FDA News Release

FDA approves first treatment for a form of Batten disease

For Immediate Release

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Release

The U.S. Food and Drug Administration today approved Brineura (cerliponase alfa) as a treatment for a specific form of Batten disease. Brineura is the first FDA-approved treatment to slow loss of walking ability (ambulation) in symptomatic pediatric patients 3 years of age and older with late infantile neuronal ceroid lipofuscinosis type 2 (CLN2), also known as tripeptidyl peptidase-1 (TPP1) deficiency.

"The FDA is committed to approving new and innovative therapies for patients with rare diseases, particularly where there are no approved treatment options," said Julie Beitz, M.D., director of the Office of Drug Evaluation III in the FDA's Center for Drug Evaluation and Research. "Approving the first drug for the treatment of this form of Batten disease is an important advance for patients suffering with this condition."

CLN2 disease is one of a group of disorders known as neuronal ceroid lipofuscinoses (NCLs), collectively referred to as Batten disease. CLN2 disease is a rare inherited disorder that primarily affects the nervous system. In the late infantile form of the disease, signs and symptoms typically begin between ages 2 and 4. The initial symptoms usually include language delay, recurrent seizures (epilepsy) and difficulty coordinating movements (ataxia). Affected children also develop muscle twitches (myoclonus) and vision loss. CLN2 disease affects essential motor skills, such as sitting and walking. Individuals with this condition often require the use of a wheelchair by late childhood and typically do not survive past their teens. Batten disease is relatively rare, occurring in an estimated two to four of every 100,000 live births in the United States.

Brineura is an enzyme replacement therapy. Its active ingredient (cerliponase alfa) is a recombinant form of human TPP1, the enzyme deficient in patients with CLN2 disease. Brineura is administered into the cerebrospinal fluid (CSF) by infusion via a specific surgically implanted reservoir and catheter in the head (intraventricular access device). Brineura must be administered under sterile conditions to reduce the risk of infections, and treatment should be managed by a health care professional knowledgeable in intraventricular administration. The recommended dose of Brineura in pediatric patients 3 years of age and older is 300 mg administered once every other week by intraventricular infusion, followed by an infusion of electrolytes. The complete Brineura infusion, including the required infusion of intraventricular electrolytes, lasts approximately 4.5 hours. Pre-treatment of patients with antihistamines with or without antipyretics (drugs for prevention or treatment of fever) or corticosteroids is recommended 30 to 60 minutes prior to the start of the infusion.

The efficacy of Brineura was established in a non-randomized, single-arm dose escalation clinical study in 22 symptomatic pediatric patients with CLN2 disease and compared to 42 untreated patients with CLN2 disease from a natural history cohort (an independent historical control group) who were at least 3 years old and had

motor or language symptoms. Taking into account age, baseline walking ability and genotype, Brineura-treated patients demonstrated fewer declines in walking ability compared to untreated patients in the natural history cohort.

The safety of Brineura was evaluated in 24 patients with CLN2 disease aged 3 to 8 years who received at least one dose of Brineura in clinical studies. The safety and effectiveness of Brineura have not been established in patients less than 3 years of age.

The most common adverse reactions in patients treated with Brineura include fever, ECG abnormalities including slow heart rate (bradycardia), hypersensitivity, decrease or increase in CSF protein, vomiting, seizures, hematoma (abnormal collection of blood outside of a blood vessel), headache, irritability, increased CSF white blood cell count (pleocytosis), device-related infection, feeling jittery and low blood pressure.

Brineura should not be administered to patients if there are signs of acute intraventricular access device-related complications (e.g., leakage, device failure or signs of device-related infection such as swelling, erythema of the scalp, extravasation of fluid, or bulging of the scalp around or above the intraventricular access device). In case of intraventricular access device complications, health care providers should discontinue infusion of Brineura and refer to the device manufacturer's labeling for further instructions. Additionally, health care providers should routinely test patient CSF samples to detect device infections. Brineura should also not be used in patients with ventriculoperitoneal shunts (medical devices that relieve pressure on the brain caused by fluid accumulation).

Health care providers should also monitor vital signs (blood pressure, heart rate, etc.) before the infusion starts, periodically during infusion and post-infusion in a health care setting. Health care providers should perform electrocardiogram (ECG) monitoring during infusion in patients with a history of slow heart rate (bradycardia), conduction disorder (impaired progression of electrical impulses through the heart) or structural heart disease (defect or abnormality of the heart), as some patients with CLN2 disease can develop conduction disorders or heart disease. Hypersensitivity reactions have also been reported in Brineura-treated patients. Due to the potential for anaphylaxis, appropriate medical support should be readily available when Brineura is administered. If anaphylaxis occurs, infusion should be immediately discontinued and appropriate treatment should be initiated.

The FDA will require the Brineura manufacturer to further evaluate the safety of Brineura in CLN2 patients below the age of 2 years, including device related adverse events and complications with routine use. In addition, a long-term safety study will assess Brineura treated CLN2 patients for a minimum of 10 years.

The FDA granted this application **Priority Review (/ForPatients/Approvals/Fast/ucm405405.htm)** and **Breakthrough Therapy (/ForPatients/Approvals/Fast/ucm405397.htm)** designations. Brineura also received **Orphan Drug (/ForIndustry/DevelopingProductsforRareDiseasesConditions/HowtoapplyforOrphanProductDesignation/default.htm)** designation, which provides incentives to assist and encourage the development of drugs for rare diseases.

The sponsor is also receiving a **Rare Pediatric Disease Priority Review Voucher (/ForIndustry/DevelopingProductsforRareDiseasesConditions/RarePediatricDiseasePriorityVoucherProgram/default.htm)** under a program intended to encourage development of new drugs and biologics for the prevention and treatment of rare pediatric diseases. A voucher can be redeemed by a sponsor at a later date to receive **Priority Review (/ForPatients/Approvals/Fast/ucm405405.htm)** of a subsequent marketing application for a different product. This is the tenth rare pediatric disease priority review voucher issued by the FDA since the program began.

The FDA granted approval of Brineura to BioMarin Pharmaceutical Inc.

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Related Information

- FDA: Approved Drugs: Questions and Answers (/Drugs/ResourcesForYou/Consumers/ucm054420.htm)
- NIH: Batten Disease Fact Sheet (https://www.ninds.nih.gov/Disorders/Patient-Caregiver-Education/Fact-Sheets/Batten-Disease-Fact-Sheet)
- NIH: CLN2 Disease (https://ghr.nlm.nih.gov/condition/cln2-disease)

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