Brineura™ (cerliponase alfa) – New orphan drug approval

- On April 27, 2017, the FDA announced the approval of BioMarin's Brineura (cerliponase alfa), to slow loss of ambulation in symptomatic pediatric patients ≥ 3 years of age with late infantile neuronal ceroid lipofuscinosis type 2 (CLN2), also known as tripeptidyl peptidase 1 (TPP1) deficiency.

- CLN2 disease is a rare inherited condition that primarily affects the nervous system. It is one of a group of disorders known as neuronal ceroid lipofuscinoses, collectively referred to as Batten disease.

    - Batten disease occurs in an estimated 2 to 4 of every 100,000 live births in the U.S.
    - In the late infantile form of the disease, signs and symptoms begin between ages 2 and 4. Initial symptoms include language delay, recurrent seizures, and difficulty coordinating movements.
    - Affected children also develop myoclonus and vision loss. These children often require use of a wheelchair by late childhood and typically do not survive past their teens.

- Brineura contains cerliponase alfa, a recombinant form of human TPP1, the enzyme that is deficient in patients with CLN2 disease.

- The efficacy of Brineura was based on a non-randomized, single-arm dose escalation study in 22 symptomatic pediatric patients with CLN2 disease. These subjects were compared to 42 untreated patients with CLN2 disease from a natural history cohort.

    - Taking into account age, baseline walking ability and genotype, Brineura-treated patients demonstrated fewer declines in walking ability vs. untreated patients in the natural history cohort.
    - Furthermore, 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. However, the safety and effectiveness of Brineura have not been established in patients less than 3 years of age.

- Brineura is contraindicated in patients with acute intraventricular access-related device complications (eg, leakage, device failure, or device-related infections) and ventriculoperitoneal shunts.

- Other warnings and precautions of Brineura include cardiovascular adverse reactions and hypersensitivity reactions.

- The most common adverse reactions (≥ 8%) with Brineura use were pyrexia, ECG abnormalities, decreased cerebrospinal fluid (CSF) protein, vomiting, seizures, hypersensitivity, increased CSF protein, hematoma, headache, irritability, pleocytosis, device-related infection, bradycardia, feeling jittery, and hypotension.

- Brineura is administered into the CSF by infusion via a specific surgically implanted reservoir and catheter in the head (intraventricular access device). The recommended dose of Brineura is 300 mg once every other week by intraventricular infusion, followed by infusion of electrolytes.

    - 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.

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  - — 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 or corticosteroids is recommended 30 to 60 minutes prior to the start of the infusion.
  - — For further details, refer to the drug label.

- To support early testing for children who experience seizures, BioMarin in partnership with a commercial lab is offering a no cost genetic testing program called Behind the Seizure.

- BioMarin RareConnections™ is a resource available to patients and families that provides a variety of personalized support services at no cost to patients, including education on CLN2 disease and Brineura, and coordination of additional services, such as information about financial assistance programs.

- The wholesale acquisition cost for Brineura is $27,000 per carton. Patients will require 1 carton every other week at a cost of $702,000 per year.

- BioMarin plans to launch Brineura in early June 2017. Brineura injection will be available as two single-dose vials (150 mg/5 mL) co-packaged with intraventicular electrolyte injection as a single-dose vial. An administration kit for use with Brineura is supplied separately and contains single-use, sterile infusion components.

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