NEW DRUG APPROVALS

Inhaled Insulin Afrezza For Diabetes

The FDA has approved a rapid-acting inhaled insulin to improve glycemic control in adults with diabetes mellitus. Insulin human inhalation powder (Afrezza, MannKind Corporation) is administered at the beginning of each meal.

The product’s safety and effectiveness were evaluated in 3,017 participants—1,026 with type-1 diabetes and 1,991 with type-2 diabetes.

The efficacy of mealtime insulin human inhalation powder in adults with type-1 diabetes was compared to mealtime insulin aspart (fast-acting insulin), both in combination with basal insulin (long-acting insulin), in a 24-week study. At week 24, treatment with basal insulin and mealtime inhaled insulin provided a mean reduction in hemoglobin A1c (HbA1c) that met the prespecified noninferiority margin of 0.4%. Insulin human inhalation powder provided less HbA1c reduction than insulin aspart by a statistically significant margin.

Insulin human inhalation powder was studied in adults with type-2 diabetes in combination with oral antidiabetic drugs; the efficacy of the inhaled mealtime insulin was compared to placebo inhalation in a 24-week study. At week 24, treatment with insulin human inhalation powder plus oral antidiabetic drugs provided a mean reduction in HbA1c that was greater, by a statistically significant margin, than the HbA1c reduction in the placebo group.

Insulin human inhalation powder is not a substitute for long-acting insulin and must be used in combination with long-acting insulin in patients with type-1 diabetes. It is not recommended for the treatment of diabetic ketoacidosis or for patients who smoke.

A boxed warning advises that acute bronchospasm has been observed in patients with asthma and chronic obstructive pulmonary disease (COPD). As a result, insulin human inhalation powder should not be used in patients with chronic lung disease, such as asthma or COPD. The most common adverse reactions in clinical trials were hypoglycemia, cough, and throat pain or irritation.

The FDA approved insulin human inhalation powder with a risk evaluation and mitigation strategy (a communication plan to inform health care professionals about the serious risk of acute bronchospasm). The FDA is requiring several postmarketing studies, including clinical trials that will evaluate: pharmacokinetics, safety, and efficacy in pediatric patients; the potential risk of pulmonary malignancy; cardiovascular risk; and the long-term effects on pulmonary function.

Source: FDA, June 20, 2014

Sivextro for Skin Infections

The FDA has approved the antibiotic Sivextro (tedizolid phosphate, Cubist Pharmaceuticals) to treat adults with acute bacterial skin and skin structure infections (ABSSSIs).

The bacteria susceptible to tedizolid include Staphylococcus aureus (including methicillin-resistant strains [MRSA] and methicillin-susceptible strains), various Streptococcus species, and Enterococcus faecalis. The drug is available for intravenous and oral use.

The application for tedizolid was designated as a qualified infectious disease product (QIDP) and received an expedited review. The drug’s safety and efficacy were evaluated in two Phase 3 trials including 1,315 adults who had ABSSSIs. Participants were randomly assigned to receive tedizolid or linezolid. Results showed tedizolid was as effective as linezolid for the treatment of ABSSSIs.

The most common side effects identified in clinical trials were nausea, headache, diarrhea, vomiting, and dizziness. The safety and efficacy of the medication have not been evaluated in patients with decreased levels of white blood cells (neutropenia), so alternative therapies should be considered. To learn more about tedizolid, see the Drug Forecast article on page 555.

Source: FDA, June 27, 2014

Beleodaq for Rare Type of Non-Hodgkin Lymphoma

Belinostat (Beleodaq, Spectrum Pharmaceuticals) has received FDA approval for the treatment of patients with peripheral T-cell lymphoma (PTCL), a rare and fast-growing type of non-Hodgkin lymphoma (NHL).

PTCL consists of a diverse group of rare diseases in which lymph nodes become cancerous. The National Cancer Institute estimates that 70,800 Americans will be diagnosed with NHL in 2014 and that 18,990 will die of the disease. PTCL represents approximately 10% to 15% of NHLs in North America.

Belinostat stops enzymes that contribute to the development of cancer in T cells. The drug is intended for patients with relapsed or refractory PTCL. The FDA approved belinostat under its accelerated approval program and gave the product an orphan drug designation.

The safety and effectiveness of belinostat were evaluated in a clinical study involving 129 patients with relapsed or refractory PTCL. All were treated with belinostat until their disease progressed or until side effects became unacceptable. A complete or partial response was achieved by 26% of the patients. The most common side effects were nausea, fatigue, pyrexia, anemia, and vomiting.

Source: FDA, July 3, 2014

Kerydin for Onychomycosis

The FDA has approved tavaborole topical solution, 5% (Kerydin, Anacor Pharmaceuticals), the first oxaborole antifungal for the topical treatment of onychomycosis of the toenails.

Source: FDA, July 3, 2014
Onychomycosis is a fungal infection of the nail and nail bed that affects approximately 35 million people in the U.S., but only 5 million to 6 million have been diagnosed by a physician. Kerydin offers a topical treatment of onychomycosis of the toenails caused by *Trichophyton rubrum* or *T. mentagrophytes*.

The clear, colorless, alcohol-based solution is applied with a dropper to the infected toenail once daily for 48 weeks. Because of its topical application, the product has low systemic absorption and has not demonstrated systemic side effects.

The efficacy and safety of tavaborole were evaluated in two multicenter, double-blind, randomized, vehicle-controlled trials. Tavaborole or vehicle was applied once daily for 48 weeks in subjects with 20% to 60% clinical involvement of the target toenail without dermatophytomas or lunula (matrix) involvement. A total of 1,194 subjects (795 using tavaborole, 399 using vehicle) 18 to 88 years of age participated. Efficacy assessments were performed at 52 weeks.

Complete cures were reported in more subjects treated with tavaborole than with vehicle in both the first trial (6.5% vs. 0.5%, respectively) and the second trial (9.1% vs. 1.5%). A complete cure was defined as a completely clear nail (no clinical involvement of the target toenail) plus a mycological cure (negative KOH wet mount and negative fungal culture) at week 52.

Common adverse reactions with tavaborole included application-site exfoliation, ingrown toenail, application-site erythema, and application-site dermatitis.

Sources: Anacor Pharmaceuticals, July 8, 2014, and Kerydin prescribing information

**Generic Approvals**

**Valsartan**

Ohm Laboratories, a subsidiary of Ranbaxy Laboratories Ltd., has received FDA approval for valsartan—the long-delayed generic version of Diovan, which has annual sales of $2.1 billion. The FDA determined that Ohm’s 40-mg, 80-mg, 160-mg, and 320-mg valsartan tablets were equivalent to Novartis’ Diovan, which is indicated for the treatment of high blood pressure and heart failure.

Diovan lost patent protection in 2012, but Ranbaxy, which had first-to-file marketing exclusivity for generic valsartan, was unable to sell the drug in the U.S. because of FDA inspection issues at its plants. Four of Ranbaxy’s five FDA-approved plants are banned from making products for the U.S. Valsartan will be manufactured at the fifth plant, an Ohm facility in New Brunswick, New Jersey. Ranbax has 180 days of marketing exclusivity for the drug.

Sources: Ohm Laboratories, June 27, 2014, and Fierce Pharma, June 26, 2014

**Erlotinib**

Mylan Pharmaceuticals’ 25-mg, 100-mg, and 150-mg erlotinib hydrochloride tablets have received FDA approval—the first generic version of the cancer drug Tarceva. Currently marketed by OSI Pharmaceuticals (an affiliate of Astellas Pharma US), Tarceva is a kinase inhibitor indicated under various circumstances for non–small-cell lung cancer and pancreatic cancer.

Sources: FDA, June 11, 2014, and Tarceva prescribing information

**NEW INDICATIONS**

**Ozurdex for Diabetic Macular Edema**

Allergan has received FDA approval for dexamethasone intravitreal implant, 0.7 mg (Ozurdex) to treat diabetic macular edema (DME) in adults who have an artificial lens implant (pseudophakic) or are scheduled for cataract surgery (phakic). The sustained-release biodegradable steroid implant demonstrated long-term efficacy without the need for monthly injections.

DME, an eye condition that affects more than 560,000 Americans, can occur in people with type-1 or type-2 diabetes. It causes fluid to leak into the macula, causing blurred vision, vision loss, and eventual blindness.

The implant uses the Novadur solid polymer delivery system—a biodegradable implant that releases medicine over an extended period—to suppress inflammation, which plays a key role in the development of DME.

Ozurdex was already FDA-approved to treat adults with macular edema following branch retinal vein occlusion or central retinal vein occlusion and to treat adults with noninfectious uveitis affecting the back segment of the eye.

The most common side effects reported in Ozurdex patients with DME include: cataract, increased eye pressure, conjunctival blood spot, reduced vision, inflammation and swelling of the conjunctiva, specks that float in the field of vision, dry eye, vitreous detachment, vitreous opacities, retinal aneurysm, foreign body sensation, corneal erosion, inflammation of the cornea, anterior chamber inflammation, retinal tear, drooping eyelid, and high blood pressure.

Source: Allergan, June 30, 2014

**NovoSeven for Glanzmann’s Thrombasthenia**

The FDA has approved coagulation factor VIIa (recombinant) (NovoSeven RT, Novo Nordisk) for bleeding episodes and perioperative management in patients with Glanzmann’s thrombasthenia (GT) with refractoriness to platelet transfusions, with or without antibodies to platelets.

GT is a rare genetic bleeding disorder that occurs because certain surface proteins on platelets are missing or do not work, significantly impacting the blood’s ability to form strong clots. GT patients may receive platelet transfusions when experiencing severe bleeding or when
surgery is required, but some patients do not respond well or at all to platelet transfusions (called refractoriness). The global Glanzmann’s Thrombasthenia Registry (GTR) collected data from 92 patients treated with NovoSeven RT for 266 severe bleeding episodes and 77 patients treated with NovoSeven RT for 160 surgical and other invasive procedures. Treatment with NovoSeven RT was successful in 94.4% of bleeding episodes and 99.4% of surgical procedures. Of 140 patients treated for 518 bleeding episodes, surgeries, or traumatic injuries, one or two patients reported these adverse reactions: deep vein thrombosis, headache, fever, nausea, and dyspnea.

NovoSeven RT is also indicated for treatment of bleeding and prevention of bleeding for surgeries and procedures in adults and children with hemophilia A or B with inhibitors and congenital factor VII deficiency, and for treatment of bleeding and prevention of bleeding for surgeries and procedures in adults with acquired hemophilia. Serious blood clots that form in veins and arteries with the use of NovoSeven RT have been reported. Source: Novo Nordisk, July 7, 2014

Lymphoseek to Gauge Spread Of Head-and-Neck Cancer

The FDA has approved use of the radioactive diagnostic imaging agent technetium 99m tilmanocept injection (Lymphoseek, Navidea Biopharmaceuticals) to help clinicians gauge the spread of squamous cell carcinoma in the head and neck.

In 2013, Lymphoseek was approved to help identify lymph nodes closest to a primary tumor in patients with breast cancer or melanoma. Lymphatic fluid may contain cancer cells, especially if the fluid drains a part of the body containing a tumor. By removing and examining the lymph nodes that drain a tumor, clinicians can sometimes determine whether a cancer has spread.

With the new approval, Lymphoseek can be used to guide the testing of lymph nodes closest to a primary tumor for cancer—a “sentinel” lymph node biopsy—in patients with cancer of the head and neck. This will allow more limited lymph-node surgery in patients with sentinel nodes negative for cancer. Doctors inject Lymphoseek into the tumor area; later, using a handheld radiation detector, they find the sentinel lymph nodes that have taken up Lymphoseek’s radioactivity.

For the new indication, the safety and effectiveness of Lymphoseek were established in a clinical study of 85 patients with squamous cell carcinoma of the lip, mouth, or skin who were injected with Lymphoseek. Surgeons subsequently removed suspected lymph nodes—those identified by Lymphoseek and those based on tumor location and surgical practice—for pathological examination. Lymphoseek-guided sentinel lymph-node biopsy accurately determined whether the cancer had spread through the lymphatic system. Source: FDA, June 13, 2014

**DRUG NEWS**

**Priority Reviews**

**Nintedanib for Pulmonary Fibrosis**

Nintedanib (Boehringer Ingelheim) has been granted priority review by the FDA for the treatment of idiopathic pulmonary fibrosis (IPF)—a rare, progressive, fatal lung disease that affects approximately 132,000 Americans and has no FDA-approved treatment. Two global phase 3 studies (INPULSIS-1 and INPULSIS-2) have evaluated the efficacy and safety of nintedanib in IPF treatment.

Nintedanib was granted an orphan drug designation in the U.S. in 2011 and a fast track designation in June 2013. It is an investigational small-molecule tyrosine kinase inhibitor that targets growth factors potentially involved in pulmonary fibrosis: the vascular endothelial growth factor receptor, the fibroblast growth factor receptor, and the platelet-derived growth factor receptor.

IPF is characterized by progressive scarring of lung tissue (fibrosis) and by the loss of lung function over time. As the tissue thickens and stiffens, the lungs lose their ability to take in and transfer oxygen into the bloodstream, and vital organs do not receive enough oxygen. As a result, individuals with IPF experience shortness of breath, cough, and often have difficulty participating in everyday physical activities.

Source: Boehringer Ingelheim, July 2, 2014

**Abbvie Hepatitis C Therapy**

Abbvie’s investigational, all-oral, interferon-free regimen for adults with chronic genotype 1 hepatitis C virus (HCV) infection has been granted priority review by the FDA. The regimen received a breakthrough therapy designation in May 2013.

The regimen consists of ABT-450/ritonavir co-formulated with ombitasvir (ABT-267) and dasabuvir (ABT-333) with or without ribavirin. The combination of three different mechanisms of action interrupts the HCV replication process with the goal of optimizing sustained virological response rates across different patient populations. The new drug application is supported by data from six phase 3 studies of more than 2,300 GT1 patients.

Source: AbbVie, June 13, 2014

**Abuse-Deterrent Hydrocodone Bitartrate**

Purdue Pharma’s once-daily, single-entity hydrocodone bitartrate tablet has received an FDA priority review designation. The investigational pain medication was formulated to incorporate abuse-deterrent properties designed to make the product more difficult to manipulate for the purpose of misuse or abuse by various routes of administration (such as chewing, snorting, and intravenous injection).
The FDA has set a target action date under the Prescription Drug User Fee Act of October 2014.

Purdue conducted a series of manipulation and extraction studies and clinical abuse liability studies to evaluate the abuse-deterring properties of this formulation. Currently available hydrocodone formulations do not incorporate abuse-deterring technologies. Hydrocodone combination products, some of the most commonly prescribed opioid analgesics in the U.S., are also the most widely abused.

Source: Purdue Pharma L.P., July 8, 2014

**Breakthrough Therapies**

**Blinatumomab for Leukemia**

The FDA has given a breakthrough therapy designation to blinatumomab (Amgen), an investigational bispecific T-cell engager (BiTE) antibody for adults with Philadelphia negative (Ph−) relapsed/refractory B-precursor acute lymphoblastic leukemia (ALL).

The designation was based on results from a phase 2 trial involving 189 adult patients with Ph− relapsed/refractory B-precursor ALL treated with blinatumomab. Blinatumomab is designed to direct T cells against target cells expressing CD19, a protein found on the surface of B-cell-derived leukemias and lymphomas. The antibody has received the FDA’s orphan drug designation for the treatment of ALL, chronic lymphocytic leukemia, hairy cell leukemia, prolymphocytic leukemia, and indolent B-cell lymphoma.

BiTE antibodies are designed to engage two different targets simultaneously, thereby juxtaposing T cells to cancer cells. BiTE antibodies help place the T cells within reach of the targeted cells, with the intent of allowing them to inject toxins and to trigger apoptosis.

Source: Amgen, July 1, 2014

**CTL019 for Relapsed/Refractory ALL**

The FDA has granted breakthrough therapy status to CTL019 (Novartis/University of Pennsylvania Perelman School of Medicine), an investigational chimeric antigen receptor (CAR) therapy for the treatment of pediatric and adult patients with relapsed/refractory acute lymphoblastic leukemia.

CTL019 uses CAR technology to reprogram a patient’s own T cells to “hunt” cancer cells that express specific proteins, called CD19. After they have been reprogrammed, the T cells (now called CTL019) are reintroduced into the patient’s blood; they proliferate and bind to the targeted CD19+ cancer cells and destroy them.

Source: Novartis, July 7, 2014

**Pradaxa Antidote**

Boehringer Ingelheim Pharmaceuticals’ idarucizumab has received an FDA breakthrough therapy designation to help speed its development as an antidote to the company’s Pradaxa (dabigatran etexilate mesylate). Idarucizumab, an investigational fully humanized antibody fragment (Fab), could be used if a patient taking dabigatran experienced uncontrolled bleeding or needed emergency surgery or another invasive procedure.

Data from a phase 1 study show that idarucizumab can achieve immediate, complete, and sustained reversal of dabigatran-induced anticoagulation in healthy humans. A phase 3 study, RE-VERSE AD, is under way in patients taking dabigatran who have uncontrolled bleeding or require emergency surgery or procedures. Preclinical studies indicate idarucizumab binds specifically to and inhibits dabigatran with no other expected interactions.

Currently, no specific antidotes for newer oral anticoagulants such as dabigatran are available.

Source: Boehringer Ingelheim Pharmaceuticals, June 26, 2014

**Fast Track Status**

**DNX-2401 for Recurrent Glioblastoma**

DNAtrix, Inc., received FDA fast track status for DNX-2401 as a potential treatment for patients with recurrent glioblastoma, a primary brain tumor resistant to conventional therapies.

DNX-2401, a conditionally replication-competent adenovirus, is being developed for the treatment of several cancers. Oncolytic virus therapy uses live viruses to selectively infect and replicate in cancer cells, limiting destruction of normal tissue. Replication amplifies the input dose of the oncolytic virus and helps spread the agent to adjacent tumor cells.

A phase 1 dose-escalating monotherapy study conducted with DNX-2401 for patients with recurrent malignant glioma showed evidence of tumor destruction and long-term survival in several patients. A second phase 1 trial evaluating DNX-2401 in combination with temozolomide is under way in Spain for patients with recurrent glioblastoma.

Source: DNAtrix, Inc., June 17, 2014

**Orphan Drug Designations**

**Mocetinostat for Myelodysplastic Syndrome**

Mocetinostat (Mirati Therapeutics, Inc.), an orally bioavailable, spectrum-selective histone deacetylase inhibitor, has received FDA orphan drug designation as a treatment for myelodysplastic syndrome (MDS). The drug is being developed in phase 2 clinical studies in combination with azacitidine (Vidaza, Celgene Corp.) as a treatment for intermediate- and high-risk MDS, and as a single-agent treatment in patients with diffuse large B-cell lymphoma and bladder cancer, targeting specific genetic mutations in histone acetylation that increase the likelihood of a response in tumor cells.

In an open-label, phase 1/2 trial, researchers evaluated 66 patients with MDS or acute myeloid leukemia. A subset continued on page 546
ENMD-2076 has also received orphan drug designation from the FDA for the treatment of ovarian cancer, multiple myeloma, and acute myeloid leukemia.

Source: CASI Pharmaceuticals, Inc., July 7, 2014

Cannabidiol for Dravet Syndrome

Cannabidiol (Insys Therapeutics, Inc.) has received FDA orphan drug designation for the treatment of Dravet syndrome, a rare pediatric-onset epilepsy. The company expects to file an investigational new drug application for the product in the second half of 2014.

Cannabidiol (one of at least 60 active cannabinoids identified in cannabis) recently received orphan drug designation as a potential treatment for another rare form of pediatric epilepsy, Lennox-Gastaut syndrome, and is being evaluated for additional indications.

Source: Insys Therapeutics, Inc., July 2, 2014

Corticosteroid Injections Don’t Help Spinal Stenosis Pain

Adding a corticosteroid to epidural injections of an anesthetic does not enhance pain reduction in patients with lumbar spinal stenosis, according to a study in the New England Journal of Medicine.

Conducted at 16 U.S. hospitals, the study included 400 patients ages 50 years and older with evidence of lumbar stenosis and at least moderate pain. Half of the patients received epidural injections of lidocaine with a corticosteroid and the other half received injections without a corticosteroid. Six weeks after treatment, the researchers found that patients whose lidocaine was supplemented with a corticosteroid experienced minimal to no additional benefit compared with patients who received injections of an anesthetic alone.

The authors observed no significant between-group differences in the Roland-Morris Disability Questionnaire score. Moreover, the adjusted difference in the average treatment effect between the lidocaine/glucocorticoid group and the lidocaine-only group was –1.0 point (P = 0.07), and the difference in the intensity of leg pain was –0.2 points (P = 0.48).

Patients given lidocaine with a corticosteroid were more likely to report side effects and to absorb the corticosteroid into their bloodstream. Taken over time, corticosteroids can result in reduced bone density, an increased risk of bone fracture, and immunosuppression.

It is estimated that more than 2.2 million lumbar epidural steroid injections are performed each year among Medicare patients. Rates and associated costs of the procedure have increased nearly 300% during the last two decades.


Docetaxel Linked to Intoxication

The intravenous chemotherapy drug docetaxel, which contains ethanol, may cause patients to experience intoxication or to feel drunk during and after treatment, says the FDA, which is revising docetaxel product labels to warn of the risk.

Health care professionals should consider docetaxel’s alcohol content when prescribing or administering the drug, particularly for patients in whom alcohol intake should be avoided or minimized, and when using it in conjunction with other medications. Patients should avoid driving, operating machinery, or performing other dangerous activities for one to two hours after an infusion of docetaxel.

Some medications, such as pain relievers and sleep aids, may interact with the alcohol in intravenous docetaxel and worsen the drug’s intoxicating effects.

Docetaxel is used to treat several kinds of cancer, including cancers of the breast, prostate, stomach, head, and neck, as well as non–small-cell lung cancer.
Different docetaxel products contain different amounts of alcohol, which is used to dissolve the active ingredients so that docetaxel can be given intravenously.

Source: FDA, June 20, 2014

Use of Lidocaine Viscous Discouraged During Teething

Prescription oral viscous lidocaine 2% solution should not be used to treat infants and children with teething pain, says the FDA, which is requiring a boxed warning on the product’s prescribing information to drive home that point.

Topical pain relievers and medications rubbed on the gums are not useful because they wash out of the baby’s mouth within minutes, the FDA says. When too much viscous lidocaine is given to infants and young children or they accidentally swallow too much, it can result in seizures, severe brain injury, heart problems, and even death.

The FDA identified 22 cases of toxicity (six of them fatal) with the use of prescription oral viscous lidocaine 2% solution in children ages 5 months to 3.5 years of age through December 2013. Yet infants and children 2 years of age and younger accounted for approximately 4% of all patients who received dispensed prescriptions in the outpatient retail setting for oral viscous lidocaine solution in 2012.

In 2011, the FDA warned that use of over-the-counter benzocaine gels and liquids applied to the gums or mouth to reduce pain was associated with methemoglobinemia, mainly in children ages 2 years and younger.

Source: FDA, June 26, 2014

Testosterone Warning Mandated

 Manufacturers must include a warning about the risk of venous thromboembolism (VTE) in the drug labeling of all approved testosterone products, the FDA says. VTE includes deep vein thrombosis and pulmonary embolism.

The risk of venous blood clots is already included in the labeling of testosterone products as a possible consequence of polycythemia, which sometimes occurs with testosterone treatment. The FDA is requiring a more general warning because of postmarket reports of venous blood clots unrelated to polycythemia.

This new warning is not related to the FDA’s ongoing evaluation of the possible risk of stroke, heart attack, and death in patients taking testosterone products. Such products are approved for use in men who lack testosterone or have low levels in conjunction with an associated medical condition.

Source: FDA, June 20, 2014

Low-Dose Aspirin May Lower Risk of Pancreatic Cancer

The longer a person takes low-dose aspirin, the lower his or her risk for pancreatic cancer, according to a study published in Cancer Epidemiology, Biomarkers & Prevention.

Men and women who took low-dose aspirin regularly had a 48% reduction in their risk for developing pancreatic cancer. Protection against pancreatic cancer ranged from a 39% reduction in risk for those who took low-dose aspirin for six years or less to a 60% reduction in risk for those who took low-dose aspirin for more than 10 years.

Study subjects (362 pancreatic cancer patients and 690 controls) were recruited from the 30 general hospitals in Connecticut between 2005 and 2009. They were interviewed to determine when they started using aspirin, the number of years they used aspirin, the type of aspirin they used (low versus regular dose), and when they stopped using aspirin, among other things. Confounding factors, including body mass index, smoking history, and history of diabetes, were taken into account. A dose of 75 to 325 mg per day was considered low-dose aspirin (usually taken for heart-disease prevention).

Discontinuation of aspirin use within two years prior to the study was associated with a threefold increased risk for pancreatic cancer compared with continuing use.

Source: American Association for Cancer Research, June 26, 2014

Sitagliptin Tied to Increased Heart Failure Hospitalizations

Use of sitagliptin (Januvia, Merck) by patients with type-2 diabetes was not associated with an increased risk for all-cause hospitalizations or death, a study concludes, but the drug was associated with an increased risk for hospitalizations related to heart failure (HF) among patients with pre-existing HF.

The observational study evaluated the effects of sitagliptin, a dipeptidyl peptidase (DPP)-4 inhibitor, in patients with type-2 diabetes and HF. The findings were published in the Journal of the American College of Cardiology.

Investigators in Canada analyzed data from a national commercially insured U.S. claims database. Patients with incident HF were identified among individuals with type-2 diabetes initially treated with metformin or sulfonylurea and followed over time. Subjects subsequently treated with sitagliptin were compared with those not treated with sitagliptin in the 90 days before the composite primary outcome of all-cause hospital admission or death.

A total of 7,620 patients with diabetes and incident HF (mean age, 54 years; 58% male) met the study’s inclusion criteria; 887 patients (12%) were exposed to sitagliptin therapy (521 patient-years of exposure) after incident HF.

The study’s composite primary end-point occurred in 4,137 patients (54%). After adjustment, sitagliptin users did not demonstrate an increased risk for the primary endpoint compared with nonusers (7.1% vs. 9.2%, respectively; adjusted odds ratio [aOR], 0.84) for each component of
the primary endpoint (hospital admission, 7.5% vs. 9.2%, aOR, 0.93; and death, 6.9% vs. 9.3%, aOR, 1.16). However, those using sitagliptin showed an increased risk for HF hospitalizations compared with nonusers (12.5% vs. 9.0%, respectively; aOR, 1.84).

Source: Journal of the American College of Cardiology, July 7, 2014

**FDA: No Clear CV Risks for Olmesartan in Diabetes**

An FDA review found no clear evidence of increased cardiovascular (CV) risks associated with use of the blood pressure medication olmesartan in diabetic patients. As a result, FDA recommendations for the use of olmesartan (Benicar, Benicar HCT, Azor, Tribenzor, and generics) will remain the same.

The review was prompted by results from the ROADMAP clinical trial, which examined the effects of olmesartan in patients with type-2 diabetes to see whether the drug could delay kidney damage. There was an unexpected finding of increased CV death risk in the olmesartan group compared with the placebo group. However, the risk of nonfatal heart attack was lower in olmesartan patients.

To evaluate these findings, the FDA reviewed additional studies, including a large study in Medicare patients. That observational study in patients ages 65 years and older examined the rate of death in patients taking olmesartan compared to other angiotensin receptor blockers (ARBs).

In diabetic patients who received the highest dose of olmesartan (40 mg daily) for more than six months, olmesartan was associated with an increased risk of death (hazard ratio [HR] 2.0; 95% confidence interval [CI] 1.1–3.8) compared with similar patients taking other ARBs. But in nondiabetic patients, high-dose olmesartan was associated with a decreased risk of death (HR, 0.46; 95% CI, 0.24–0.86) compared to similar patients taking other ARBs. The conflicting results “raise uncertainty about the credibility of the findings in either group,” the FDA says.

Source: FDA, June 24, 2014

**Fixed-Dose Heart Regimen Aids Adherence, Not Results**

Patients and physicians both liked a fixed-dose combination of cardiovascular drugs—but despite extremely high adherence, patients’ symptoms did not improve in a statistically significant way, say University of Auckland researchers.

The study, IMPACT (IMProving Adherence using Combination Therapy), involved 513 adults with a history of or high risk for cardiovascular disease; 97% of enrollees completed 12 months of follow-up. Participants were randomly assigned to continued usual care or to fixed-dose treatment with aspirin 75 mg, simvastatin 40 mg, and lisinopril 10 mg, with either atenolol 50 mg or hydrochlorothiazide 12.5 mg. Their general practitioners could choose the combination, change combinations, or discontinue treatment at any stage, with no limitations on use of any concomitant drugs (including cardiovascular medications).

At 12 months, nearly twice as many fixed-dose patients were adherent to all four recommended drugs compared with usual-care patients (81% vs. 46%), but the study found no statistically significant improvement in risk factor control between the groups. The difference was ~2.2 mm Hg in systolic blood pressure (BP); ~1.2 mm Hg in diastolic BP; and ~0.05 mmol/L in low-density lipoprotein cholesterol.

One problem appeared to be that the patients were very well treated when the study started, the researchers say. Thus, researchers found limited scope for testing the effects of the fixed-dose combination treatment among patients who most need strategies to improve adherence—those taking few or no preventive drugs.

Source: BMJ, May 27, 2014

**Linezolid Aids Success With MRSA Pneumonia**

Veterans with methicillin-resistant Staphylococcus aureus pneumonia who were treated with linezolid were 53% more likely to be discharged as “clinical successes,” according to researchers from VAMC Providence, University of Rhode Island, and Brown University.

The researchers conducted a nested case-control study among 3,732 Veterans Affairs patients with MRSA pneumonia who received linezolid or vancomycin. They compared factors that might contribute to success, defined as discharge from the hospital or intensive care unit (ICU) by day 14 after treatment initiation. The 1,290 control patients represented nonsuccess: that is, therapy change, intubation, ICU admission, readmission, or death between treatment initiation and day 14.

Potential predictors included treatment, patient demographic and admission characteristics, previous health care and medication, comorbidities, and medical history. The clinical-success patients were more likely to be older and to have a current diagnosis of respiratory disease and diagnosis of pneumonia in the year before the MRSA pneumonia.

Only two predictors of clinical success were significant: treatment with linezolid and previous complication of an implant or graft in the year before admission for MRSA pneumonia. Clinical success also was more likely when length of therapy was shorter. The researchers aren’t sure why having an implant or graft complication was associated with clinical success; they theorize that those instances might have prompted more aggressive treatment.

Predictors associated with nonsuccess included: diagnosis of concomitant urinary tract infection, use of an intravenous line, previous coagulopathy, previous amputation procedure, current coagulopathy diagnosis, dialysis, multiple
inpatient procedures, inpatient surgery, and previous endocarditis.

The researchers say the only modifiable variable was linezolid treatment.

Source: Clinical Therapeutics, April 2014

Oral Treatment Prolongs Ovarian Cancer Survival

A near-doubling of progression-free survival (PFS) is among preliminary findings from a phase 2 study of the first oral combination of drugs for recurrent platinum-sensitive ovarian cancer, researchers reported at the annual meeting of the American Society of Clinical Oncology.

The study, conducted by the National Cancer Institute, compared a combination of olaparib and cediranib with olaparib alone. Olaparib is a PARP inhibitor, blocking poly ADP-ribose polymerase, an enzyme involved in many cell functions, including repair of DNA damage. Cediranib is an anti-angiogenic drug.

Olaparib has been used as monotherapy in recurrent ovarian cancer; it recently received priority review by the FDA for treatment of platinum-sensitive relapsed ovarian cancer in patients with a BRCA mutation. Cediranib, in the phase 3 ICON 6 trial, significantly improved PFS and overall survival in platinum-sensitive relapsed ovarian cancer compared with chemotherapy alone.

Preclinical studies suggested that the two drugs would be synergistic, and a phase 1 trial showed the combination was well tolerated. Based on those early findings, 90 patients were randomly assigned to one of two study arms for the phase 2 trial. One group took olaparib capsules (400 mg twice daily), and the other took olaparib 200 mg twice daily and cediranib tablets 30 mg once daily. The study arms were stratified by BRCA gene mutation status and prior anti-angiogenic therapy.

Patients were enrolled from October 2011 to June 2013. As of March 2014, median PFS was 17.7 months for the combination therapy versus 9.2 months for olaparib alone. Toxicity was higher in the combination group, with fatigue, diarrhea, and hypertension being the most common adverse effects, all manageable.

Sources: NIH, June 2, 2014; AstraZeneca, May 31

Better Results, Lower Price With Heparin Vs. Bivalirudin?

Using heparin to prevent blood-clot formation during emergency treatment of heart attacks could result in improved outcomes compared with far more costly bivalirudin (Angiomax, The Medicines Company), according to a study published in The Lancet.

Patients who undergo primary percutaneous coronary intervention (PPCI)—the most common treatment for heart attack—usually receive a combination of antithrombotic drugs to prevent further blood clots during and after the procedure. The most commonly used antithrombotic drugs are unfractionated heparin and bivalirudin. Bivalirudin is around 400 times more expensive than heparin.

The HEAT-PPCI trial at the Liverpool Heart and Chest Hospital in the United Kingdom recruited 1,829 patients undergoing emergency angiography. More than 80% went on to receive PPCI; approximately half received heparin and half received bivalirudin. The researchers recorded how many patients experienced a major adverse cardiac event, such as death or another heart attack, within 28 days after surgery.

The overall rates of major adverse cardiac events were significantly lower in the heparin group than the bivalirudin group, including death (4.3% vs. 5.1%, respectively) and another heart attack (0.8% vs. 2.7%). There was no significant difference between the two groups in the rate of complications.

A related editorial says that although the study had limitations—including including an open-label, single-center design—it resembled clinical practice by including patients who would have been excluded from earlier trials that compared the drugs.

Source: Lancet, July 5, 2014

Recalls

Bristol-Myers Squibb Coumadin Injection

Bristol-Myers Squibb recalled six lots of Coumadin for Injection, 5-mg single-use vials, after visible particulate matter was found in a small number of unreleased samples. The recall includes lots 2011125, 2011126, 2011127, 201228, 201229, and 201230, distributed from November 2011 through January 2014. Contact GENCO at 1-855-838-5784 to arrange for return of remaining stock.

Source: Bristol-Myers Squibb, June 30, 2014

One Lot of Hospira 0.5% Marcaine

Hospira, Inc., recalled lot 33-545-DD of 0.5% Marcare (bupivacaine HCl injection, USP), 30 mL, single-dose vial, preservative free, due to particulates embedded in the glass vial and visible in the solution. Hospira attributed the embedded particulates to a supplier’s glass defect and is working with its supplier on corrective and preventative actions. The lot was distributed from November 2013 through March 2014. For assistance, call Stericycle at 1-888-656-6380, Monday through Friday, 8 a.m. to 5 p.m. Eastern time.

Source: Hospira, Inc., June 17, 2014

DEVICE NEWS

Approvals

ReWalk Wearable Exoskeleton

The FDA has approved marketing of the ReWalk Personal System (ReWalk Robotics), a wearable robotic exoskeleton that provides powered hip and knee motion to enable people with spinal cord injury to stand upright and walk at home and in the community.
The device provides user-initiated mobility through the integration of a wearable brace support, a computer-based control system, and motion sensors. The system allows independent, controlled walking while mimicking the natural gait patterns of the legs, similar to that of an able-bodied person.

Clinical studies of the system showed significant health benefits to the user on a physiological and psychological level, including potential improvements in cardiovascular health, loss of fat tissue, building of lean muscle mass, and improved bowel function. Feedback from users also supports such potential benefits as better pain management, fewer medications, and potentially reduced hospitalizations.

The FDA cleared the device after multiple clinical studies demonstrated the technology’s safety and effectiveness. ReWalk has been tested extensively in the U.S., Europe, and Israel, and is used by more people worldwide than all other exoskeleton systems combined.

The ReWalk Personal System is custom-fitted to each individual and designed for daily use in a range of environments, such as indoors and outdoors on different surfaces or terrains. Users must meet the requirements of a medical examination and complete a training program.

Source: ReWalk Robotics, June 27, 2014

**Medtronic Transcatheter Use Extended to More Patients**

The FDA has approved use of the self-expanding transcatheter CoreValve System (Medtronic, Inc.) for patients at high risk for surgery. The system previously received FDA approval for patients at extreme risk.

The latest approval was based on research showing clinical outcomes at one year with the CoreValve System were superior to open-heart surgery for aortic valve replacement. The FDA approved the CoreValve System without an independent device advisory panel review due to positive results demonstrated in the High Risk Study of the CoreValve U.S. Pivotal Trial, which compared transcatheter aortic valve replacement (TAVR) with the CoreValve System to traditional surgical aortic valve replacement. Survival at one year for patients receiving the CoreValve System (85.8%) was statistically superior to patients receiving a surgical valve (80.9%).

For patients treated with the CoreValve System, rates of stroke were not statistically different than rates experienced by surgery patients. The rate of major adverse cardiovascular or cerebral events was significantly better for CoreValve patients at one year, and overall hemodynamic performance was better in CoreValve patients than in surgical patients across all time points.

The FDA approved the entire CoreValve platform—including the 23-mm, 26-mm, 29-mm, and 31-mm size valves—which are put into place using the smallest commercially available TAVR delivery system (approximately 0.25 inch), making it possible to treat patients with difficult or small vasculature.

Source: Medtronic, Inc., June 12, 2014

**Edwards Aortic Heart Valve**

The FDA has approved the Sapien XT transcatheter aortic heart valve (Edwards Lifesciences Corporation) for the treatment of high-risk and inoperable patients suffering from severe symptomatic aortic stenosis. The system, which includes a 29-mm valve size for patients with a large native annulus, will permit the treatment of more patients.

In the PARTNER II trial that evaluated the Sapien XT valve, the results in inoperable U.S. patients demonstrated a reduction in complications with the transcatheter aortic valve replacement procedure, as well as improved patient outcomes over earlier trials.

Source: Edwards Lifesciences Corporation, June 16, 2014

**A “Fly-Through” Surgical Simulator for Brain Surgery**

The FDA has given clearance to a product that combines flight simulation technology with advanced imaging so surgeons can perform a “fly-through” of a patient’s brain surgery.

The Surgical Navigation Advanced Platform (SNAP) provides virtual-reality guidance to surgeons to help them determine the safest and most efficient pathway to remove cerebral tumors and treat vascular anomalies.

SNAP (Surgical Theater, LLC) integrates with operating room technology to provide advanced 3D capabilities. Surgeons can execute their surgery plan while in the operating room utilizing a patient’s computerized tomography and magnetic resonance imaging scans.

SNAP provides the ability to rotate an image or make it semitransparent to see behind arteries and other critical structures. In addition, SNAP’s augmented reality and simulation capabilities allow surgeons to analyze virtual “what if” scenarios before making the actual incision.

Source: Surgical Theater, LLC, June 30, 2014

**Injectable Gel to Improve Lip Volume, Smooth Wrinkles**

The FDA has approved marketing of a transparent injectable hyaluronic acid gel that may temporarily increase the volume of patients’ lips and smooth wrinkles around the mouth. Hyaluronic acid is a protective, lubricating gel that is produced naturally by the body.

A doctor injects Restylane Silk ( Valeant Pharmaceuticals North America LLC/Medicis) into a patient’s lips and wrinkles around the mouth one or two times as needed over a period of two weeks. In a clinical study, patients needed one or two
injections to achieve the best lip volume and wrinkle appearance. The effect lasts for about six months. Restylane Silk is used in patients over the age of 21 years with thin or very thin lips.

Side effects may include bruising, redness, swelling, pain, tenderness, and itching. The product should not be used in patients who have severe allergies, bleeding disorders, and hypersensitivity to local anesthetics.

Source: FDA, July 1, 2014

**Rapid Molecular Flu Test**

The Alere Influenza A & B test (Alere Inc.)—the first molecular test to detect and differentiate influenza A and B viruses in less than 15 minutes—has been cleared for marketing by the FDA.

The test’s performance was established in a prospective study conducted at U.S. sites during the 2012–2013 flu season, when 585 nasal swab specimens, collected from patients with flu-like symptoms, were evaluated with the Alere test and the results were compared with viral culture. All specimens generating discrepant results between the Alere test and culture were further evaluated using an FDA-approved reverse transcription polymerase chain reaction (RT-PCR) assay to confirm the specimens’ influenza status.

The Alere Influenza A & B Test is intended to aid in the differential diagnosis of influenza A and B viral infections, but negative results should not be used as the sole basis for treatment or other management decisions.

Sources: Alere Inc., June 16, 2014

**Study Backs 3D Mammography**

Three-D mammography (digital breast tomosynthesis) found significantly more invasive cancers than a traditional mammogram alone and reduced call-backs for additional imaging, according to a study published in the Journal of the American Medical Association.

The retrospective study looked at 281,187 digital mammography examinations and 173,663 examinations with both tomosynthesis and digital mammography between 2010 and 2012. The data included women from a wide range of geographically diverse breast cancer screening programs in 13 academic and community practices.

The primary measured outcomes were recall rate (proportion of patients requiring additional imaging based on a screening examination result), cancer detection rate, positive predictive value for recall (proportion of patients recalled after screening who were diagnosed as having breast cancer), and positive predictive value for biopsy (proportion of patients undergoing biopsies who were diagnosed as having breast cancer).

Analysis indicated that the model-adjusted rates per 1,000 screens were as follows for digital mammography compared with digital mammography plus tomosynthesis: for recall rate, 107 versus 91 (an overall decrease in recall rate of 16 per 1,000 screens); for biopsies, 18.1 versus 19.3; for cancer detection, 4.2 versus 5.4; and for invasive cancer detection, 2.9 versus 4.1, respectively. Adding tomosynthesis increased the positive predictive value for recall from 4.3% to 6.4% and for biopsy from 24.2% to 29.2%.

Tomosynthesis allows for 3D reconstruction of the breast tissue, giving radiologists a clearer view of the overlapping slices of breast tissue. In 2011, the FDA approved tomosynthesis to be used in combination with standard digital mammography for breast cancer screening.

Sources: University of Pennsylvania and JAMA, June 24, 2014

**RECALLS**

**Flexi-Seal CONTROL Fecal Management System**

A system used in health care facilities to manage fecal incontinence—marketed without FDA clearance—has been recalled after reports of 12 serious injuries and one death.

The Flexi-Seal CONTROL Fecal Management System Kit is used to collect liquid to semi-liquid stool and to provide access to administer medications. The kit contains a soft catheter, inserted into the rectum, that contains and diverts fecal waste to protect the patient’s skin and keep the bedding clean. There is a low-pressure retention balloon at the far end and a connector for attaching the collection bag at the other end.

The system’s unique Auto-Valve feature “has not consistently performed relative to the inflation and deflation of the device’s retention balloon,” the FDA said. “This feature is one of the reasons a 510(k) application should have been submitted.” Inflation problems may result in rectal damage, expulsion of the device, leakage, and skin deterioration around the anus due to contact with fecal matter.

ConvaTec, Inc., launched the device (model number ICC 411107) in February 2013 and distributed it through April 14, 2014, as part of its Flexi-Seal product family. Customers should stop using the device and contact ConvaTec at 1-800-422-8811, Monday through Friday, 8:30 a.m. to 7 p.m. Eastern time.

Source: FDA, June 20, 2014

**Hydrofinity Hydrophilic Guidewire**

Nitinol Devices & Components (NDC) is recalling HydroFinity Hydrophilic Guidewires, which it makes and Covidien distributes, due to 12 reports of product damage during use.

The nitinol-core, polymer-jacketed guidewire with a hydrophilic coating is used in catheter placement and other procedures to treat vascular diseases. In two cases, the polymer jacket separated from the device and embolized; one case required surgical intervention.

Unused product should be returned...

Source: FDA, June 20, 2014
to Covidien. For information or to report problems, contact NDC Customer Service at 1-510-683-2000, Monday through Friday, 8 a.m. to 5 p.m. Pacific time.
Source: Nitinol Devices & Components, June 18, 2014

Vascular Solutions Catheters
Vascular Solutions, Inc., recalled some Langston V2 Dual Lumen Pressure Monitoring Catheters after reports that some inner catheters have separated from the device hub during use, which may require a procedure to retrieve the separated piece from the patient’s vascular system.

The device is used to deliver contrast medium into a patient’s blood vessels during angiographic studies and to measure pressure within the blood vessel. The devices were distributed from March 2014 to May 2014. Affected lot numbers are available at http://vasc.com. For information, contact Customer Service at 1-888-240-6001, Monday through Friday, 8 a.m. to 5 p.m. Central time, or via email at customerservice@vasc.com.
Source: Vascular Solutions, Inc., May 23, 2014

Medtronic Duet External Drainage and Monitoring
Medtronic Neurosurgery has recalled 58 lots of its Medtronic Duet External Drainage and Monitoring System because the patient line tubing may separate from the patient line connectors (especially during frequent handling).

The system externally drains and monitors cerebrospinal fluid (CSF) and monitors intracranial pressure. Device failure may result in pneumocephalus, infection, and too much or too little CSF drainage.

The affected products were distributed from April 10, 2013, through May 19, 2014. Affected catalog and lot numbers are listed in the FDA recall notice (available at http://tinyurl.com/MedtronicRecall).

Customers with questions may contact the firm’s Director of Quality at 805-571-8725, Monday through Friday, 8 a.m. to 5 p.m. Pacific time.
Source: FDA, July 2, 2014

NEW MEDICAL DEVICES

Marvin M. Goldenberg, PhD, RPh, MS

Name: BD MAX Enteric Bacterial Panel
Manufacturer: BD Diagnostics (Becton, Dickinson, and Company), Sparks, Maryland
Approval Date: May 7, 2014

Purpose: The BD MAX Enteric Bacterial Panel for use on the BD MAX System is a qualitative in vitro diagnostic test detecting DNA from Campylobacter species (jejuni and coli), Salmonella species, Shigella species, and enteroinvasive E. coli, as well as stx 1 and stx 2 genes in stool specimens. These pathogens are responsible for up to 95% of the bacteria causing gastroenteritis, accounting for millions of deaths annually.

Description: The BD MAX Enteric Bacterial Panel is designed to detect bacterial pathogens in line with widely recommended clinical algorithms for testing. These algorithms utilize patient history and clinical presentation in selecting diagnostic tests. Specimen types include unpreserved and Cary Blair preserved stool specimens from symptomatic patients with suspected acute gastroenteritis, enteritis, or colitis, adding to the flexibility of use for the laboratory.

Benefit: Infectious gastroenteritis accounts for approximately 1.7 billion cases of diarrhea globally and more than 2 million deaths annually. These infections may be caused by viruses, bacteria, or parasites, which often take two to four days or more to identify in the clinical laboratory using conventional methods. The BD MAX Enteric Bacterial Panel will provide clinicians with fast, accurate results that will enable more rapid diagnosis compared with conventional culture methods and will help improve standard of care and clinical efficiencies. The use of focused panels enables the implementation of enteric molecular testing in a cost-effective manner.

The use of the BD MAX Enteric Bacterial Panel also allows laboratories to implement Shiga toxin-producing E. coli screening recommended by the Centers for Disease Control and Prevention and required by the Joint Commission.
Source: www.bd.com

Name: Inspire Upper Airway Stimulation
Manufacturer: Inspire Medical Systems, Inc., Maple Grove, Minnesota
Approval Date: April 30, 2014

Purpose: The Inspire Upper Airway Stimulation (UAS) system is an implantable nerve stimulator used to treat a subset of patients with moderate-to-severe obstructive sleep apnea (OSA). On the apnea-hypopnea index (AHI), their OSA should be at least 20 and no more than 65. The system is intended for use in patients 22 years of age and older who have been confirmed to fail or cannot tolerate positive airway pressure treatments (such as continuous positive airway pressure [CPAP] or bilevel positive airway pressure [BPAP] machines) and who do not have a complete concentric collapse (as seen during drug-induced sleep endoscopy) at the soft palate level.

Description: The Inspire UAS system consists of implanted components, including the pulse generator (IPG), stimulation lead, and sensing lead, and external components, including the physician programmer and the patient programmer (sleep remote).

The IPG detects the patient’s breathing pattern and maintains an open airway with mild stimulation of the hypoglossal nerve, which controls tongue movement, during inhaled breathing. The physician...
adjusts the stimulation settings using the external physician programmer. The patient sleep remote allows patients to turn therapy on before they go to sleep and to turn therapy off when they wake up.

**Benefit:** In a clinical study of 126 patients at 22 sites, Inspire UAS therapy provided the majority of patients with significant reductions in the severity of their OSA and improvements in their quality of life. More than half of the patients experienced at least a 50% reduction in AHI and an AHI of less than 20 events per hour at the end of the 12-month study. Inspire UAS therapy patients also experienced at least a 25% reduction in oxygen desaturation index.

**Source:** www.fda.gov

**Name:** Invenia ABUS (Automated Breast Ultrasound System)

**Manufacturer:** GE Healthcare, Milwaukee, Wisconsin

**Approval Date:** June 3, 2014

**Purpose:** Invenia ABUS breast-imaging technology has been proven to help clinicians find 35.7% more cancers in women with dense breasts than mammograms alone. Since breast-cancer screenings can be emotionally stressful for the patient, Invenia ABUS was designed with a reverse curve transducer to conform to a woman’s anatomy, for better comfort and image performance. The system uses compression assist, which applies light levels of compression automatically to the breast for increased ease and image reproducibility.

**Description:** The Invenia ABUS uses 3D ultrasound technology to comfortably and quickly image women with dense breast tissue in approximately 15 minutes with new features that conform to a woman’s body and provide enhanced images.

**Benefit:** There is growing awareness of the increased risk of cancer among women with high breast density. The more dense a woman’s breast tissue, the higher her risk of developing breast cancer—up to six times greater than women who do not have dense breast tissue.

A growing body of research suggests the importance of screening ultrasound for women with dense breast tissue—about 40% of women. Mammography is still considered the gold standard for breast-cancer screening, but it is less sensitive in women who have dense breast tissue. Supplementing the mammogram with automated breast ultrasound screenings should help find tumors that cannot be seen on the mammogram and at an earlier stage than they would have otherwise been found.

**Sources:** www3.gehealthcare.com, www.medicaldevicenetwork.com