NEW DRUG APPROVALS

Kybella for Submental Fat

Deoxycholic acid (Kybella, Kythera Biopharmaceuticals Inc.) has received FDA approval to treat moderate-to-severe fat below the chin, called submental fat. The product is not approved or recommended to treat fat outside of the submental area.

Kybella is identical to the deoxycholic acid produced in the body, which helps the body absorb fats. A cytolytic drug, it destroys the cell membrane when injected into tissue. When properly injected into the fat tissue in the submental area, the drug destroys fat cells; however, it can also destroy other types of cells, such as skin cells, if it is inadvertently injected into the skin.

Adults may receive up to 50 injections in a single treatment, with up to six single treatments administered no less than one month apart. Only a licensed health care professional should provide the injections, and patients should understand the associated risks before considering treatment.

The safety and effectiveness of deoxycholic acid for treatment of submental fat were established in two clinical trials: 1,022 adults with moderate or severe submental fat were randomly assigned to receive deoxycholic acid or a placebo for up to six treatments. Reductions in submental fat were observed more frequently in participants who received deoxycholic acid versus placebo.

Deoxycholic acid can cause serious side effects, including nerve injury in the jaw that can cause an uneven smile or facial muscle weakness, and trouble swallowing. The most common side effects include swelling, bruising, pain, numbness, redness, and areas of hardness in the treatment area.

Deoxycholic acid is being provided in single-patient-use vials and should not be diluted or mixed with other compounds.

Source: FDA, April 30, 2015

Tuzistra XR for Cough Relief

The FDA has approved codeine polistirex/chlorpheniramine polistirex extended-release oral suspension (Tuzistra XR, Vernalis LLC/Tris Pharma Inc.) to relieve coughs and symptoms associated with upper respiratory allergies or a common cold in patients 18 years of age and older.

Tuzistra XR, a Schedule III controlled substance, is meant to be dosed orally with or without food every 12 hours; it is not indicated for patients younger than 18 years of age. Codeine is an opiate agonist antitussive and chlorpheniramine is a histamine H1 receptor antagonist.

Tuzistra XR is contraindicated for postoperative pain management in children who have undergone tonsillectomy, adenoidectomy, or both. Respiratory depression and death have occurred in children who received codeine following those procedures and had evidence of being ultra-rapid metabolizers of codeine due to a cytochrome P450 CYP2D6 polymorphism. Tuzistra XR is also contraindicated in patients with known hypersensitivity to codeine, chlorpheniramine, or any of Tuzistra XR’s inactive ingredients. Persons known to be hypersensitive to certain other opioids may exhibit cross-sensitivity to codeine.

Source: Vernalis, May 1, 2015

Generic Approvals

Aripiprazole From Four Companies

Four companies have received FDA approval to market aripiprazole, the first generic versions of the second-generation antipsychotic drug Abilify (Otsuka America Pharmaceutical, Inc.). Abilify has annual U.S. sales of approximately $7.8 billion, according to IMS Data.

Alembic Pharmaceuticals, Hetero Labs Ltd., Teva Pharmaceuticals, and Torrent Pharmaceuticals can sell aripiprazole in multiple strengths and dosage forms. Otsuka is still seeking to protect some Abilify patents in court, but according to Teva (which has already launched its aripiprazole), a federal court has found that Otsuka’s likelihood of success is low.

Aripiprazole is approved to treat schizophrenia and bipolar disorder. Like all second-generation antipsychotics, it carries a boxed warning about an increased risk of death associated with off-label use to treat behavioral problems in older people with dementia-related psychosis. Its boxed warning also includes an increased risk of suicidal thinking and behavior in children, adolescents, and young adults taking antidepressants. Aripiprazole must be dispensed with a medication guide that describes important information about the drug’s uses and risks.

Sources: FDA and Teva Pharmaceuticals, April 28, 2015

Orally Disintegrating Vardenafil Tablets

The FDA has approved Watson Laboratories’ vardenafil hydrochloride orally disintegrating tablets, 10 mg (base), the first generic version of Bayer Healthcare’s Staxyn orally disintegrating tablets. Staxyn is a phosphodiesterase 5 inhibitor indicated for the treatment of erectile dysfunction.

Sources: FDA, April 22, 2015, and Staxyn prescribing information

Nebivolol Tablets

The marketing of 2.5-, 5-, 10-, and 20-mg nebivolol tablets by Amerigen Pharmaceuticals, Ltd., has received FDA approval. This is the first generic version of Bystolic (Forest Laboratories), a beta-adrenergic blocking agent indicated for the treatment of hypertension.

Sources: FDA, April 16, 2015, and Bystolic prescribing information

Fluorouracil Cream USP, 0.5%

Spear Pharmaceuticals has received FDA approval to market fluorouracil cream USP, 0.5%—the first generic ver- continued on page 356
Aurobindo Pharma Ltd. has secured FDA approval to market sildenafil injection, 10 mg/12.5 mL (0.8 mg/mL), the first generic version of Pfizer’s Revatio (Ranbaxy). This topical corticosteroid is indicated for relief of inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses.

Sources: FDA, April 13, 2015, and Kenalog prescribing information

**NEW INDICATIONS**

**Cyramza for Colorectal Cancer**

Ramucirumab injection 10 mg/mL solution (Cyramza, Eli Lilly) is now FDA-approved in combination with FOLFIRI chemotherapy (irinotecan, folinic acid, and 5-fluorouracil) to treat metastatic colorectal cancer that has progressed on or after therapy with bevacizumab, oxaliplatin, and a fluoropyrimidine.

The approval—ramucirumab’s fourth—was based on results from the phase 3 RAISE trial, which compared ramucirumab plus FOLFIRI (n = 536) with placebo plus FOLFIRI (n = 536) every two weeks in this patient population. Patients treated with ramucirumab/FOLFIRI compared with placebo/FOLFIRI achieved a median overall survival of 13.3 months versus 11.7 months and a median progression-free survival of 5.7 months versus 4.5 months, respectively.

Ramucirumab is a vascular endothelial growth factor (VEGF) receptor-2 antagonist that specifically blocks the binding of VEGF receptor ligands VEGF-A, -C, and -D. In the U.S., it is approved for use as a single agent or in combination with paclitaxel to treat advanced or metastatic gastric or gastroesophageal junction adenocarcinoma that has progressed on or after prior fluoropyrimidine- or platinum-containing chemotherapy, and in combination with docetaxel for metastatic non–small-cell lung cancer that has progressed on or after platinum-based chemotherapy.

Ramucirumab’s labeling contains boxed warnings for hemorrhage, gastrointestinal perforation, and impaired wound healing as well as additional warnings and precautions for arterial thromboembolic events, hypertension, infusion-related reactions, clinical deterioration in patients with Child-Pugh B or C cirrhosis, reversible posterior leukoencephalopathy syndrome, proteinuria (including nephrotic syndrome), thyroid dysfunction, and embryofetal toxicity. The most common adverse events observed in ramucirumab/FOLFIRI patients included diarrhea, neutropenia, decreased appetite, epistaxis, and stomatitis.

Source: Eli Lilly, April 24, 2015

**Avelox for Plague**

The FDA has approved moxifloxacin (Avelox, Bayer HealthCare Pharmaceuticals) to treat patients with pneumonic and septicemic plague. Avelox is also approved to prevent plague in adults.

Avelox is a phosphodiesterase 5 inhibitor indicated for the treatment of pulmonary arterial hypertension in adults to improve exercise ability and delay clinical worsening.

Sources: FDA, April 20, 2015, and Reva-tio prescribing information

**NEW DRUGS**

**Triamcinolone Acetonide Topical Spray**

The FDA has approved triamcinolone acetonide topical aerosol, USP, 0.147 mg/g, from Perrigo UK Finco Ltd.—the first generic formulation of Kenalog spray (Ranbaxy). This topical corticosteroid is indicated for relief of inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses.

Sources: FDA, April 20, 2015, and Carac prescribing information

**Sildenafil Injection**

Breo Ellipta (Breo Ellipta, GlaxoSmithKline/Theravance, Inc.) to include once-daily treatment of asthma in patients 18 years of age and older.

Breo Ellipta was approved in May 2013 for long-term, once-daily maintenance treatment of airflow obstruction and for reducing exacerbations in patients with chronic obstructive pulmonary disease. It is not indicated for the relief of acute bronchospasm.

Breo Ellipta is a fixed-dose combina-
tion of the inhaled corticosteroid fluticasone furoate and the long-acting beta2 agonist (LABA) vilanterol. Two strengths, 100/25 mcg and 200/25 mcg, have been approved for use in asthma patients, administered once daily with the Ellipta dry-powder inhaler.

The FDA issued a complete response letter on the proposed use of the medication in patients ages 12 to 17 years stating that the data did not show an adequate risk–benefit ratio to support this approval. Additional data will be required to demonstrate the medication’s safety and efficacy in this population.

LABAs increase the risk of asthma-related death, and data from controlled clinical trials suggest that LABAs increase the risk of asthma-related hospitalization in pediatric and adolescent patients. When treating asthma patients, physicians should prescribe fluticasone furoate/vilanterol only for patients not adequately managed on a long-term asthma-control medication, such as an inhaled corticosteroid, or whose disease severity clearly warrants the initiation of treatment with both an inhaled corticosteroid and a LABA.

Once asthma control is achieved and maintained, the patient should be assessed at regular intervals; Breo Ellipta should be discontinued if possible without loss of asthma control and the patient should be kept on a long-term asthma control medication, such as an inhaled corticosteroid.

Sources: GlaxoSmithKline, April 30, 2015, and Breo Ellipta prescribing information

**NEW DRUGS**

**Breakthrough Therapies**

**Venetoclax for CLL**

Venetoclax (AbbVie/Roche) has received an FDA breakthrough therapy designation for the treatment of chronic lymphocytic leukemia (CLL) in relapsed/refractory patients with the 17p deleterious genetic mutation. Up to 10% of CLL patients have this mutation at diagnosis, and it occurs in up to 50% of patients with relapsed/refractory CLL.

Venetoclax is an investigational oral B-cell lymphoma-2 (BCL-2) inhibitor being evaluated for the treatment of several cancers. The BCL-2 protein prevents apoptosis of some cells, including lymphocytes, and can be expressed in some cancers. Venetoclax is being evaluated in phase 2 and 3 clinical trials for the treatment of CLL.

Source: AbbVie, May 6, 2015

**Xalkori for ROS1-Positive NSCLC**

Crizotinib (Xalkori, Pfizer Inc.) has received an FDA breakthrough therapy designation for the treatment of ROS1-positive non–small-cell lung cancer (NSCLC), which accounts for approximately 1% of NSCLC.

The designation was based on data from an expansion cohort of the phase 1 Study 1001, which evaluated crizotinib in 50 patients with ROS1-positive advanced NSCLC. Crizotinib exhibited marked antitumor activity. Crizotinib, a kinase inhibitor, is FDA-approved to treat patients with metastatic NSCLC whose tumors are anaplastic lymphoma kinase–positive as detected by an FDA-approved test.

Source: Pfizer Inc., April 21, 2015

**Priority Reviews**

**Idarucizumab to Reverse Dabigatran**

The FDA has granted priority review to idarucizumab (Boehringer Ingelheim Pharmaceuticals, Inc.), a specific reversal agent for the anticoagulant effect of dabigatran, the active ingredient in the company’s Pradaxa. Idarucizumab would be used in patients needing emergency surgery or experiencing uncontrolled bleeding. The application for idarucizumab (which received breakthrough therapy status in June 2014) will be reviewed under the accelerated approval pathway. Currently, none of the novel oral anticoagulants has an approved reversal agent.

Phase 1 data showed the potential for idarucizumab, a humanized antibody fragment, to immediately reverse dabigatran’s anticoagulant effect with no clinically relevant adverse events. A phase 3 study, RE-VERSE AD, is ongoing.

Source: Boehringer Ingelheim Pharmaceuticals, Inc., April 23, 2015

**AbbVie Genotype 4 HCV Drug**

The FDA has awarded priority review to AbbVie’s all-oral, interferon-free treatment for adults chronically infected with hepatitis C virus genotype 4 (HCV GT4). The treatment combines ombitasvir/paritaprevir/ritonavir with ribavirin.

The FDA granted priority review based in part on results from HCV GT4 patients in the open-label, phase 2b PEARL-I study. After 12 weeks of treatment with the regimen, all of the 42 patients without cirrhosis who were new to therapy, and all of the 49 patients who had failed previous treatment with pegylated interferon and ribavirin, achieved a sustained virological response 12 weeks after the end of treatment (SVR12). Additionally, 40 of 44 patients (91%) who were new to therapy achieved SVR12 after taking the treatment without ribavirin.

HCV GT4 infection accounts for up to 6% of HCV infections. AbbVie’s regimen was granted a breakthrough therapy designation in June 2014.

Source: AbbVie, April 24, 2015

**Brilinta After Heart Attacks**

Ticagrelor (Brilinta, AstraZeneca) will receive FDA priority review for a new indication: use in patients more than one year after a heart attack.

The new application is based on the PEGASUS-TIMI 54 study, in which 21,162 patients who had had a myocardial infarction (MI) one to three years earlier received ticagrelor 90 mg twice daily,
ticagrelor 60 mg twice daily, or placebo, as well as low-dose aspirin. After a median 33 months of follow-up, the primary efficacy endpoint—a composite of cardiovascular death, MI, or stroke—was 7.85% for ticagrelor 90 mg, 7.77% for ticagrelor 60 mg, and 9.04% for placebo. Rates of Thrombolysis in Myocardial Infarction major bleeding were 2.60% with ticagrelor 90 mg, 2.30% with ticagrelor 60 mg, and 1.06% with placebo.

Brilinta, a direct-acting, selective, reversibly binding P2Y12 receptor antagonist, inhibits platelet activation. The 90-kg tablets are indicated to reduce the rate of thrombotic cardiovascular events in patients with acute coronary syndromes.

Sources: AstraZeneca, April 29, 2015, and New England Journal of Medicine, March 14, 2015

Medication Recalls
Mylan Injectable Products

Mylan Institutional recalled eight lots of four injectable products due to the presence of particulate matter observed during sample testing. The recalls cover injectable gemcitabine, carboplatin, methotrexate, and cytarabine with expiration dates from May 2015 to August 2016 packaged by Agila Onco Therapies Ltd., a Mylan subsidiary; some carry Pfizer Injectable labels. A list is available at http://tinyurl.com/MylanInjectablesRecall. For information, contact Mylan Customer Relations at 1-800-796-9526, Monday through Friday, 8 a.m. to 5 p.m. Eastern time.

Source: Mylan Institutional, April 23, 2015

Teva Adrucil

Teva Parenteral Medicines recalled eight lots of fluorouracil injection, USP (Adrucil) 5 g/100 mL because of the potential presence of an aggregate of silicone rubber pieces from a filler dia-phragm and fluorouracil crystals. Adrucil is distributed in pharmacy bulk packages of five 5 g/100 mL vials per shelf pack. Numbers of the lots (expiring from November 2015 to July 2016) are available at http://tinyurl.com/TevaAdrucilRecall. Call Teva Customer Service with questions at 1-800-545-8800, Monday through Friday, 8 a.m. to 5 p.m. Eastern time.

Source: Teva, May 4, 2015

Hospira Bupivacaine HCl Injection

Hospira, Inc. recalled lot 38-515-DK of preservative-free bupivacaine HCl injection, USP, 0.5% (5 mg/mL), 30 mL single-dose vials, after iron oxide particles were found in one glass tear top vial. The lot, expiring in February 2016, was distributed from July 2014 to September 2014. For assistance, call Stericycle at 1-866-918-8770, Monday through Friday, 8 a.m. to 5 p.m. Eastern time.

Source: Hospira, Inc., April 23, 2015

RESEARCH BRIEFS
Pharmacists Help Lower BP

Patients referred to a pharmacist-run hypertension program had significantly improved blood pressure one year later, according to a study at Roudebush Veterans Affairs (VA) Medical Center in Indianapolis.

The study compared 465 patients with high blood pressure (BP) with 1,268 control participants. Six clinical pharmacists provided the hypertension care management program in four primary care clinics as part of the VA’s Patient-Aligned Care Team model. Patients were discharged from the program once they reached their BP goals, but could be sent back to the pharmacist for additional management.

At six and 12 months, systolic BP fell from baseline by –4.0 and –7.1 mm Hg, respectively, among program participants, compared with –1.6 and –2.6 mm Hg among controls. Diastolic BP dropped by –2.5 and –3.2 mm Hg at six and 12 months among the program’s patients, compared with –1.1 and –1.2 mm Hg in the control group. The researchers say their findings support pharmacists’ expanded role as part of the patient-centered model for improving hypertension and cardiovascular outcomes.

The pharmacists’ effect on BP was not necessarily due to improved adherence. Similar proportions of patients in both groups adhered to their antihypertensive medication regimen: 35% of the program’s patients and 32% of controls.

Instead, the improvements may have occurred because the pharmacists were tasked with changing the medication regimens to maximize effectiveness, “balancing the efficacy and safety of the medications with the preferences of the patient.”

It’s possible, the researchers say, that the hypertension drug regimens the pharmacists initiated were more potent while avoiding or mitigating adverse effects.

Source: American Journal of Medicine, May 2015

Oncology Drug Spending Soars

Total global spending on oncology medications (including therapeutic treatments and supportive care) reached $100 billion in 2014, the IMS Institute for Healthcare Informatics reports. Spending on oncology drugs in the U.S. rose at a compounded annual growth rate of 5.3% in 2014 to reach $42.4 billion.

The report says the pace of change in cancer care is accelerating. Innovative treatments, often combined with other new or existing medicines and often associated with biomarkers, are emerging from the research-and-development pipeline. Many are for tumor types with low survival rates and limited treatment options.

The changing landscape is adding complexity for oncologists, payers, and governments seeking to provide appropriate patient care while ensuring the sustainability of health care systems. Earlier
diagnosis, longer treatment duration, and increased effectiveness of drug therapies are contributing to rising spending. In most instances, five-year survival rates have risen through continuous small improvements in detection and treatment, including refinements with existing therapies.

Assessing oncology products’ value has become more complicated because most products have multiple indications. Of 88 cancer drugs marketed in 2014, 40 were for single indications and 48 were for multiple indications. By 2020, most cancer drugs will carry multiple indications, reflecting developers’ pursuit of genetic targets across multiple tumors and the rise of immuno-oncologic agents that may have more than six indications, the report predicts.

Sources: IMS Institute for Healthcare Informatics and Formulary Watch, May 5, 2015

Home Health Care Infections

About 3.5% of patients being treated at home develop infections that lead to emergency care or hospitalization, Columbia University researchers say.

The researchers analyzed 2010 data from 199,462 patients and 8,255 home health care (HHC) agencies included in the national Outcome and Assessment Information Set. Of that sample, 11,476 patients (6%) received emergency care during HHC treatment, nearly always leading to hospital admission. About 5% of hospitalizations were planned, but 18% were not, and of those unplanned hospitalizations, 17% were caused by infections. In fact, three of the top six reasons for unplanned hospitalization were related to infections, most commonly respiratory, wound, urinary tract, and intravenous/catheter–related infections. The average time to developing an infection while receiving HHC was 24 days.

Agency-level infection rates varied from 0 to 100%, the researchers say, with an average of 3%. Because some agencies had very few patients, the researchers calculated the infection rate with agencies caring for 10 or more patients, yielding a rate of 3.5%. Approximately one-fourth of those agencies had no infections.

Infection rates may vary because the agencies follow different infection control practices. The researchers cite a 2002 article that estimated 1.2 million infections in HHC every year and called for national HHC infection surveillance—a system that has not been established. Moreover, the researchers say, evidence of infection control policy and practice in HHC is “sparse.” A study using a national representative sample, they suggest, could help HHC policy-makers understand practice adherence and make recommendations that improve HHC quality.

Source: American Journal of Infection Control, May 2015

Aiding Constipation From Opioids

The combination of prolonged-release (PR) oxycodone and naloxone relieves pain and opioid-induced constipation (OIC) significantly better than PR oxycodone alone, Belgian researchers say.

In their study, 65 patients with laxative-refractory OIC received PR oxycodone alone or with naloxone at a median dose of 20 mg per day. Pain and constipation relief were assessed at three visits over 12 weeks.

The combination was superior to oxycodone alone in improving pain relief, OIC, and quality of life. The Bowel Function Index (BFI) showed a statistically significant improvement of 48.5 points from visit 1 to visit 3. A BFI change of 12 points or more has proven to be related to clinically meaningful changes in OIC patients’ bowel habits. The average BFI was less than 28.8 after patients took the combination for six weeks, indicating that most were no longer constipated.

The mean pain score was significantly lower with the combination. On a scale of 0 to 10, scores fell by an average of 2.1 during treatment to a mean score of 3.8 at 18 weeks.

The researchers say the median oxycodone/naloxone dose remained constant throughout the study and the number of patients who used analgesic rescue medication in the seven days before each visit fell from 44 (65%) to 26 (42%). That means increased doses or use of rescue medication can’t explain the improved pain relief, which is probably related to improved constipation relief.

Quality-of-life scores increased significantly and the number of patients using laxatives in the seven days before each visit dropped from 65 to 24 by visit 3. Only two patients reported adverse events, which were mild or unrelated to the study treatment.

Source: Clinical Therapeutics, April 2015

A Targeted Approach to RA

Some patients with rheumatoid arthritis (RA) do well when their dose of tumor necrosis factor (TNF) inhibitor is reduced or stopped, but the results aren’t easy to predict. Findings from the Dose Reduction Strategy of Subcutaneous TNF Inhibitors (DRESS) study suggest that, in general, it may be alright to try a treat-to-target approach, in which the intervals between injections are lengthened until the patient has a flare or the drug can be stopped.

In this study of RA patients with low disease activity at two Dutch rheumatology outpatient clinics, 121 were assigned to dose-reduction treatment with adalimumab (Humira, AbbVie) or etanercept (Enbrel, Immunex) and 59 to usual care. The disease-activity strategy guided dose reduction stepwise, increasing the injection interval every three months.

At 18 months, the researchers found
Spirometry Underused in Asthma

Spirometry is recommended to help diagnose asthma, but its use—already low—has declined, University of Texas researchers report.

In 2007, the National Asthma Education and Prevention Program published comprehensive, evidence-based guidelines that included spirometry. Evaluating trends over the past 10 years, the Texas researchers analyzed data on 134,208 patients diagnosed with asthma and found that only 48% had spirometry within a year of diagnosis.

Spirometry plays a vital role in diagnosing and managing asthma by accurately measuring air volumes and flows. Guidelines recommend spirometry at the initial assessment; after treatment is initiated and symptoms and peak expiratory flow have stabilized; during periods of progressive or prolonged loss of asthma control; and at least every one to two years. But according to the American Academy of Allergy, Asthma, and Immunology, the researchers say, clinicians often rely on symptoms alone to diagnose and manage asthma, and symptoms may be misleading.

The decrease in spirometry use could be explained by a concurrent increase in asthma patients being treated solely by primary care practitioners, the researchers say. Patients who received care from a specialist, including allergists and pulmonary specialists, were more likely to receive spirometry. Of the 4,756 patients who were co-managed by primary care physicians, allergists, and pulmonary specialists, 92% had spirometry.

Use of short-acting bronchodilators and controller therapies was higher in asthma patients who had spirometry than those who did not. Among patients who did not have spirometry, 78% received at least one inhaler and more than 50% were on controller inhaler medications.

Although studies have found spirometry helps improve asthma care, surveys have revealed barriers to its use, such as lack of equipment and training. Still, the researchers cite some cost comparisons: spirometry, about $42; unnecessary use of an inhaled corticosteroid, $200 to $300 a month; and an emergency department visit for an asthma episode, about $3,500.

Source: BMJ, April 9, 2015

PTSD Increases Heart Failure

Veterans with post-traumatic stress disorder (PTSD) are nearly 50% more likely to develop heart failure than veterans without PTSD, according to an analysis of records from the Veterans Affairs Pacific Islands Health Care System.

Researchers reviewed medical records for 8,248 veterans treated as outpatients from 2005 to 2012. During the study, 1,712 veterans were diagnosed with PTSD. Over an average follow-up of seven years, 287 veterans without PTSD and 84 veterans with PTSD developed heart failure.

The difference between the two groups’ rates held up even after researchers controlled for known clinical risk factors and military-specific factors, such as combat service.

The evidence linking PTSD to coronary heart disease is “substantial,” the researchers say. They note that veterans with PTSD are significantly more likely to have abnormal electrocardiograph results, myocardial infarctions, and atrioventricular conduction deficits than veterans without PTSD. They cite several hypotheses for the mechanisms by which PTSD contributes to heart disease. For instance, a hallmark symptom of PTSD—hyperarousal—and the subsequent sustained sympathetic nervous system activation affect the release of neurotransmitters and endocrine function, harming the cardiovascular system.

Source: American Journal of Public Health, April 2015

DEVICE NEWS

Ionsys Pain-Drug Device Approved for Hospital Use

The FDA has approved the fentanyl iontophoretic transdermal system (Ionsys, The Medicines Company), the first needle-free, patient-controlled, pre-programmed fentanyl delivery system, for the short-term management of acute postoperative pain in hospitalized adults who require opioid analgesia.

Patients recovering from surgery control their analgesic dosing by pushing a button to dispense fentanyl transdermally via an imperceptible electrical current as needed for pain. The device is to be used only for hospitalized patients enrolled in the Ionsys risk evaluation and mitigation strategy (REMS) program and is not meant for home use. The Ionsys REMS aims to mitigate the risk of respiratory depression resulting from accidental exposure to persons for whom it is not prescribed.
Ionsys, originally developed by Johnson & Johnson (J&J), won FDA approval in 2006. But after its launch in Europe in 2008, it was recalled because of device stability issues and never reached the U.S. market. The Medicines Company gained access to the treatment through its 2012 acquisition of Incline Therapeutics Inc., which had acquired the device from J&J in 2010.

Sources: The Medicines Company, April 29, 2015, and Reuters, April 30, 2015

Medtronic, FDA Agree on Synchronaed II Restrictions

Medtronic, Inc., will stop making most Synchronaed II Implantable Infusion Pump Systems—at least for now—after repeatedly failing to correct violations that FDA inspectors found at its production facilities, the agency said.

Medtronic and the FDA agreed to a consent decree, now awaiting federal court approval, against the company and two of its officers, S. Omar Ishrak and Thomas M. Tefft. The violations occurred at Medtronic’s Neuromodulation facilities in Columbia Heights, Minnesota, where the devices are made.

The Synchronaed systems deliver medication to treat cancer, chronic pain, and severe spasticity. The consent decree requires Medtronic to stop manufacturing, designing, and distributing them except in very limited cases, such as when a physician determines that the system is medically necessary for a patient’s treatment.

Medtronic must also retain a third-party expert to help develop and submit plans to the FDA to correct violations. Until the FDA determines that the company has complied with all of the consent decree’s provisions, it will remain in effect. Once Medtronic receives FDA permission to resume the design, manufacture, and distribution of these products, the company must continue to submit audit reports to the FDA, which will also conduct its own inspections.

Medtronic said it expects to implement design changes to the Synchromed II pumps and enhance the Neuromodulation quality system.

The FDA approved the Synchronaed II pumps in 2004, and first identified manufacturing problems in 2006 that can result in over- or under-infusion or a delay in therapy for patients. Between 2006 and 2013, the FDA conducted five inspections at Neuromodulation that resulted in three warning letters for major violations, including inadequate processes for identifying, investigating, and correcting quality problems; failure to document design changes; and failure to ensure that finished products meet design specifications.

Patients with an implanted Synchromed II pump should maintain regular follow-up appointments with their physicians. There is no need for patients to change their current course of therapy or have the pump removed.

Sources: FDA and Medtronic, Inc., April 27, 2015

Device Recalls

OriGen Recalls VV13F ECMO Catheters

OriGen Biomedical has recalled one lot of VV13F Reinforced Dual Lumen Extracorporeal Membrane Oxygenation (ECMO) Catheters because a clear extension tube can potentially separate from its hub. One product failure resulted in a patient’s death, the company said.

The class I recall involves lot N18549, which was distributed from February 16, 2015, to March 26, 2015, and expires in September 2018.

The catheter is indicated for use as a single cannula for both venous drainage and re-infusion of blood in the internal jugular vein during extracorporeal life support procedures of six hours or less in neonatal intensive care and pediatric intensive care ECMO centers. Customers with questions can contact the company at 512-474-7278, Monday through Friday, 8 A.M. to 5 P.M. Central time.

Source: OriGen Biomedical, April 15, 2015

TigerPaw Occlusion Fastener

The FDA has recalled all 4,154 units of the TigerPaw System II (LAAx, Inc., a subsidiary of Maquet Medical Systems), a surgical staple used to close tissue in the left atrial appendage of the heart. Incomplete closure may result in tissue tears and/or bleeding, and the left atrial wall may tear during use of the device. The firm has received 51 reports of adverse events, including one death.

The units were distributed from April 1, 2013, through March 23, 2015. Customers with questions about the class I recall can contact Maquet Customer Service at 1-888-880-2874, 6 A.M. to 5 P.M. Pacific time.

Source: FDA, April 23, 2015, and May 7, 2015

Ebola Virus One-Step Test Kits

Ebola Virus One-Step Test Kits (LuSys Laboratories, Inc.) have been recalled because the FDA has not cleared or approved them for use or sale. The results from the tests have not been shown to be accurate and should not be used as in vitro diagnostic tests for Ebola infection, the agency said.

This class I recall covers all lots of the kits, which were sold in California and exported to Sierra Leone, Canada, and Denmark between October 2014 and January 2015. Questions should be directed to LuSys Laboratories at 858-546-0902, Monday through Friday, 9 A.M. to 5:30 P.M. Pacific time.

Source: April 23, 2015

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DEVICE SPOTLIGHT
Kunj Gohil, PharmD, RPh

Name: Myopore Sutureless Myocardial Pacing Lead
Manufacturer: Greatbatch Medical, Clarence, New York
Approval Date: April 30, 2015
Purpose: The Myopore Sutureless Myocardial Pacing Lead is indicated when ventricular epicardial attachment is required or when a transvenous lead cannot provide effective pacing.
Description: This device is a surgically implanted, insulated, and sutureless wire with a screw-in tip. It is part of a permanently implanted cardiac resynchronization therapy (CRT) device, pacemaker, or defibrillator.
Benefit: The Myopore pacing lead can be implanted using a small incision under the breastbone, allowing a less-invasive procedure for eligible patients; the lead is placed on the surface of the heart muscle and the screw-in tip can electrically stimulate the heart's ventricles. This lead allows for use of a CRT device when other leads cannot be implanted, which gives various types of patients a viable option in controlling heart rhythm.
Sources: www.greatbatchmedical.com, www.fda.gov

Name: Raplixa
Manufacturer: The Medicines Company, Parsippany, New Jersey
Approval Date: April 30, 2015
Purpose: Raplixa helps control bleeding during surgery from small blood vessels when standard surgical techniques, such as suture, ligature, or cautery, are ineffective or impractical.
Description: Raplixa is a biological product containing fibrinogen and thrombin. It can be applied directly from the product vial or sprayed onto a bleeding site with the RaplixaSpray delivery device.
Benefit: This product provides surgeons with a convenient option to control bleeding during surgical procedures; the easy-to-use agent also works well across multiple bleeding settings. Approval was granted based on results from a phase 3, multicenter trial, which demonstrated that hemostasis was superior with Raplixa when compared to sponge alone.
Sources: www.fda.gov, http://ir.themedicinescompany.com

Name: Senza System
Manufacturer: Nevro Corporation, Menlo Park, California
Approval Date: May 8, 2015
Purpose: This system aids in the management of chronic intractable pain of the trunk and/or limbs.
Description: A minimally invasive procedure is performed to implant the system into the patient’s body. It then delivers electrical stimulation to the lower-mid region of the back through implanted leads, which are connected to a rechargeable pulse generator that is implanted into the patient's upper buttocks or abdomen. A remote control is used to operate the pulse generator within ranges programmed by the clinician.
Benefit: An increasing prevalence of chronic pain is seen in today’s society, with several options available to patients. Unfortunately, many of these systems are associated with paresthesia (a tingling sensation), which patients do not like. The Senza System can reduce pain without producing paresthesia by providing high-frequency stimulation (at 10 KHz) and low stimulation amplitudes, which may be preferred by patients suffering from chronic pain.
Sources: www.fda.gov, www.nevro.com