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

Second FDA Approved Therapy for Neuromyelitis Optica Spectrum Disorder Offers Patients Additional Treatment Option

The U.S. Food and Drug Administration today 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.

"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 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 effectiveness of Uplizna for the treatment of NMOSD was demonstrated in a clinical study of 230 adult patients that evaluated the efficacy and safety of intravenous Uplizna. In the trial, 213 of the 230 patients had antibodies against AQP4 (anti-AQP4 antibody positive). During the 197-day study, the risk of an NMOSD relapse in the 161 anti-AQP4 antibody positive patients who were treated with Uplizna was reduced by 77% when compared to the placebo treatment group. There was no evidence of a benefit in patients who were anti-AQP4 antibody negative.

The prescribing information for Uplizna includes a warning for infusion reactions, potential depletion of certain proteins (hypogammaglobulinemia), and potential increased risk of infection – including Progressive Multifocal Leukoencephalopathy, and potential reactivation of hepatitis B and tuberculosis. The most common adverse reactions in the NMOSD clinical trial were urinary tract infection, headache, joint pain (arthralgia), nausea and back pain. Women who are pregnant should not take Uplizna because it may cause harm to a developing fetus or newborn baby. The FDA advises health care professionals to inform females of reproductive age to use effective contraception during treatment with Uplizna and for six months after the last dose. Vaccination with live-attenuated or live vaccines is not recommended during treatment and should be administered at least four weeks prior to initiation of Uplizna.

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

The FDA granted approval of Uplizna to Viela Bio.

FDA News released June 11, 2020. www.fda.gov.

FDA Approves New Indication for Drug Containing an Active Ingredient Derived from Cannabis to Treat Seizures in Rare Genetic Disease

Today, the U.S. Food and Drug Administration approved Epidiolex (cannabidiol) [CBD] oral solution for the treatment of seizures associated with tuberous sclerosis complex (TSC) in patients one year of age and older. Epidiolex was previously approved for the

treatment of seizures associated with two rare and severe forms of epilepsy, Lennox-Gastaut syndrome (LGS) and Dravet syndrome (DS). This is the only FDA-approved drug that contains a purified drug substance derived from cannabis. It is also the second FDA approval of a drug for the treatment of seizures associated with TSC.

CBD is a chemical component of the Cannabis sativa plant. However, CBD does not cause intoxication or euphoria (the "high") that comes from tetrahydrocannabinol (THC). It is THC (and not CBD) that is the primary psychoactive component of cannabis.

"The FDA continues to believe the drug approval process represents the best way to make new medicines, including any drugs derived from cannabis, available to patients in need of appropriate medical therapy such as the treatment of seizures associated with these rare conditions. This paradigm ensures new therapies are safe, effective, and manufactured to a high quality that provides uniform and reliable dosing for patients," said Douglas Throckmorton, M.D., deputy center director for regulatory programs in the FDA's Center for Drug Evaluation and Research. "The agency is committed to supporting rigorous scientific research on the potential medical uses of cannabis-derived products and working with product developers who are interested in bringing patients safe and effective, high quality products."

TSC is a rare genetic disease that causes non-cancerous (benign) tumors to grow in the brain and other parts of the body like the eyes, heart, kidneys, lungs, and skin. TSC usually affects the central nervous system and can result in a combination of symptoms including seizures, developmental delay, and behavioral problems, although the signs and symptoms of the condition, as well as the severity of symptoms, vary widely. TSC affects about 1 in 6,000 people.

Epidiolex's effectiveness for the treatment of seizures associated with TSC was established in a randomized, double-blind, placebo-controlled trial where 148 patients out of a total of 224 in the study received Epidiolex. The study measured the change from baseline in seizure frequency. In the study, patients treated with Epidiolex had a significantly greater reduction in the frequency of seizures during the treatment period than patients who received placebo (inactive treatment). This effect was seen within eight weeks and remained consistent throughout the 16-week treatment period.

The most common side effects that occurred in Epidiolex-treated patients with TSC in the clinical trial were: diarrhea, elevated liver enzymes, decreased appetite, sleepiness, fever, and vomiting. Additional side effects for patients with LGS, DS, or TSC include: liver injury, decreased weight, anemia, and increased creatinine.

Epidiolex must be dispensed with a patient Medication Guide that describes important information about the drug's uses and risks. As is true for all drugs that currently treat epilepsy, including Epidiolex, the most serious risks may include an increase in suicidal thoughts and behavior, or thoughts of self-harm. Patients, their caregivers, and their families should be advised to monitor for any unusual changes in mood or behavior, such as worsening depression, suicidal thoughts or behavior. Patients, caregivers, and families should report behaviors of concern immediately to healthcare providers. Epidiolex also caused liver injury in some patients. Most cases were generally mild, but a risk of rare, but more severe liver injury exists. More severe liver injury can cause nausea, vomiting, abdominal pain, fatigue, anorexia, jaundice, and/or dark urine.

The FDA granted Priority Review designation for this application. The approval of Epidiolex was granted to Greenwich Biosciences Inc., of Carlsbad, California.

FDA News released July 31, 2020. www.fda.gov.

FDA Approves Targeted Treatment for Rare Duchenne Muscular Dystrophy Mutation

Today, the U.S. Food and Drug Administration granted accelerated approval to Viltepso (viltolarsen) injection for the treatment of Duchenne muscular dystrophy (DMD) in patients who have a confirmed mutation of the DMD gene that is amenable to exon 53 skipping. This is the second FDA-approved targeted treatment for patients with this type of mutation. Approximately 8% of patients with DMD have a mutation that is amenable to exon 53 skipping.

"The FDA is committed to fostering drug development for serious neurological disorders like Duchenne muscular dystrophy," 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 Viltepso provides an important

treatment option for Duchenne muscular dystrophy patients with this confirmed mutation."

DMD is a rare genetic disorder characterized by progressive muscle deterioration and weakness. It is the most common type of muscular dystrophy. DMD is caused by mutations in the DMD gene that results in an absence of dystrophin, a protein that helps keep muscle cells intact. The first symptoms are usually seen between three and five years of age and worsen over time. DMD occurs in approximately one out of every 3,600 male infants worldwide; in rare cases, it can affect females.

Viltepso was evaluated in two clinical studies with a total of 32 patients, all of whom were male and had genetically confirmed DMD. The increase in dystrophin production was established in one of those two studies, a study that included 16 DMD patients, with 8 patients receiving Viltepso at the recommended dose. In the study, dystrophin levels increased, on average, from 0.6% of normal at baseline to 5.9% of normal at week 25.

The FDA concluded that the applicant's data demonstrated an increase in dystrophin production that is reasonably likely to predict clinical benefit in patients with DMD who have a confirmed mutation of the dystrophin gene amenable to exon 53 skipping. A clinical benefit of the drug has not been established. In making this decision, the FDA considered the potential risks associated with the drug, the life-threatening and debilitating nature of the disease, and the lack of available therapies.

As part of the accelerated approval process, the FDA is requiring the company to conduct a clinical trial to confirm the drug's clinical benefit. The ongoing study is designed to assess whether Viltepso improves the time to stand for DMD patients with this confirmed mutation. If the trial fails to verify clinical benefit, the FDA may initiate proceedings to withdraw approval of the drug.

The most common side effects observed in DMD patients (pooled from the two studies) treated with 80 mg/kg once a week were: Upper respiratory tract infection, injection site reaction, cough and fever.

Although kidney toxicity was not observed in the Viltepso clinical studies, the clinical experience with Viltepso is limited, and kidney toxicity, including potentially fatal glomerulonephritis, has been observed after administration of some antisense oligonucleotides. Kidney function should be monitored in patients taking Viltepso.

Viltepso was approved under the FDA's accelerated approval pathway, which provides for the approval of drugs that treat serious or life-threatening diseases and generally offer a meaningful advantage over existing treatments. Approval under this pathway can be based on adequate and well-controlled studies showing the drug has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit to patients (i.e., how patients feel or function or whether they survive). This pathway provides earlier patient access to promising new drugs while the company conducts clinical trials to verify the predicted clinical benefit.

The FDA granted this application Priority Review designation.

The FDA is granting the approval to NS Pharma, Inc.

FDA News released Aug 12, 2020. www.fda.gov.

Source: FDA