FDA Approves New Antibiotic to Treat Community-acquired Bacterial Pneumonia

The U.S. Food and Drug Administration today approved Xenleta (lefamulin) to treat adults with community-acquired bacterial pneumonia.

"This new drug provides another option for the treatment of patients with community-acquired bacterial pneumonia, a serious disease," said Ed Cox, M.D., M.P.H., director of FDA's Office of Antimicrobial Products. "For managing this serious disease, it is important for physicians and patients to have treatment options. This approval reinforces our ongoing commitment to address treatment of infectious diseases by facilitating the development of new antibiotics."

Community-acquired pneumonia occurs when someone develops pneumonia in the community (not in a hospital). Pneumonia is a type of lung infection that can range in severity from mild to severe illness and can affect people of all ages. According to data from the Centers from Disease Control and Prevention, each year in the United States, about one million people are hospitalized with community-acquired pneumonia and 50,000 people die from the disease.

The safety and efficacy of Xenleta, taken either orally or intravenously, was evaluated in two clinical trials with a total of 1,289 patients with CABP. In these trials, treatment with Xenleta was compared to another antibiotic, moxifloxacin with or without linezolid. The trials showed that patients treated with Xenleta had similar rates of clinical success as those treated with moxifloxacin with or without linezolid.

The most common adverse reactions reported in patients taking Xenleta included diarrhea, nausea, reactions at the injection site, elevated liver enzymes and vomiting. Xenleta has the potential to cause a change on an ECG reading (prolonged QT interval). Patients with prolonged QT interval, patients with certain irregular heart rhythms (arrhythmias), patients receiving treatment for certain irregular heart rhythms (antiarrhythmic agents), and patients receiving other drugs that prolong the QT interval should avoid Xenleta. In addition, Xenleta should not be used in patients with known hypersensitivity to lefamulin or any other members of the pleuromutilin antibiotic class, or any of the components of Xenleta. Based on findings of fetal harm in animal studies, pregnant women and women who could become pregnant should be advised of the potential risks of Xenleta to a fetus. Women who could become pregnant should be advised to use effective contraception during treatment with Xenleta and for two days after the final dose.

Xenleta received FDA's Qualified Infectious Disease Product (QIDP) designation. The QIDP designation is given to antibacterial and antifungal drug products intended to treat serious or life-threatening infections under the Generating Antibiotic Incentives Now (GAIN) title of the FDA Safety and Innovation Act. As part of QIDP designation, Xenleta was granted Priority Review under which the FDA's goal is to take action on an application within an expedited time frame.

The FDA granted the approval of Xenleta to Nabriva Therapeutics.

A key global challenge the FDA faces as a public health agency is addressing the threat of antimicrobial-resistant infections. Among the FDA's other efforts to address antimicrobial resistance, is the focus on facilitating the development of safe and effective new treatments to give patients more options to fight serious infections.

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FDA Approves First Oral GLP-1 Treatment for Type 2 Diabetes

The U.S. Food and Drug Administration today approved Rybelsus (semaglutide) oral tablets to improve control of blood sugar in adult patients with type 2 diabetes, along with diet and exercise. Rybelsus is the first glucagon-like peptide (GLP-1) receptor protein treatment approved for use in the United States that does not need to be injected. GLP-1 drugs are non-insulin treatments for people with type 2 diabetes.

"Patients want effective treatment options for diabetes that are as minimally intrusive on their lives as possible, and the FDA welcomes the advancement of new therapeutic options that can make it easier for patients to control their condition," said Lisa Yanoff, M.D, acting director of the Division of Metabolism and Endocrinology Products in the FDA's Center for Drug Evaluation and Research. "Before this approval, patients did not have an oral GLP1 option to treat their type 2

diabetes, and now patients will have a new option for treating type 2 diabetes without injections."

Type 2 diabetes is the most common form of diabetes, occurring when the pancreas cannot make enough insulin to keep blood sugar at normal levels. GLP-1, which is a normal body hormone, is often found in insufficient levels in type 2 diabetes patients. Like GLP-1, Rybelsus slows digestion, prevents the liver from making too much sugar, and helps the pancreas produce more insulin when needed.

The efficacy and safety of Rybelsus in reducing blood sugar in patients with type 2 diabetes were studied in several clinical trials, two of which were placebo-controlled and several of which were compared to other GLP-1 injection treatments. Rybelsus was studied as a stand-alone therapy and in combination with other diabetes treatments, including metformin, sulfonylureas (insulin secretagogues), sodium-glucose co-transporter-2 (SGLT-2) inhibitors, insulins and thiazolidinediones, all in patients with type 2 diabetes.

In the placebo-controlled studies, Rybelsus as a stand-alone therapy resulted in a significant reduction in blood sugar (hemoglobin A1c) compared with placebo, as determined through HbA1c tests, which measure average levels of blood sugar over time. After 26 weeks, 69% of those taking 7 mg once daily and 77% of those taking 14 mg once daily of Rybelsus decreased their HbA1c to lower than 7%, compared with 31% of patients on placebo.

The prescribing information for Rybelsus includes a boxed warning to advise health care professionals and patients about the potential increased risk of thyroid c-cell tumors, and that Rybelsus is not recommended as the first choice of medicine for treating diabetes. Patients who have ever had medullary thyroid carcinoma (MTC) or who have a family member who has ever had MTC are advised not to use Rybelsus. Additionally, patients who have ever had an endocrine system condition called multiple endocrine neoplasia syndrome type 2 (MEN 2) are advised not to use Rybelsus. Rybelsus is not for use in patients with type 1 diabetes and people with diabetic ketoacidosis.

Rybelsus also has warnings about pancreatitis (inflammation of the pancreas), diabetic retinopathy (damage to the eye's retina), hypoglycemia (low blood sugar), acute kidney injury and hypersensitivity reactions. It is not known whether Rybelsus can be used by patients who have had pancreatitis. The risk of hypoglycemia increased when Rybelsus was used in combination with sulfonylureas or insulin.

Rybelsus should be taken at least 30 minutes before the first food, beverage or other oral medication of the day, with no more than 4 ounces of plain water. Rybelsus slows digestion, so patients should discuss other medications they are taking with their health care provider before starting Rybelsus. The most common side effects are nausea, diarrhea, vomiting, decreased appetite, indigestion and constipation.

The approval of Rybelsus was granted to Novo Nordisk.

FDA News released Sep 20, 2019. www.fda.gov.

FDA Approves New Type of Therapy to Treat Advanced Urothelial Cancer

Today, the U.S. Food and Drug Administration 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.

"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 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 auristantin E."

Padcev was approved based on the results of a clinical trial that enrolled 125 patients with locally advanced or metastatic urothelial cancer who received prior treatment with a PD-1 or PD-L1 inhibitor and platinum-based chemotherapy. The overall response rate, reflecting the percentage of patients who had a certain amount of tumor shrinkage, was 44%, with 12% having a complete response and 32% having a partial response. The median duration of response was 7.6 months.

The most common side effects for patients taking Padcev were fatigue, peripheral neuropathy (nerve damage resulting in tingling or numbness), decreased appetite, rash, alopecia (hair loss), nausea, altered taste, diarrhea, dry eye, pruritis (itching) and dry skin. Patients may experience hyperglycemia (high blood sugar levels) regardless of whether they have diabetes or not, and blood sugar levels should be monitored closely in patients receiving Padcev. Patients should also be monitored for new or worsening peripheral neuropathy and have the dose of Padcev interrupted, reduced or discontinued if needed. Patients may experience eye disorders, including dry eyes and vision changes, while taking Padcev. Health care professionals may consider prophylactic artificial tears for dry eyes and referral to an ophthalmologist for any new symptoms related to the eye. Patients who experience infusion site extravasation (leakage of medications administered through veins into the surrounding tissue) may experience delayed extravasation site reactions with pain, blisters and peeling of skin. Adequate venous access should be ensured prior to starting Padcev.

The FDA advises health care professionals to tell patients of reproductive age to use effective contraception during treatment with Padcev, and for a period of time thereafter. Women who are pregnant or breastfeeding should not take Padcev because it may cause harm to a developing fetus or newborn baby, or cause delivery complications.

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 News released Dec 18, 2019. www.fda.gov.

Source: FDA