

REGULATORY INTELLIGENCE

YEAR-END REPORT - 2020

Published 21-Dec-2020
HPTS Issue Brief 12-21-20.37

Health Policy Tracking Service - Issue Briefs
Pharmaceuticals and Medical Devices
FDA Oversight

**This Issue Brief was written Robert S. White, a Compliance Attorney
on the publisher's editorial staff and a member of the Oklahoma bar.**

12/21/2020

I. Drug Approvals

FDA Approves Use Of Drug To Reduce Risk Of Cardiovascular Events In Certain Adult Patient Groups

On December 13, 2019, the FDA approved the use of Vascepa (icosapent ethyl) as an adjunctive (secondary) therapy to reduce the risk of cardiovascular events among adults with elevated triglyceride levels (a type of fat in the blood) of 150 milligrams per deciliter or higher. Patients must also have either established cardiovascular disease or diabetes and two or more additional risk factors for cardiovascular disease. Patients are advised to continue physical activity and maintain a healthy diet. ^[FN2]

Vascepa is the first FDA approved drug to reduce cardiovascular risk among patients with elevated triglyceride levels as an add-on to maximally tolerated statin therapy. Statins are drugs used to treat elevated cholesterol levels and reduce the risk of cardiovascular events.

"The FDA recognizes there is a need for additional medical treatments for cardiovascular disease," said John Sharretts, M.D., acting deputy director of the Division of Metabolism and Endocrinology Products in the FDA's Center for Drug Evaluation and Research. "Today's approval will give patients with elevated triglycerides and other important risk factors, including heart disease, stroke and diabetes, an adjunctive treatment option that can help decrease their risk of cardiovascular events."

High levels of triglycerides can play a role in the hardening of arteries or thickening of the artery wall, which can increase the risk of a heart attack or stroke; however, the mechanisms of action that contribute to reduced cardiovascular events among patients taking Vascepa are not completely understood.

Vascepa was initially approved in 2012 for adults with severe triglyceride levels. This supplement application received Priority Review. The FDA grants priority review to applications for drugs that, if approved, would improve the safety or effectiveness of the treatment, diagnosis, or prevention of serious conditions.

The approval of Vascepa was granted to Amarin Pharma Inc.

FDA Approves New Type Of Therapy To Treat Advanced Urothelial Cancer

On December 18, 2019, the FDA granted accelerated approval to Padcev (enfortumab vedotin-ejfv), a Nectin-4-directed antibody and microtubule inhibitor conjugate, meaning the drug specifically targets cancer cells. In this case, the cell adhesion molecule Nectin-4, which is highly expressed in urothelial cancers. Padcev is indicated for the treatment of adult patients with locally advanced (when cancer has grown too large to be surgically removed) or metastatic (when cancer cells spread to other parts of the body) urothelial cancer who have previously received a programmed death receptor-1 (PD-1) or programmed death ligand 1 (PD-L1) inhibitor and a platinum-containing chemotherapy. Platinum-containing chemotherapy, PD-1 and PD-L1 inhibitors are standard treatments for patients with bladder cancer, the sixth most common cancer in the U.S. Urothelial cancer, accounting for more than 90% of bladder cancers, begins in cells that line the bladder and nearby organs. Padcev represents a new type of therapy for patients with advanced urothelial cancer whose disease has progressed on chemotherapy and immunotherapy. ^[FN3]

"Antibody-drug conjugates are strategic tools in the targeted treatment of cancer. These conjugates combine the ability of monoclonal antibodies to target specific receptors on cancer cells and then deliver a drug to the cancer cell," said Richard Pazdur, M.D., director of the FDA's Oncology Center of Excellence and acting director of the Office of Oncologic Diseases in the FDA's Center for Drug



THOMSON REUTERS™

© 2021 Thomson Reuters. No claim to original U.S. Government Works.

Evaluation and Research. “Padcev is an antibody-drug conjugate that targets Nectin-4, a cell surface protein expressed on bladder cancer cells and a cell-killing agent, monomethyl auristatin E.”

Padcev was granted Accelerated Approval, which enables the FDA to approve drugs for serious conditions to fill an unmet medical need based on a result that is reasonably likely to predict a clinical benefit to patients. A further clinical trial is required to verify and describe Padcev's clinical benefit.

The FDA granted this application Priority Review and Breakthrough Therapy designation, which expedites the development and review of drugs that are intended to treat a serious disease or condition and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over available therapies. Padcev received approval approximately three months before the goal date.

The FDA granted the approval of Padcev to Astellas Pharma US Inc.

FDA Approves Vaccine For The Prevention Of Ebola Virus Disease

On December 19, 2019, the FDA announced the approval of Ervebo, the first FDA-approved vaccine for the prevention of Ebola virus disease (EVD), caused by Zaire ebolavirus in individuals 18 years of age and older. Cases of EVD are very rare in the U.S., and those that have occurred have been the result of infections acquired by individuals in other countries who then traveled to the U.S., or health care workers who became ill after treating patients with EVD. ^[FN4]

“While the risk of Ebola virus disease in the U.S. remains low, the U.S. government remains deeply committed to fighting devastating Ebola outbreaks in Africa, including the current outbreak in the Democratic Republic of the Congo,” said Anna Abram, FDA Deputy Commissioner for Policy, Legislation, and International Affairs. “Today's approval is an important step in our continuing efforts to fight Ebola in close coordination with our partners across the U.S. Department of Health and Human Services, as well as our international partners, such as the World Health Organization. These efforts, including today's landmark approval, reflect the FDA's unwavering dedication to leveraging our expertise to facilitate the development and availability of safe and effective medical products to address urgent public health needs and fight infectious diseases, as part of our vital public health mission.”

The FDA granted this application Priority Review and a Tropical Disease Priority Review Voucher under a program intended to encourage development of new drugs and biologics for the prevention and treatment of certain tropical diseases. The FDA also granted Breakthrough Therapy designation for Ervebo to facilitate the development and scientific evaluation of the vaccine. Because of the public health importance of a vaccine to prevent EVD, the FDA worked closely with the company and completed its evaluation of the safety and effectiveness of Ervebo in less than six months.

The approval was granted to Merck & Co., Inc.

FDA Approves New Treatment Option For Patients With HER2-Positive Breast Cancer Who Have Progressed On Available Therapies

On December 20, 2019, the FDA granted accelerated approval to Enhertu (fam-trastuzumab deruxtecan-nxki) for the treatment of adults with unresectable (unable to be removed with surgery) or metastatic (when cancer cells spread to other parts of the body) HER2-positive breast cancer who have received two or more prior anti-HER2-based regimens in the metastatic setting. Enhertu is a human epidermal growth factor receptor 2 (HER2)-directed antibody and topoisomerase inhibitor conjugate, meaning that the drug targets the changes in HER2 that help the cancer grow, divide and spread, and is linked to a topoisomerase inhibitor, which is a chemical compound that is toxic to cancer cells. ^[FN5]

“There have been many advances in the development of drugs for HER2-positive breast cancer since the introduction of Herceptin (trastuzumab) in 1998. The approval of Enhertu represents the newest treatment option for patients who have progressed on available HER2-directed therapies,” said Richard Pazdur, M.D., director of the FDA's Oncology Center of Excellence and acting director of the Office of Oncologic Diseases in the FDA's Center for Drug Evaluation and Research. “Drug development in the area of targeted therapies builds on our scientific understanding of malignant diseases not only in breast cancer, but in multiple other diseases.”

HER2-positive breast cancer is a type of breast cancer that tests positive for a protein called human epidermal growth factor receptor 2 (HER2), which promotes the growth of cancer cells. Approximately one of every five breast cancers have a gene mutation in the cancer cells that makes an excess of the HER2 protein. HER2-positive breast cancers are an aggressive type of breast cancer.

Enhertu was granted Accelerated Approval, which enables the FDA to approve drugs for serious conditions to fill an unmet medical need based on a result that is reasonably likely to predict a clinical benefit to patients. Further clinical trials may be required to verify and describe Enhertu's clinical benefit.

The FDA granted this application Breakthrough Therapy designation, which expedites the development and review of drugs that are intended to treat a serious condition, when preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over available therapies. Enhertu was also granted Fast Track designation, which expedites the review of drugs to treat serious conditions and fill an unmet medical need. This application was approved four months prior to the FDA goal date.

The FDA granted the approval of Enhertu to Daiichi Sankyo.

FDA Approves New Treatment For Migraines



On December 23, 2019, the FDA approved Ubrelvy (ubrogepant) tablets for the acute (immediate) treatment of migraine with or without aura (a sensory phenomenon or visual disturbance) in adults. Ubrelvy is not indicated for the preventive treatment of migraine. It is the first drug in the class of oral calcitonin gene-related peptide receptor antagonists approved for the acute treatment of migraine. ^[FN6]

“Migraine is an often disabling condition that affects an estimated 37 million people in the U.S.,” said Billy Dunn, M.D., acting director of the Office of Neuroscience in the FDA’s Center for Drug Evaluation and Research. “Ubrelvy represents an important new option for the acute treatment of migraine in adults, as it is the first drug in its class approved for this indication. The FDA is pleased to approve a novel treatment for patients suffering from migraine and will continue to work with stakeholders to promote the development of new safe and effective migraine therapies.”

Migraine headache pain is often described as an intense throbbing or pulsating pain in one area of the head. Additional symptoms include nausea and/or vomiting and sensitivity to light and sound. Approximately one third of individuals who suffer from migraine also experience aura shortly before the migraine. An aura can appear as flashing lights, zig-zag lines, or a temporary loss of vision. Migraines can often be triggered by various factors including stress, hormone changes, bright or flashing lights, lack of food or sleep and diet. Migraine is three times more common in women than in men and affects more than 10% of people worldwide.

The FDA granted the approval of Ubrelvy to Allergan USA, Inc.

FDA Approves The First Targeted Therapy To Treat A Rare Mutation In Patients With Gastrointestinal Stromal Tumors

On January 9, 2020, the FDA approved Ayvakit (avapritinib) for the treatment of adults with unresectable (unable to be removed with surgery) or metastatic (when cancer cells spread to other parts of the body) gastrointestinal stromal tumor (GIST) ? a type of tumor that occurs in the gastrointestinal tract, most commonly in the stomach or small intestine ? harboring a platelet-derived growth factor receptor alpha (PDGFRA) exon 18 mutation. This approval includes GIST that harbors a PDGFRA D842V mutation, which is the most common exon 18 mutation. Ayvakit is a kinase inhibitor, meaning it blocks a type of enzyme called a kinase and helps keeps the cancer cells from growing. ^[FN7]

“GIST harboring a PDGFRA exon 18 mutation do not respond to standard therapies for GIST. However, today’s approval provides patients with the first drug specifically approved for GIST harboring this mutation,” said Richard Pazdur, M.D., director of the FDA’s Oncology Center of Excellence and acting director of the Office of Oncologic Diseases in the FDA’s Center for Drug Evaluation and Research. “Clinical trials showed a high response rate with almost 85% of patients experiencing tumor shrinkage with this targeted drug.”

GISTs arise from specialized nerve cells found in the walls of the gastrointestinal tract. One or more mutations in the DNA of one of these cells may lead to the development of GIST. These cells aid in the movement of food through the intestines and control various digestive processes. More than half of GISTs start in the stomach. Most of the others start in the small intestine, but GISTs can start anywhere along the gastrointestinal tract. The activating mutations in PDGFRA have been linked to the development of GISTs, and up to approximately 10% of GIST cases involve mutations of this gene.

The FDA granted this application Breakthrough Therapy designation, which expedites the development and review of drugs that are intended to treat a serious condition, when preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over available therapies. Ayvakit was also granted Fast Track designation, which expedites the review of drugs to treat serious conditions and fill an unmet medical need. Ayvakit received Orphan Drug designation, which provides incentives to assist and encourage the development of drugs for rare diseases.

The FDA granted approval of Ayvakit to Blueprint Medicines Corporation.

FDA Approves First Treatment For Thyroid Eye Disease

On January 21, 2020, FDA approved Tepezza (teprotumumab-trbw) for the treatment of adults with thyroid eye disease, a rare condition where the muscles and fatty tissues behind the eye become inflamed, causing the eyes to be pushed forward and bulge outwards (proptosis). Today’s approval represents the first drug approved for the treatment of thyroid eye disease. ^[FN8]

“Today’s approval marks an important milestone for the treatment of thyroid eye disease. Currently, there are very limited treatment options for this potentially debilitating disease. This treatment has the potential to alter the course of the disease, potentially sparing patients from needing multiple invasive surgeries by providing an alternative, non-surgical treatment option,” said Wiley Chambers, M.D., deputy director of the Division of Transplant and Ophthalmology Products in the FDA’s Center for Drug Evaluation and Research. “Additionally, thyroid eye disease is a rare disease that impacts a small percentage of the population, and for a variety of reasons, treatments for rare diseases are often unavailable. This approval represents important progress in the approval of effective treatments for rare diseases, such as thyroid eye disease.”

Thyroid eye disease is associated with the outward bulging of the eye that can cause a variety of symptoms such as eye pain, double vision, light sensitivity or difficulty closing the eye. This disease impacts a relatively small number of Americans, with more women than men affected. Although this condition impacts relatively few individuals, thyroid eye disease can be incapacitating. For example, the troubling ocular symptoms can lead to the progressive inability of people with thyroid eye disease to perform important daily activities, such as driving or working.



THOMSON REUTERS™

© 2021 Thomson Reuters. No claim to original U.S. Government Works.

The FDA granted this application Priority Review, in addition to Fast Track and Breakthrough Therapy Designation. Additionally, Tepezza received Orphan Drug designation, which provides incentives to assist and encourage the development of drugs for rare diseases or conditions. Development of this product was also in part supported by the FDA Orphan Products Grants Program, which provides grants for clinical studies on safety and efficacy of products for use in rare diseases or conditions.

The FDA granted the approval of Tepezza to Horizon Therapeutics Ireland DAC.

FDA Approves First Treatment Option Specifically For Patients With Epithelioid Sarcoma, A Rare Soft Tissue Cancer

On January 23, 2020, the FDA granted accelerated approval to Tazverik (tazemetostat) for the treatment of adults and pediatric patients aged 16 years and older with metastatic (when cancer cells spread to other parts of the body) or locally advanced (when cancer has grown outside the organ it started in, but has not yet spread to distant parts of the body) epithelioid sarcoma not eligible for complete resection (surgically removing all of a tissue, structure, or organ). Epithelioid sarcoma is a rare sub-type of soft tissue sarcoma that often occurs in young adults.^[FN9]

“Epithelioid sarcoma accounts for less than one percent of all soft tissue sarcomas,” said Richard Pazdur, M.D., director of the FDA’s Oncology Center of Excellence and acting director of the Office of Oncologic Diseases in the FDA’s Center for Drug Evaluation and Research. “Until today, there were no treatment options specifically for patients with epithelioid sarcoma. The approval of Tazverik provides a treatment option that specifically targets this disease. When we brought Tazverik’s application to the Oncologic Drugs Advisory Committee last month, the committee voted unanimously that the benefits of the drug outweighed the risks.”

Tazverik blocks activity of the EZH2 methyltransferase, which may help keep the cancer cells from growing. Most cases of epithelioid sarcoma begin in the soft tissue under the skin of an extremity, though it can start in other areas of the body. Surgical removal is considered the main treatment when the cancer is localized to one area of the body. Chemotherapy or radiation may also be given. However, there is a high likelihood for local and regional spread of the disease even with treatment and approximately 50% of patients have metastatic disease at the time of diagnosis. Metastatic disease is considered life-threatening to the patient.

Tazverik was granted Accelerated Approval, which enables the FDA to approve drugs for serious conditions to fill an unmet medical need based on a result that is reasonably likely to predict a clinical benefit to patients. Further clinical trials may be required to verify and describe Tazverik’s clinical benefit. Tazverik also received Orphan Drug designation, which provides incentives to assist and encourage the development of drugs for rare diseases.

The FDA granted the approval of Tazverik to Epizyme Inc.

FDA Approves First Drug For Treatment Of Peanut Allergy For Children

On January 31, 2020, the FDA approved Palforzia [Peanut (Arachis hypogaea) Allergen Powder-dnfp] to mitigate allergic reactions, including anaphylaxis, that may occur with accidental exposure to peanuts. Treatment with Palforzia may be initiated in individuals ages 4 through 17 years with a confirmed diagnosis of peanut allergy and may be continued in individuals 4 years of age and older. Those who take Palforzia must continue to avoid peanuts in their diets.^[FN10]

“Peanut allergy affects approximately 1 million children in the U.S. and only 1 out of 5 of these children will outgrow their allergy. Because there is no cure, allergic individuals must strictly avoid exposure to prevent severe and potentially life-threatening reactions,” said Peter Marks, M.D., Ph.D., director of the FDA’s Center for Biologics Evaluation and Research. “Even with strict avoidance, inadvertent exposures can and do occur. When used in conjunction with peanut avoidance, Palforzia provides an FDA-approved treatment option to help reduce the risk of these allergic reactions in children with peanut allergy.”

Peanut allergy is a condition in which the body’s immune system mistakenly identifies even small amounts of peanut as harmful. Allergic reactions to peanut are unpredictable in occurrence and in how they present, with some individuals experiencing severe reactions from even trace amounts. Physical symptoms can develop within seconds of exposure and may include skin reactions (e.g., hives, redness or swelling), digestive discomfort, or more dangerous reactions, such as constriction of the throat and airways, and loss of adequate blood flow to vital organs of the body. Antihistamines and epinephrine can be used to treat allergic reactions, but severe reactions can be fatal even with appropriate, prompt treatment. Palforzia cannot be used for the emergency treatment of allergic reactions, including anaphylaxis.

The FDA granted approval of Palforzia to Aimmune Therapeutics.

FDA Approves Three Drugs For Nonprescription Use Through Rx-To-OTC Switch Process

On February 14, 2020, the FDA approved three drugs for nonprescription, or over-the-counter (OTC), use through a process called a prescription (Rx)-to-OTC switch. The FDA approved Voltaren Arthritis Pain (diclofenac sodium topical gel, 1%) for the temporary relief of arthritis pain; Pataday Twice Daily Relief (olopatadine HCl ophthalmic solution/drops, 0.1%) for the temporary relief of itchy and red eyes due to pollen, ragweed, grass, animal hair or dander; and Pataday Once Daily Relief (olopatadine HCl ophthalmic solution/drops, 0.2%) for the temporary relief of itchy eyes due to pollen, ragweed, grass, animal hair or dander, for nonprescription use.^[FN11]

“As a result of the Rx-to-OTC switch process, many products sold over-the-counter today use ingredients or dosage strengths that were available only by prescription 30 years ago,” said Karen Mahoney, M.D., acting deputy director of the Office of Nonprescription Drugs in the FDA’s Center for Drug Evaluation and Research. “Approval of a wider range of nonprescription drugs has the potential to improve



public health by increasing the types of drugs consumers can access and use that would otherwise only be available by prescription. This includes providing the millions of people that suffer with joint pain from arthritis daily over-the-counter access to another non-opioid treatment option.”

The process of changing the status of a drug from prescription to nonprescription is called an Rx-to-OTC switch. It is usually initiated by the manufacturer of the prescription drug. For a drug to switch to nonprescription status, the data provided must demonstrate that the drug is safe and effective for use in self-medication as directed in proposed labeling. The manufacturer must show that consumers can understand how to use the drug safely and effectively without the supervision of a healthcare professional.

All three products will be marketed in the U.S. as nonprescription drugs and will no longer be available as prescription drugs.

The FDA granted the approval of nonprescription Voltaren Arthritis Pain to GlaxoSmithKline plc. The FDA granted the approvals of nonprescription Pataday Twice Daily Relief and Pataday Once Daily Relief to Alcon.

FDA Approves First Generic Of Proair HFA

On February 24, 2020, the FDA approved the first generic of ProAir HFA (albuterol sulfate) Inhalation Aerosol for the treatment or prevention of bronchospasm in patients four years of age and older with reversible obstructive airway disease and the prevention of exercise-induced bronchospasm in patients four years of age and older. ^[FN12]

“Today’s approval of the first generic drug product for one of the most commonly used rescue inhalers in the U.S. is part of our longstanding commitment to advance patient access to lower-cost, high-quality generic drug products that are as safe and effective as their brand name counterparts, and to expand opportunities to bring generic copies of complex drugs to the market,” said FDA Commissioner Stephen M. Hahn, M.D. “Metered dose inhalers like these are known as complex generics, which are traditionally harder to copy because of their complex formulation or mode of delivery. As a result, too many complex drugs lack generic competition even after patents and exclusivities no longer block generic approval. Supporting development and approval of generic copies of these complex medicines so that these products can get to patients has been a major focus of our efforts to improve competition and access and to lower drug prices. Getting more generic copies of complex drugs to the market is a key priority for how we’ll help bring new savings to consumers.”

According to the National Heart, Lung, and Blood Institute, bronchospasms occur when the muscles surrounding the airways swell and tighten, squeezing the airways and making them smaller. Exercise and other physical activity can bring on symptoms in most people who have asthma and may occur either during or right after being active. Asthma causes recurring periods of wheezing (a whistling sound when breathing), chest tightness, shortness of breath and coughing. The coughing often worsens at night or early in the morning. Asthma affects people of all ages, but it most often starts during childhood. In the United States, more than 26 million people are known to have asthma, about 7 million of these people are children.

The FDA granted approval of this generic albuterol sulfate inhalation aerosol to Perrigo Pharmaceutical Co.

FDA Approves First Generic of Daraprim

On February 28, 2020, the FDA approved an application for the first generic of Daraprim (pyrimethamine) tablets for the treatment of toxoplasmosis (an infection caused by the parasite *Toxoplasma gondii*) when used with a sulfonamide (a group of medicines used to treat bacterial infections). ^[FN13]

“The FDA has a longstanding commitment to increasing competition in markets with limited or no generic alternatives. Through the FDA’s Drug Competition Action Plan, we’ve worked to remove barriers in generic drug development by not only taking actions that improve the efficiency of the development, review and approval of generic drugs, but also by closing loopholes that allow brand-name drug companies to “game” the rules in ways that delay generic competition that Congress intended,” said FDA Commissioner Stephen M. Hahn, M.D. “Empowering patients and promoting choice and competition are top priorities for the FDA. These important efforts include improving access to safe, effective and high-quality generic medications. Today’s approval is especially important for populations that are more susceptible to toxoplasmosis infections, such as pregnant women and individuals with HIV or AIDS by paving the way for more choices in treatment options.”

Toxoplasmosis is an infection caused by a single-celled parasite called *Toxoplasma gondii* that, when severe, can cause damage to the brain, eyes or other organs. A *Toxoplasma* infection can occur, among other ways, by eating undercooked, contaminated meat or shellfish; drinking water contaminated with *Toxoplasma*; or by accidental swallowing of the parasite through contact with cat feces that contain *Toxoplasma*. It is considered to be the leading cause of death attributed to foodborne illness in the United States.

Severe toxoplasmosis is more likely in pregnant women and individuals who have weak immune systems, such as those with HIV or AIDS, those taking certain types of chemotherapy and those who have recently received an organ transplant. However, occasionally even persons with healthy immune systems may experience eye damage from toxoplasmosis.

The sponsor of the approved generic version of Daraprim Tablets is Cerovene Inc.

FDA Approves New Therapy for Patients with Previously Treated Multiple Myeloma

On March 2, 2020, the FDA approved Sarclisa (isatuximab-irfc), in combination with pomalidomide and dexamethasone, for the treatment of adult patients with multiple myeloma who have received at least two prior therapies including lenalidomide and a



THOMSON REUTERS™

© 2021 Thomson Reuters. No claim to original U.S. Government Works.

proteasome inhibitor. Sarclisa, administered through intravenous (IV) infusion, is a CD38-directed cytolytic antibody that works by helping certain cells in the immune system attack multiple myeloma cancer cells. ^[FN14]

"Targeting cells has led to the development of important oncology treatments. While there is no cure for multiple myeloma, Sarclisa is now another CD38-directed treatment option added to the list of FDA-approved treatments of patients with multiple myeloma who have progressive disease after previous therapies," said Richard Pazdur, M.D., director of the FDA's Oncology Center of Excellence and acting director of the Office of Oncologic Diseases in the FDA's Center for Drug Evaluation and Research. "In the clinical trial, there was a 40% reduction in the risk of disease progression or death with this therapy."

Multiple myeloma is a form of blood cancer that occurs in infection-fighting plasma cells (a type of white blood cell) found in the bone marrow. These cancerous cells multiply, produce an abnormal protein and push out other healthy blood cells from the bone marrow. The disease may result in a weakened immune system and cause other bone or kidney problems. The National Cancer Institute estimates there would be 32,270 new cases of multiple myeloma and 12,830 related deaths in the United States in 2020.

Sarclisa received Orphan Drug designation, which provides incentives to assist and encourage the development of drugs for rare diseases.

The FDA granted approval of Sarclisa to Sanofi-Aventis U.S. LLC.

FDA Approves New Treatment for Adults with Cushing's Disease

On March 6, 2020, the FDA approved Isturisa (osilodrostat) oral tablets for adults with Cushing's disease who either cannot undergo pituitary gland surgery or have undergone the surgery but still have the disease. Cushing's disease is a rare disease in which the adrenal glands make too much of the cortisol hormone. Isturisa is the first FDA-approved drug to directly address this cortisol overproduction by blocking the enzyme known as 11-beta-hydroxylase and preventing cortisol synthesis. ^[FN15]

"The FDA supports the development of safe and effective treatments for rare diseases, and this new therapy can help people with Cushing's disease, a rare condition where excessive cortisol production puts them at risk for other medical issues," said Mary Thanh Hai, M.D., acting director of the Office of Drug Evaluation II in the FDA's Center for Drug Evaluation and Research. "By helping patients achieve normal cortisol levels, this medication is an important treatment option for adults with Cushing's disease."

Cushing's disease is caused by a pituitary tumor that releases too much of a hormone called adrenocorticotropin, which stimulates the adrenal gland to produce an excessive amount of cortisol. The disease is most common among adults between the ages of 30 to 50, and it affects women three times more often than men. Cushing's disease can cause significant health issues, such as high blood pressure, obesity, type 2 diabetes, blood clots in the legs and lungs, bone loss and fractures, a weakened immune system and depression. Patients may have thin arms and legs, a round red full face, increased fat around the neck, easy bruising, striae (purple stretch marks) and weak muscles.

Isturisa received Orphan Drug Designation, which is a special status granted to a drug intended to treat a rare disease or condition.

The FDA granted the approval of Isturisa to Novartis.

FDA Approves First Treatment for Group of Progressive Interstitial Lung Diseases

On March 9, 2020, the FDA approved Ofev (nintedanib) oral capsules to treat patients with chronic fibrosing (scarring) interstitial lung diseases (ILD) with a progressive phenotype (trait). It is the first FDA-approved treatment for this group of fibrosing lung diseases that worsen over time. ^[FN16]

"The FDA continues to encourage the development of therapies for patients with limited or no treatment options," said Banu Karimi-Shah, M.D., acting deputy director of the Division of Pulmonary, Allergy, and Rheumatology Products in the FDA's Center for Drug Evaluation and Research. "Today's approval helps to fulfill an unmet treatment need, as patients with these life-threatening lung diseases have not had an approved medication until now."

Chronic fibrosing ILD with a progressive phenotype encompasses a group of fibrotic lung diseases caused by different underlying diseases or conditions, including autoimmune ILD, hypersensitivity pneumonitis and idiopathic nonspecific interstitial pneumonia. Characteristics of chronic fibrosing ILD include lung scarring and rapid disease progression, as assessed through worsening lung function tests, symptoms and/or imaging. Progressive lung scarring leads to breathlessness and respiratory failure. Lung function declines over time among these patients and can be debilitating and life-threatening.

Ofev was previously approved to treat idiopathic pulmonary fibrosis and to slow the rate of decline in pulmonary function among patients with ILD associated with systemic sclerosis or scleroderma.

The FDA granted the approval of Ofev to treat ILD with a progressive phenotype to Boehringer Ingelheim Pharmaceuticals, Inc.

FDA Approves Additional Treatment for Adults and Adolescents with Hemophilia A or B and Inhibitors

On April 1, 2020, the FDA approved Sevenfact [coagulation factor VIIa (recombinant)-jncw] for the treatment and control of bleeding episodes occurring in adults and adolescents 12 years of age and older with hemophilia A or B with inhibitors (neutralizing antibodies). Sevenfact contains an active ingredient expressed in genetically engineered rabbits. ^[FN17]



"Today's approval provides another treatment option for the control of bleeding episodes in adults and adolescents with hemophilia who have developed inhibitors," said Dr. Peter Marks, M.D., Ph.D., director of the FDA's Center for Biologics Evaluation and Research. "In addition to being an important option for patients, Sevenfact is the first product for hemophilia treatment that contains an active ingredient obtained from rabbits genetically engineered to produce a protein necessary for blood coagulation. This approval is an example of our efforts to advance safe biotechnology innovations to support patient health."

Hemophilia A or B is a congenital bleeding disorder caused by a dysfunction or deficiency of Coagulation Factor (F) VIII or IX, respectively. People with hemophilia may bleed for a longer time than others after injury or surgery. They may also have spontaneous bleeding in muscles, joints and organs, which may be life-threatening. Individuals with inhibitors may not respond to factor replacement therapy. According to the Centers for Disease Control and Prevention (CDC), there are an estimated 20,000 people living with hemophilia in the United States. Bleeding episodes in these individuals are managed by either on-demand treatment or prophylaxis using products containing FVIII or FIX. However, when inhibitors to FVIII or FIX develop in these individuals, treatment of bleeding episodes with FVIII or FIX products may no longer be effective. In these situations, the administration of products such as Sevenfact, which bypass the Factor VIII and Factor IX reactions, promotes clot formation and controls bleeding.

The FDA granted approval of Sevenfact to Laboratoire Francais du Fractionnement et des Biotechnologies S.A.

FDA Approves First Generic of a Commonly Used Albuterol Inhaler to Treat and Prevent Bronchospasm

On April 8, 2020, the FDA approved the first generic of Proventil HFA (albuterol sulfate) Metered Dose Inhaler, 90 mcg/Inhalation, for the treatment or prevention of bronchospasm in patients four years of age and older who have reversible obstructive airway disease, as well as the prevention of exercise-induced bronchospasm in this age group. ^[FN18]

"The FDA recognizes the increased demand for albuterol products during the novel coronavirus pandemic," said FDA Commissioner Stephen M. Hahn, M.D. "We remain deeply committed to facilitating access to medical products to help address critical needs of the American public."

The FDA granted approval of this generic albuterol sulfate inhalation aerosol to Cipla Limited.

FDA Approves First Therapy for Children with Debilitating and Disfiguring Rare Disease

On April 10, 2020, the FDA approved Koselugo (selumetinib) for the treatment of pediatric patients, 2 years of age and older, with neurofibromatosis type 1 (NF1), a genetic disorder of the nervous system causing tumors to grow on nerves. Koselugo is the first drug approved by the FDA to treat this debilitating, progressive and often disfiguring rare disease that typically begins early in life. ^[FN19]

"Everyone's daily lives have been disrupted during the COVID-19 pandemic, and in this critical time we want patients to know that the FDA remains committed to making patients with rare tumors and life threatening diseases, and their unique needs, a top priority. We continue to expedite product development for these patients," said Richard Pazdur, M.D., director of the FDA's Oncology Center of Excellence and acting director of the Office of Oncologic Diseases in the FDA's Center for Drug Evaluation and Research.

Koselugo is approved specifically for patients who have symptomatic, inoperable plexiform neurofibromas (PN), which are tumors involving the nerve sheaths (coating around nerve fibers) and can grow anywhere in the body, including the face, extremities, areas around the spine and deep in the body where they may affect organs. Koselugo is a kinase inhibitor, meaning it functions by blocking a key enzyme, which results in helping to stop the tumor cells from growing.

The FDA granted approval of Koselugo to AstraZeneca Pharmaceuticals LP.

FDA Approves First Therapy for Treatment of Low-Grade Upper Tract Urothelial Cancer

On April 15, 2020, the FDA approved Jelmyto (mitomycin gel), the first therapy to treat low-grade upper tract urothelial cancer (UTUC). Urothelial cancer is a cancer of the lining of the urinary system. ^[FN20]

"Although our nation's emphasis is on the need to combat COVID-19, patients with cancer and their unique needs continue to be a top priority for the FDA," said Richard Pazdur, M.D., director of the FDA's Oncology Center of Excellence and acting director of the Office of Oncologic Diseases in the FDA's Center for Drug Evaluation and Research. "We continue to expedite oncology product development in this critical time. Our staff is continuing to meet virtually with drug developers, academic investigators and patient advocates to push forward the coordinated review of drugs, biologics and devices for cancer."

While the majority of urothelial cancers occur in the bladder, UTUC corresponds to a subset of urothelial cancers that arise in the lining of the kidney or the ureter (the long, thin tube that connects that kidney to the bladder). UTUC can block the ureter or kidney, causing swelling, infections and impairment of kidney function in some patients. UTUCs can develop as low-grade or high-grade tumors. In general, low-grade tumors are not invasive and very rarely spread from the kidney or ureter. However, they often recur and management involves treating visible tumors and trying to preserve the urinary tract, as these tumors are more likely to recur in the urinary system than they are to spread. Low-grade UTUC is rare, but affects 6,000-8,000 new patients in the United States every year.

"This is the first approval specifically for patients with low-grade UTUC and provides an option for some patients who may otherwise require a nephroureterectomy," said Pazdur. "Due to substantial treatment challenges associated with the complex anatomy of the



upper urinary tract, many patients need to be treated with radical surgery ? usually complete removal of the affected kidney, ureter and bladder cuff. Jelmyto gives patients, for the first time, an alternative treatment option for low-grade UTUC.”

The FDA granted approval of Jelmyto to UroGen Pharma, Inc.

FDA Approves First New Drug Under International Collaboration, A Treatment Option for Patients with HER2-Positive Metastatic Breast Cancer

On April 17, 2020, as part of Project Orbis, the FDA approved Tukysa (tucatinib) in combination with chemotherapy (trastuzumab and capecitabine) for the treatment of adult patients with advanced forms of HER2-positive breast cancer that can't be removed with surgery, or has spread to other parts of the body, including the brain, and who have received one or more prior treatments. ^[FN21]

The FDA collaborated with the Australian Therapeutic Goods Administration (TGA), Health Canada, Health Sciences Authority (HSA, Singapore) and Swissmedic (SMC, Switzerland) on this review. This is the first Project Orbis partnership between the FDA, HSA and Swissmedic. While the FDA approved Tukysa today, the application is still under review at the other agencies. Collaboration among international regulators may allow patients with cancer to receive earlier access to products in other countries where there may be significant delays in regulatory submissions, regardless of whether the product has received FDA approval. Early availability of new therapies and adoption as standard of care around the world may have an impact on the increasingly international conduct of cancer clinical trials, potentially accelerating the development of anticancer products. With a framework for concurrent submission and review of oncology drugs, Project Orbis facilitates a collaborative review to identify any regulatory divergence across review teams.

“The FDA's Project Orbis provides a framework for concurrent submission and review of oncology drug applications among the FDA's international collaborators. We are pleased to work with our Singapore and Switzerland colleagues for the first time, and to continue working alongside our Australian and Canadian colleagues as we facilitate new treatment options for patients ? like today's first new molecular entity under Project Orbis,” said Richard Pazdur, M.D., director of the FDA's Oncology Center of Excellence and acting director of the Office of Oncologic Diseases in the FDA's Center for Drug Evaluation and Research. “This approval represents an additional targeted treatment option for patients with HER2-positive breast cancer. The clinical trial supporting this approval enrolled and specifically studied patients with active brain metastases in addition to the overall population enrolled, which also demonstrated benefit in this subgroup.”

HER2-positive breast cancer, which makes up approximately one-fifth of breast cancers, has too much of a protein called human epidermal growth factor receptor 2 (HER2), which promotes the growth of cancer cells. More than 25% of women with metastatic HER2-positive breast cancer will develop brain metastases.

“We recognize that patients with cancer constitute a vulnerable population at risk of contracting the coronavirus disease,” said Pazdur. “In this critical time, we remain steadfast in our commitment to patients with cancer and doing everything we can to expedite oncology product development. Tukysa was approved four months prior to the FDA goal date, providing an example of this commitment and showing how our regular work in reviewing treatments for patients with cancer is moving forward without delay.”

The FDA granted approval of Tukysa to Seattle Genetics, Inc.

FDA Approves First Targeted Treatment for Patients with Cholangiocarcinoma, a Cancer of Bile Ducts

On April 17, 2020, the FDA granted accelerated approval to Pemazyre (pemigatinib), the first treatment approved for adults with certain types of previously treated, advanced cholangiocarcinoma. ^[FN22]

“This approval demonstrates that while we continue to focus our efforts on addressing the COVID-19 pandemic, the FDA remains committed to the important work of reviewing treatments for patients with cancer and other serious conditions,” said Richard Pazdur, M.D., director of the FDA's Oncology Center of Excellence and acting director of the Office of Oncologic Diseases in the FDA's Center for Drug Evaluation and Research. “With Pemazyre, we considered the observed efficacy results to be clinically meaningful and the overall risk to benefit assessment for patients with tumors harboring FGFR2 gene fusions and other rearrangements to be favorable, particularly when we considered that these patients have no other good options following first line treatment with chemotherapy.”

Cholangiocarcinoma is a rare form of cancer that forms in bile ducts, which are slender tubes that carry the digestive fluid bile from the liver to gallbladder and small intestine. Today's approval is for patients with cholangiocarcinoma that is locally advanced (when cancer has grown outside the organ it started in, but has not yet spread to distant parts of the body) or metastatic (when cancer cells spread to other parts of the body) and who have tumors that have a fusion or other rearrangement of a gene called fibroblast growth factor receptor 2 (FGFR2).

The FDA granted approval of Pemazyre to Incyte Corporation.

FDA Issues Emergency Use Authorization for Potential COVID-19 Treatment

On May 1, 2020, the FDA issued an emergency use authorization ^[FN23] for the investigational antiviral drug remdesivir for the treatment of suspected or laboratory-confirmed COVID-19 in adults and children hospitalized with severe disease. While there is limited information known about the safety and effectiveness of using remdesivir to treat people in the hospital with COVID-19, the investigational drug was shown in a clinical trial to shorten the time to recovery in some patients. ^[FN24]



The emergency use authorization allows for remdesivir to be distributed in the U.S. and administered intravenously by health care providers, as appropriate, to treat suspected or laboratory-confirmed COVID-19 in adults and children hospitalized with severe disease. Severe disease is defined as patients with low blood oxygen levels or needing oxygen therapy or more intensive breathing support such as a mechanical ventilator.

The issuance of an EUA is different than FDA approval. In determining whether to issue an EUA, the FDA evaluates the available evidence and carefully balances any known or potential risks of any unproven products with any known or potential benefits of making them available during the emergency.

The EUA was issued to Gilead Sciences Inc. The FDA previously allowed for study of the investigational drug under clinical trials, as well as expanded access use for individual patients and through a multi-patient expanded access program coordinated by Gilead.

The EUA will be effective until the declaration that circumstances exist justifying the authorization of the emergency use of drugs and biologics for prevention and treatment of COVID-19 is terminated and may be revised or revoked if it is determined the EUA no longer meets the statutory criteria for issuance.

FDA Approves New Treatment for a Type of Heart Failure

On May 5, 2020, the FDA approved Farxiga (dapagliflozin) oral tablets for adults with heart failure with reduced ejection fraction to reduce the risk of cardiovascular death and hospitalization for heart failure. Heart failure occurs when the heart does not pump enough blood to support the body's needs, and this type of heart failure happens when the heart's main pumping chamber, the left ventricle, is weakened. With the approval, Farxiga is the first in this particular drug class, sodium-glucose co-transporter 2 (SGLT2) inhibitors, to be approved to treat adults with New York Heart Association's functional class II-IV heart failure with reduced ejection fraction. ^[FN25]

"Heart failure is a serious health condition that contributes to one in eight deaths in the U.S. and impacts nearly 6.5 million Americans," said Norman Stockbridge, M.D., Ph.D., director of the Division of Cardiology and Nephrology in the FDA's Center for Drug Evaluation and Research. "This approval provides patients with heart failure with reduced ejection fraction an additional treatment option that can improve survival and reduce the need for hospitalization."

Farxiga is also FDA-approved to improve glycemic control in adults with type 2 diabetes in addition to diet and exercise, and to reduce the risk of hospitalization for heart failure among adults with type 2 diabetes and known cardiovascular disease or other risk factors.

The FDA granted the approval of Farxiga related to heart failure to AstraZeneca Pharmaceuticals LP Wilmington, DE.

FDA Approves First Targeted Therapy to Treat Aggressive Form of Lung Cancer

On May 6, 2020, the FDA approved Tabrecta (capmatinib) for the treatment of adult patients with non-small cell lung cancer (NSCLC) that has spread to other parts of the body. Tabrecta is the first FDA-approved therapy to treat NSCLC with specific mutations (those that lead to mesenchymal-epithelial transition or MET exon 14 skipping). ^[FN26]

The FDA also approved the FoundationOne CDx assay (F1CDx) as a companion diagnostic for Tabrecta today. Most patients had tumor samples that were tested for mutations that lead to MET exon 14 skipping using local tests and confirmed with the F1CDx, which is a next-generation sequencing based in vitro diagnostic device that is capable of detecting several mutations, including mutations that lead to MET exon 14 skipping.

"Lung cancer is increasingly being divided into multiple subsets of molecularly defined populations with drugs being developed to target these specific groups," said Richard Pazdur, M.D., director of the FDA's Oncology Center of Excellence and acting director of the Office of Oncologic Diseases in the FDA's Center for Drug Evaluation and Research. "Tabrecta is the first approval specifically for the treatment of patients with non-small cell lung cancer whose tumors have mutations that lead to MET exon 14 skipping. This patient population now has an option for a targeted therapy, which they didn't have prior to today."

The FDA granted approval of Tabrecta to Novartis Pharmaceuticals Corporation. The approval of the F1CDx companion diagnostic was granted to Foundation Medicine, Inc.

FDA Approves First Therapy for Patients with Lung and Thyroid Cancers with a Certain Genetic Mutation or Fusion

On May 8, 2020, the FDA approved Retevmo (selpercatinib) capsules to treat three types of tumors ? non-small cell lung cancer, medullary thyroid cancer and other types of thyroid cancers ? in patients whose tumors have an alteration (mutation or fusion) in a specific gene (RET or "rearranged during transfection"). Retevmo is the first therapy approved specifically for cancer patients with the RET gene alterations. ^[FN27]

"Innovations in gene-specific therapies continue to advance the practice of medicine at a rapid pace and offer options to patients who previously had few," said Richard Pazdur, M.D., director of the FDA's Oncology Center of Excellence and acting director of the Office of Oncologic Diseases in the FDA's Center for Drug Evaluation and Research. "The FDA is committed to reviewing treatments like Retevmo that are targeted to specific subsets of patients with cancer."

Specifically, the cancers that Retevmo is approved to treat include:

Non-small cell lung cancer (NSCLC) that has spread in adults,



THOMSON REUTERS™

© 2021 Thomson Reuters. No claim to original U.S. Government Works.

Advanced medullary thyroid cancer (MTC) or MTC that has spread, in patients 12 and older who require systemic therapy (a treatment option that spreads across the entire body, is not targeted), and

Advanced RET fusion-positive thyroid cancer in those age 12 and older that requires systemic therapy that has stopped responding to radioactive iodine therapy or is not appropriate for radioactive iodine therapy.

Retevmo is a kinase inhibitor, meaning it blocks a type of enzyme (kinase) and helps prevent the cancer cells from growing. Before beginning treatment, the identification of a RET gene alteration must be determined using laboratory testing.

The FDA granted approval of Retevmo to Loxo Oncology, Inc., a subsidiary of Eli Lilly and Company.

FDA Approves First Drug for Fourth-Line Treatment of Advanced Gastrointestinal Stromal Tumors

On May 15, 2020, the FDA approved Qinlock (ripretinib) tablets as the first new drug specifically approved as a fourth-line treatment for advanced gastrointestinal stromal tumor (GIST), a type of tumor that originates in the gastrointestinal tract. Qinlock is indicated for adult patients who have received prior treatment with three or more kinase inhibitor therapies, including imatinib. ^[FN28]

"Despite the progress that has been made over the past 20 years in developing treatments for GIST, including four FDA-approved targeted therapies ? imatinib in 2002, sunitinib in 2006, regorafenib in 2013 and avapritinib earlier this year ? some patients don't respond to treatment and their tumors continues to progress. Today's approval provides a new treatment option for patients who have exhausted all FDA-approved therapies for GIST," said Richard Pazdur, M.D., director of the FDA's Oncology Center of Excellence and acting director of the Office of Oncologic Diseases in the FDA's Center for Drug Evaluation and Research.

Each year, approximately 4,000 to 6,000 adults in the United States are diagnosed with a GIST. GISTs arise when abnormal cells form in the tissues of the gastrointestinal tract. GISTs most commonly occur in the stomach, small intestine, and large intestine but can start anywhere along the gastrointestinal tract.

Qinlock is a kinase inhibitor, meaning it works by blocking a type of enzyme called a kinase, which helps keep the cancer cells from growing.

The FDA granted approval of Qinlock to Deciphera Pharmaceuticals, Inc.

FDA Approves First Treatment for a Form of Bladder Dysfunction in Pediatric Patients as Young as 2 Years of Age

On May 26, 2020, the FDA approved VESIcare LS (solifenacin succinate) oral suspension, a liquid taken by mouth, for the treatment of neurogenic detrusor overactivity (NDO), a form of bladder dysfunction related to neurological impairment, in children ages two years and older. VESIcare (solifenacin succinate) tablets were initially approved in 2004 for the treatment of overactive bladder in adults 18 years and older. ^[FN29]

"This is the first FDA-approved treatment for NDO patients as young as two years of age," said Christine P. Nguyen, M.D., acting director, FDA's Division of Urology, Obstetrics and Gynecology, Office of Rare Diseases, Pediatrics, Urologic and Reproductive Medicine, Center for Drug Evaluation and Research. "In addition, prior to today's approval, the current standard of care for many of these patients required up to three times a day dosing, and this treatment requires only once a day dosing."

NDO is a dysfunction of the bladder that results from disease or injury in the nervous system. NDO may be related to congenital conditions (often-inherited conditions beginning at or before birth), such as spina bifida (myelomeningocele), or other conditions such as spinal cord injury. With NDO, there is overactivity of the bladder wall muscle, which normally relaxes to allow storage of urine. The bladder wall muscle overactivity results in sporadic bladder muscle contraction, which increases pressure in the bladder and decreases the volume of urine the bladder can hold. If NDO is not treated, increased pressure in the bladder can put the upper urinary tract at risk of harm, including possible permanent damage to the kidneys. In addition, spontaneous bladder muscle contractions can lead to unexpected and frequent leakage of urine with symptoms of urinary urgency (immediate urge to urinate), frequency (urinating more often than normal) and incontinence (loss of bladder control).

The approval of VESIcare LS was granted to Astellas Pharma US, Inc.

FDA Approves First Drug to Image Tau Pathology in Patients Being Evaluated for Alzheimer's Disease

On May 28, 2020, the FDA approved Tauvid (flortaucipir F18) for intravenous injection, the first drug used to help image a distinctive characteristic of Alzheimer's disease in the brain called tau pathology. Tauvid is a radioactive diagnostic agent for adult patients with cognitive impairment who are being evaluated for Alzheimer's disease. Tauvid is indicated for positron emission tomography (PET) imaging of the brain to estimate the density and distribution of aggregated tau neurofibrillary tangles (NFTs), a primary marker of Alzheimer's disease. ^[FN30]

"Alzheimer's disease is a devastating condition that affects millions of Americans. This approval will provide health care professionals with a new type of brain scan to use in patients being evaluated for Alzheimer's disease," said Charles Ganley, M.D., director of Office of Specialty Medicine in FDA's Center for Drug Evaluation and Research. "While there are FDA approved imaging drugs for amyloid pathology, this is the first drug approved for imaging tau pathology, one of the two neuropathological hallmarks of Alzheimer's disease, and represents a major advance for patients with cognitive impairment being evaluated for the condition."



THOMSON REUTERS™

© 2021 Thomson Reuters. No claim to original U.S. Government Works.

Two proteins ? tau and amyloid ? are recognized as hallmarks of Alzheimer's disease. In patients with Alzheimer's disease, pathological forms of tau proteins develop inside neurons in the brain, creating neurofibrillary tangles. After Tauvid is administered intravenously, it binds to sites in the brain associated with this tau protein misfolding. The brain can then be imaged with a PET scan to help identify the presence of tau pathology.

Alzheimer's disease is a progressive disease that typically begins with mild memory loss. It is one of the top 10 leading causes of death in the United States. According to the U.S. Centers for Disease Control and Prevention, in 2014, there were as many as 5 million Americans living with Alzheimer's disease. This number is projected to nearly triple to 14 million by 2060. Currently, Alzheimer's disease can only be definitively diagnosed by pathologic evaluation of a patient's brain once they have died (post-mortem). There are three imaging agents approved for post-mortem amyloid pathology with PET scans.

The FDA granted the manufacturer of Tauvid Priority Review, under which the FDA's goal is to take action on an application within six months where the agency determines that the drug, if approved, would significantly improve the safety or effectiveness of treating, diagnosing or preventing a serious condition.

The FDA granted approval of Tauvid to Avid Radiopharmaceuticals, Inc.

FDA Approves New Option to Treat Heavy Menstrual Bleeding Associated with Fibroids in Women

On May 29, 2020, the FDA approved Oriahnn (an estrogen and progestin combination product consisting of elagolix, estradiol and norethindrone acetate) capsules, co-packaged for oral use, for the management of heavy menstrual bleeding associated with uterine leiomyomas (fibroids) in premenopausal women. ^[FN31]

"Uterine fibroids are the most common benign tumors affecting premenopausal women, and one of the most common symptoms from fibroids is heavy menstrual bleeding," said Christine P. Nguyen, MD, Acting Director, Division of Urology, Obstetrics and Gynecology in FDA's Center for Drug Evaluation and Research. "Although surgical treatments, such as hysterectomy, are available, patients may not qualify for surgery or want the procedure. Various non-surgical therapies are used to treat fibroid-related heavy menstrual bleeding, but none have been FDA-approved specifically for this use. Today's approval provides an FDA-approved medical treatment option for these patients."

Fibroids are benign (non-cancerous) muscle tumors of the uterus that can cause heavy menstrual bleeding, pain, bowel or bladder problems and infertility. Some women may not experience any symptoms, but many do, including heavy bleeding with periods. Fibroids can occur at any age but are most common in women 35 to 49 years of age. They typically resolve after menopause but are a leading reason for hysterectomy (surgical removal of the uterus) in the United States when they cause severe symptoms.

The approval of Oriahnn was granted to AbbVie Inc.

FDA Approves Antibiotic to Treat Hospital-Acquired Bacterial Pneumonia and Ventilator-Associated Bacterial Pneumonia

On June 4, 2020, the FDA approved Recarbrio (a combination of imipenem-cilastatin and relebactam) to treat hospital-acquired bacterial pneumonia and ventilator-associated bacterial pneumonia (HABP/VABP) in patients 18 years of age and older. Recarbrio was previously FDA-approved to treat patients with complicated urinary tract infections and complicated intra-abdominal infections who have limited or no alternative treatment options. ^[FN32]

"As a public health agency, the FDA addresses the threat of antimicrobial-resistant infections by facilitating the development of safe and effective new treatments," said Sumathi Nambiar, M.D., M.P.H., director of the Division of Anti-Infectives within the Office of Infectious Disease in FDA's Center for Drug Evaluation and Research. "These efforts provide more options to fight serious bacterial infections and get new, safe and effective therapies to patients as soon as possible."

HABP and VABP are a type of pneumonia that occurs in hospitalized patients and can cause symptoms such as fever, chills, cough, chest pain and increased oxygen requirements. Recarbrio is a combination of imipenem-cilastatin and relebactam. The drug is administered intravenously by a health care professional.

FDA Approves New Therapy for Rare Disease Affecting Optic Nerve, Spinal Cord

On June 11, 2020, the FDA approved Uplizna (inebilizumab-cdon) injection for intravenous use for the treatment of neuromyelitis optica spectrum disorder (NMOSD) in adult patients with a particular antibody (patients who are anti-aquaporin-4 or AQP4 antibody positive). NMOSD is a rare autoimmune disease of the central nervous system that mainly affects the optic nerves and spinal cord. Uplizna is only the second approved treatment for the disorder. ^[FN33]

"Until recently, patients with NMOSD had no FDA-approved treatment options," said Billy Dunn, M.D., Director of the Office of Neuroscience in the FDA's Center for Drug Evaluation and Research. "Uplizna now represents the second approved therapy for these patients within the past year. We continue to remain highly committed to the development of additional safe and effective drugs for this rare and devastating disease."

In patients with NMOSD, the body's immune system mistakenly attacks healthy cells and proteins in the body, most often those in the optic nerves and spinal cord. Individuals with NMOSD typically have attacks of optic neuritis, which causes eye pain and vision loss. Individuals also can have attacks resulting in transverse myelitis, which often causes numbness, weakness, or paralysis of the



THOMSON REUTERS™

© 2021 Thomson Reuters. No claim to original U.S. Government Works.

arms and legs, along with loss of bladder and bowel control. Most attacks occur in clusters, days to months to years apart, followed by partial recovery during periods of remission. Approximately 50% of patients with NMOSD have permanent visual impairment and paralysis caused by NMOSD attacks. According to the National Institutes of Health, women are more often affected by NMOSD than men and African Americans are at greater risk of the disease than are Caucasians. Estimates vary, but NMOSD is thought to impact approximately 4,000 to 8,000 patients in the United States.

NMOSD can be associated with antibodies that bind to a protein called aquaporin-4 (AQP4). Binding of the anti-AQP4 antibody appears to activate other components of the immune system, causing inflammation and damage to the central nervous system.

The FDA granted approval of Uplizna to Viela Bio.

FDA Approves Drug to Treat Infants and Children with HIV

On June 12, 2020, the FDA approved Tivicay (dolutegravir) tablets and Tivicay PD (dolutegravir) tablets for suspension to treat HIV-1 infection in pediatric patients at least four weeks old and weighing at least 3 kg (6.61 pounds) in combination with other antiretroviral treatments. ^[FN34]

“For babies and young children with HIV, getting treatment early is very important. HIV can progress more quickly in children than adults,” said Debra Birnkrant, M.D., director of the Division of Antivirals in FDA’s Center for Drug Evaluation and Research. “While the incidence of pediatric HIV infections continues to decline, the availability and early initiation of effective treatment are critical for infants and children living with HIV. Tivicay and Tivicay PD are taken once daily, which could help patients and caregivers better adhere to the regimen. Today’s approval gives our youngest HIV patients more options, helping them live longer, healthier lives.”

According to the U.S. Centers for Disease Control and Prevention, at the end of 2016, there were 2,238 children younger than 13 years old living with HIV in the U.S. and dependent areas, with 99 new HIV-1 infections diagnosed in this age group in 2017. Effective treatment is important in reducing the amount of virus in the blood.

Tivicay and Tivicay PD are intended to treat pediatric patients at least 4 weeks old and 3 kg who have never been treated for HIV or who have been treated, but not with an integrase strand transferase inhibitor (INSTI) class drug.

The FDA is granting the approval of Tivicay and Tivicay PD to ViiV Healthcare.

FDA Approves First Therapy for Rare Disease that Causes Low Phosphate Blood Levels, Bone Softening

On June 18, 2020, the FDA approved Crysvida (burosumab-twza) injection to treat patients age two and older with tumor-induced osteomalacia (TIO), a rare disease that is characterized by the development of tumors that cause weakened and softened bones. The tumors associated with TIO release a peptide hormone-like substance known as fibroblast growth factor 23 (FGF23) that lowers phosphate levels. ^[FN35]

“Treatment for TIO focuses on identifying and removing the tumor that causes the disease. However, when that is not possible, Crysvida can help increase the levels of phosphate in the blood,” said Theresa E. Kehoe, M.D., acting director of the Division of General Endocrinology in the FDA’s Center for Drug Evaluation and Research. “As the first FDA-approved therapy to treat this debilitating disease, today’s action is an important step in finding treatment options for patients living with TIO whose tumor cannot be found or removed.”

FGF23 regulates levels of phosphate, an electrolyte that plays important roles in bone maintenance, energy production by cells and nerve function. When there is not enough phosphate in the body, bones begin to soften and weaken, causing osteomalacia (marked softening of bones).

The FDA granted approval of Crysvida to Ultragenyx Pharmaceutical Inc.

FDA Approves New Therapy for Dravet Syndrome

On June 25, 2020, the FDA approved Fintepla (fenfluramine), a Schedule IV controlled substance, for the treatment of seizures associated with Dravet syndrome in patients age 2 and older. Dravet syndrome is a life-threatening, rare and chronic form of epilepsy. It is often characterized by severe and unrelenting seizures despite medical treatment. ^[FN36]

“Dravet syndrome is a debilitating disease that takes a tremendous toll on both patients and their families,” said Billy Dunn, M.D., director of the Office of Neuroscience in the FDA’s Center for Drug Evaluation and Research. “Fintepla offers an additional effective treatment option for the treatment of seizures associated with Dravet syndrome. The FDA will continue to work with companies on drug development for Dravet syndrome and other types of epilepsy.”

The FDA granted approval of Fintepla to Zogenix, Inc.

FDA Approves Breast Cancer Treatment That Can Be Administered At Home By Health Care Professional

On June 29, 2020, the FDA approved Phesgo[®] a combination of pertuzumab, trastuzumab and hyaluronidase[®] for injection under the skin to treat adult patients with HER2-positive breast cancer that has spread to other parts of the body, and for treatment of adult patients with early HER2-positive breast cancer. Patients should be selected based on an FDA-approved companion diagnostic test. ^[FN37]



THOMSON REUTERS™

© 2021 Thomson Reuters. No claim to original U.S. Government Works.

HER2-positive breast cancer, which makes up approximately one-fifth of breast cancers, has too much of a protein called human epidermal growth factor receptor 2 (HER2), which promotes the growth of cancer cells. Pertuzumab and trastuzumab bind to sites on HER2 and disrupt signaling to stop cancer cell growth. Phesgo is initially used in combination with chemotherapy and could continue to be administered at home by a qualified health care professional once the chemotherapy regimen is finished.

“Currently, most patients with HER2-positive breast cancer receive trastuzumab and pertuzumab at infusion centers. With a new administration route, Phesgo offers an out-patient option for patients to receive trastuzumab and pertuzumab,” said Richard Pazdur, M.D., director of the FDA's Oncology Center of Excellence and acting director of the Office of Oncologic Diseases in the FDA's Center for Drug Evaluation and Research. “As part of the FDA's ongoing commitment to address the novel coronavirus pandemic, we continue to keep a strong focus on patients with cancer who constitute a vulnerable population at risk of contracting the disease. At this critical time, we continue to expedite oncology product development. This application was approved about four months ahead of the FDA goal date.”

The FDA granted approval of Phesgo to Genentech Inc.

FDA Approves First-Line Immunotherapy for Patients with MSI-H/dMMR Metastatic Colorectal Cancer

On June 29, 2020, the FDA approved Keytruda (pembrolizumab) for intravenous injection for the first-line treatment of patients with unresectable or metastatic microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) colorectal cancer. This marks the first immunotherapy approved for this patient population as a first-line treatment and which is administered to patients without also giving chemotherapy. ^[FN38]

MSI-H and dMMR tumors contain abnormalities that affect the proper repair of DNA inside the cell. The frequency of MSI-H varies across tumor types and stages, and approximately 5% of patients with metastatic colorectal cancer have MSI-H or dMMR tumors.

“Metastatic colorectal cancer is a serious and life-threatening disease with a poor prognosis. Available current therapy with chemotherapy combinations and other biologics are associated with substantial toxicity,” said Richard Pazdur, M.D., director of the FDA's Oncology Center of Excellence and acting director of the Office of Oncologic Diseases in the FDA's Center for Drug Evaluation and Research. “Having a non-chemotherapy option available for selected patients is a noteworthy paradigm shift in treatment.”

The FDA granted this approval of Keytruda to Merck & Co.

FDA Approves New HIV Treatment for Patients With Limited Treatment Options

On July 2, 2020, the FDA approved Rukobia (fostemsavir), a new type of antiretroviral medication for adults living with HIV who have tried multiple HIV medications and whose HIV infection cannot be successfully treated with other therapies because of resistance, intolerance or safety considerations. ^[FN39]

“This approval marks a new class of antiretroviral medications that may benefit patients who have run out of HIV treatment options,” said Jeff Murray, M.D., deputy director of the Division of Antivirals in the FDA's Center for Drug Evaluation and Research. “The availability of new classes of antiretroviral drugs is critical for heavily treatment-experienced patients living with multidrug resistant HIV infection?helping people living with hard-to-treat HIV who are at greater risk for HIV-related complications, to potentially live longer, healthier lives.”

The FDA granted this application Fast Track, Priority Review and Breakthrough Therapy designations.

The FDA granted approval of Rukobia to ViiV Healthcare.

FDA Approves New Therapy for Myelodysplastic Syndromes (MDS) That Can Be Taken at Home

On July 7, 2020, the FDA approved Inqovi (decitabine and cedazuridine) tablets for treatment of adult patients with myelodysplastic syndromes (MDS) and chronic myelomonocytic leukemia (CMML). This represents an important advance in treatment options for patients with MDS, a type of blood cancer, who previously needed to visit a health care facility to receive intravenous therapy. ^[FN40]

“The FDA remains committed to providing additional treatments to patients during the coronavirus pandemic. In this case, the FDA is making available an oral outpatient treatment option that can reduce the need for frequent visits to health care facilities,” said Richard Pazdur, M.D., director of the FDA's Oncology Center of Excellence and acting director of the Office of Oncologic Diseases in the FDA's Center for Drug Evaluation and Research. “At this critical time, we continue to focus on providing options to patients with cancer, including regimens that can be taken at home.”

The FDA collaborated with international agency counterparts on the review of this application as part of Project Orbis.

The FDA granted this approval to Astex Pharmaceuticals, Inc., a subsidiary of Otsuka Pharmaceutical Co. Ltd.

FDA Approves First Cell-Based Gene Therapy For Adult Patients with Relapsed or Refractory MCL

On July 24, 2020, the FDA approved Tecartus (brexucabtagene autoleucl), a cell-based gene therapy for treatment of adult patients diagnosed with mantle cell lymphoma (MCL) who have not responded to or who have relapsed following other kinds of treatment. Tecartus, a chimeric antigen receptor (CAR) T cell therapy, is the first cell-based gene therapy approved by the FDA for the treatment of MCL. ^[FN41]



“Tremendous progress has been made in the discovery of new therapies for debilitating diseases that are difficult to treat. This approval is yet another example of customized treatments that use a patient’s own immune system to help fight cancer, while using a scientific advance in this promising new area of medicine,” said Peter Marks, M.D., Ph.D., director of the FDA’s Center for Biologics Evaluation and Research. “We’re seeing continued advances in the field of gene therapy and remain committed to supporting innovation in this promising new area of medicine.”

MCL is a rare form of cancerous B-cell non-Hodgkin’s lymphoma that usually occurs in middle-aged or older adults. In patients with MCL, B-cells, a type of white blood cell which help the body fight infection, change into cancer cells that start to form tumors in the lymph nodes and quickly spread to other areas of the body.

FDA Approves First Cell-Based Gene Therapy For Adult Patients with Relapsed or Refractory MCL

On July 24, 2020, the FDA approved Tecartus (brexucabtagene autoleucel), a cell-based gene therapy for treatment of adult patients diagnosed with mantle cell lymphoma (MCL) who have not responded to or who have relapsed following other kinds of treatment. Tecartus, a chimeric antigen receptor (CAR) T cell therapy, is the first cell-based gene therapy approved by the FDA for the treatment of MCL. ^[FN42]

“Tremendous progress has been made in the discovery of new therapies for debilitating diseases that are difficult to treat. This approval is yet another example of customized treatments that use a patient’s own immune system to help fight cancer, while using a scientific advance in this promising new area of medicine,” said Peter Marks, M.D., Ph.D., director of the FDA’s Center for Biologics Evaluation and Research. “We’re seeing continued advances in the field of gene therapy and remain committed to supporting innovation in this promising new area of medicine.”

MCL is a rare form of cancerous B-cell non-Hodgkin’s lymphoma that usually occurs in middle-aged or older adults. In patients with MCL, B-cells, a type of white blood cell which help the body fight infection, change into cancer cells that start to form tumors in the lymph nodes and quickly spread to other areas of the body.

FDA Approves Oral Treatment for Spinal Muscular Atrophy

On August 7, 2020, the FDA approved Evrysdi (risdiplam) to treat patients two months and older with spinal muscular atrophy (SMA), a rare and often fatal genetic disease affecting muscle strength and movement. This is the second drug and the first oral drug approved to treat this disease. ^[FN43]

“Evrysdi is the first drug for this disease that can be taken orally, providing an important treatment option for patients with SMA, following the approval of the first treatment for this devastating disease less than four years ago,” said Billy Dunn, M.D., director of the Office of Neuroscience in the FDA’s Center for Drug Evaluation and Research.

SMA is a hereditary disease that causes weakness and muscle wasting because patients lose lower motor neurons (nerve cells) that control movement. Evrysdi contains a survival of motor neuron 2-directed RNA splicing modifier.

The FDA granted this approval of Evrysdi to Genentech, Inc.

FDA Approves New Opioid for Intravenous Use in Hospitals, Other Controlled Clinical Settings

On August 7, 2020, the FDA approved Olinvyk (oliceridine), an opioid agonist for the management of moderate to severe acute pain in adults, where the pain is severe enough to require an intravenous opioid and for whom alternative treatments are inadequate. ^[FN44]

Olinvyk is indicated for short-term intravenous use in hospitals or other controlled clinical settings, such as during inpatient and outpatient procedures. It is not indicated for at-home use.

“Addressing the opioid crisis remains a top priority for the FDA. We will continue to do everything we can to reduce the number of Americans who are addicted to opioids and cut the rate of new addiction through a number of cross-agency initiatives,” said Douglas Throckmorton M.D., deputy director for regulatory programs in the FDA’s Center for Drug Evaluation and Research. “Importantly, the FDA will only approve new drug applications, including those for opioid medications, following a rigorous review to evaluate the risks and benefits and ultimate determination that the data support safety and effectiveness. Of note, this particular medication is only indicated for use in a controlled clinical setting, meaning under medical supervision and not for use in a take-home prescription.”

The FDA granted approval of Olinvyk to Trevena Inc.

FDA Approves Treatment for Rare Disease Affecting Optic Nerves, Spinal Cord

On August 17, 2020, the FDA approved Enspryng (satralizumab-mwge) for the treatment of neuromyelitis optica spectrum disorder (NMOSD) in adults with a particular antibody ? patients who are anti-aquaporin-4 or AQP4 antibody-positive. NMOSD is a rare autoimmune disease of the central nervous system that mainly affects the optic nerves and spinal cord. Enspryng is the third approved treatment for the disorder. ^[FN45]

“Until last year, there were no FDA-approved treatments for patients with this rare, debilitating and sometimes fatal disease. Now there are three,” said Billy Dunn, M.D., director of the Office of Neuroscience in the FDA’s Center for Drug Evaluation and Research.



"Today's approval of Enspryng highlights the FDA's commitment to rapidly advancing safe and effective therapies for NMOSD and other neurological diseases."

In patients with NMOSD, the body's immune system mistakenly attacks healthy cells and proteins in the body, most often those in the optic nerves and spinal cord. Individuals with NMOSD typically have attacks of optic neuritis, which causes eye pain and vision loss. Approximately 50% of patients with NMOSD have permanent visual impairment and paralysis caused by NMOSD attacks. Estimates vary, but NMOSD is thought to impact approximately 4,000 to 8,000 Americans.

NMOSD can be associated with antibodies that bind to a protein called aquaporin-4 (AQP4). Binding of the anti-AQP4 antibody appears to activate other components of the immune system, causing inflammation and damage to the central nervous system.

The FDA is granting the approval to Genentech Inc.

FDA Approves Drug to Treat Group of Rare Blood Disorders

On September 25, 2020, the FDA approved Nucala (mepolizumab) for adults and children aged 12 years and older with hypereosinophilic syndrome (HES) for six months or longer without another identifiable non-blood related cause of the disease. The new indication for Nucala is the first approval for HES patients in nearly 14 years. ^[FN46]

"Today's approval marks the first time in over a decade that there is a new FDA-approved treatment option for patients with hypereosinophilic syndrome," said Ann Farrell, M.D., director of the Division of Nonmalignant Hematology in the FDA's Center for Drug Evaluation and Research. "FDA is committed to helping develop safe and effective treatment options for this group of rare and debilitating blood diseases and other rare conditions."

HES is a heterogeneous group of rare disorders associated with persistent eosinophilia (higher than normal levels of a type of disease-fighting white blood cell) with evidence of organ damage. Symptoms include skin rashes, itching, asthma, difficulty breathing, abdominal pain, vomiting, diarrhea, arthritis, muscle inflammation, congestive heart failure, deep venous thrombosis (blood clots in the veins) and anemia.

The FDA is granting the approval to GlaxoSmithKline of Research Triangle Park, North Carolina.

FDA Approves Drug Combination for Treating Mesothelioma

On October 2, 2020, the FDA approved Opdivo (nivolumab) in combination with Yervoy (ipilimumab) for the first-line treatment of adults with malignant pleural mesothelioma that cannot be removed by surgery. This is the first drug regimen approved for mesothelioma in 16 years and the second FDA-approved systemic therapy for mesothelioma. ^[FN47]

"Today's approval of nivolumab plus ipilimumab provides a new treatment that has demonstrated an improvement in overall survival for patients with malignant pleural mesothelioma," said Richard Pazdur, M.D., director of the FDA's Oncology Center of Excellence and acting director of the Office of Oncologic Diseases in the FDA's Center for Drug Evaluation and Research. "In 2004, FDA approved pemetrexed in combination with cisplatin for this indication, and now patients now have an important, additional treatment option after more than a decade with only one FDA-approved drug regimen."

Malignant pleural mesothelioma (MPM) is a life-threatening cancer of the lungs' lining caused by inhaling asbestos fibers that about 20,000 Americans are diagnosed with each year. MPM accounts for most mesothelioma diagnoses, and most patients have an unresectable (unable to be removed with surgery) tumor at time of diagnosis. With currently available therapy, overall survival is generally poor. Opdivo and Yervoy are both monoclonal antibodies that, when combined, decrease tumor growth by enhancing T-cell function.

The FDA granted approval to Bristol-Myers Squibb Company.

FDA Approves First Treatment for Ebola Virus

On October 14, 2020, the FDA approved Inmazeb (atoltivimab, maftivimab, and odesivimab-ebgn), a mixture of three monoclonal antibodies, as the first FDA-approved treatment for Zaire ebolavirus (Ebola virus) infection in adult and pediatric patients.

"Today's action demonstrates the FDA's ongoing commitment to responding to public health threats both domestically and abroad? on the basis of science and data," said FDA Commissioner Stephen M. Hahn, M.D. "This approval was made possible because of our steadfast dedication to facilitate the development of safe and effective treatments for infectious diseases as part of our vital public health mission."

Zaire ebolavirus, commonly known as Ebola virus, is one of four Ebolavirus species that can cause a potentially fatal human disease. Ebola virus is transmitted through direct contact with blood, body fluids and tissues of infected people or wild animals, as well as with surfaces and materials, such as bedding and clothing, contaminated with these fluids. Individuals who provide care for people with Ebola virus, including health care workers who do not use correct infection control precautions, are at the highest risk for infection.

The FDA is granting the approval to Regeneron Pharmaceutica.

FDA Approves First Treatment for COVID-19



THOMSON REUTERS™

© 2021 Thomson Reuters. No claim to original U.S. Government Works.

On October 22, 2020, the FDA approved the antiviral drug Veklury (remdesivir) for use in adult and pediatric patients 12 years of age and older and weighing at least 40 kilograms (about 88 pounds) for the treatment of COVID-19 requiring hospitalization. Veklury should only be administered in a hospital or in a healthcare setting capable of providing acute care comparable to inpatient hospital care. Veklury is the first treatment for COVID-19 to receive FDA approval.

This approval does not include the entire population that had been authorized to use Veklury under an Emergency Use Authorization (EUA) originally issued on May 1, 2020. In order to ensure continued access to the pediatric population previously covered under the EUA, the FDA revised the EUA for Veklury to authorize the drug's use for treatment of suspected or laboratory confirmed COVID-19 in hospitalized pediatric patients weighing 3.5 kg to less than 40 kg or hospitalized pediatric patients less than 12 years of age weighing at least 3.5 kg. Clinical trials assessing the safety and efficacy of Veklury in this pediatric patient population are ongoing.

"The FDA is committed to expediting the development and availability of COVID-19 treatments during this unprecedented public health emergency," said FDA Commissioner Stephen M. Hahn, M.D. "Today's approval is supported by data from multiple clinical trials that the agency has rigorously assessed and represents an important scientific milestone in the COVID-19 pandemic. As part of the FDA's Coronavirus Treatment Acceleration Program, the agency will continue to help move new medical products to patients as soon as possible, while at the same time determining whether they are effective and if their benefits outweigh their risks."

The FDA granted this application Fast Track and Priority Review designations. The Agency also granted this application a Material Threat Medical Countermeasure Priority Review Voucher, which provides additional incentives for certain medical products intended to treat or prevent harm from specific chemical, biological, radiological and nuclear threats.

The FDA granted approval and reissued the revised EUA to Gilead Sciences Inc.

FDA Approves Lotion for Nonprescription Use to Treat Head Lice

On October 27, 2020, the FDA approved a lotion to treat head lice for nonprescription, or over-the-counter (OTC), use through a process called a prescription (Rx)-to-OTC switch. The FDA initially approved Sklice (ivermectin) lotion, 0.5% for the treatment of head lice infestation in patients 6 months of age and older as a prescription drug in February 2012.

"The Rx-to-OTC switch process aims to promote public health by increasing consumer access to drugs that would otherwise only be available by prescription," said Theresa Michele, M.D., acting director of the Office of Nonprescription Drugs in the FDA's Center for Drug Evaluation and Research. "Today's approval expands access to another effective topical treatment for the thousands of people with head lice."

Rx-to-OTC switches are generally initiated by the manufacturer of the prescription drug. For a drug to switch from prescription to nonprescription status, the data provided must demonstrate that the drug is safe and effective when used as directed in the proposed labeling. The manufacturer must show that consumers can understand how to use the drug safely and effectively without the supervision of a healthcare professional.

In the United States, it is estimated that between 6 and 12 million cases of head lice infestation occur each year in children 3 to 11 years of age, according to the U.S. Centers for Disease Control and Prevention. Head lice are most common among preschool children attending child care, elementary school children and members of a household where children have lice.

The FDA granted the approval of nonprescription Sklice (ivermectin) lotion, 0.5% for the topical treatment of head lice infestations in patients 6 months of age and older to Arbor Pharmaceuticals LLC.

FDA Authorizes Monoclonal Antibody for Treatment of COVID-19

On November 9, 2020, the FDA issued an emergency use authorization (EUA) for the investigational monoclonal antibody therapy bamlanivimab for the treatment of mild-to-moderate COVID-19 in adult and pediatric patients. Bamlanivimab is authorized for patients with positive results of direct SARS-CoV-2 viral testing who are 12 years of age and older weighing at least 40 kilograms (about 88 pounds), and who are at high risk for progressing to severe COVID-19 and/or hospitalization. This includes those who are 65 years of age or older, or who have certain chronic medical conditions.

While the safety and effectiveness of this investigational therapy continues to be evaluated, bamlanivimab was shown in clinical trials to reduce COVID-19-related hospitalization or emergency room visits in patients at high risk for disease progression within 28 days after treatment when compared to placebo.

Bamlanivimab is not authorized for patients who are hospitalized due to COVID-19 or require oxygen therapy due to COVID-19. A benefit of bamlanivimab treatment has not been shown in patients hospitalized due to COVID-19. Monoclonal antibodies, such as bamlanivimab, may be associated with worse clinical outcomes when administered to hospitalized patients with COVID-19 requiring high flow oxygen or mechanical ventilation.

"As illustrated by today's action, the FDA remains committed to expediting the development and availability of potential COVID-19 treatments and providing sick patients timely access to new therapies where appropriate, while at the same time supporting research to further evaluate whether they are safe and effective," said FDA Commissioner Stephen M. Hahn, M.D. "Through our Coronavirus Treatment Acceleration Program, the FDA continues to work around the clock and use every tool at our disposal toward these efforts."



THOMSON REUTERS™

© 2021 Thomson Reuters. No claim to original U.S. Government Works.

Monoclonal antibodies are laboratory-made proteins that mimic the immune system's ability to fight off harmful antigens such as viruses. Bamlanivimab is a monoclonal antibody that is specifically directed against the spike protein of SARS-CoV-2, designed to block the virus' attachment and entry into human cells.

"The FDA's emergency authorization of bamlanivimab provides health care professionals on the frontline of this pandemic with another potential tool in treating COVID-19 patients," said Patrizia Cavazzoni, M.D., acting director of the FDA's Center for Drug Evaluation and Research. "We will continue to evaluate new data on the safety and efficacy of bamlanivimab as they become available."

The issuance of an EUA is different than FDA approval. In determining whether to issue an EUA, the FDA evaluates the available evidence and carefully balances any known or potential risks with any known or potential benefits of the product for use during an emergency. Based on the FDA's review of the totality of the scientific evidence available, the agency determined that it is reasonable to believe that bamlanivimab may be effective in treating non-hospitalized patients with mild or moderate COVID-19. And, when used to treat COVID-19 for the authorized population, the known and potential benefits outweigh the known and potential risks for the drug. There are no adequate, approved and available alternative treatments to bamlanivimab for the authorized population. As part of the evaluation of the EUA, the agency imposed several quality measures to protect patients. The company is required to implement these quality measures to manufacture this drug under the EUA.

The EUA was issued to Eli Lilly and Company.

FDA Authorizes Drug Combination for Treatment of COVID-19

On November 19, 2020, the FDA issued an emergency use authorization (EUA) for the drug baricitinib, in combination with remdesivir, for the treatment of suspected or laboratory confirmed COVID-19 in hospitalized adults and pediatric patients two years of age or older requiring supplemental oxygen, invasive mechanical ventilation, or extracorporeal membrane oxygenation (ECMO).^[FN48]

In a clinical trial of hospitalized patients with COVID-19, baricitinib, in combination with remdesivir, was shown to reduce time to recovery within 29 days after initiating treatment compared to patients who received a placebo with remdesivir. The safety and effectiveness of this investigational therapy for use in the treatment of COVID-19 continues to be evaluated. Baricitinib is not authorized or approved as a stand-alone treatment for COVID-19.

"Today's action demonstrates the FDA's steadfast efforts to make potential COVID-19 treatments available in a timely manner, where appropriate, while continuing to support research to further evaluate whether they are safe and effective," said FDA Commissioner Stephen M. Hahn, M.D. "As part of our Coronavirus Treatment Acceleration Program, the FDA continues to use every possible avenue to facilitate new treatments for patients as quickly as possible to combat COVID-19."

The EUA was issued to Eli Lilly and Company.

FDA Approves First Treatment for Hutchinson-Gilford Progeria Syndrome and Some Progeroid Laminopathies

On November 20, 2020, the FDA approved Zokinvy (lonafarnib) capsules to reduce the risk of death due to Hutchinson-Gilford progeria syndrome and for the treatment of certain processing-deficient progeroid laminopathies in patients one year of age and older. Zokinvy is not approved for use in patients with other progeroid syndromes or laminopathies.^[FN49]

"Hutchinson-Gilford progeria syndrome and progeroid laminopathies are rare genetic diseases that cause premature aging and death and have a debilitating effect on people's lives," said Hylton V. Joffe, M.D., M.M.Sc, director of the Office of Rare Diseases, Pediatrics, Urologic and Reproductive Medicine in the FDA's Center for Drug Evaluation and Research. "With today's approval, Zokinvy is the first FDA-approved medication for these devastating diseases. The FDA will continue to work with stakeholders to advance the development of additional new, effective and safe therapies for these patients."

Patients with Hutchinson-Gilford progeria syndrome and progeroid laminopathies experience accelerated cardiovascular disease from the buildup of defective progerin or progerin-like protein in cells. Most patients die before the age of 15 years from heart failure, heart attack or stroke. Before this approval, the only treatment options included supportive care and therapies directed towards the complications arising from the disease.

The FDA granted the approval of Zokinvy to Eiger BioPharmaceuticals, Inc.

FDA Authorizes Monoclonal Antibodies for Treatment of COVID-19

On November 21, 2020, the FDA issued an emergency use authorization (EUA) for casirivimab and imdevimab to be administered together for the treatment of mild to moderate COVID-19 in adults and pediatric patients (12 years of age or older weighing at least 40 kilograms [about 88 pounds]) with positive results of direct SARS-CoV-2 viral testing and who are at high risk for progressing to severe COVID-19. This includes those who are 65 years of age or older or who have certain chronic medical conditions.^[FN50]

In a clinical trial of patients with COVID-19, casirivimab and imdevimab, administered together, were shown to reduce COVID-19-related hospitalization or emergency room visits in patients at high risk for disease progression within 28 days after treatment when compared to placebo. The safety and effectiveness of this investigational therapy for use in the treatment of COVID-19 continues to be evaluated.

Casirivimab and imdevimab must be administered together by intravenous (IV) infusion.



THOMSON REUTERS™

© 2021 Thomson Reuters. No claim to original U.S. Government Works.

Casirivimab and imdevimab are not authorized for patients who are hospitalized due to COVID-19 or require oxygen therapy due to COVID-19. A benefit of casirivimab and imdevimab treatment has not been shown in patients hospitalized due to COVID-19. Monoclonal antibodies, such as casirivimab and imdevimab, may be associated with worse clinical outcomes when administered to hospitalized patients with COVID-19 requiring high flow oxygen or mechanical ventilation.

The EUA was issued to Regeneron Pharmaceuticals Inc.

FDA Approves First Drug to Treat Rare Metabolic Disorder

On November 23, 2020, the FDA approved Oxlumio (lumasiran) as the first treatment for primary hyperoxaluria type 1 (PH1), a rare genetic disorder. This approval is a culmination of the work of experts and community members coordinated by the Oxalosis & Hyperoxaluria Foundation and the Kidney Health Initiative. ^[FN51]

"The approval of Oxlumio represents a great triumph of community involvement to address a rare disease. It is a result of input from patients, treating physicians, experts and sponsors at a patient-focused drug development meeting and through other collaborative efforts," said Norman Stockbridge, M.D., Ph.D., director of the Division of Cardiology and Nephrology in the FDA's Center for Drug Evaluation and Research.

Primary hyperoxalurias (PHs) are caused by excess production of oxalate, a substance consumed in food and also produced by the body. PH1 is the most common and severe type. PH1 affects an estimated one to three individuals per million in North America and Europe and accounts for approximately 80% of PH cases.

The FDA granted the approval of Oxlumio to Alnylam Pharmaceuticals, Inc.

II Enforcements

FDA Requests Removal of All Ranitidine Products (Zantac) from the Market

On April 1, 2020, the FDA announced it is requesting manufacturers withdraw all prescription and over-the-counter (OTC) ranitidine drugs from the market immediately. This is the latest step in an ongoing investigation of a contaminant known as N-Nitrosodimethylamine (NDMA) in ranitidine medications (commonly known by the brand name Zantac). The agency has determined that the impurity in some ranitidine products increases over time and when stored at higher than room temperatures and may result in consumer exposure to unacceptable levels of this impurity. As a result of this immediate market withdrawal request, ranitidine products will not be available for new or existing prescriptions or OTC use in the U.S. ^[FN52]

NDMA is a probable human carcinogen (a substance that could cause cancer). In the summer of 2019, the FDA became aware of independent laboratory testing that found NDMA in ranitidine. Low levels of NDMA are commonly ingested in the diet, for example NDMA is present in foods and in water. These low levels would not be expected to lead to an increase in the risk of cancer. However, sustained higher levels of exposure may increase the risk of cancer in humans. The FDA conducted thorough laboratory tests and found NDMA in ranitidine at low levels. At the time, the agency did not have enough scientific evidence to recommend whether individuals should continue or stop taking ranitidine medicines, and continued its investigation and warned the public in September 2019 of the potential risks and to consider alternative OTC and prescription treatments.

New FDA testing and evaluation prompted by information from third-party laboratories confirmed that NDMA levels increase in ranitidine even under normal storage conditions, and NDMA has been found to increase significantly in samples stored at higher temperatures, including temperatures the product may be exposed to during distribution and handling by consumers. The testing also showed that the older a ranitidine product is, or the longer the length of time since it was manufactured, the greater the level of NDMA. These conditions may raise the level of NDMA in the ranitidine product above the acceptable daily intake limit.

III Other Developments

FDA Issue Statement on Signing of the COVID-19 Emergency Relief Bill

On March 30, 2020, the FDA released a statement ^[FN53] regarding the COVID-19 Emergency Relief Bill indicating the legislation will help the FDA deliver support and guidance to protect and promote public health during the pandemic.

The statement indicates that the legislation provided an additional \$80 million in funding to continue the Agency's COVID-19 response efforts, including the development of medical countermeasures and vaccines, promoting the advanced manufacturing of medical products and monitoring of the medical product supply chain.

Additionally, the FDA specifically highlights that a portion of the bill reforms and modernizes the way certain over-the-counter (OTC) drugs are regulated in the United States – a landmark step that will have an impact lasting long after the current public health emergency.

FDA Continues to Accelerate Development of Novel Therapies for COVID-19

On March 31, 2020, the FDA announced a new program to expedite the development of potentially safe and effective life-saving treatments to combat the COVID-19 pandemic. The program, known as the Coronavirus Treatment Acceleration Program (CTAP), is using every tool at the agency's disposal to bring new therapies to sick patients as quickly as possible, while at the same time



THOMSON REUTERS™

© 2021 Thomson Reuters. No claim to original U.S. Government Works.

supporting research to further evaluate whether these medical countermeasures are safe and effective for treating patients infected with this novel virus. ^[FN54]

To support these goals, the FDA has, among other things, redeployed medical and regulatory staff to serve on review teams dedicated to COVID-19 therapies, streamlined processes and operations for developers and scientists to send inquiries and requests and provided resources to health care providers and researchers to help them submit emergency requests to use investigational products.

There are a variety of therapeutic areas being evaluated, including antiviral drugs like remdesivir that might treat the specific virus, as well as host targets, such as interleukin-6 (IL-6) receptor inhibitors that may be helpful in reducing lung inflammation and improving lung function in COVID-19 patients. There's also interest in examining whether therapies such as convalescent plasma and hyperimmune globulin, antibody-rich blood products that are taken from blood donated by people who have recovered from the virus, could shorten the length or lessen the severity of the illness. Work is also ongoing to evaluate whether existing therapies such as chloroquine and hydroxychloroquine (with or without other medications) help treat patients with COVID-19.

The FDA also recognizes the potential for many different real-world data sources to complement traditional clinical studies and speed the process of evaluating the impact of potential COVID-19 therapies. To that end, the agency is advancing relationships with partners in the public and private sectors to rapidly collect and analyze information in areas such as illness patterns and treatment outcomes.

FDA Issues Drug Safety Communication regarding Hydroxychloroquine or Chloroquine for COVID-19

On April 24, 2020, the FDA cautioned against use of hydroxychloroquine or chloroquine for COVID-19 outside of the hospital setting or a clinical trial due to risk of heart rhythm problems. ^[FN55]

The safety communication indicates that hydroxychloroquine and chloroquine have not been shown to be safe and effective for treating or preventing COVID-19. They are being studied in clinical trials for COVID-19, and the FDA authorized their temporary use during the COVID-19 pandemic for treatment of the virus in hospitalized patients when clinical trials are not available, or participation is not feasible, through an Emergency Use Authorization (EUA). The medicines being used under the hydroxychloroquine/chloroquine EUA are supplied from the Strategic National Stockpile, the national repository of critical medical supplies to be used during public health emergencies. This safety communication reminds physicians and the public of risk information set out in the hydroxychloroquine and chloroquine healthcare provider fact sheets that were required by the EUA.

Hydroxychloroquine and chloroquine can cause abnormal heart rhythms such as QT interval prolongation and a dangerously rapid heart rate called ventricular tachycardia. These risks may increase when these medicines are combined with other medicines known to prolong the QT interval, including the antibiotic azithromycin, which is also being used in some COVID-19 patients without FDA approval for this condition. Patients who also have other health issues such as heart and kidney disease are likely to be at increased risk of these heart problems when receiving these medicines.

FDA Requiring Labeling Changes for Benzodiazepines

On September 23, 2020, the FDA announced in a Drug Safety Communication that it is requiring an update to the Boxed Warning, the agency's most prominent safety warning, and requiring class-wide labeling changes for benzodiazepines to include the risks of abuse, misuse, addiction, physical dependence and withdrawal reactions to help improve their safe use. ^[FN56]

In 2019, an estimated 92 million benzodiazepine prescriptions were dispensed from U.S. outpatient pharmacies, with alprazolam (38%) being the most common followed by clonazepam (24%) and lorazepam (20%). In 2018, an estimated 50% of patients dispensed oral benzodiazepines received them for two months or longer. Most benzodiazepines are recommended for use for periods of weeks or months. Benzodiazepines are important approved treatment options for generalized anxiety disorder, insomnia, seizures, social phobia and panic disorder. They are also used as premedication before some medical procedures. The dose, frequency and duration of treatment vary depending on the patient, the particular benzodiazepine being prescribed and the medical condition that the drug is being used to treat.

"While benzodiazepines are important therapies for many Americans, they are also commonly abused and misused, often together with opioid pain relievers and other medicines, alcohol and illicit drugs," said FDA Commissioner Stephen M. Hahn, M.D. "We are taking measures and requiring new labeling information to help health care professionals and patients better understand that while benzodiazepines have many treatment benefits, they also carry with them an increased risk of abuse, misuse, addiction and dependence."

Physical dependence can occur when benzodiazepines are taken steadily for several days to weeks. Patients who have been taking a benzodiazepine for weeks or months can have withdrawal signs and symptoms when the medicine is discontinued abruptly or continued in lower doses to avoid withdrawal. Stopping benzodiazepines abruptly or reducing the dosage too quickly can result in acute withdrawal reactions, including seizures, which can be life-threatening. Prior to stopping benzodiazepines, patients should talk to their health care provider to develop a plan for slowly tapering the medication.

In addition to requiring an update to the Boxed Warning, the FDA is requiring other changes to the Warnings and Precautions, Drug Abuse and Dependence and Patient Counseling Information sections of the prescribing information for all benzodiazepine products. The agency is also requiring revisions to the existing patient Medication Guides for these medicines to help educate patients and caregivers about these risks.



THOMSON REUTERS™

© 2021 Thomson Reuters. No claim to original U.S. Government Works.

[FN2]

. 2019 WLNR 37477240

[FN3]

. 2019 WLNR 38010839

[FN4]

. 2019 WLNR 38150140

[FN5]

. <https://www.fda.gov/news-events/press-announcements/fda-approves-new-treatment-option-patients-her2-positive-breast-cancer-who-have-progressed-available>

[FN6]

. 2019 WLNR 38494763

[FN7]

. 2020 WLNR 858368

[FN8]

. 2020 WLNR 2062322

[FN9]

. 2020 WLNR 2325390

[FN10]

. 2020 WLNR 3174842

[FN11]

. 2020 WLNR 4639573

[FN12]

. 2020 WLNR 5613107

[FN13]

. 2020 WLNR 6102486

[FN14]

. 2020 WLNR 6358380

[FN15]

. 2020 WLNR 6840268

[FN16]

. 2020 WLNR 7093764

[FN17]

. 2020 WLNR 9474696

[FN18]

. 2020 WLNR 10149124

[FN19]



THOMSON REUTERS™

. 2020 WLNR 10366480

[FN20]

. 2020 WLNR 10826564

[FN21]

. 2020 WLNR 11069782

[FN22]

. 2020 WLNR 11067836

[FN23]

. <https://www.fda.gov/media/137564/download>

[FN24]

. 2020 WLNR 12425308

[FN25]

. 2020 WLNR 12751485

[FN26]

. 2020 WLNR 12878027

[FN27]

. 2020 WLNR 13101886

[FN28]

. 2020 WLNR 13806503

[FN29]

. 2020 WLNR 14806101

[FN30]

. 2020 WLNR 15021864

[FN31]

. 2020 WLNR 15128854

[FN32]

. 2020 WLNR 15743166

[FN33]

. 2020 WLNR 16425045

[FN34]

. 2020 WLNR 16531124

[FN35]

. 2020 WLNR 17108485

[FN36]

. 2020 WLNR 17918796

[FN37]

. 2020 WLNR 18162202

[FN38]

. 2020 WLNR 18162308



THOMSON REUTERS™

© 2021 Thomson Reuters. No claim to original U.S. Government Works.

[FN39]
. 2020 WLNR 18525632

[FN40]
. 2020 WLNR 18969315

[FN41]
. 2020 WLNR 20745081

[FN42]
. 2020 WLNR 20745081

[FN43]
. 2020 WLNR 22246488

[FN44]
. 2020 WLNR 22246265

[FN45]
. 2020 WLNR 23179274

[FN46]
. 2020 WLNR 27238587

[FN47]
. 2020 WLNR 27970645

[FN48]
. 2020 WLNR 33143833

[FN49]
. 2020 WLNR 33591666

[FN50]
. 2020 WLNR 33322270

[FN51]
. 2020 WLNR 33512260

[FN52]
. 2020 WLNR 9474680

[FN53]
. <https://www.fda.gov/news-events/press-announcements/fda-signing-covid-19-emergency-relief-bill-including-landmark-over-counter-drug-reform-and-user-fee>

[FN54]
. 2020 WLNR 9358449

[FN55]
. 2020 WLNR 11720769

[FN56]
. 2020 WLNR 26992534