 30-mg/PE Tann, 25-mg/Brom Tann, 10-mg suspension; and PE Tann, 20-mg/CP Tann, 4-mg suspension.

Source: FDA, April 20, 2009

… and Narcotics for Pain

The FDA has requested that nine companies stop manufacturing 14 unapproved, widely used narcotics to treat pain. The products include high-concentrate morphine sulfate oral solutions and immediate-release tablets containing morphine sulfate, hydromorphone, or oxycodone. This action does not include oxycodone capsules.

Manufacturers will be allowed to temporarily continue to market and distribute a high-concentrate 20-mg/mL morphine sulfate oral solution in order to avoid a shortage. This product is used to alleviate pain in terminally ill patients. The FDA has determined that this dosage form is medically necessary, and it can remain on the market until an approved alternative becomes available.

The nine companies include Mallinckrodt, Physicians Total Care, Boehringer Ingelheim, Roxane, Cody, Glenmark, Lannett, Lehigh Valley Technologies, and Xanodyne. Manufacturers have 60 days to stop making these products, and distributors have 90 days to stop shipping existing products.

Source: FDA, April 2 and April 9, 2009

Better Survival With Drug-Coated Stents

Patients 65 years of age and older with heart disease who receive drug-eluting stents to prevent arterial blockages are more likely to survive and may be less likely to have heart attacks than patients receiving bare-metal stents.

Researchers from Duke University, the Agency for Healthcare Research and Quality (AHRQ), and Kaiser Permanente found that patients with coated stents had an 18% better survival rate over the 30-month study period and were 16% less likely to have a heart attack.

The FDA approved two drug-coated stents in 2003 and 2004 but issued precautionary advisories in 2006 after receiving reports of blood clot formation and deaths. Subsequent studies produced conflicting results.

Better outcomes with drug-eluting stents might be explained as follows. Patients receiving coated stents must take anticoagulants for a long time after the procedure. Patients who receive bare-metal stents usually take anticoagulants for a shorter period of time and may take them less often. Patients with coated stents might also visit their doctors more often after hospital discharge and may receive drugs to lower cholesterol levels and manage other heart conditions more often than patients who receive bare-metal stents.

Source: AHRQ, March 28; http://effectivehealthcare.ahrq.gov

Levonorgestrel Emergency Contraception (Plan B) Now Available to Younger Women

On March 23, 2009, a federal court issued an order directing the FDA, within 30 days, to permit Duramed’s Plan B to be made available to women 17 years of age and older without a prescription. The government does not intend to appeal this decision. In accordance with the
Vancomycin (Vancocin) May Prolong Extubation

Patients in intensive-care units (ICUs) with acute, severe hospital-acquired pneumonia tend to spend more time receiving mechanical ventilation and may need a longer time to extubate if they are taking vancomycin (Vancocin, Viropharma).

Researchers at Duke University in Durham and at Drexel University in Philadelphia studied 219 patients, 83 of whom died. Vancomycin was one of the independent predictors of mortality, nearly doubling the risk of death. The median time to extubation was six days; vancomycin extended the duration of mechanical ventilation by almost one week. The median was eight days, with a range of three to 17 days.

Other than the association between vancomycin and the time to extubation, the researchers found no specific empirical antimicrobial regimen linked to adverse clinical outcomes. However, because most of the patients were treated with combination therapy, it was difficult to analyze individual variables.

Source: Am J Infect Control 2009;37:143–149

Hydromorphone and Older Adults

In the past decade, the number of adults 65 years of age and older who visited emergency departments (EDs) grew by 11%, with pain their most common chief complaint. Researchers from Montefiore Medical Center in Bronx, New York, say that these patients tended to receive too little analgesia. As EDs become more crowded, the risk of undertreated pain is expected to worsen.

Although morphine is a first-line parenteral opioid used for severe pain, a significant minority of patients have intolerable adverse effects or inadequate pain relief, or both. Thus, hydromorphone, which is more than seven times more potent than morphine, is being used more often even though evidence for such a strategy may be lacking, the investigators add. Studies have compared hydromorphone with morphine in younger adults, but it is unclear whether older adults respond differently.

In a double-blind study, 194 patients with severe, acute pain were randomly assigned to receive a single dose of 0.0075 mg/kg of IV hydromorphone or 0.05 mg/kg of IV morphine. The patients rated their pain on a scale ranging from zero (no pain) to 10 (the worst pain possible). The mean decreases in pain from the baseline to 30 minutes were 3.8 for hydromorphone and 3.3 with morphine. The data suggest that hydromorphone and morphine did not differ clinically or statistically in efficacy or safety in older adults. The incidence of adverse effects also did not differ.

A key point is that neither drug provided more than 50% pain relief for most patients—an amount considered “largely unsatisfactory,” the researchers emphasize. Approximately one-third of patients in both groups reported fair or poor satisfaction with pain medication, and about one-third also reported sligt or no pain relief. The findings suggest that higher initial doses, more frequent administration by titration, or both, might be necessary for older patients.

Source: Am J Geriatr Pharmacother 2009;7:1–10

Life-Threatening Effect Of Levofloxacin (Levaquin)

Hypoglycemia is a rare but potentially fatal adverse effect of levofloxacin (Levaquin, PriCara). Seven cases have been reported; physicians from Caritas Saint Elizabeth’s Medical Center of Boston and Tufts University, reporting on another case, suggest that the very rarity of the adverse effect may mean that it is easily overlooked. In a recent survey, 80% of physicians were unaware that levofloxacin could cause hypoglycemia, even though in four of the seven reported cases, delays in recognizing the cause of the hypoglycemia led to unfortunate consequences.

Their patient, a 65-year-old woman with type-2 diabetes, chronic obstructive pulmonary disease, chronic kidney disease, and cirrhosis, presented with a two-day history of cough, worsening dyspnea, and acute renal failure. She was treated with diuretics, corticosteroids, and levofloxacin. The last dose of glipizide (Glucotrol, Pfizer), which was used to treat patients with diabetes, was given eight hours before the first dose of levofloxacin.

The next day, the patient had several episodes of hypoglycemia and received repeated infusions of 50% dextrose. The hypoglycemia persisted over the next 72 hours, during which she received more dextrose infusions and glucagon. On the fourth day, levofloxacin was discontinued. After two days, her glycemic values gradually returned to baseline levels.

According to the Naranjo Adverse Drug Reaction Probability Scale, the hypoglycemia was possibly caused by levofloxacin.

The authors say that the patient’s persistent, severe hypoglycemia; her lack of response to dextrose despite steroid therapy; and her elevated serum insulin levels, even with low blood glucose values, imply a different mechanism for the hypoglycemia than the usual suspects—renal failure, hepatic dysfunction, and glucose-lowering medications. They note
that the inappropriately uninhibited levels of insulin were consistent with an effect of levofloxacin on beta-cell function, and they cite data from animal studies showing that fluoroquinolones directly stimulate insulin secretion from pancreatic B cells.

Source: Am J Med 122:e3–e4

DEVICES IN THE NEWS

Quick Test for Avian Flu Virus

The FDA has approved a rapid test for detecting influenza A/H5N1, a disease-causing subtype of the avian influenza A virus that can infect humans.

Arbor Vita’s Advantage A/H5N1 Flu Test detects influenza A/H5N1 in throat or nose swabs collected from patients who have flu-like symptoms. In less than 40 minutes, the test identifies a specific protein (NS1) that indicates the presence of the influenza A/H5N1 virus subtype. Previous tests to detect this subtype took three or four hours to produce results.

The H5N1 subtype is found mostly in birds, but it has also occurred in humans who have come into contact with infected poultry. The subtype also has the potential to mutate further, causing an influenza pandemic and life-threatening illness, although it has not been detected in the Americas.

Source: FDA, April 9, 2009

Securus Suture System In Arthroscopic Surgery

Core Essence Orthopaedics, Inc., has received approval for Securus, a knotless suture system. The device makes it easier for surgeons to use minimally invasive techniques in rotator cuff repairs at a time when the demand for arthroscopic surgery is increasing. Only a small fraction of shoulder tendon repairs are performed with less invasive arthroscopic surgical approaches.

Unlike most current knotless anchors, Securus can be adjusted during the operation.

Source: Core Essence, April 8, 2009

Genetic Test for Hair Loss

PharmaGenoma, Inc., and its subsidiary, HairDx LLC, have announced an agreement with an Italian company to provide genetic testing to predict androgenetic alopecia, the most common type of hair loss in men and women. Biodue Srl will initially offer the test to patients through Italian dermatologists.

The HairDx test collection kit is listed with the FDA as a Class I medical device.

Source: HairDx, April 14, 2009, www.hairdx.it

FDA to Review Pre-1976 Medical Devices

Manufacturers of 25 types of medical devices that were marketed before 1976 must submit safety and effectiveness data to the FDA so that the devices can be evaluated for their levels of risk.

These 25 device types were sold in the U.S. before the Medical Device Amendments to the Food, Drug, and Cosmetic Act of 1976, which authorized the FDA to review new devices. The FDA’s announcement is the first step toward completing the review of Class III devices predating the 1976 law.

The FDA classifies medical devices into three categories of risk. Class III devices (e.g., heart valves, intraocular lenses) represent the highest level of risk and must be shown to be safe and effective before they may be marketed. Class I and Class II devices (e.g., adhesive bandages, wheelchairs) are associated with lower risks.

Source: FDA, April 9, 2009

New Gel for Wound Care

American Biotech Labs, LLC, has been granted formal approval by the FDA to market its ASAP Wound Dressing Gel throughout the U.S.

The topical gel is indicated for treating cuts, lacerations, abrasions, first-degree and second-degree burns, and skin irritations. The product utilizes the company’s SilverSol Technology.


NEW MEDICAL DEVICES

Marvin M. Goldenberg, PhD, RPh, MS

Name: LifeStent FlexStar and FlexStar XL Vascular Stent Systems

Manufacturer: Bard Peripheral Vascular, Inc., Tempe, Ariz.

Approval Date: February 13, 2009

Use Classification: This stent is used to treat patients with narrowing of the superficial femoral or proximal popliteal artery caused by atherosclerosis.

Description: A catheter with a deflated balloon at its tip is inserted into a blood vessel in the groin. The catheter is advanced within the vessel to the narrowed section of the superficial femoral or proximal popliteal artery. The balloon is inflated to open the narrowed artery by pushing the plaque against the artery wall. The angioplasty balloon and its catheter are removed, and the stent system is advanced through the same vessel and positioned within the expanded artery. The stent, constructed of nickel-titanium alloy (nitinol) tubing, is then deployed by retracting the outer sheath after it is positioned in the artery, and it opens automatically over the blockage. The delivery catheter is removed. The stent remains permanently in the artery and supports the newly opened section of the vessel.

Purpose: The stent is used to reopen narrowed regions of the superficial femoral and proximal popliteal arteries, which supply blood to the legs.

Benefit: The inside lining of the artery grows over the stent approximately eight weeks after the stent is inserted. The stent holds open the narrowed artery...
and improves blood flow to the legs.

Source: FDA, www.fda.gov

**Name:** Reclain Deep Brain Stimulation (DBS) Therapy

**Manufacturer:** Medtronic, Inc., Minneapolis, Minn.

**Approval Date:** February 19, 2009

**Use Classification:** The deep brain stimulator is used to treat patients with severe obsessive–compulsive disorder (OCD). The stimulator was approved through a Human Device Exemption policy.

**Description:** An implanted pulse generator is connected with a lead extension to a lead with four electrodes. The electrodes are in contact at a specific anatomical structure within the brain. The generator, which is implanted under the skin of either the abdomen or under the clavicle, sends programmable electrical pulses to output electrodes within the brain. Two of these device systems may be implanted to stimulate both sides of the brain in order to relieve symptoms, or one device with two lead outputs may be used. The surgically implanted device delivers carefully controlled electrical pulses to targeted areas of the brain. The clinician can make adjustments to find the most appropriate type and amount of stimulation for each patient to maximize symptom control and minimize adverse effects.

**Purpose:** The neurostimulators are the same as those used to treat common movement disorders like Parkinson’s disease. However, because the area of the brain targeted is different in patients with OCD, a unique lead was designed. For OCD and treatment-resistant depression, the anatomical target in the brain is the anterior limb of the internal capsule and a region (the ventral capsule/ventral striatum), believed to regulate mood and anxiety. Standard treatments such as medications and cognitive behavioral therapy do not always work for all patients. Reclain DBS is the first FDA-approved medical device to treat OCD.

**Benefit:** DBS therapy for OCD should improve some symptoms associated with OCD for a small subset of patients, but individual results may vary. The stimulator is expected to be available in the U. S. by mid-2009.

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

**Device Recalls**

**Shiley 3.0PED Cuffless Pediatric Tracheostomy Tube.** A tracheostomy tube is usually placed through the wind-pipe to provide an airway and to remove fluid from a patient’s trachea and lungs. In January, Covidien, Inc., recalled several lots of the tubes because practitioners found it difficult to insert two of the device’s components. In some instances, the tracheostomy tube had to be removed and replaced. The action has been deemed a Class I recall, the FDA’s most urgent type of recall.

**Source:** FDA, March 9, 2009

**Colleague Single-Channel and Triple-Channel Volumetric Infusion Pumps.** Electronic infusion pumps deliver controlled amounts of medications or other fluids to patients through an IV, intra-arterial, epidural, or other route of administration. On January 23, 2009, Baxter Healthcare sent a correction letter to its customers about failures that could lead to interruption of therapy, damaged battery messages, smoke and fire hazards, and serious injury or death.

The letter advised hospitals to have contingency plans to verify that back-up pumps are available and included instructions for handling an interruption of therapy with any failure code, for addressing damaged battery messages, and for cleaning the device properly.

**Source:** FDA, March 11, 2009

**Select AED 10 Defibrillators.** There is a slight chance that some automated external defibrillators (AEDs) made by Welch Allyn might experience problems. In such cases, defibrillation may be prevented and patients in cardiac arrest could die. There have been 20 reported instances of low-energy shock, eight reports of electromagnetic noise interference, and 11 reports of unexpected shutdowns.

Because the chance of malfunction is remote, customers should keep using AED 10 or MRL–Welch Allyn JumpStart units until they receive replacements. If a unit warns of a low-energy shock during use, consumers should continue to use the device and should follow the voice prompts and directions. A low-energy shock may still be clinically effective, and a full-energy shock can follow a low-energy shock.

**Source:** Welch Allyn, March 11, 2009

**Innervision Snap Shunt Ventricular Catheter, BioGlide, and Snap Shunt Ventricular Catheter.** Ventricular catheters are part of a surgically implanted system that redirects excess fluid from the brain to another part of the body, such as in patients with hydrocephalus. The product was recalled because of the potential for the ventricular catheter to become detached from the snap base assembly and because of its tendency to increase the need for emergency corrective surgery.

Medtronic Neurologic Technologies sent customers a recall notice on February 13, 2009, informing them that they should stop implanting the device. Customers were asked to return all unused products to the company, to account for each used (implanted) device, and to advise surgeons about the recall.

**Source:** FDA, updated March 30, 2009