NEW DRUG APPROVALS

Trumenba Meningitis Vaccine

Trumenba (Wyeth/Pfizer) has received FDA approval as the first U.S. vaccine licensed to prevent invasive meningococcal disease caused by Neisseria meningitidis serogroup B in people 10 through 25 years of age.

N. meningitidis is a leading cause of life-threatening bacterial meningitis. According to the Centers for Disease Control and Prevention, serogroup B caused about 160 U.S. cases of meningococcal disease in 2012.

Vaccination is the most effective way to prevent meningococcal disease, the FDA says. Until now, U.S.-approved meningococcal vaccines have covered only four of the five main serogroups of N. meningitidis bacteria that cause meningococcal disease: A, C, W, and Y.

Trumenba is administered as a three-dose series; individuals receive the second shot two months after the first and the third shot four months after the second.

Three randomized studies were conducted in the U.S. and Europe in approximately 2,800 adolescents. Among those who received three doses of Trumenba, 82% had antibodies in their blood that killed four N. meningitidis serogroup B strains after vaccination compared with less than 1% before vaccination. These four strains cause serogroup B meningococcal disease in the U.S.

The safety of Trumenba was assessed in about 4,500 individuals who received it in global studies. The most common adverse events included injection-site pain and swelling, headache, diarrhea, muscle pain, joint pain, fatigue, and chills.

Sources: FDA and Pfizer, October 29, 2014

Xigduo XR for Diabetes

The FDA has approved dapagliflozin/metformin (Xigduo XR, AstraZeneca) as the first once-daily tablet in the U.S. to combine a sodium-glucose cotransporter 2 (SGLT2) inhibitor with the biguanide metformin.

AstraZeneca recently launched the SGLT2 inhibitor dapagliflozin as Farxiga. SGLT2 is responsible for most glucose reabsorption in the kidneys, which contribute to normal glucose balance in part by filtering and subsequently returning glucose to circulation. Selective inhibition of SGLT2 reduces the reabsorption of glucose and allows its disposal via the urine.

Xigduo XR is indicated as an adjunct therapy to diet and exercise to improve glycemic control in adults with type-2 diabetes when treatment with both dapagliflozin and metformin is appropriate. It is not approved for use in patients with type-1 diabetes or diabetic ketoacidosis. The product has a boxed warning for lactic acidosis, and it is contraindicated in patients with moderate-to-severe renal impairment, a history of serious hypersensitivity to dapagliflozin or metformin, or metabolic acidosis.

Xigduo XR is available in multiple dosage strengths of dapagliflozin/metformin, including 5 mg/500 mg, 5 mg/1,000 mg, 10 mg/500 mg, and 10 mg/1,000 mg. It should be taken once daily in the morning with food, with gradual dose escalation to reduce the risk of gastrointestinal side effects due to metformin. The maximum daily recommended dose is 10 mg for dapagliflozin and 2,000 mg for metformin.

Sources: Reuters, October 30, 2014, and Xigduo XR prescribing information

Obizur for Acquired Hemophilia A

The FDA has approved antihemophilic factor (recombinant), porcine sequence (Obizur, Baxter International) for the treatment of bleeding episodes in adults with acquired hemophilia A (AHA).

Obizur is the first recombinant porcine factor VIII (FVIII) therapy approved for AHA that allows physicians to manage the treatment’s efficacy and safety by measuring FVIII activity levels in addition to clinical assessments. It replaces the inhibited human FVIII with a recombinant porcine sequence FVIII based on the rationale that it is less susceptible to inactivation by circulating human FVIII antibodies.

The approval was based on a global, prospective, controlled, phase 2/3 open-label trial that examined Obizur for the treatment of serious bleeding episodes in adults with AHA; 29 patients were evaluated for safety and 28 for efficacy. All patients treated with Obizur showed a positive response (an effective or partially effective response with bleeding stopped or reduced and clinical improvement) at 24 hours after the initial infusion. The most common adverse reaction was the development of inhibitors to porcine FVIII.

The safety and efficacy of Obizur have not been established in patients with baseline anti-porcine FVIII inhibitor titers greater than 20 BU. The treatment is not indicated for patients with congenital hemophilia A or von Willebrand disease.

Source: Baxter, October 24, 2014

Esbriet for Idiopathic Pulmonary Fibrosis

Pirfenidone (Esbriet, InterMune, Inc.) has received FDA approval for the treatment of idiopathic pulmonary fibrosis.

Pirfenidone’s safety and effectiveness were established in three clinical trials involving 1,247 patients. The decline in forced vital capacity (FVC)—the amount of air that can be forcibly exhaled after taking the deepest breath possible—was significantly reduced in patients receiving pirfenidone versus placebo. The ASCEND trial, a placebo-controlled, randomized, double-blind, phase 3 study, enrolled 555 patients with mild-to-moderate idiopathic pulmonary fibrosis. From baseline to the end of the study at 52 weeks, a FVC decline of at least 10% took place in 17% of patients who received pirfenidone compared with 32% of patients who received placebo.

Pirfenidone is believed to interfere with the production of transforming growth factors.
factor-beta, a small protein involved in cell growth, and tumor necrosis factor-alpha, a small protein involved in inflammation. Pirfenidone is not recommended for patients who have severe liver problems or end-stage kidney disease or who require dialysis. It should be taken with food to minimize the potential for nausea and dizziness. Patients should avoid or minimize exposure to sunlight and sunlamps and wear sunscreen and protective clothing, as pirfenidone may cause patients to sunburn more easily.

The most common side effects are nausea, rash, abdominal pain, upper respiratory tract infection, diarrhea, fatigue, headache, dyspepsia, dizziness, vomiting, decrease or loss of appetite, gastroesophageal reflux disease, sinusitis, insomnia, decreased weight, and arthralgia.

Sources: FDA and InterMune, October 15, 2014

Ofev for Idiopathic Pulmonary Fibrosis

The FDA has approved nintedanib (Ofev, Boehringer Ingelheim) for the treatment of idiopathic pulmonary fibrosis (IPF).

Nintedanib, a kinase inhibitor, blocks multiple pathways that may be involved in the scarring of lung tissue. Its safety and effectiveness were established in three randomized, double-blind, placebo-controlled clinical trials involving 1,231 IPF patients. The studies assessed forced vital capacity (FVC)—the amount of air that can be forcibly exhaled after taking the deepest breath possible—in patients receiving nintedanib 150 mg twice daily compared with placebo.

All three trials—the phase 2 TOMORROW study and the phase 3 INPULSIS-1 and INPULSIS-2 studies—demonstrated a consistent, statistically significant reduction in the annual rate of decline in FVC with nintedanib compared with placebo. The relative reductions in FVC decline were 68% in TOMORROW, 52% in INPULSIS-1, and 45% in INPULSIS-2. In addition, the time to the first acute IPF exacerbation was significantly reduced in patients receiving nintedanib compared with those given placebo in TOMORROW and INPULSIS-2 (but not in INPULSIS-1).

The most common side effects included diarrhea, nausea, abdominal pain, vomiting, liver enzyme elevation, decreased appetite, headache, decreased weight, and high blood pressure.

Nintedanib is not recommended for patients with moderate-to-severe liver problems, and treatment can cause birth defects or death to an unborn baby.

Sources: FDA and Boehringer Ingelheim, October 15, 2014

Uceris for Distal Ulcerative Colitis

Budesonide rectal foam (Uceris, Salix Pharmaceuticals) has been given FDA approval for the induction of remission in patients with active mild-to-moderate distal ulcerative colitis (UC) extending up to 40 cm from the anal verge. The foam, a rectally administered corticosteroid, overcomes treatment limitations associated with other approved therapies, which are often ineffective because not enough active drug reaches the distal colon.

In UC, the colon’s lining becomes inflamed and develops ulcers that produce pus and mucous. The combination of inflammation and ulceration can cause abdominal discomfort and frequent emptying of the colon. Rectal therapy can be used alone or in combination with oral aminosalicylic acid for mild-to-moderate distal UC. Limitations of other rectal therapies include difficulty of administration and retention (enemas) and limited proximal spread (suppositories). When glucocorticosteroids are used chronically, systemic effects such as hypercorticism and adrenal suppression may occur.

Source: Salix Pharmaceuticals, October 8, 2014

Lumason to Aid Ultrasound

The FDA has approved sulfur hexafluoride lipid microsphere (Lumason, Bracco Diagnostics Inc.) for patients whose echocardiograms are hard to see with ultrasound waves.

Sulfur hexafluoride lipid microsphere is a contrast agent made up of gas-filled microbubbles that reflect the sound waves to allow for clearer imaging of the left ventricle chamber and endocardium.

The agent’s safety and efficacy were established in three clinical trials involving 191 patients with suspected cardiac disease whose echocardiograms were difficult to read. The agent helped doctors see the lining of the left ventricle more clearly, with visual improvement observed in the majority of the patients who received a 2-mL dose. Lumason also helped independent reviewers in all three studies more clearly and completely see inside the patient’s left ventricle.

Like all microbubble contrast agents, it carries a boxed warning about the risk of serious cardiopulmonary reactions, including fatal cardiac or respiratory arrest. This risk may increase among patients with certain heart conditions; most serious reactions occur within 30 minutes of administration. The most commonly reported side effects were headache and nausea.

Source: FDA, October 10, 2014

Generic Approvals

Valganciclovir

The FDA has approved valganciclovir tablets USP, 450 mg, made by Endo Pharmaceuticals and Dr. Reddy’s Laboratories, Inc.—the first generic versions of Hoffmann La Roche’s Valcyte tablets.

Valganciclovir is a cytomegalovirus (CMV) nucleoside analogue DNA polymerase inhibitor indicated for treatment of CMV retinitis in adults with acquired immunodeficiency syndrome; prevention of CMV disease in adult kidney, heart,
or kidney-pancreas transplant patients at high risk; and prevention of CMV disease in pediatric kidney or heart transplant patients at high risk. It has a boxed warning for hematological toxicity, carcinogenicity, teratogenicity, and impairment of fertility.

Valcyte had U.S. sales of $368.5 million in 2013. Ranbaxy Laboratories Ltd. originally received tentative approval to launch the first Valcyte generic, but Ranbaxy said that the FDA had rescinded its approval because of quality control issues at its manufacturing plants.

Sources: FDA, November 4, 2014, Reuters, November 7, 2014, and Valcyte prescribing information

Olopatadine HCl nasal spray

The first generic version of Patanase Nasal Spray has received FDA approval. Olopatadine hydrochloride nasal solution, 665 mcg/spray, will be marketed by Apotex Inc. Patanase (Alcon Inc.) is an H1 receptor antagonist indicated for the relief of the symptoms of seasonal allergic rhinitis in patients 12 years of age and older.

Sources: FDA, October 8, 2014, and Patanase prescribing information

Ivermectin

The FDA has approved the application of Edenbridge Pharmaceuticals, LLC, to offer ivermectin tablets USP, 3 mg—the first generic form of Merck’s Stromectol tablets. Ivermectin is indicated for the treatment of strongyloidiasis of the intestinal tract due to the nematode parasite *Strongyloides stercoralis* and onchocerciasis due to the nematode parasite *Onchoerca volvulus*.

Sources: FDA, October 24, 2014, and Stromectol prescribing information

NEW INDICATIONS

Rumucirumab/Paclitaxel For Advanced Gastric Cancer

The FDA has approved ramucirumab (Cyramza, Eli Lilly) in combination with paclitaxel chemotherapy as a treatment for patients with advanced or metastatic gastric or gastroesophageal junction adenocarcinoma whose cancer has progressed on or after prior fluoropyrimidine- or platinum-containing chemotherapy.

In April, the FDA approved ramucirumab as a single agent for this population. The latest approval was based on results from the randomized, double-blind, placebo-controlled phase 3 RAINBOW trial, which compared ramucirumab plus paclitaxel with placebo plus paclitaxel among 665 patients.

Ramucirumab plus paclitaxel significantly extended median overall survival compared with placebo plus paclitaxel (9.6 months versus 7.4 months, respectively). Ramucirumab plus paclitaxel also significantly delayed disease progression; progression-free survival was 4.4 months for ramucirumab plus paclitaxel versus 2.9 months for placebo plus paclitaxel.

The most common serious adverse events with ramucirumab plus paclitaxel in the RAINBOW trial included neutropenia and febrile neutropenia. Ramucirumab’s labeling contains a boxed warning regarding an increased risk of hemorrhage.

Ramucirumab, an antiangiogenic therapy, binds to and blocks the activation of vascular endothelial growth factor receptor-2 by interfering with the binding of receptor ligands.

Source: Eli Lilly, November 5, 2014

Simeprevir/Sofosbuvir for HCV

The FDA has approved simeprevir (Olysio, Medivir/Janssen) in combination with sofosbuvir (400 mg once daily), with or without ribavirin, in HCV genotype-1 chronically infected treatment-naive and treatment-experienced adults with compensated liver disease. Among all patients, 93% (26 of 28) achieved a sustained virological response at 12 weeks after the end of therapy (SVR12) following 12 weeks of treatment and 97% (30 of 31) achieved SVR12 after 24 weeks.

The most common adverse events reported during 12 weeks of treatment with simeprevir and sofosbuvir without ribavirin were fatigue (25%), headache (21%), nausea (21%), insomnia (14%), and pruritus (11%). During 24 weeks of treatment, dizziness (16%) and diarrhea (16%) were also reported.

Simeprevir is an NS3/4A protease inhibitor approved for the treatment of chronic HCV infection as part of an antiviral regimen in combination with pegylated interferon and ribavirin in genotype-1–infected adults with compensated liver disease, including cirrhosis.

Source: Medivir, November 6, 2014

NEW FORMULATION

Sotylize for Ventricular Arrhythmia

An oral solution of the antiarrhythmic sotalol hydrochloride (Sotylize, Arbor Pharmaceuticals) has received FDA approval. Sotalol hydrochloride is indicated for the treatment of ventricular arrhythmias, such as sustained ventricular tachycardia, that in a physician’s judgment are life-threatening, and for the maintenance of normal sinus rhythm in patients with symptomatic atrial fibrillation/atrial flutter who are in sinus rhythm.

Previously, sotalol was available only in tablet form. Pharmacists often compound the tablets into a liquid suspension using

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Previously, sotalol was available only in tablet form. Pharmacists often compound the tablets into a liquid suspension using
simple syrup for pediatric and elderly patients who cannot swallow pills.

The product carries a boxed warning about life-threatening proarrhythmia. It can cause life-threatening ventricular tachycardia associated with QT interval prolongation. Patients should be hospitalized in a facility that can provide cardiac resuscitation and continuous electrocardiographic monitoring, and the dosing interval should be adjusted based on creatinine clearance.

Source: Arbor Pharmaceuticals, October 23, 2014

**DRUG NEWS**

**TAS-102 on Fast Track For Colorectal Cancer**

The FDA has granted fast-track designation to TAS-102 (trifluridine/tipiracil hydrochloride, Taiho Oncology, Inc.), an oral combination drug under investigation for the treatment of refractory metastatic colorectal cancer (mCRC). The company has initiated a rolling new drug application submission to the FDA.

The phase 3 RECURRENT trial forms the foundation for the submission. The randomized, double-blind, placebo-controlled comparison trial evaluated TAS-102 in 800 patients with refractory mCRC who had received at least two prior regimens of standard chemotherapies and were refractory to or failed those chemotherapies. Patients receiving TAS-102 had statistically significant improvements in overall survival (hazard ratio [HR], 0.68) and decreases in the risk of disease progression (HR, 0.48) compared with placebo. Trifluridine, an antineoplastic nucleoside analog, is incorporated directly into DNA, interfering with its function. Trifluridine’s blood concentration is maintained via tipiracil hydrochloride, which inhibits the trifluridine-degrading enzyme thymidine phosphorylase.

Source: Taiho Oncology, Inc., October 20, 2014, and June 28, 2014

**Breakthrough Therapy Status**

**Keytruda in Advanced NSCLC**

Pembrolizumab (Keytruda, Merck) has received its second FDA breakthrough therapy designation—this time for the treatment of patients with non-small-cell lung cancer (NSCLC) whose disease is epidermal growth factor receptor mutation-negative, is anaplastic lymphoma kinase rearrangement-negative, and has progressed on or following platinum-based chemotherapy.

Pembrolizumab is indicated for the treatment of patients with unresectable or metastatic melanoma and disease progression following ipilimumab and, if BRAF V600 mutation-positive, a BRAF inhibitor. The FDA previously granted pembrolizumab breakthrough therapy status for advanced melanoma. The breakthrough therapy designation in advanced NSCLC is supported by data from the ongoing phase 1b KEYNOTE-001 study.

Pembrolizumab is a humanized monoclonal antibody that blocks the interaction between programmed death receptor-1 (PD-1) and its ligands, PD-L1 and PD-L2. This releases the PD-1 pathway-mediated inhibition of the immune response, including the antitumor immune response.

Source: Merck, October 27, 2014

**NBI-98854 for Tardive Dyskinesia**

Neurocrine Biosciences, Inc., has received an FDA breakthrough therapy designation for its vesicular monoamine transporter 2 (VMAT2) inhibitor, NBI-98854, for tardive dyskinesia. The designation was granted, in part, based on the results of the phase 2b Kinect studies of NBI-98854 in approximately 220 patients. VMAT2 is a protein concentrated in the brain that is primarily responsible for repackaging and transporting monoamines in presynaptic neurons. NBI-98854 is a highly selective VMAT2 inhibitor that modulates dopamine release during nerve communication with minimal impact on other monoamines, reducing the likelihood of “off-target” side effects. Modulation of neuronal dopamine levels in diseases such as tardive dyskinesia, which is characterized, in part, by a hyperdopaminergic state, should provide symptomatic benefits.

Source: Neurocrine Biosciences, Inc., October 30, 2014

**SPK-RPE65 for Nyctalopia**

SPK-RPE65 (Spark Therapeutics) has received breakthrough therapy designation from the FDA for the treatment of nyctalopia in patients with Leber’s congenital amaurosis due to mutations in the RPE65 gene. SPK-RPE65 targets a group of blinding conditions known as inherited retinal dystrophies caused by autosomal recessive mutations in this gene.

In two clinical trials, results to date and reports from the clinical study team suggest that SPK-RPE65 enables patients to perform activities of daily living with greater independence than they could prior to treatment and has long-lasting effects in restoring functional vision. After a single injection of SPK-RPE65 in one eye, children in the trials no longer depended on visual aids to carry out classroom activities and were able to walk and play more like normally sighted children. SPK-RPE65 is undergoing a fully enrolled pivotal phase 3 clinical trial.

Source: Spark Therapeutics, November 6, 2014

**Priority Review Status**

**Lenvatinib for Thyroid Cancer**

The application for lenvatinib mesylate (Eisai Inc.) as a treatment for progressive radioactive iodine-refractory differentiated thyroid cancer (RAI-refractory DTC) has been accepted by the FDA with priority review status.

Lenvatinib is an oral multiple receptor tyrosine kinase inhibitor with a unique binding mode that selectively inhibits the
kinase activities of vascular endothelial growth factor receptors, in addition to other proangiogenic and oncogenic pathway-related tyrosine kinases suspected in tumor proliferation.

A multicenter, randomized, double-blind, placebo-controlled phase 3 trial (SELECT) compared the progression-free survival of 392 patients with RAI-refractory DTC and radiographic evidence of disease progression within the prior 12 months, treated with once-daily, oral lenvatinib versus placebo.

Source: Eisai Inc., October 14, 2014

**Blinatumomab for ALL**

The FDA has granted priority review to blinatumomab (Amgen) for the treatment of adults with Philadelphia-negative (Ph−) relapsed/refractory B-precursor acute lymphoblastic leukemia (ALL).

Amgen’s biologics license application includes data from a phase 2 trial that met its primary endpoint among adults with this disease. The Prescription Drug User Fee Act target date is May 19, 2015.

Blinatumomab is an investigational specific T-cell engager antibody construct being investigated for fighting cancer by helping the body’s immune system to detect and target malignant cells. Blinatumomab is designed to direct T cells against target cells expressing CD19, a protein found on the surface of B-cell–derived leukemias and lymphomas.

The therapy has received an FDA orphan drug designation for the treatment of ALL, chronic lymphocytic leukemia, hairy cell leukemia, prolymphocytic leukemia, and indolent B-cell lymphoma.

Source: Amgen, October 9, 2014

**Lucentis in Diabetic Retinopathy**

The FDA has granted priority review to a supplemental biologics license application for ranibizumab injection (Lucentis, Genentech) in the treatment of diabetic retinopathy. The action date is February 6, 2015. If approved, ranibizumab would be the first eye medication available for patients with diabetic retinopathy.

The submission is based on two phase 3 trials (RISE and RIDE) that found meaningful improvements in diabetic retinopathy in a clinically significant proportion of patients treated with ranibizumab at two years compared with patients treated with sham injections. The benefits of ranibizumab treatment were maintained during the third year of treatment.

Ranibizumab is designed to bind to and inhibit vascular endothelial growth factor A, a protein that is believed to play a critical role in angiogenesis and in the hyperpermeability of the vessels.

Source: Genentech, October 8, 2014

**Orphan Drug Designations**

**AC-201 for Epidermolysis Bullosa**

Twi Biotechnology, Inc., has received an FDA orphan drug designation for the topical use of AC-201 to treat epidermolysis bullosa, a very rare genetic connective tissue disorder. Patients have extremely fragile skin that blisters and tears from friction or trauma. The topical formulation of AC-201 seeks to prevent or reduce the blisters. The company will soon proceed to clinical trials.

AC-201 has shown the ability to inhibit the production and activity of caspase-1 and the cytokine interleukin-1 beta (IL-1β) and to down-regulate IL-1β receptors. Inhibition of IL-1β signaling has been demonstrated to be effective in treating a variety of diseases.

Source: Twi Pharmaceuticals, Inc., October 21, 2014

**Isavuconazole for Invasive Candidiasis**

The FDA has awarded an orphan drug status for the treatment of invasive aspergillosis and invasive mucormycosis, and the FDA has designated the drug as a qualified infectious disease product for all three indications.

Isavuconazole (the active moiety of the prodrug isavuconazonium) is an investigational once-daily intravenous and oral broad-spectrum antifungal being developed for the treatment of severe invasive and life-threatening fungal infections. It has demonstrated in vitro and in vivo coverage of a broad range of yeasts and molds.

Source: Astellas, November 3, 2014

**Benefits, Risks of Pradaxa**

An FDA-sponsored study of more than 134,000 Medicare patients found that dabigatran etexilate mesylate (Pradaxa, Boehringer Ingelheim) was associated with significantly reduced risks of ischemic stroke, intracranial hemorrhage, and death but a significantly increased risk of major gastrointestinal (GI) hemorrhage compared with warfarin in patients with nonvalvular atrial fibrillation (NVAF). The study found no difference in major bleeds or in myocardial infarction with dabigatran compared with warfarin.

Boehringer Ingelheim says the study, which was published online October 30 in *Circulation*, reinforces dabigatran’s favorable benefit–risk profile.

The FDA study was based on data from Medicare patients older than 65 years of age who started therapy with dabigatran or warfarin between October 2010 and December 2012. Each group comprised 67,207 patients. The analysis showed that dabigatran was generally associated with better patient outcomes than warfarin.

The outcomes included: a 20% reduced risk of ischemic stroke; no difference in major hemorrhage; a 66% reduced risk of intracranial hemorrhage; a 28% increased risk of GI bleeding; no statistical differ-
Embeda is an opioid analgesic meant to reduce the risk of abuse when crushed. When swallowed intact, however, Embeda can still be abused or misused because the naltrexone is not expected to substantially block the euphoric effects of the morphine.

It will not be known whether the abuse-deterrent properties will reduce intravenous abuse until post-marketing data are available. The FDA is requiring post-marketing studies to assess the effects of the drug’s abuse-deterrent features on the risk and consequences of abuse.

Embeda is part of the risk evaluation and mitigation strategy for extended-release/long-acting opioid analgesics. The FDA is requiring post-marketing studies to assess the effects of the drug’s abuse-deterrent features on the risk and consequences of abuse.

The FDA required Geron to provide follow-up information from imetelstat-treated patients who had experienced liver function test (LFT) abnormalities until such abnormalities resolved to normal or baseline. Geron’s analysis found that LFT abnormalities had resolved to normal or baseline in 23 of 27 patients in company-sponsored phase 2 trials in essential thrombocytopenia and multiple myeloma. LFT abnormalities showed improvement in three other patients and were unresolved in one patient; two of these patients continue in follow-up. No emergent hepatic adverse events were reported during follow-up in either study.

The FDA also requested information about the reversibility of liver toxicity after chronic imetelstat administration in animals. Company studies did not identify any clinical pathology changes indicating hepatocellular injury or any clear signals of LFT abnormalities.

A phase 2 clinical trial in MF is expected to begin in 2015. Geron does not intend to further study or develop imetelstat for the treatment of essential thrombocytopenia or polycythemia vera.

Sources: Sanofi Pasteur, November 3, 2014

**Fluzone Label Asserts Efficacy**

Fluzone High-Dose influenza vaccine (Sanofi Pasteur) provided improved protection against influenza infection compared with standard-dose Fluzone vaccine (trivalent intramuscular formulation) in adults 65 years of age and older, according to updated prescribing information.

The FDA approved a supplemental biologics license application allowing Sanofi to add efficacy data from a large trial published in the *New England Journal of Medicine*. In the double-blind, post-licensure efficacy trial, adults 65 years of age and older received either Fluzone High-Dose vaccine or Fluzone vaccine over the 2011–2012 and 2012–2013 flu seasons. Each vaccine was given to about 16,000 participants. Fluzone High-Dose vaccine was 24.2% more effective than standard-dose Fluzone vaccine in preventing laboratory-confirmed influenza caused by any influenza viral type or subtype in association with influenza-like illness.

Sources: Sanofi Pasteur, November 3, 2014, and *NEJM*, August 14, 2014

**Imetelstat Clinical Hold Ends**

The FDA has removed its full clinical hold on the investigational new drug application for imetelstat and has decided that Geron Corporation’s clinical development plan for the drug, focused on high-risk myeloid malignancies such as myelofibrosis (MF), is acceptable.

The FDA required Geron to provide follow-up information from imetelstat-treated patients who had experienced liver function test (LFT) abnormalities until such abnormalities resolved to normal or baseline. Geron’s analysis found that LFT abnormalities had resolved to normal or baseline in 23 of 27 patients in company-sponsored phase 2 trials in essential thrombocytopenia and multiple myeloma. LFT abnormalities showed improvement in three other patients and were unresolved in one patient; two of these patients continue in follow-up. No emergent hepatic adverse events were reported during follow-up in either study.

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Sources: Geron Corporation, November 3, 2014

**Hospira Lifecare Product Recall**

Hospira, Inc., has recalled 54 lots of 11 products in its LifeCare line of intravenous solutions due to potential leakage. The issue was identified during re-inspection of a lot in which a single puncture mark was identified going through the overwrap and primary container.

The company blames a defect in a conveyor system and has implemented corrective actions. A list of affected products and lots (distributed from September 2013 through October 2014) can be found at http://tinyurl.com/HospiraLifeCare.

Sources: Hospira, Inc., October 14, 2014

**RESEARCH BRIEFS**

**Better Handoffs Cut Errors**

Improvements in verbal and written communication between health care providers during patient handoffs can reduce injuries due to medical errors by 30%, according to a multicenter study led by Boston Children’s Hospital researchers.

The results, published in the *New England Journal of Medicine* (NEJM), show that I-PASS—a system of bundled communication and training tools for handoff of patient care between providers—can increase patient safety without significantly burdening clinical workflows.

I-PASS includes: standardized communication and handoff training; a verbal handoff process organized around the mnemonic “I-PASS” (illness severity, patient summary, action list, situational awareness and contingency planning, continued on page 820
and synthesis by receiver); computerized handoff tools to share patient information between providers using an I-PASS structure; engagement of supervising attending physicians to observe and oversee handoff communications; and a campaign promoting the adoption of I-PASS as part of institutional process and culture.

In the NEJM paper, patient handoffs by residents were monitored and assessed for a six-month pre-intervention period at nine U.S. hospitals. Residents were then trained on I-PASS processes and required to use the system going forward. An additional six months of monitoring and assessment followed the intervention.

Across participating centers, the rate of medical errors decreased by 23%, from 24.5 to 18.8 errors per 100 admissions, after the introduction of I-PASS. Preventable adverse events decreased by 30%, from 4.7 to 3.3 errors per 100 admissions.

Time-motion analyses of providers’ activities showed that implementing I-PASS did not add time to patient handoffs or decrease time spent at patient bedside or on other tasks.

Sources: NEJM, November 6, 2014, and Boston Children’s Hospital, November 5, 2014

Is MRSA Isolation Necessary?
Many patients hospitalized with a history of methicillin-resistant Staphylococcus aureus (MRSA) are isolated unnecessarily, say researchers at the Christiana Care Health System in Delaware, who suggest that screening patients first is better for them and cost-effective.

Hospitals often automatically isolate patients with known past MRSA colonization. When surveyed as part of Christiana’s nine-month pilot project, the patients said the isolation made them feel stigmatized, contaminated, neglected, and distressed. The researchers also found that more than 80% of the patients on the MRSA list were put at needless risk, especially when housed with another patient who had an active MRSA infection.

In the study, seven medical-surgical units admitted 211 patients who were listed as MRSA-positive but had not had a positive MRSA culture for at least 12 months. Twenty-three percent did not complete screening because they were discharged or were receiving antibiotics. Of the patients who completed screening, only 20% were still colonized. Thirty-two percent were placed in isolation; 41% of them said isolation affected their hospital stay. Some reported fewer visitors, different treatment by staff, or emotional distress.

The annual costs of screening for the seven medical-surgical units were projected at about $8,000. The costs associated with unnecessary isolation? Nearly $109,000 a year.

Source: American Journal of Infection Control, October 2014

**DEVICE NEWS**

**EverFlex Stent System**
The FDA has approved marketing of the EverFlex Self-Expanding Peripheral Stent System (ev3, Inc.), which can be implanted in the iliac arteries. The system consists of a stent, made of nitinol tubing laser-cut into a mesh shape, and a delivery catheter. The system is indicated for improving luminal diameter in patients with atherosclerotic disease of the common and/or external iliac arteries up to 100 mm in length, with a reference vessel diameter of 4.5–7.5 mm. Once in place, the stent permanently holds open a narrowed iliac artery and improves blood flow to the pelvis and legs.

Source: FDA, October 24, 2014

**XIENCE Stent Systems**
The XIENCE family of everolimus eluting coronary stent systems (Abbott Vascular) can now be used to treat chronic total occlusions, the FDA has ruled.

The agency also approved marketing of a new design for the delivery catheters. The systems include a cobalt chromium alloy stent coated with the drug everolimus and the revised delivery catheter. The design of the stent differs between the XIENCE V and the XIENCE PRIME, while the XIENCE PRIME, XIENCE Xpedition, and XIENCE Alpine have identical stent designs, which remain unchanged.

The safety and efficacy of the systems were established in the EXPERT CTO trial, a prospective, multicenter, one-arm, nonrandomized, open-label trial with clinical follow-up through five years.

Source: FDA, October 29, 2014

**Device Recalls**

**Hospira GemStar Power Supply**
Hospira, Inc., is recalling its GemStar Power Supply, 3VDC (an accessory to the GemStar Infusion Pump) because it may not deliver electricity properly. Loss of power could delay infusion therapy if no backup power supply is used.

Hospira has received 20 reports of incidents, and found that the infusion pump was operating on battery power while connected to the 3VDC power supply. The GemStar Supply converts alternating current voltage of 120 or 240 volts to direct current of 3.3 volts. In the U.S., the class I recall affects 5,687 units: the Wall Mount Power Supply, distributed from February 2013 through April 2013, and the Desk Top Power Supply, distributed from November 2011 through April 2013. A list of recalled lots is available at http://tinyurl.com/GemStar3VDC. For information and technical assistance, customers may call the Hospira Advanced Knowledge Center, 1-800-241-4002, option 4, 24 hours a day, seven days a week.

Source: FDA, November 11, 2014
software versions below 2.8 because a potential software problem can cause the ventilator to stop working after the air and oxygen gas supply lines are disconnected and then reconnected.

The ventilators were distributed from March 3, 2014, through August 22, 2014. A list of serial numbers in this class I recall is available at http://tinyurl.com/PB980. Covidien will update the software on the ventilators. For assistance, contact Covidien’s Technical Support Department at 1-800-255-6774, option 4, and then option 1, Monday through Friday, 6 a.m. to 4 p.m. Pacific time.

Source: FDA, October 28, 2014

**Covidien Defibrillation Electrodes**

Covidien is recalling automated external defibrillator (AED) electrodes sold under several names because the electrodes will not work with FR3 and FRx AEDs manufactured by Philips, which has changed the design of its connectors.

Use of the electrodes could delay electrical therapy needed to revive patients. Covidien has received two reports of injuries; a delay in resuscitation may have contributed to one patient’s death.

The class I recall covers all Medi-Trace Cadence Adult Multi-Function Defibrillation Electrodes Radiotransparent, Medi-Trace Cadence Adult Multi-Function Defibrillation Electrodes Preconnect, Kendall Adult Multi-Function Defibrillation Electrodes, Kendall 1710H Multi-Function Defibrillation Electrodes, MediChoice Multifunction Electrode, and Philips HEARTSTART Multifunction Electrode Pads. These electrodes, distributed from September 1, 2012, to August 24, 2014, will work with the appropriate Philips AEDs.

For information, contact Covidien Quality Assurance at 1-800-962-9888, option 8, extension 2500, Monday through Friday, 8 a.m. to 5 p.m. Eastern time.

Source: FDA, October 21, 2014

**Richard-Allan Scientific Formalin**

Richard-Allan Scientific recalled seven lots of 10% neutral buffered formalin products after discovering that some contained 0% to 3% formalin instead of the required 10%. A too-low concentration of formalin (used to preserve tissue samples for examination) will not properly protect them and can lead to damage, potentially preventing or delaying diagnoses and treatments.

The products and lots included in this class I recall, available at http://tinyurl.com/RASformalin, were distributed from July 18 through September 17, 2014. For questions, contact product support at 1-800-522-7270, option 2, Monday through Friday, 8 a.m. to 5 p.m. Eastern time.

Source: FDA, October 31, 2014

**DEVICE SPOTLIGHT**

**Kunj Gohil, PharmD, RPh**

**Name:** Implantable Miniature Telescope (part of the Implantable Telescope Technology platform)

**Manufacturer:** VisionCare Ophthalmic Technologies, Inc., Saratoga, California

**Approval Date:** October 13, 2014

**Purpose:** The Implantable Miniature Telescope is surgically placed in the eye and magnifies images onto the healthy areas of the light-sensing retina to help improve central vision.

**Description:** The Implantable Miniature Telescope improves visual acuity and quality of life for suitable patients with age-related macular degeneration (AMD) whose sight is permanently obstructed by a blind spot in their central vision, making it difficult or impossible to see faces, read, and perform everyday activities such as watching television, preparing meals, and performing self-care. The telescope, which functions similarly to a telephoto lens, is part of VisionCare’s platform based on wide-angle micro-optics that, in combination with the optics of the cornea, create a telephoto system that magnifies objects in view.

**Benefit:** AMD is the leading cause of vision loss among Americans 60 years of age and older, affecting an estimated 15 million people. Despite pharmacological advances in treatment, once patients progress to end-stage AMD they will experience a permanent obstruction in the center of their vision. This technology will yield better results than other surgical options. Interestingly, the implantable technology was approved years ago for older patients, but its availability has now been expanded to include patients ages 65–74 who suffer from AMD.

Source: www.visioncareinc.net

**Name:** Lutonix 035 Drug-Coated Balloon Percutaneous Transluminal Angioplasty Catheter (Lutonix DCB)

**Manufacturer:** Lutonix, Inc. (part of BARD Peripheral Vascular, Tempe, Arizona)

**Approval Date:** October 10, 2014

**Purpose:** This drug-coated balloon is used to re-open arteries in the thigh (superficial femoral arteries) and knee (popliteal arteries) that have been narrowed or blocked as a result of peripheral artery disease (PAD).

**Description:** The Lutonix DCB is a percutaneous transluminal angioplasty catheter with a balloon used to re-open the artery. The balloon is coated on its outer surface with the drug paclitaxel, which may help to prevent recurrent narrowing of arteries (restenosis) after the procedure. During the procedure, the artery is first partially opened with a traditional angioplasty balloon, without a drug coating. The Lutonix DCB is then used to fully open the narrowed portion of the artery and apply the drug to the artery wall.

**Benefit:** PAD is characterized by plaque buildup in the arteries that transport blood to the limbs; this narrowing of the arteries limits the flow of oxygen-rich
blood. This disease is extremely dangerous, and preventing additional blockages is just as important as removing the initial blockage. Clinical data demonstrate that the new Lutonix technology may be more effective than traditional procedures in preventing blockages in the artery. FDA approval is contingent on two post-marketing studies to further monitor the safety and efficacy of this technology.

**Sources:** www.fda.gov, www.bardpv.com

**Name:** inFlow Intraurethral Valve-Pump

**Manufacturer:** Vesiflo, Inc., Redmond, Washington

**Approval Date:** October 14, 2014

**Purpose:** A replaceable urinary prosthesis for use in female adults who cannot contract the muscles necessary to push urine out of the bladder (impaired detrusor contractility, or IDC).

**Description:** The device has four components: a sterilized, single-use urethral insert component with silicone shaft, fins, and flange; an introducer; an activator; and a sizing component. The device draws urine out to empty the bladder and blocks urine flow when continence is desired. A physician sizes the patient for an inFlow device and performs the initial insertion. After training, device insertion and removal can be performed by the patient or a caregiver. Each inserted component must be replaced at least once every 29 days.

**Benefit:** IDC leads to the inability to urinate because of impaired bladder muscle contraction, which can result from a number of conditions. Patients have traditionally been managed by various catheters, but current therapies limit the patient’s mobility. The inFlow device allows women with IDC to urinate without daily catheterization or a urine drainage bag.

**Sources:** www.fda.gov, www-vesiflo.com