FDA Approves New Treatment for Pneumonia Caused by Certain Difficult-to-Treat Bacteria

Today, the U.S. Food and Drug Administration approved Xacduro (sulbactam for injection; durlobactam for injection), a new treatment for hospital-acquired bacterial pneumonia (HABP) and ventilator-associated bacterial pneumonia (VABP) caused by susceptible strains of bacteria called Acinetobacter baumannii-calcoaceticus complex, for patients 18 years of age and older.

According to the World Health Organization, Acinetobacter species top the list of critical bacterial pathogens that pose the greatest threat to human health, highlighting the high level of need for additional treatment options amid growing global resistance to antimicrobial medicines.

"The FDA is dedicated to supporting the development of safe and effective treatment options for infections caused by difficult-to-treat bacteria like Acinetobacter baumannii-calcoaceticus complex," said Peter Kim, M.D., M.S., director of the Division of Anti-Infectives in the FDA's Center for Drug Evaluation and Research. "Today's approval helps address a high unmet medical need by providing an additional treatment option for some of the sickest patients in our nation's hospitals."

Acinetobacter baumannii-calcoaceticus complex (henceforth referred to as A. baumannii) includes four species of bacteria in the Acinetobacter family. These bacteria can cause infections in various parts of the body, occurring most frequently in healthcare settings and predominantly causing pneumonia. A. baumannii can become highly resistant to multiple antibacterial drugs and current treatment options for drug-resistant A. baumannii are limited.

Xacduro consists of sulbactam, a drug structurally related to penicillin, and durlobactam. Sulbactam kills A. baumannii whereas durlobactam protects sulbactam from being degraded by enzymes that may be produced by A. baumannii. Xacduro is administered by intravenous infusion.

Xacduro's efficacy was established in a multicenter, active-controlled, open-label (investigator-unblinded, assessor-blinded), non-inferiority clinical trial in 177 hospitalized adults with pneumonia caused by carbapenem-resistant A. baumannii. Patients received either Xacduro or colistin (a comparator antibiotic) for up to 14 days. Both treatment arms also received an additional antibiotic, imipenem/cilastatin, as background therapy for potential HABP/VABP pathogens other than Acinetobacter baumannii-calcoaceticus complex. The primary measure of efficacy was mortality from all causes within 28 days of treatment in patients with a confirmed infection with carbapenem-resistant A. baumannii. Of those who received Xacduro, 19% (12 of 63 patients) died, compared to 32% (20 of 62 patients) who received colistin; this demonstrated that Xacduro was noninferior to colistin.

The most common adverse reaction with Xacduro was liver function test abnormalities. Xacduro comes with certain warnings and precautions, such as hypersensitivity reactions and Clostridioides, difficile-associated diarrhea.

Patients should not receive Xacduro if they have a history of known severe hypersensitivity to components of Xacduro, sulbactam or other beta-lactam antibacterial drugs.

The FDA granted Xacduro Fast Track, Qualified Infectious Disease Product and Priority Review designations for this application.

The FDA granted the approval of Xacduro to Entasis Therapeutics.

FDA News released May 23, 2023. www.fda.gov.

FDA Approves First Cellular Therapy to Treat Patients with Type 1 Diabetes

Today, the U.S. Food and Drug Administration approved Lantidra, the first allogeneic (donor) pancreatic islet cellular therapy made from deceased donor pancreatic cells for the treatment of type 1 diabetes. Lantidra is approved for the treatment of adults with type 1 diabetes who are unable to approach target glycated hemoglobin (average blood glucose levels) because of current repeated episodes of severe hypoglycemia (low blood sugar) despite intensive diabetes management and education.

"Severe hypoglycemia is a dangerous condition that can lead to injuries resulting from loss of consciousness or seizures," said Peter Marks, M.D., Ph.D., director of the FDA's Center for Biologics Evaluation and Research. "Today's approval, the first-ever cell therapy to treat patients with type 1 diabetes, provides individuals living with type 1 diabetes and recurrent severe hypoglycemia an additional treatment option to help achieve target blood glucose levels."

Type 1 diabetes is a chronic autoimmune disease that requires lifelong care including requiring insulin, either through multiple daily injections or continuous infusion using a pump, every day to live. People with type 1 diabetes also perform blood glucose checks several times a day to guide the management of their diabetes.

Some people with type 1 diabetes have trouble managing the amount of insulin needed every day to prevent hyperglycemia (high blood sugar) without causing hypoglycemia. They may also develop hypoglycemia unawareness, where they are unable to detect their blood glucose is dropping and may not have a chance to treat themselves to prevent their blood glucose from further dropping. This makes it difficult to dose insulin. Lantidra provides a potential treatment option for these patients.

The primary mechanism of action of Lantidra is believed to be the secretion of insulin by the infused allogeneic islet beta cells. In some patients with type 1 diabetes, these infused cells can produce enough insulin, so the patient no longer needs to take insulin (by injections or pump) to control their blood sugar levels. Lantidra is administered as a single infusion into the hepatic (liver) portal vein. An additional infusion of Lantidra may be performed depending on the patient's response to the initial dose.

The safety and effectiveness of Lantidra was evaluated in two non-randomized, single-arm studies in which a total of 30 participants with type 1 diabetes and hypoglycemic unawareness received at least one infusion and a maximum of three infusions. Overall, 21 participants did not need to take insulin for a year or more, with 11 participants not needing insulin for one to five years and 10 participants not needing insulin for more than five years. Five participants did not achieve any days of insulin independence.

Adverse reactions associated with Lantidra varied with each participant depending on the number of infusions they received and the length of time they were followed and may not reflect the rates observed in practice The most common adverse reactions included nausea, fatigue, anemia, diarrhea and abdominal pain. A majority of participants experienced at least one serious adverse reaction related to the procedure for infusing Lantidra into the hepatic portal vein and the use of immunosuppressive medications needed to maintain the islet cell viability. Some serious adverse reactions required discontinuation of immunosuppressive medications, which resulted in the loss of islet cell function and insulin independence. These adverse events should be considered when assessing the benefits and risks of Lantidra for each patient. Lantidra is approved with patient-directed labeling to inform patients with type 1 diabetes about benefits and risks of Lantidra.

The FDA granted approval of Lantidra to CellTrans Inc.

FDA News released June 28, 2023. www.fda.gov.

FDA Approves New Drug to Prevent RSV in Babies and Toddlers

Today, the U.S. Food and Drug Administration approved Beyfortus (nirsevimab-alip) for the prevention of Respiratory Syncytial Virus (RSV) lower respiratory tract disease in neonates and infants born during or entering their first RSV season, and in children up to 24 months of age who remain vulnerable to severe RSV disease through their second RSV season.

"RSV can cause serious disease in infants and some children and results in a large number of emergency department and physician office visits each year," said John Farley, M.D., M.P.H., director of the Office of Infectious Diseases in the FDA's Center for Drug Evaluation and Research. "Today's approval addresses the great need for products to help reduce the impact of RSV disease on children, families and the health care system."

RSV is a virus that causes acute respiratory infection in individuals of all age groups. While most infants and young children experience mild, cold-like symptoms, some infants, especially with their first infection, develop lower respiratory tract disease such as pneumonia and bronchiolitis (swelling of the small airway passages in the lungs), that often leads to an emergency department or physician office visit. Premature infants, and those with chronic lung disease of prematurity or significant congenital heart disease, are at highest risk for severe RSV disease. Approximately 1% to 3% of children under 12 months of age in the United States are hospitalized each year due to RSV, according to the American Academy of Pediatrics.

In most parts of the U.S., RSV circulation is seasonal, typically starting during the fall and peaking in the winter; it is transmitted from person to person through close contact with someone who is infected.

Beyfortus is a monoclonal antibody with activity against RSV. Monoclonal antibodies are laboratory-

made proteins that mimic the immune system's ability to fight off harmful pathogens such as viruses. One dose of Beyfortus, administered as a single intramuscular injection prior to or during RSV season, may provide protection during the RSV season.

The safety and efficacy of Beyfortus were supported by three clinical trials (Trials 03, 04 and 05). The key measure of efficacy was the incidence of medically attended RSV lower respiratory tract infection (MA RSV LRTI), evaluated during the 150 days after Beyfortus administration. MA RSV LRTI included all health care provider visits (physician office, urgent care, emergency room visits and hospitalization) for lower respiratory tract disease with worsening clinical severity and a positive RSV test. Trials 03 and 04 were randomized, double-blind, placebo-controlled, multicenter clinical trials.

Trial 03 included 1,453 preterm infants (born at greater than or equal to 29 weeks of gestational age up to less than 35 weeks of gestation) who were born during or entering their first RSV season. Of the 1,453 preterm infants in the trial, 969 received a single dose of Beyfortus and 484 received placebo. Among infants who were treated with Beyfortus, 25 (2.6%) experienced MA RSV LRTI compared with 46 (9.5%) infants who received placebo. Beyfortus reduced the risk of MA RSV LRTI by approximately 70% relative to placebo.

For Trial 04, the primary analysis group within the trial included 1,490 term and late preterm infants (born at greater than or equal to 35 weeks in gestational age), 994 of whom received a single dose of Beyfortus and 496 of whom received placebo. Among infants who were treated with Beyfortus, 12 (1.2%) experienced MA RSV LRTI compared with 25 (5.0%) infants who received placebo. Beyfortus reduced the risk of MA RSV LRTI by approximately 75% relative to placebo.

Trial 05, a randomized, double-blind, active (palivizumab)-controlled, multicenter trial, supported the use of Beyfortus in in children up to 24 months of age who remain vulnerable to severe RSV disease through their second RSV season. The trial enrolled 925 preterm infants and infants with chronic lung disease of prematurity or congenital heart disease. The safety and pharmacokinetic data from Trial 05 provided evidence for the use of Beyfortus to prevent MA RSV LRTI in this population.

Possible side effects of Beyfortus include rash and injection site reactions. Beyfortus should not be given to infants and children with a history of serious hypersensitivity reactions to Beyfortus' active ingredients or any of its excipients.

Beyfortus comes with warnings and precautions about serious hypersensitivity reactions, including anaphylaxis, which have been observed with other human IgG1 monoclonal antibodies. Beyfortus should be given with caution to infants and children with clinically significant bleeding disorders.

Beyfortus received a Fast Track designation for this indication.

The FDA granted this approval to AstraZeneca.

FDA News released July 17, 2023. www.fda.gov.

Source: FDA