NEW DRUG APPROVALS

Keytruda for Treatment Of Advanced Melanoma

The FDA has approved pembrolizumab (Keytruda, Merck) to treat certain melanoma patients—the first anti-programmed death receptor-1 (PD-1) therapy authorized in the U.S.

At 2 mg/kg every three weeks, pembrolizumab is indicated for the treatment of patients with unresectable or metastatic melanoma and disease progression after treatment with ipilimumab (Yervoy, Bristol-Myers Squibb) and, if those patients are BRAF V600 mutation-positive, a BRAF inhibitor. This indication received accelerated approval based on the tumor response rate and the durability of response; an improvement in survival or disease-related symptoms has not been established. Pembrolizumab received FDA breakthrough therapy designation for the treatment of advanced melanoma.

The approval was based on data from an open-label, randomized, dose-comparative cohort in the ongoing KEYNOTE-001 phase 1b trial in patients with unresectable or metastatic melanoma and disease progression. For the recommended 2-mg/kg dose (based on data from 89 patients), the overall response rate was 24%, with one complete response and 20 partial responses. At the time of the analysis, 18 of the 21 patients with objective responses (86%) had ongoing responses of more than 1.4 to more than 8.5 months. Phase 2 and 3 studies are being conducted to provide confirmatory evidence for this indication.

Pembrolizumab is a humanized monoclonal antibody that works by helping the body’s immune system fight advanced melanoma. The drug blocks the interaction between PD-1 and its ligands, PD-L1 and PD-L2. Immune-mediated adverse reactions have included pneumonitis, colitis, hepatitis, hypophysitis, nephritis, hyperthyroidism, and hypothyroidism. Pembrolizumab may cause fetal harm when administered to a pregnant woman.

Sources: FDA and Merck, September 4, 2014

Contrave to Manage Weight

Naltrexone hydrochloride/bupropion hydrochloride (Contrave, Takeda Pharmaceuticals America/Orexigen Therapeutics) has received FDA approval as a treatment option for chronic weight management in addition to a reduced-calorie diet and physical activity.

The drug is approved for adults with a body mass index (BMI) of 30 or greater, and for adults with a BMI of 27 or greater who have at least one weight-related condition, such as hypertension, type-2 diabetes, or dyslipidemia.

Contrave combines naltrexone and bupropion in an extended-release formulation. Both are FDA-approved: naltrexone for alcohol and opioid dependence, and bupropion for depression, seasonal affective disorder, and smoking cessation.

The medication’s effectiveness was evaluated in clinical trials that included approximately 4,500 obese and overweight patients with and without significant weight-related conditions who were treated for one year. All ate a reduced-calorie diet and added physical activity.

In one trial, patients without diabetes lost 4.1% of their weight, on average, compared with placebo at one year; 42% of patients on Contrave lost at least 5% of their weight compared with 17% of those on placebo. In another trial, patients with type-2 diabetes lost 2% of their weight, on average, compared with placebo at one year; 36% of those using Contrave lost at least 5% of their weight, compared with 18% of the placebo group.

Contrave has a boxed warning regarding the increased risk of suicidal thoughts and behaviors associated with antidepressant drugs such as bupropion. This warning also notes that serious neuropsychiatric events have been reported in patients taking bupropion for smoking cessation.

Contrave can cause seizures and must not be used in patients with seizure disorders. The drug can also raise blood pressure and heart rate and must not be used in patients with uncontrolled hypertension. The most common adverse events with Contrave include nausea, constipation, headache, vomiting, dizziness, insomnia, dry mouth, and diarrhea.

The FDA is requiring post-marketing studies to assess Contrave’s cardiovascular risk; its efficacy, safety, and pharmacology in pediatric patients; its effect on cardiac conduction; its dosing in patients with hepatic or renal impairment; and its potential for interactions with other drugs. A nonclinical juvenile toxicity study will focus on growth and development.

Source: FDA, September 10, 2014

Triumeq, One Pill for HIV-1

The FDA has approved Triumeq (ViiV Healthcare), a single-pill regimen for patients infected with human immunodeficiency virus-1 (HIV-1) that contains abacavir 600 mg, dolutegravir 50 mg, and lamivudine 300 mg. Dolutegravir is an integrase strand transfer inhibitor (INSTI); abacavir and lamivudine are nucleoside reverse transcriptase inhibitors (NRTIs).

The FDA’s approval was based primarily on data from two clinical studies: the phase 3 SINGLE trial in treatment-naïve adults, conducted with dolutegravir and abacavir/lamivudine as separate pills; and a bioequivalence study of the fixed-dose combination of abacavir, dolutegravir, and lamivudine when taken as a single pill compared with the administration of dolutegravir and abacavir/lamivudine as separate pills.

In SINGLE, more patients in the dolutegravir and abacavir/lamivudine arm had undetectable HIV-1 compared with patients treated with Atripla (efavirenz, emtricitabine, and tenofovir, Bristol-
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Myers Squibb/Gilead Sciences)—the most commonly used single-pill regimen. The difference, which was statistically significant and met the prespecified test for superiority, was driven by a higher rate of discontinuation due to adverse events in the Atripla arm.

At 96 weeks, 80% of patients treated with the dolutegravir-based regimen were virologically suppressed compared with 72% of patients treated with Atripla. Treatment-emergent adverse reactions with the dolutegravir-based regimen included insomnia, headache, and fatigue. Triumeq has a boxed warning regarding the potential for hypersensitivity reactions, lactic acidosis, severe hepatomegaly, and exacerbations of hepatitis B.

Triumeq alone is not recommended for use in patients with resistance to any of its components, with resistance-associated integrase substitutions, or with clinically suspected INSTI resistance. Before initiating treatment, clinicians should screen for the HLA-B*5701 allele; products containing abacavir should not be used in patients with that genetic marker.

Source: ViiV Healthcare, August 22, 2014

**Cerdelga for Gaucher Disease**

Eliglustat (Cerdelga, Genzyme) has won FDA approval for the long-term treatment of adults with type-1 Gaucher disease, a rare genetic disorder.

In Gaucher disease, the body does not produce enough of the enzyme glucocerebrosidase. This deficiency causes fatty materials to collect in the spleen, liver, and bone marrow. The major signs of Gaucher disease include liver and spleen enlargement, anemia, low platelet counts, and bone problems. Eliglustat, taken orally, slows the production of the fatty materials by inhibiting the metabolic process that forms them.

Eliglustat was evaluated in two clinical trials involving 199 subjects with type-1 Gaucher disease. In a randomized, double-blind, placebo-controlled trial among people who had not previously received enzyme replacement therapy (ERT), eliglustat treatment resulted in a greater reduction in spleen volume from baseline to the end of the study (by week 39) and greater improvement in liver volume, blood platelet count, and hemoglobin level compared with placebo.

The other trial compared eliglustat to ERT in 159 subjects with type-1 Gaucher disease previously treated with and stabilized on ERT. They received either eliglustat or the ERT drug imiglucerase (Cerezyme, Genzyme). Treatment with eliglustat resulted in similar stabilization of the hemoglobin level, platelet count, and spleen and liver volumes compared with imiglucerase.

The most common side effects in trials of eliglustat were fatigue, headache, nausea, diarrhea, back pain, pain in the extremities, and upper abdominal pain.

Source: FDA, August 19, 2014

**Ferric Citrate for Hyperphosphatemia**

The FDA has approved ferric citrate (formerly known as Zerenex, Keryx Biopharmaceuticals, Inc.) for the control of serum phosphorus levels in patients with chronic kidney disease (CKD) on dialysis.

In phase 3 clinical trials, ferric citrate effectively reduced serum phosphorus levels to well within the Kidney Disease Outcomes Quality Initiative guidelines range of 3.5 mg/dL to 5.5 mg/dL. In addition, ferric citrate’s pharmacodynamic properties resulted in increased ferritin and transferrin saturation (TSAT), while these parameters remained relatively constant in patients treated with active control (sevelamer carbonate [Renvela, Sanofi-Aventis] and/or calcium acetate [Phoslo, Fresenius Medical Care]).

The most common adverse events with ferric citrate were gastrointestinal, including diarrhea, nausea, vomiting, and constipation. The product labeling includes a warning about the potential for iron overload. Physicians should monitor ferritin and TSAT, and should assess the need to reduce the dose of or discontinue intravenous iron therapy.

The FDA recently informed the company that approval of the brand name Zerenex had been rescinded.

Sources: Keryx Biopharmaceuticals, Inc., September 5, 2014, and ferric citrate prescribing information

**Arnuity Ellipta for Asthma**

The FDA has approved fluticasone furoate inhalation powder (Arnuity Ellipta, GlaxoSmithKline), a once-daily inhaled corticosteroid medication for maintenance treatment of asthma as prophylactic therapy in patients 12 years of age and older.

The efficacy and safety of Arnuity Ellipta have been evaluated in more than 3,600 patients with asthma. The approved doses, 100 mcg and 200 mcg, are administered once daily via the Ellipta dry-powder inhaler.

Arnuity Ellipta is not indicated for the relief of acute bronchospasm. The medication is contraindicated for the primary treatment of status asthmaticus or acute episodes of asthma requiring intensive measures and in patients with severe hypersensitivity to milk proteins or any ingredients of Arnuity Ellipta.

*Candida albicans* infection of the mouth and throat may occur in patients treated with Arnuity Ellipta. Patients who use corticosteroids are at risk for potential worsening of existing tuberculosis; fungal, bacterial, viral, or parasitic infections; or ocular herpes simplex. A more serious or even fatal course of chickenpox or measles may occur in susceptible patients.

Source: GlaxoSmithKline, August 20, 2014
Hyqvia for Primary Immunodeficiency

Immune globulin infusion 10% (human) with recombinant human hyaluronidase (Hyqvia, Baxter International/Halozyme Therapeutics) has received FDA approval for adults with primary immunodeficiency (PI).

Hyqvia is the first subcutaneous immune globulin treatment approved for PI patients with a dosing regimen requiring only one infusion up to once a month (every three to four weeks) and one injection site per infusion to deliver a therapeutic dose. Most PI patients receive intravenous infusions in a physician’s office or an infusion center, and current subcutaneous immune globulin treatments require weekly or biweekly treatment with multiple infusion sites per treatment.

The immune globulin component of Hyqvia—a 10% solution that is prepared from large pools of human plasma consisting of at least 98% immune globulin G (IgG)—contains a broad spectrum of antibodies and provides the treatment’s therapeutic effect. The recombinant human hyaluronidase in Hyqvia increases the dispersion and absorption of the immune globulin infusion 10% (human).

Hyqvia has a boxed warning noting that thrombosis may occur with immune globulin products.

Source: Baxter International, September 12, 2014

Generic Approvals Entecavir

Teva Pharmaceutical Industries Ltd. has launched the first U.S. generic entecavir tablets, 0.5 mg and 1.0 mg. The brand-name product, Baraclude (Bristol-Myers Squibb), had annual U.S. sales of approximately $328 million as of June 2014, according to IMS data.

Entecavir is a hepatitis B virus (HBV) nucleoside analog reverse transcriptase inhibitor indicated for the treatment of chronic HBV infection in adults with evidence of active viral infection. Patients should have either evidence of persistent elevations in serum aminotransferases (ALT or AST) or histologically active disease. The labeling includes a boxed warning regarding the potential for severe acute exacerbations of hepatitis B; use in patients with human immunodeficiency virus and HBV; and lactic acidosis and hepatomegaly.

Sources: Teva Pharmaceutical Industries Ltd., September 4, 2014, and Entecavir package insert

Decitabine for Injection

InnoPharma, Inc., has received FDA approval for decitabine for injection, a generic version of Eisai Inc.’s Dacogen. Sandoz, Inc., will sell, market, and distribute InnoPharma’s generic formulation in the U.S. According to IMS data, U.S. sales of Dacogen were approximately $251 million for the 12 months ending in April 2014.

Decitabine for injection will be sold in 20-mL single-dose glass vials containing 50 mg of decitabine. It is indicated for the treatment of patients with myelodysplastic syndromes.

Source: InnoPharma, Inc., August 29, 2014

Potassium Chloride Extended Release

Mylan Inc. has launched potassium chloride extended release tablets USP, 8 mEq (600 mg) and 10 mEq (750 mg), the generic version of Upsher-Smith’s Klor-Con. The medication is indicated for the treatment of patients with hypokalemia, with or without metabolic alkalosis; in digitalis intoxication; and in patients with hypokalemic familial periodic paralysis.

These dosages of the medication had U.S. sales of approximately $135 million for the 12 months ending June 30, 2014, according to IMS Health.

Source: Mylan Inc., August 22, 2014

Tacrolimus Topical Ointment

Fougera Pharmaceuticals has received FDA approval for tacrolimus topical ointment 0.03% and 0.1%, the first generic versions of Protopic ointment marketed by Astellas Pharma U.S., Inc.

The topical ointment of tacrolimus (a macrolide immunosuppressant) is indicated for second-line therapy for short-term, noncontinuous chronic treatment of moderate-to-severe atopic dermatitis in nonimmunocompromised patients who have failed to respond adequately to other topical prescription treatments for atopic dermatitis, or when those treatments are not advisable.

Sources: FDA, September 9, 2014, and Protopic ointment prescribing information

Frovatriptan Succinate

The FDA has approved Mylan Inc.’s frovatriptan succinate tablets 2.5 mg (base), the first generic version of Endo Pharmaceutical’s Frova, which is used to treat acute migraine headaches in adults.

In 2013, frovatriptan had U.S. sales of approximately $66 million, according to IMS Health. Mylan’s launch of the product will be governed by a court settlement of patent litigation between Endo and Mylan.


Ibandomate Sodium Injection

Mylan Inc. has launched ibandomate sodium injection, 1 mg (base)/mL, packaged in 3 mg (base)/3 mL pre-filled glass syringes, the generic version of Hoffmann-La Roche’s Boniva Injection. Ibandomate sodium injection is indicated for the treatment of osteoporosis in postmenopausal women.

Source: Mylan Inc., September 5, 2014
NEW INDICATIONS
Xtandi’s Use Extended For Prostate Cancer

The FDA has expanded the use of enzalutamide (Xtandi, Medivation/Astellas Pharma) among men with metastatic castration-resistant prostate cancer (CRPC) after a priority review of a supplemental new drug application based on results from the phase 3 PREVAIL trial.

The FDA approved enzalutamide, an oral, once-daily androgen receptor inhibitor, in August 2012 for use in patients with metastatic CRPC who had received chemotherapy with docetaxel. The new indication approves enzalutamide for use in men with metastatic CRPC who have not received chemotherapy.

In PREVAIL, men receiving enzalutamide and gonadotropin-releasing hormone (GnRH) therapy showed a statistically significant improvement in both overall survival and the time to radiographic progression or death compared with men receiving placebo and GnRH therapy. Enzalutamide reduced the risk of radiographic progression or death by 83% and the risk of death by 29% compared with placebo. Enzalutamide also delayed the time to initiation of chemotherapy and the time to a skeletal-related event.

Seizure occurred in 0.9% of patients treated with enzalutamide who had received docetaxel and in 0.1% of chemotherapy-naïve patients. The most common adverse reactions in two randomized clinical trials included back pain, decreased appetite, constipation, arthralgia, diarrhea, hot flush, upper respiratory tract infection, peripheral edema, dyspnea, musculoskeletal pain, decreased weight, headache, hypertension, and dizziness/vertigo.

Enzalutamide, an androgen receptor inhibitor, acts on three different steps in the androgen receptor signaling pathway.

Source: Astellas Pharma, September 10, 2014

Eliquis for DVT, PE

Apixaban (Eliquis, Bristol-Myers Squibb/Pfizer) has received FDA approval for the treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE) and for reducing the risk that those conditions will recur after initial therapy.

DVT, a blood clot in a vein that partially or totally blocks the flow of blood, can progress to PE, a blood clot blocking one or more vessels in the lungs that carries the risk of sudden death.

This approval is based on data from the global AMPLIFY and AMPLIFY-EXT studies. AMPLIFY, a randomized, double-blind trial, included patients with confirmed symptomatic DVT or PE; 2,609 received apixaban and 2,635 received standard of care (initial enoxaparin treatment for at least five days, overlapped by oral warfarin therapy for six months). Apixaban 10 mg twice daily for one week followed by 5 mg twice daily for six months demonstrated efficacy comparable with that of standard of care for the primary efficacy composite endpoint of recurrent, symptomatic venous thromboembolism (VTE) or VTE-related death (2.3% vs. 2.7%, respectively).

Apixaban, compared with standard of care, demonstrated less major bleeding (0.6% vs. 1.8%, respectively), less clinically relevant nonmajor bleeding (3.9% vs. 8.0%), and a lower discontinuation rate due to bleeding events (0.7% vs. 1.7%).

The prescribing information for Eliquis includes boxed warnings for the increased risk of thrombotic events in patients who prematurely discontinue the drug and for the increased risk of epidural or spinal hematoma in patients using apixaban and undergoing spinal epidural anesthesia or spinal puncture.

Source: Pfizer, August 21, 2014

Promacta for Aplastic Anemia

The FDA has approved eltrombopag (Promacta, GlaxoSmithKline) for patients with severe aplastic anemia (SAA) who have shown an insufficient response to immunosuppressive therapy.

SAA is a rare blood disorder in which the bone marrow fails to produce enough red blood cells (RBCs), white blood cells (WBCs), and platelets. Eltrombopag, an oral thrombopoietin receptor agonist, helps induce proliferation and differentiation of bone-marrow stem cells to increase blood-cell production.

The new approval is based on a single-arm, open-label, phase 2 study by the National Heart, Lung, and Blood Institute. The treated population had a median age of 45 years, 56% were male, and 84% had received at least two prior immunosuppressive therapies. When patient’s hematological responses were assessed after 12 weeks of treatment, 17 patients (40%) had experienced a response in at least one lineage (platelets, RBCs, or WBCs).

In an extension phase, eight patients achieved a multilineage response; four of these patients tapered off treatment and maintained their response (median follow-up: 8.1 months).

At baseline, 91% of the patients were platelet transfusion-dependent; the median platelet transfusion-free period in responders was 200 days. While 86% of patients were RBC-transfusion-dependent at baseline, the median RBC transfusion-free period in responders was 208 days.

The most common adverse reactions among 43 SAA patients who received eltrombopag included nausea, fatigue, cough, diarrhea, and headache. New cytogenetic abnormalities were found in eight patients (19%).

Eltrombopag is also indicated for thrombocytopenia treatment in certain cases.

Source: GlaxoSmithKline, August 26, 2014

Zorvolex for Osteoarthritis Pain

Diclofenac (Zorvolex, Iroko Pharmaceuticals, LLC), a nonsteroidal anti-inflammatory drug (NSAID), has
received FDA approval for the management of osteoarthritis pain. In October 2013, the FDA approved diclofenac for the treatment of mild-to-moderate acute pain in adults.

Vimpat was developed in line with recommendations from the FDA and medical organizations that NSAIDs be used at the lowest effective dose for the shortest possible duration consistent with individual patient treatment goals. Proprietary technology can produce diclofenac as submicron particles that are approximately 20 times smaller than their original size; this reduction provides an increased surface area, leading to faster dissolution.

The new approval was supported by data from a 12-week, randomized, double-blind, parallel-group, placebo-controlled trial that enrolled 305 patients with osteoarthritis of the hip or knee, as well as data from a 12-month open-label safety study of 602 patients.

Source: Iroko Pharmaceuticals, LLC, August 25, 2014

**Vimpat as Epilepsy Monotherapy**

The FDA has approved lacosamide (Vimpat, UCB) as monotherapy for the treatment of partial-onset seizures in patients ages 17 years and older with epilepsy. The drug was previously approved as adjunctive treatment for partial-onset seizures in this age group. With the new indication, adults with partial-onset seizures can be started on lacosamide monotherapy and patients already being treated with an anti-epileptic drug can be converted to lacosamide monotherapy.

The new approval was based on a phase 3 historical-control conversion to lacosamide monotherapy study in adult epilepsy patients with partial-onset seizures. The most common adverse events were similar to those in adjunctive-therapy studies, which included dizziness, headache, nausea, and diplopia. Insomnia was observed at a rate not reported in previous studies, but causality could not be established. Insomnia has also been seen in post-marketing experience.

The FDA also approved a new single-loading dose-administration option for lacosamide as monotherapy or adjunctive treatment. This option allows initiation of the drug as a single loading dose of 200 mg (oral or injection), followed approximately 12 hours later by a 100-mg twice-daily dose (200 mg/day). The loading dose should be administered under medical supervision.

Source: UCB, September 1, 2014

**Drug News**

**Nuplazid Gains Breakthrough Status for Parkinson’s Psychosis**

The FDA has given a breakthrough therapy designation to pimavanserin (Nuplazid, Acadia Pharmaceuticals Inc.) for the treatment of Parkinson’s disease psychosis (PDP).

If approved, pimavanserin—a selective serotonin inverse agonist—will establish a new pharmacological approach to treating psychosis. Pimavanserin, administered orally once daily, preferentially targets 5-HT2A receptors believed to play an important role in psychosis and has successfully completed a pivotal phase 3 trial. Acadia plans to submit a new drug application to the FDA in late 2014.

PDP, a debilitating disorder that occurs in an estimated 40% of Parkinson’s patients, commonly consists of visual hallucinations and delusions. There is no FDA-approved therapy to treat PDP.

Source: Acadia Pharmaceuticals Inc., September 2, 2014

**Ivabradine for Chronic Heart Failure**

The FDA has granted priority review to ivabradine (Amgen) for the treatment of chronic heart failure.

Ivabradine is an oral drug that inhibits the If current in the sinoatrial node—the body’s cardiac pacemaker. The drug works to slow the heart rate without having negative effects on myocardial contractility or ventricular repolarization.

The application for ivabradine was based on global clinical trial data from SHIFT, a pivotal phase 3, randomized, double-blind, placebo-controlled outcomes study. SHIFT compared ivabradine to placebo on top of standard-of-care therapies, including beta-blockers, in more than 6,500 patients in sinus rhythm with reduced left ventricular function and a
Somatuline Depot for GEP-NETs
The FDA has awarded priority review to a supplemental new drug application for lanreotide acetate (Somatuline Depot, Ipsen) 120-mg injection for the treatment of gastroenteropancreatic neuroendocrine tumors (GEP-NETs). A decision is expected in early 2015.

GEP-NETs are a heterogeneous group of tumors often arising from cells in the gastrointestinal tract and the pancreas; although rare, they have been on the rise.

The CLARINET study demonstrated lanreotide’s antitumor effect in the treatment of patients with GEP-NETs. CLARINET was a 96-week, phase 3, randomized, double-blind, placebo-controlled study of 204 patients with well or moderately differentiated nonfunctioning enteropancreatic neuroendocrine tumors. Lanreotide substantially prolonged time to disease progression or death versus placebo (hazard ratio, 0.47; \( P = 0.0002 \)).

Lanreotide acetate is a somatostatin analogue that inhibits the secretion of several endocrine, exocrine, and paracrine amines and peptides. It is approved in the U.S. for the long-term treatment of patients with acromegaly who have had an inadequate response to or cannot be treated with surgery and/or radiotherapy.

Source: Ipsen, September 1, 2014

Fast-Track Designations
Motolimod for Ovarian Cancer
The FDA has given fast-track status to motolimod (VTX-2337, VentiRx Pharmaceuticals, Inc.) in combination with pegylated liposomal doxorubicin (PLD) for the treatment of women with ovarian cancer that has progressed on or recurred after platinum-based chemotherapy.

Motolimod, a Toll-like Receptor 8 (TLR8) agonist that directly activates multiple components of the innate immune system, is being evaluated in two randomized, placebo-controlled phase 2 trials.

VentiRx has enrolled more than 290 patients in the GOG-3003 trial of motolimod in combination with PLD in patients with recurrent or persistent epithelial ovarian, fallopian tube, or primary peritoneal cancer who have failed prior platinum-based chemotherapy. The primary endpoint is overall survival. In April 2014, the FDA granted orphan drug designation to motolimod for the treatment of ovarian cancer. The second trial, Active8, involves patients with locally advanced and metastatic squamous cell carcinoma of the head and neck.

Source: VentiRx Pharmaceuticals, Inc., September 2, 2014

Relebactam for Certain Infections
Merck’s relebactam (previously called MK-7655), an investigational beta-lactamase inhibitor, has received FDA designation as a qualified infectious disease product with fast-track status. The designations apply to intravenous use of relebactam to treat complicated urinary tract infections, complicated intra-abdominal infections, and hospital-acquired bacterial pneumonia/ventilator-associated bacterial pneumonia.

Beta-lactamases are a family of enzymes produced by some bacteria that can cause resistance to several widely used beta-lactam antibiotics, including penicillins, cephalosporins, and carbapenems. By combining a beta-lactamase inhibitor with a beta-lactam antibiotic, it may be possible to overcome the resistance.

Relebactam is being evaluated in combination with imipenem/cilastatin in phase 2 clinical trials for the treatment of complicated urinary tract infections and complicated intra-abdominal infections. In preclinical studies, the drug combination demonstrated antibacterial activity against a broad range of gram-negative and beta-lactam-resistant pathogens.

Source: Merck, September 4, 2014

PF-06425090 for Clostridium Difficile
PF-06425090, an investigational Clostridium difficile (C. difficile) vaccine candidate now in phase 2 clinical development by Pfizer Inc., has received FDA fast-track designation. C. difficile-associated disease can include life-threatening diarrhea and pseudomembranous colitis. In the U.S. alone, approximately 250,000 cases of C. difficile-associated disease result in approximately 14,000 deaths each year.

Source: Pfizer Inc., August 28, 2014

PEGPH20 for Pancreatic Cancer
The FDA has granted fast-track designation to pegylated recombinant human hyaluronidase (PEGPH20, Halozyme Therapeutics, Inc.) in combination with gemcitabine and nab-paclitaxel for the treatment of patients with metastatic pancreatic cancer.

Source: Halozyne Therapeutics, Inc., September 3, 2014

Orphan Drug Designations
APD811 for Pulmonary Arterial Hypertension
Arena Pharmaceuticals, Inc., has received FDA orphan drug status for APD811 for the treatment of pulmonary arterial hypertension (PAH). The company expects to begin a phase 2 clinical trial program later this year.

PAH is a progressive, life-threatening disorder characterized by increased pressure in the arteries that carry blood from the heart to the lungs. The increased pressure strains the heart.

APD811, an orally available agonist of...
the prostacyclin receptor, is an investigational drug candidate intended for the treatment of vasospastic diseases such as PAH.

Source: Arena Pharmaceuticals, Inc., September 2, 2014

PRM-151 for Myelofibrosis
The FDA has granted orphan drug status to PRM-151 (Promedior, Inc.) for the treatment of myelofibrosis, a serious, life-limiting cancer characterized by fibrosis of the bone marrow. Symptomatic myelofibrosis affects about 18,000 people a year in the U.S.

Preliminary data from a phase 2 study of PRM-151 demonstrated benefits across all clinically relevant measures of myelofibrosis, including decreases in bone marrow fibrosis, symptom responses, improvements in hemoglobin and platelets, and reductions in spleen size, with a well-tolerated safety profile and no treatment-related myelosuppression.

PRM-151 is a recombinant form of an endogenous human protein, pentraxin 2, that is specifically active at the site of tissue damage. PRM-151 is an agonist that acts as a monocyte/macrophage differentiation factor to prevent and potentially reverse fibrosis. PRM-151 also has orphan designation for treatment of idiopathic pulmonary fibrosis.

Source: Promedior, Inc., September 2, 2014

Cannabidiol for Glioblastoma Multiforme
Cannabidiol (Insys Therapeutics, Inc.) has received FDA orphan drug status for the treatment of glioblastoma multiforme, the most common and most aggressive malignant primary brain tumor in humans. Cannabidiol previously received orphan drug status for the treatment of Lennox-Gastaut Syndrome and Dravet Syndrome, both rare forms of epilepsy. Insys is evaluating the potential use of the drug in additional indications.


Hydrocodone Combination Products Move to Schedule II
The Drug Enforcement Administration is moving hydrocodone combination products (HCPs) from Schedule III to the more-restrictive Schedule II under the Controlled Substances Act on October 6, 2014, ending a review process that proceeded in fits and starts for 15 years.

HCPs contain both hydrocodone, which by itself is a Schedule II drug, and specified amounts of other substances, such as acetaminophen or aspirin. Nearly 137 million prescriptions for HCPs were dispensed in 2013. The most frequently prescribed HCPs combine hydrocodone and acetaminophen (such as Vicodin and Lortab).

Schedule II products, which have a high potential for abuse that may lead to severe psychological or physical dependence, are subject to rules and sanctions regarding registration, security, labeling, packaging, manufacturing quotas, inventory, records, and reports.

No prescription for HCPs issued on or after October 6, 2014, can authorize refills. Any prescriptions for HCPs that are issued before that date and authorized for refilling may be dispensed in accordance with the law until April 8, 2015.

Data and surveys from multiple agencies show the extent of HCP abuse. For example, Monitoring the Future surveys of eighth-, 10th-, and 12th-graders from 2002 to 2011 found that twice as many high school seniors used Vicodin nonmedically as used OxyContin, a Schedule II substance that is more tightly controlled.

The rescheduling of HCPs was initiated by a physician’s petition in 1999.

Sources: Drug Enforcement Administration, August 21, 2014, and Federal Register, August 22, 2014

Medication Recalls
Martin Avenue Pharmacy Sterile Preparations
Martin Avenue Pharmacy, Inc., is recalling all in-date compounded sterile preparations after FDA inspectors observed quality control procedures that present a risk to sterility assurance. The company has ceased production of compounded sterile preparations until further notice.

Martin Avenue Pharmacy supplied compounded sterile preparations to medical professionals and individual patients by prescription until August 20, 2014, in multiple states, including Illinois, Wisconsin, Ohio, Michigan, Florida, Alabama, and Texas. The recall does not pertain to nonsterile compounded medications.

To identify which products are being recalled, visit www.martinavenue.com/voluntaryrecall. For further information, contact the company at 630-355-6400 or 888-355-6492, Monday through Friday, 9 a.m. to 7 p.m. Central time, or by email at info@martinavenue.com.

Source: Martin Avenue Pharmacy, Inc., August 27, 2014

Pharmacy Creations
Pharmacy Creations voluntarily recalled four product lots after testing results from Front Range, Inc. (its former independent testing laboratory, which it no longer uses) indicated that the products might not be sterile.

The preparations were distributed in Florida, New Jersey, New York, and Puerto Rico between March 4, 2014, and June 18, 2014, and were mailed directly to patients and physicians. The products, lot numbers, and expiration dates follow: ascorbic acid, 500 mg/mL in a 50-mL vial, 05082014@7, November 4, 2014; glutathione, 100 mg/mL in a 30-mL vial, 05122014@4, September 9, 2014; magnesium chloride, 200 mg/mL in a 50-mL vial, 05202014@7, November 2014.
19, 2014; and tropi/cyclo/phenyl/tobra/flurb (1/1/10/0.3/0.3)% in a 3-mL bottle, 05202014®3, November 16, 2014. Customers with questions can contact the company by mail at 540 Route 10, West Randolph, NJ 07869, or call 858-366-8389.

Source: Pharmacy Creations, September 5, 2014

RESEARCH BRIEFS
Bolstering Gemcitabine To Improve Outcomes

Gemcitabine (GEM) is standard treatment for locally advanced/metastatic pancreatic cancer, but many studies have sought combinations that might extend its efficacy, say researchers from Beijing Friendship Hospital.

Most studies showed no improvement in overall survival (OS) until researchers found that nanoparticle albumin-bound paclitaxel plus GEM significantly improved OS by nearly nine months and progression-free survival (PFS) by nearly six months compared with GEM monotherapy. Other research found combining GEM with platinum, fluoropyrimidine, irinotecan, and biotherapy marginally but significantly extended survival compared with GEM monotherapy, but the combinations were associated with increased toxicity.

Some research has focused on targeted agents (TA). Studies that added drugs targeting epidermal growth factor receptor, which is overexpressed in pancreatic tumors and associated with poor prognosis, have had mixed results. That prompted researchers in this study to conduct a systematic survey of 10 randomized clinical trials.

Of 3,899 patients, 1,989 received GEM plus TA and 1,910 received GEM with or without placebo (PLC). In a subgroup of GEM plus antiangiogenic agents, 733 patients received GEM plus axitinib or bevacizumab and cilengitide, and 693 received GEM with or without PLC.

A marginal difference was seen in one-year survival between the GEM/TA and GEM/PLC groups. In the subgroup analysis, the researchers found a significant increase in objective response rate with GEM plus antiangiogenic agents versus GEM with or without PLC, but they found no significant difference in OS, one-year survival, or PFS between those groups.

The researchers suggested further research that concentrates on clarifying the “concrete targets” involved in the occurrence and progression of pancreatic cancer. Personalized therapy based on a patient’s stratification, tumor stage, and genetic background should also be considered.

Source: American Journal of Medicine, August 2014

Finding the Right Dose of MTX

Experience suggests that the most effective dose of methotrexate (MTX) for rheumatoid arthritis is 15 mg to 25 mg a week and that early, rapid control of disease activity minimizes damage. The result has been to start hard and go fast, with an initial dose of 10 mg to 15 mg per week and escalation by 5 mg every month.

But researchers from the Post Graduate Institute of Medical Education and Research in Chandigarh, India, say the recommendation to start with 15 mg is based on “weak evidence.” What’s more, only a limited number of studies have compared fixed MTX doses head to head, and many are 20 to 30 years old.

The higher starting dose may improve efficacy but can lead to adverse effects, intolerance, and withdrawal from therapy, the researchers say. They sought a balance between efficacy, speed, and tolerability by comparing two dosage regimens of oral MTX, starting at 7.5 mg or 15 mg a week and escalating 2.5 mg every two weeks over 12 weeks, to a possible maximum of 25 mg per week.

In group one, 47 patients were started on the lower dose, reaching a mean dose of 12 weeks of 17.3 mg per week. In group two, 53 patients were started on the higher dose and reached a mean dose of 23.6 mg per week. In patients who completed the study, the mean doses were 19.2 mg and 24.5 mg per week, respectively.
Nine patients withdrew from group one and seven from group two. Withdrawals due to adverse effects did not differ significantly between groups. However, group two had a higher incidence of nausea than group one (42% versus 19%), although the severity and duration of nausea were similar in both groups. There were no significant differences in cytopenia, transaminitis, or disease activity.

The researchers say one limitation of the study is the short duration. They found “a relatively poor response” to MTX by week 12, they say, and future studies might benefit from extending the follow-up to 24 weeks.

Source: Clinical Therapeutics, July 2014

An Antibiotic-Free Way to Reduce S. Aureus Carriage

Between 20% and 40% of healthy people carry Staphylococcus aureus in their nasal passages, raising the risk that they will infect themselves or others. Nasal antibiotics can’t be used safely for long periods and aren’t appropriate for everyone. An effective, convenient nonantibiotic preparation that could be used daily would help.

In a randomized, double-blind, placebo-controlled study, researchers from Medical University of South Carolina (MUSC) and Johns Hopkins recruited 387 volunteers from the MUSC Hospital nursing and technical staff; 78 tested positive for S. aureus. Of 39 who tested positive and completed the study, 20 were assigned to antiseptic treatment and 19 to placebo.

Participants refrained from using nasal sprays or washes from the time of their screening through their study period (a single 10-hour workday). The researchers swabbed both nasal vestibules of each volunteer at the start of the day and immediately applied placebo or the test preparation, Nozin Nasal Sanitizer antiseptic, which is composed of 70% ethanol active combined with natural oil emollients and a preservative. The preparations were reapplied at hours 4 and 8. Subjects’ nasal samples were collected at hour 10.

Antiseptic treatment reduced colony-forming units at a median 99% for S. aureus and 91% for total bacteria. Reductions in bacteria were consistent across subjects, with a median decrease in the antiseptic-treated group of 98.8% at the end of the workday.

The study did not determine the rate of bacterial killing. However, the researchers cite another study that found the bactericidal activity of 70% ethanol with emollients resulted in near-maximum activity within minutes of application.

The 20% prevalence of S. aureus carriage among the 387 volunteers fell at the low end of the spectrum seen in health care professionals, the researchers say. Some data suggest that women may have a lower prevalence than men; this study group consisted mostly of women. The researchers found few distinguishing characteristics among carriers. Potential contributors to colonization risk included the presence at home of one or more children between ages 6 months and 11 years or the presence of dogs and cats.

Source: American Journal of Infection Control, August 2014

Bureaucracy Is Costly For U.S. Hospitals

A Health Affairs study of hospital administrative costs in eight nations finds that hospital bureaucracies consumed 25.3% of U.S. hospital budgets in 2011—far more than in other nations. Administrative costs were lowest (about 12%) in Scotland and Canada, where single-payer systems fund hospitals through lump-sum budgets.

The study was conducted by a team from the U.S., the United Kingdom, France, Germany and the Netherlands, and was coordinated by researchers at the City University of New York and the London School of Economics. The researchers analyzed accounting data that virtually all hospitals in each nation reported to their governments.

Hospital administrative spending totaled $667 per capita in the U.S., $158 in Canada, $164 in Scotland, $211 in Wales, $225 in England, and $325 in the Netherlands. Comparable estimates could not be calculated for French and German hospitals because of accounting differences, but their administration costs were approximately 20% higher than in Canada and Scotland and 40% below U.S. levels.

The study found that U.S. hospital administrative costs rose from 23.5% of hospital budgets in 2000 to 25.3% in 2011. Researchers found no evidence that high U.S. administrative costs yielded benefits.

The article attributes the high administrative costs in the U.S. to the complexity of billing a multiplicity of insurers and the entrepreneurial imperative for hospitals to achieve profits (or, for nonprofit hospitals, surpluses) in order to fund modernization and upgrades.

Sources: Physicians for a National Health Program, September 8, 2014, and Health Affairs, September 2014

Hypertension ER Visits Up 25% in 2006–2011

The number of people going to the emergency room (ER) for essential hypertension increased by 25% from 2006 to 2011, according to a study presented at the American Heart Association’s High Blood Pressure Research Scientific Sessions 2014 in San Francisco.

Sourabh Aggarwal, MD, of the Western Michigan University School of Medicine, and colleagues reviewed data on approximately 3.9 million ER visits in 2006–2011 in which hypertension was the first listed diagnosis. Their key findings include the following:

• ER visits for essential hypertension increased by 25%, but the admission percentage for these patients fell 15%.
• ER visits for hypertension with complications and for secondary hypertension increased by 19%, but the admission percentage for these patients fell by 12%.
• Among admitted patients, the percentage who died in the hospital dropped 36%.

The decrease in admissions and deaths may be due to ER and hospital physicians becoming more skilled at treating high blood pressure, Dr. Aggarwal said.

Source: American Heart Association, September 9, 2014

DEVICE APPROVALS
SenoClaire for 3D Mammography

The FDA has approved SenoClaire, a breast tomosynthesis device with three-dimensional (3D) imaging technology developed by General Electric Healthcare in collaboration with Massachusetts General Hospital.

The device uses a low-dose, short x-ray sweep around the positioned breast, acquiring nine exposures with a “step-and-shoot” method. This technique removes potential motion from the tube, which helps to reduce blur and increase image sharpness.

A key challenge in screening mammography is keeping radiation levels low. With the SenoClaire device, according to GE, there is no increase in the radiation dose from a standard 2D mammogram to a 3D view. 3D breast-screening technology helps clinicians uncover small cancers, which can be a limiting factor in standard 2D mammography.

SenoClaire also helps to improve workflow, GE says. The device is compatible with Centricity PACS with Universal Viewer and supports the DICOM standard that can be read by capable PACS vendors. When SenoClaire is combined with GE Healthcare’s Centricity PACS and Centricity Clinical Archive solution, clinicians have access to the patient’s longitudinal record, providing data that allow better patient care, the company says.

Source: GE Healthcare, September 3, 2014

Assay for Type-1 Diabetes

The FDA has allowed marketing of the Kronus zinc transporter 8 autoantibody (ZnT8Ab) Elisa assay—the first ZnT8Ab test to help determine whether a person has type-1 diabetes rather than another form of diabetes.

According to the developer (Kronus Market Development Associates, Inc.), when used with other tests and patient clinical information, the ZnT8Ab assay may help some people with type-1 diabetes receive timely diagnosis and treatment for their disease.

Type-1 diabetes is the most common form of diabetes diagnosed in children and adolescents, but it can also develop in adults. The immune system of many people with type-1 diabetes produces ZnT8Ab, but patients with other forms of diabetes (i.e., type-2 and gestational) do not. The Kronus assay detects the presence of the ZnT8 autoantibody in a patient’s blood.

The FDA reviewed data from a study of 569 blood samples—323 from patients diagnosed with type-1 diabetes, and 246 from patients diagnosed with other kinds of diabetes, other autoimmune diseases, and other clinical conditions. The Kronus assay was able to detect ZnT8Ab in 65% of the samples from patients with type-1 diabetes and incorrectly gave a positive result in less than 2% of the samples from patients with other diseases.

Source: FDA, August 20, 2014

Shilla Growth Guidance System

Medtronic, Inc., has received FDA clearance to launch the Shilla Growth Guidance System, designed to treat skeletally immature pediatric patients less than 10 years of age diagnosed with severe, progressive, life-threatening, early-onset spinal deformities.

The system uses new growth-sparing technology that allows correction of the deformity while maintaining the corrections over time, minimizing the need for periodic lengthening procedures. Current operative treatments are distraction-based systems that require lengthening every six to nine months.

The existing gold standard for long-term management of scoliosis is to fuse the spine, but this can create serious complications in growing children. The Shilla system permits effective management of the curvature of the spine while still harnessing the child’s natural growth.

The system utilizes a unique nonlocking set screw at the proximal and distal portions of the construct’s rods. This feature allows the rod to slide through the screw heads as the child’s spine grows while providing correction of the spinal deformity. The system is meant to be removed after skeletal maturity.

Source: Medtronic, Inc., August 28, 2014

TMJD Pain-Relief Device

A device to reduce pain from temporomandibular joint disorder (TMJD) has received FDA clearance. TMJ NexGen-eration (TMJ Health, LLC) consists of two custom-made, hollow ear canal inserts that allow full passage of sound and are practically invisible from the outside.

Traditionally, TMJD has been treated with bite splints—plastic mouthpieces that fit over the upper or lower teeth to prevent them from coming together and reduce clenching or grinding. They cannot be worn while eating, can affect speech, and are typically worn only while sleeping.

The ear canal is located close to the temporomandibular joint (TMJ), and the volume of the ear canal increases when the jaw is opened through movements
such as chewing, smiling, and speaking. The TMJ NextGeneration Device uses this anatomical change to treat TMJD.

Patients wearing the devices in a three-month clinical study experienced a significant reduction in the pain and dysfunction associated with TMJD—at least as much as that experienced by patients wearing a bite splint. In addition to the pain reduction, all of the subjects indicated excellent (71%) or good (29%) overall satisfaction with the device.

Source: TMJ Health, LLC, August 13, 2014

**Low-Profile Visualized Intraluminal Support Device**

The FDA has given MicroVention, Inc., approval to market the Low-Profile Visualized Intraluminal Support Device (LVIS and LVIS Jr.), a stent and delivery system used to treat unruptured intracranial saccular aneurysms.

The stent is a self-expanding, nickel-titanium (nitinol) single wire braid. The delivery system consists of an introducer and delivery wire and is used to deliver the stent to the aneurysm. The stent keeps the soft platinum coils that are put into the aneurysm from slipping back into the main blood vessel.

Source: FDA, July 25, 2014

**Device Recalls**

**DePuy Synthes Craniomaxillofacial Distraction System**

DePuy Synthes is recalling approximately 200 lots of its Craniomaxillofacial Distraction System AB Distractor Bodies and BC Distractor Bodies because the devices may reverse direction and lose the desired distraction distance after surgery. The devices have been linked with 15 reports of injury.

The system (also called an external mandibular fixator and/or distractor and a bone plate) is an implant used to lengthen and/or stabilize the mandibular body and ramus. By gradually lengthening the bone (distraction), it can help correct congenital or post-traumatic defects. Reversing occurs when the distractor screw turns in the opposite direction, causing the device to lose distraction distance.

Infants are at the highest risk for injury if the device fails because sudden tracheal obstruction may occur, which could lead to potentially fatal respiratory arrest. Older patients, who can maintain an open airway, are at less risk for serious injury because a device failure would not obstruct the trachea. However, surgical intervention may be needed to replace a failed device in any patient.

The products and lots affected by the recall are available at [http://tinyurl.com/DePuyCMF](http://tinyurl.com/DePuyCMF). Those with questions can call 610-719-5450.

Sources: FDA, August 28, 2014, and DePuy Synthes, April 16, 2014

**Customed Surgical Convenience Packs**

Customed, Inc., is recalling more than 459,000 convenience surgical packs because packaging, storage, and manufacturing issues may compromise sterility.

Each of the packs—manufactured between January 9, 2009, and May 20, 2014—contains instruments or other items used during surgical procedures. In some cases, the plastic packaging of one bag has adhered to the end seal of an adjacent pack. When the bags are separated, the plastic film can tear and compromise the sterility of the contents.

In addition, the FDA says, “the products have been exposed to uncontrolled and inadequate storage conditions and there are serious deficiencies in the manufacturing process.”

A list of the 234 catalog items and 3,562 lots involved in the recall is available at [http://tinyurl.com/Customed](http://tinyurl.com/Customed). Customers with questions may reach the Customed recall coordinator at 787-622-5151, extension 7510, Monday through Friday, 8 a.m. to 5 p.m. Eastern time.

Sources: FDA, August 26, 2014, and Customed, August 21, 2014

**Diamondback 360 Peripheral Orbital Atherectomy System**

Cardiovascular Systems is recalling six lots of the Diamondback 360 Peripheral Orbital Atherectomy Systems because they may contain defective saline sheaths that could fracture during use. If this occurs, fragments of the sheath could potentially block blood vessels.

The system—a high-speed cutting tool inserted via a catheter into a patient’s blood vessel—is used to re-establish blood flow in narrowed arteries or arterio-venous dialysis shunts. The affected lot numbers are 100573, 100575, 100674, 100676, 100678, and 100680; 48 devices were distributed in May 2014. For more information, contact Cardiovascular Systems Customer Service at 1-877-274-0901.

Source: FDA, August 19, 2014

**Gel-E Donut and Squishon 2**

Children’s Medical Ventures is recalling the Gel-E Donut and Squishon 2 due to complaints about mold on the outer surface. The mold was identified as Cladosporium and Penicillium fungi, which can cause difficulty in breathing or an allergic reaction. Cladosporium can also cause invasive infections, especially in vulnerable populations.

These gel-filled products are used in hospitals, under a caregiver’s supervision, to support and cradle an infant’s head and/or body, help ease pressure caused by long periods of stillness, and allow for head movement while maintaining a supportive surface. They were distributed from July 1, 2012, to December 31, 2013. Contact Children’s Medical Ventures Customer Support at 412-380-8881 with questions.

Source: FDA, August 22, 2014
CloverSnare Vascular Retrieval Snare
Cook Medical is recalling 696 CloverSnare 4-Loop Vascular Retrieval Snare devices because of a potential for the loop to separate from the shaft, resulting in loss of device function, potential for embolization of snare fragments, and the potential need for intervention to retrieve the separated snare.

In six cases, customers reported separation of the loop snare from the shaft during use. The separation was caused by the application of lateral force to the snare in an effort to change the shape of the device. In four cases of separation, medical intervention was required to retrieve the separated snare.

The recall affects products distributed between March 8, 2013, and July 1, 2014. A list of the lots involved is available at http://tinyurl.com/CloverSnare. Customers with questions may contact Cook Medical Customer Relations at 800-457-4500 or 812-339-2235, Monday through Friday, 7:30 a.m. to 5 p.m. Eastern time.

Source: FDA, August 27, 2014

**DEVICE SPOTLIGHT**

**Kunj Gohil, PharmD, RPh**

**Name:** NephroCheck Test System  
**Manufacturer:** Astute Medical, Inc., San Diego, California  
**Approval Date:** September 5, 2014  
**Purpose:** NephroCheck utilizes a single-use cartridge designed to detect biomarkers of acute kidney injury (AKI), tissue inhibitor of metalloproteinase 2 (TIMP-2) and insulin-like growth factor binding protein 7 (IGFBP-7). The NephroCheck Test System should be used as an aid in risk assessment for moderate-to-severe AKI within 12 hours of patient assessment. Patients should be 21 years of age and older. The test provides results in 20 minutes.

**Description:** The test operator applies a fresh or thawed (i.e., previously frozen) clinical urine sample (mixed with labeled fluorescent conjugate) to the NephroCheck Test Cartridge, and then inserts the test cartridge into the Astute140 Meter for incubation, reading, result calculation, and result display.

**Benefit:** AKI is one of the more prevalent and serious morbidities in critically ill hospitalized patients and is associated with a multitude of acute and chronic conditions. The economic and public health burden of AKI is staggering, with substantially increased mortality, morbidity, length of intensive-care-unit stay, and in-hospital costs, as well as longer-term health consequences. Tests to assess AKI provide important information to physicians and, in conjunction with other available clinical information, can aid physicians in optimizing patient management.

**Source:** www.astutemedical.com, www.fda.gov

**Name:** Levo System  
**Manufacturer:** Otoharmonics, Portland, Oregon  
**Approval Date:** September 3, 2014  
**Purpose:** The Levo System is a personalized, neuroscience-based sound therapy indicated for temporarily relieving the symptoms of tinnitus. It works to create, reroute, or reduce neural connections to ease the effects of tinnitus. The device is used overnight with an interactive application on an iPad or iPod to help the brain learn to ignore tinnitus sounds.

**Description:** The brain reorganizes itself when patients sleep and, in turn, prioritizes new and stored information to lock in learning and memory. Personalized earbuds are designed for the patient and the specific tinnitus is identified through a series of interactive activities involving a proprietary application. By using the Levo System while sleeping, patients leverage the brain’s natural ability to diminish the effects of tinnitus over time through the creation and change of neural pathways in the brain.

**Benefit:** Tinnitus, a “ringing in the ears” as a result of false signaling in the brain, can have a significant effect on a patient’s quality of life. It is estimated that 50 million people in the United States experience tinnitus. Certain patients only have minor symptoms, but for two million to three million people it can cause serious problems, such as sleep loss, emotional distress, and anxiety.

**Source:** http://otoharmonics.com

**Name:** AliveCor Heart Monitor  
**Manufacturer:** AliveCor, Inc., San Francisco, California  
**Approval Date:** August 21, 2014  
**Purpose:** The AliveCor Heart Monitor’s analysis program has been developed to detect atrial fibrillation. Electrocardiogram (ECG) readings are taken and analyzed through mobile phones; the readings are then processed and analyzed for the presence of atrial fibrillation.

**Description:** The AliveCor Heart Monitor is attached to a mobile phone and an ECG is taken using the fingertips. Data is transferred from the heart monitor device to the mobile phone, where a proprietary application reviews the ECG for the presence of atrial fibrillation. The ECG can be forwarded to a board-certified cardiologist or a personal physician for further review.

**Benefit:** One in four adults ages 40 years and older can develop atrial fibrillation, which can increase the risk of stroke fivefold. Symptoms, which include heart palpitations and chest discomfort, can sometimes be mild or nonexistent. This device is a very accessible way for patients to know if atrial fibrillation is present in their ECG. This allows people to seek medical treatment sooner, which can decrease the risk of further complications from this abnormal heartbeat.

**Source:** www.alivecor.com

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Name: Viva CRT-P device with the AdaptivCRT algorithm

Manufacturer: Medtronic, Inc., Minneapolis, Minnesota

Approval Date: August 25, 2014

Purpose: The Viva CRT-P device with the AdaptivCRT algorithm is indicated for patients with heart failure. This next-generation cardiac resynchronization therapy (CRT) pacemaker expands Medtronic’s cardiovascular portfolio and advances its proprietary technology for heart rhythm therapy.

Description: The Viva CRT-P includes Medtronic’s AdaptivCRT algorithm, which preserves normal heart rhythms and automatically adjusts to the patient’s needs, creating a customized therapy for each patient. It is the only algorithm demonstrated to improve heart failure patients’ response to the therapy and reduce the risk of atrial fibrillation. It includes advanced diagnostic tools, such as OptiVol Fluid Status Monitoring and the Monitoring and Cardiac Compass Report, which provide detailed insight into patients’ physiological condition.

Benefit: Heart failure affects 5.1 million Americans and results in more than one million hospitalizations yearly. Recent data show the AdaptivCRT algorithm reduced 30-day hospital readmissions for heart failure by 47% and atrial fibrillation-related health care utilizations (hospitalizations, emergency department visits, or clinic visits) by 55%—important benefits, since heart failure is a costly problem and represents a leading cause of 30-day hospital readmissions.

Sources: www.medtronic.com, www.fiercemedicaldevices.com
