FDA NEWS RELEASE

FDA Approves First Treatment for Acid Sphingomyelinase Deficiency, a Rare Genetic Disease

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Today, the U.S. Food and Drug Administration approved Xenpozyme (Olipudase alfa) for intravenous infusion in pediatric and adult patients with Acid Sphingomyelinase Deficiency (ASMD), a rare genetic disease that causes premature death. Xenpozyme is the first approved medication to treat symptoms that are not related to the central nervous system in patients with ASMD.

"ASMD has a debilitating effect on people's lives and there is a critical need to increase treatment options for patients who suffer from this rare disease," said Christine Nguyen, M.D., deputy director of the Office of Rare Diseases, Pediatrics, Urologic and Reproductive Medicine in the FDA's Center for Drug Evaluation and Research. "The challenges involved with developing treatments for rare diseases are significant and unique. We believe patients who suffer from ASMD, their families and their physicians will welcome this long-awaited advancement."

ASMD is caused by the lack of an enzyme needed to break down a complex lipid, called sphingomyelin, that accumulates in the liver, spleen, lung, and brain. Patients with ASMD have enlarged abdomens that can cause pain, vomiting, feeding difficulties, and falls. They also have abnormal liver and blood tests. The most severely affected patients have profound neurologic symptoms and rarely survive beyond two to three years of age. Other patients may survive into adulthood but die prematurely from respiratory failure.

Xenpozyme is an enzyme replacement therapy that helps reduce sphingomyelin accumulation in the liver, spleen, and lung. The efficacy of Xenpozyme for the treatment of ASMD was demonstrated in a randomized, double-blind, placebo-controlled study of 31 patients randomized to take Xenpozyme or placebo. Because the study had the placebo comparator and measured treatment benefits that could be detected during the study's duration, the FDA was able to conclude that Xenpozyme is effective. Overall, treatment with Xenpozyme improved lung function and reduced liver and spleen size.

The most common side effects of Xenpozyme include headache, cough, fever, joint pain, diarrhea, and low blood pressure. Xenpozyme carries a boxed warning for severe hypersensitivity reactions including anaphylaxis. Some patients treated with Xenpozyme developed laboratory test abnormalities, such as abnormal liver blood tests. Routine blood laboratory testing should be obtained periodically.

Xenpozyme should not be started during pregnancy due to the potential for fetal harm, which was observed during animal studies. Additionally, in the clinical trials, 75% of pediatric patients and 50% of adult patients experienced reactions including headaches, nausea and vomiting while receiving Xenpozyme through intravenous infusion.

Xenpozyme received fast track (https://www.fda.gov/patients/fast-track-breakthrough-therapy-accelerated-approval-priority- review/fast-track), breakthrough therapy, (https://www.fda.gov/patients/fast-track-breakthrough-therapy-accelerated-approval- priority-review/breakthrough-therapy) and priority review (https://www.fda.gov/patients/fast-track-breakthrough-therapy- accelerated-approval-priority-review/priority-review) designations. It also received orphan drug (https://www.fda.gov/industry/medical-products-rare-diseases-and-conditions/designating-orphan-product-drugs-and-biological-products) designation, which provides incentives to

assist and encourage the development of drugs for rare diseases. The FDA awarded the sponsor a rare pediatric disease priority review voucher (https://www.fda.gov/regulatory-information/search-fda-guidance- documents/rare-pediatric-disease-priority-review-vouchers), an incentive to encourage development of new drugs and biologics that prevent and treat rare diseases in children.

More than 7,000 rare diseases affect more than 30 million people in the United States. Many rare conditions are life threatening and most do not have treatments. The FDA estimates that half of these serious or life-threatening diseases affect children.

The FDA granted the approval of Xenpozyme to Genzyme.

Related Information

- Office of Rare Diseases, Pediatrics, Urologic and Reproductive Medicine-Division of Rare Diseases and Medical Genetics (DRDMG) (https://www.fda.gov/about-fda/center-drug-evaluation-and-research-cder/office-rare-diseases-pediatrics-urologic-and-reproductive-medicine-division-rare-diseases-and)
- Medical products for rare diseases and conditions (https://www.fda.gov/industry/medical-products-rare-diseases-and- conditions)
- CDER's ARC Program (https://www.fda.gov/about-fda/center-drug-evaluation-and-research-cder/cders-arc-program)

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