**NEW DRUGS**

**Rixubis for Hemophilia B**

Coagulation factor IX (Rixubis, Baxter Healthcare) has been approved for patients with hemophilia B who are 16 years of age and older. The medication is the first recombinant coagulation factor IX specifically indicated for routine use in preventing bleeding episodes.

Hemophilia B, an inherited blood-clotting disorder, affects mostly males. It is caused by factor IX gene mutations and affects about 3,300 people in the U.S.

Rixubis is a purified protein produced by recombinant DNA technology. It does not contain human or animal proteins. It is supplied in single-use vials of freeze-dried powder and is administered intravenously. When used for routine prophylaxis, it is administered twice weekly.

Sources: FDA and MedPage Today, June 27, 2013

**Zubsolv for Opioid Dependence**

Zubsolv, a menthol-flavored tablet that dissolves under the tongue, has been approved for the maintenance treatment of opioid dependence. Made by Orexo AB, Zubsolv combines buprenorphine and naloxone. Comparators include Subutex and Suboxone sublingual film (Reckitt Benckiser). Zubsolv is classified as a Schedule CIII medication. The product’s launch is planned for September 2013.

Sources: Orexo, July 5, 2013; Healo, July 11, 2013

**Brisdelle for Hot Flashes**

The FDA has approved paroxetine mesylate (Brisdelle, Noven) for the treatment of hot flashes associated with menopause. This product is the only nonhormonal therapy for hot flashes approved by the FDA. Other approved therapies for menopausal vasomotor symptoms contain either estrogen alone or estrogen plus a progestin.

Brisdelle capsules contain 7.5 mg of paroxetine and are taken once daily at bedtime. Paxil (GlaxoSmithKline) and Pexeva (Noven) contain higher doses of paroxetine and approved for major depressive disorder, obsessive–compulsive disorder, panic disorder, and generalized anxiety disorder. All paroxetine drugs approved for treating depression have a boxed warning about a risk of suicide in children and young adults. A patient medication guide will be dispensed at each refill. For more information, please see the Pharmaceutical Approval Update column, page 445.

Source: FDA, June 28, 2013

**Gilotrif and a Diagnostic Test For Lung Cancer**

Afatinib (Gilotrif, formerly Tomtovok, Boehringer Ingelheim) is now approved for patients with metastatic non–small-cell lung cancer (NSCLC) whose tumors express specific epidermal growth factor receptor (EGFR) gene mutations. The FDA also concurrently approved a companion diagnostic device, the therascreen EGFR RGQ PCR Kit (Qiagen), to help determine whether a patient’s lung cancer cells express the EGFR mutations.

Afatinib, a tyrosine kinase inhibitor, is intended for patients whose tumors express the EGFR exon 19 deletions or exon 21 L858R substitution gene mutations. This is the second drug approved this year for patients with metastatic NSCLC whose tumors express these mutations. In May, the FDA approved a new indication for erlotinib (Tarceva, OSI/Genentech) in NSCLC, along with Roche’s Cobas EGFR Mutation Test, a companion diagnostic.

Warnings include serious skin disorders and severe diarrhea, which may cause dehydration and renal failure. Afatinib was evaluated under the FDA’s priority review program.

Source: FDA; July 12, 2013

**Generic Approvals**

**Norethindrone Oral Contraceptives**

Mylan Pharmaceuticals, Inc., has launched norethindrone tablets USP, 0.35 mg. The tablets are the generic version of Janssen’s Micronor 28-day cycle tablets. Mylan’s partner, Famy Care Ltd., received final approval from the FDA for its Abbreviated New Drug Application (ANDA).

Source: Mylan, June 26, 2013

**Metronidazole for Rosacea**

Sandoz, a division of Novartis, has launched metronidazole 1% topical gel, the first generic version of Galderma’s Metrogel in the U.S. The product, a nitroimidazole, is indicated for the topical treatment of inflammatory lesions of rosacea. This drug is not indicated for intravaginal or ophthalmic use.

Sources: Sandoz, July 2, 2013; [www.metrogel.com](http://www.metrogel.com)

**Rizatriptan for Migraine**

Glenmark Generics Inc. USA has announced the FDA’s approval of its rizatriptan benzoate orally disintegrating tablets (5 mg and 10 mg) for the treatment of migraine headaches. The tablets are a generic version of Maxalt (Merck).

Source: Glenmark, July 2, 2013

**ER Methylphenidate for ADHD**

Kremers Urban Pharmaceuticals, Inc., a subsidiary of UCB, has received approval for extended-release (ER) methylphenidate HCl (18 mg and 27 mg). The central nervous system stimulant is indicated for patients with attention-deficit hyperactivity disorder. Kremers also received tentative approval for the 36-mg and 54-mg strengths, which will be eligible for final approval after exclusivity expiration in September.

The generic product is bioequivalent to Concerta (Alza Corp./McNeil/Johnson & Johnson). Each tablet is designed to be
effective for 12 hours.

In September 2011, Kremers announced that it reached a settlement dismissing all pending litigation arising from its ANDA to market an ER methylphenidate HCl product. The agreement allows Kremers to launch its methylphenidate ANDA product under Alza’s existing patents.

Source: UCB, July 10, 2013

Dextroamphetamine Liquid Solution For ADHD and Narcolepsy
Tris Pharma has launched dextroamphetamine sulfate oral solution, the first generic equivalent of ProCentra (FSC Pediatrics). The drug is used to treat ADHD and narcolepsy. The generic product, approved by the FDA on May 29, 2013, is being distributed in accordance with FDA and U.S. Drug Enforcement Administration (DEA) regulations governing the handling of Schedule CII controlled substances.

Source: Tris Pharma, July 10, 2013

Oxydometorone ER for Pain
Actavis has received the FDA’s approval for its ANDA of oxymorphone HCl extended-release (ER) tablets in strengths of 5, 10, 20, 30, and 40 mg.

Actavis’ product is the generic equivalent to the previously marketed formulation of Endo’s Opana ER, which was voluntarily withdrawn from sale in 2012. Actavis previously received approval for, and is currently marketing, oxymorphone HCl ER 7.5-mg and 15-mg tablets. Actavis is defending ongoing patent litigation initiated by Endo concerning the 7.5-mg and 15-mg strengths and is evaluating launch plans for the newly approved additional dosage strengths.

This opioid agonist is indicated for the relief of moderate-to-severe pain in patients who need continuous, extended-around-the-clock opioid treatment.

Source: Actavis, July 12, 2013

NEW INDICATIONS
Latan demonstrating for Bipolar Depression
The FDA has approved two new indications for lurasidone HCl (Latan, Sunovian)—as monotherapy and as adjunctive therapy, with either lithium or valproate, for adults with major depressive episodes associated with bipolar I disorder (bipolar depression). This second-generation antipsychotic agent was originally approved in 2010 for patients with schizophrenia.

A boxed warning advises against use by elderly patients with dementia-related psychosis and mentions a risk of suicidal thoughts and actions in some children, teenagers, and young adults.

Source: Sunovian, July 1, 2013

Plan B One-Step Now OK for All Ages, No Prescription Needed
Levonorgestrel (Plan B One-Step, Teva), an emergency oral contraceptive (OC), is now approved as a nonprescription product for all women of childbearing age. This action complies with the April 5, 2013, order of the U.S. District Court in New York to make levonorgestrel-containing emergency OCs available over the counter without age restrictions at the point of sale. This single-dose, 1.5-mg tablet should be taken as soon as possible within 3 days after unprotected sex.

Plan B One-Step was first approved in July 2009 for use without a prescription in women 17 years of age and older and as a prescription-only option for females younger than age 17. In April 2013, the tablet was approved for non-prescription use for females as young as age 15.

Source: FDA, June 20, 2013

Mycamine Injection For Pediatric Patients
Micafungin sodium injection (Mycamine, Astellas) is now approved to treat pediatric patients 4 months of age and older with infections caused by Candida. The Supplemental New Drug Application (sNDA) for this drug is also indicated as prophylaxis of candidal infections in patients undergoing hematopoietic stem-cell transplantation.

Micafungin inhibits an enzyme essential for fungal cell-wall synthesis. It was approved in 2005 for adults with esophageal candididiasis and in 2008 for adults with candidemia, acute disseminated candidiasis, candidal peritonitis, and abscesses. This is the only echinocandin antifungal agent approved for preventing candidal infections in adults (and now pediatric patients) undergoing stem-cell transplantation. The drug’s efficacy against infections caused by fungi other than Candida is not known.


Vibativ, an Antibiotic for Hospital-Acquired Pneumonia
Telavancin injection (Vibativ, Theravance) has been approved to treat patients with hospital-acquired pneumonia (HAP) and ventilator-associated bacterial pneumonia caused by Staphylococcus aureus. The drug was originally approved in 2009 to treat complicated skin and skin-structure infections, such as those caused by gram-positive bacteria.

HAP, the second most common nosocomial infection, is often caused by S. aureus, particularly the methicillin-resistant form (MRSA). Until now, only vancomycin (Vancocin, ViroPharma) and linezolid (Zyvox, Pfizer) were recommended for treating HAP caused by MRSA. However, vancomycin has slow bactericidal action and poor lung penetration. Therefore, the recent FDA approval of once-daily telavancin for HAP could be good news.

Telavancin is a lipoglycopeptide with potent bactericidal action against gram-positive pathogens. It was compared with vancomycin for safety and effectiveness
in two phase 3 clinical trials (ATTAIN I and ATTAIN II).

Telavancin brought about higher cure rates compared with vancomycin and was effective in patients with pneumonia caused by MRSA and by meticillin-susceptible *S. aureus* (MSSA). In *vitro*, telavancin is rapidly bactericidal against gram-positive bacteria, including MRSA, vancomycin-intermediate *S. aureus*, and penicillin-resistant *S. pneumoniae*. Currently, telavancin is approved to treat only *S. aureus* in HAP patients.

More telavancin patients than vancomycin patients experienced serious adverse drug events (ADEs) or discontinued treatment stemming from an ADE, but incidence rates of most common ADEs (anemia, abnormal serum potassium levels, and elevated hepatic enzymes) were similar in both groups. Telavancin patients were more likely to have significant creatinine increases compared with vancomycin patients (16% vs. 10%, respectively).

More telavancin patients with pre-existing kidney disease died, compared with those who received vancomycin. For most patients, renal impairment had resolved or was resolving at the last follow-up visit. The researchers emphasized that many patients enrolled in the ATTAIN studies were critically ill.

Mortality rates were comparable between the two arms, except among patients with pre-existing kidney disease. In the first study, 80 telavancin-treated patients (21.5%) and 62 vancomycin patients (16.6%) died. In the second study, 70 telavancin patients (18.5%) and 78 vancomycin patients (20.6%) died. The findings, which incorporated data from more than 250 sites, are robust and consistent.

The FDA states that telavancin should be used to treat HAP only when an alternative therapy is not available. Telavancin can also cause new or existing kidney problems. This information has been added to the product's boxed warning.


**Exelon Patch for Severe Alzheimer’s Disease**

The FDA has expanded the indication for transdermal rivastigmine (Exelon, Novartis) to include patients with severe Alzheimer’s disease (AD). The patch is also approved for the treatment of mild-to-moderate dementia of the Alzheimer’s type. Rivastigmine is also indicated for the treatment of mild-to-moderate dementia associated with Parkinson’s disease.

The expanded approval was based on the ACTION trial (ACTivities of Daily Living and CogniTION in Patients with Severe Dementia of the Alzheimer’s Type). The trial results were reported at this year’s meetings of the American Academy of Neurology and the American Association for Geriatric Psychiatry.

Sources: Medscape, June 28, 2013; MedPage Today, July 1, 2013

**DRUG NEWS**

**PPIs and Heart Problems**

Proton pump inhibitors (PPIs), which are widely used to treat patients with acid reflux, have been associated with cardiovascular disease, according to researchers at Houston Methodist Hospital.

In human tissue and mouse models, the drugs caused constriction of blood vessels and interfered with the ability of blood vessels to relax. It taken regularly, PPIs could be expected to result in hypertension and a weakened heart.

This was an unexpected effect, although PPIs have been noted to increase the risk of a second heart attack in hospitalized patients with acute coronary syndrome. The researchers suggest that patients use another drug to protect the stomach if they are at risk for a heart attack.

PPIs such as lansoprazole (Prevacid, Novartis) and omeprazole (Prilosec, AstraZeneca) are indicated for gastrointestinal reflux disease, *Helicobacter pylori* infection, Zollinger–Ellison syndrome, and Barrett’s esophagus.

Sources: *Circulation* July 3, 2013 (online); *Science Daily*, July 10, 2013; Houston Methodist Hospital

**Recalls**

**Aspirin Mixup**

Advance Pharmaceutical has recalled one lot of 81-mg enteric-coated aspirin tablets that could contain acetaminophen instead. The company received a complaint that one bottle of lot 13A206 contained 500-mg acetaminophen tablets, not aspirin. The recalled lot is sold under the Rugby Laboratories label in bottles containing 120 tablets each, with an expiration date of January 2015. The product was distributed nationwide to wholesalers and retail stores.

National Drug Code numbers are 0536-3086-41 and UPC 3 0536-3086-41 9.

According to the bottle’s label, the recommended dose is four to eight tablets every 4 hours, up to a maximum of 48 tablets per day. A patient swallowing that many 500-mg acetaminophen tablets would ingest a total of 24,000 mg, about six times the recommended maximum daily dose.

Sources: American Society of Health-System Pharmacists and MedPage Today, June 20, 2013

**Estarylla Birth Control Pills**

Sandoz has recalled one lot of Estarylla, an oral contraceptive, after a patient found a placebo tablet among the pills designated as containing the active drug. The affected norgestimate–ethinyl estradiol tablets are in lot LF01213A, with an expiration date of February 2014. The National Drug Code number is 00781-4058-15.
The pills are supplied in cartons containing three blister cards of 28 tablets each. This lot was distributed only in the U.S. Of 10,855 blister cards, 10,848 were distributed to a single wholesaler and were returned.

The packaging flaw is easily visible. The risk of pregnancy is low even if one blue (active-ingredient) tablet is skipped.

This action is similar to one that occurred in April. Toronto-based Apotex Canada recalled several lots of its Alysera-28 contraceptives because some packages were thought to contain a 2-week supply of placebo tablets instead of the prescribed 1-week supply.


Benztropine for Parkinson’s Disease

On June 30, 2013, the FDA announced the voluntary recall of four lots of injectable benztropine mesylate because of the presence of glass particles. Benztropine is indicated for the treatment of Parkinson’s disease and extrapyramidal disorders.

The affected lots were manufactured by Allergy Laboratories and distributed by Fresenius Kabi USA. The label might say Nexus Pharmaceuticals or APP. The recall includes 2-mg/2-mL single-dose vials. NDC numbers are 14789-300-02 or 63323-970-02; lot numbers are 030712, 071212, 090512, and 111412. Expiration dates are March, July, September, and November, respectively, all in 2014.

The use of an injectable drug tainted with glass particles can cause thromboembolism, pulmonary embolism, vein inflammation, and blocked capillaries, and a risk of low-grade inflammation. When glass vessels are manufactured at high temperatures or fluid drug mixtures have a highly alkaline pH, the internal surface of the vial may become delaminated, causing glass particles within the medication. The particles might or might not visible.

Originally made by Merck, benztropine (Cogentin) was approved in 1954.


Label Changes

Sprue May Be Linked to Benicar

The FDA is warning that the blood pressure drug olmesartan medoxomil (e.g., Benicar, Benicar HCT, Azor, and Tribenzor, Daiichi Sankyo) may cause intestinal problems known as sprue-like enteropathy. The labels of these drugs are being changed to include this concern.

Olmesartan medoxomil, an angiotensin II receptor blocker (ARB), was approved as monotherapy for the treatment of hypertension or with other antihypertensive agents in 2002. Sprue-like enteropathy has not been detected with ARBs other than olmesartan.


Boxed Warning

For Blood Volume Expander

Corn-based hydroxyethyl starch solutions, which are used to treat hypovolemia, must now carry a boxed warning about an increased risk of kidney injury and death. The change comes 2 weeks after advisers in Europe urged that these products be pulled from the market entirely.

Hydroxyethyl starch is a key component of infusion solutions used to expand blood volume in patients with septic shock and in those undergoing open-heart surgery with cardiopulmonary bypass. An intravenous (IV) solution of hydroxyethyl starch (e.g., Hespan, B. Braun; Voluven, Fresenius Kabi) is commonly used to prevent shock following severe blood loss caused by trauma, surgery, or a medical problem. Increasing the blood volume allows red blood cells to continue to deliver oxygen to the body.

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Amyvid (Florbetapir F18 Injection) before it approves coverage of the imaging test for its beneficiaries. The CMS said that it needs more evidence that the test will improve outcomes. A final decision is expected in October.

Amyvid is used to estimate beta-amyloid neuritic plaque density in patients being assessed for Alzheimer’s disease and other causes of cognitive decline. Approved by the FDA in 2012, the liquid helps to identify insoluble deposits of amyloid plaque or beta-amyloid found in the brain.

Eli Lilly, which acquired Avid in 2010, said that restricting coverage of this adjunctive tool could hinder a timely and accurate diagnosis for patients with cognitive impairment.


**NEW MEDICAL DEVICES**

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

**Name:** Hepatitis C Diagnostic (Abbott RealTime HCV Genotype II, Control Kit, and Uracil-N-Glycosylase)

**Manufacturer:** Abbott Diagnostics, Abbott Park, Ill.

**Approval Date:** June 20, 2013

**Purpose:** The Genotype II test has the capability of detecting seven different genotypes of the hepatitis C virus (HCV) in a patient’s blood sample.

**Description:** The test is designed to be used with Abbott’s m2000 molecular diagnostic system, which is used to diagnose herpes, HCV, and other viral infections. By accurately determining the genotype of a patient’s HCV infection, the technology is intended to help reduce the occurrence of liver cancer and other symptoms associated with the disease.

This *in vitro* reverse transcription–polymerase chain reaction (PCR) assay is used to quantify HCV RNA in human serum and plasma from HCV-infected individuals. It is not used to screen blood, plasma, serum, or tissue donors for HCV, and it is not a diagnostic test to confirm the presence of HCV infection.

The control kit is used to establish validity of the Abbott RealTime HCV Genotype II assay.

The uracil-N-glycosylase procedure is used in conjunction with the Abbott RealTime HCV Genotype II assay as an optional contamination control for laboratories using amplification techniques that incorporate uracil into the amplification product.

**Benefit:** Physicians can provide personalized treatment for the reported 3.2 million American patients with HCV infection, thereby achieving better patient outcomes. According to the Centers for Disease Control and Prevention (CDC), baby-boomers are 50% more likely to carry HCV compared with the general population. CDC officials recommend that everyone born between 1945 and 1965 be tested for hepatitis.

The assay provides consistently accurate test results and the ability to predict the patient’s response to treatment. There are no substantial clinical concerns associated with the approval of this device. It is safe and effective when used according to the directions in the labeling.

Sources: www.abbottmolecular.com; www.fda.gov; www.ivdtechnology.com; www.ncbi.nlm.nih.gov/pmc/articles/PMC2738061

**Name:** Trulign Toric Accommodating Posterior Chamber Intraocular Lens and Calculator

**Manufacturer:** Bausch + Lomb, Aliso Viejo, Calif.

**Date of Approval:** May 20, 2013

**Purpose:** The Trulign artificial intraocular lens (IOL) is used restore vision after the eye’s natural lens is removed during cataract surgery. The IOL also corrects blurry vision caused by corneal astigmatism. This IOL is used for patients with both cataracts and corneal astigmatism.

**Description:** The IOL focuses light on the retina. Traditional IOLs are monofocal, offering vision at one distance only (e.g., far, intermediate, or near). With conventional IOLs, patients must wear eyeglasses or contact lenses in order to read, use a computer, or view objects at arm’s length. Accommodating IOLs offer the possibility of seeing well at more than one distance without glasses or contact lenses.

The calculator is used solely to assist physicians in determining the appropriate IOL cylinder power and axis of placement.

**Upgraded Sumavel DosePro Toolbox for Migraine**

Zogenix, Inc., has announced the launch of an improved Sumavel DosePro Migraine Toolbox to help patients have access to the appropriate triptan medication to address the type of migraine they are experiencing. The Sumavel DosePro needle-free delivery system (sumatriptan injection) was originally approved in 1992.

The updated compact toolbox is provided by physicians. It includes a carrying case for treatments, a sample dose of medication, a journal for tracking attacks and the effectiveness of treatments, a product brochure, a key card to access an online video, an instruction card, copay information, and a product card worth $15 to simplify pharmacy purchases.

Sumavel DosePro is indicated for the acute treatment of migraine attacks, with or without aura, and the acute treatment of cluster headaches; it should not be used to prevent migraine or to manage hemiplegic or basilar migraine. The medication is injected into the stomach or thigh only; it should not be administered intravenously.

Source: Zogenix, June 25, 2013
Benefit: This is the first accommodating IOL that also corrects corneal astigmatism between 0.83 and 2.50 diopters. Patients have clear distance, intermediate, and near vision without glasses after cataract surgery. Most surgeons who treat astigmatism in cataract patients tend to use astigmatic keratotomy or to make incisions in the cornea. Lenticular astigmatism, caused by irregularity in the shape of the natural lens inside the eye, can also be corrected with a toric IOL.

Precautions: Risks of the procedure include poor vision if the lens rotates out of position, with the possible need for further surgery to reposition or replace the IOL. The tendency of the lens to rotate may affect some patients more than others.

There are no known contraindications, but the product’s safety and effectiveness have not been evaluated in patients younger than 50 years of age and in those with diabetic retinopathy, amblyopia, chronic drug-induced miosis, and a history of retinal detachment.

Sources: www.fda.gov; www.allaboutvision.com/conditions/iols.htm

Recall

In May, Endologix, Inc., initiated a Class I recall of AFX Introducer System Model S17-45 after the dilator was reported to have broken during implantation procedures. The device is used to introduce catheters and other instruments into blood vessels with minimal blood loss.

The product was distributed and manufactured from April 1 through April 30, 2013, in Florida, Indiana, Michigan, New Hampshire, New Jersey, and New York. Lot numbers 1079840, 1079843, 1079844, and 1079845 are affected.

The FDA has since assigned its most serious warning, saying the problem could cause serious injury or death. The company warned customers not to use or further distribute any affected products.

Sources: FDA, May 13, 2013; Fierce Medical Devices, June 18, 2013