Roadmap to Brineura® (cerliponase alfa) treatment

In April 2017, the US Food and Drug Administration (FDA) approved Brineura® (cerliponase alfa) for children with symptoms of CLN2 disease who are 3 years of age and older to slow the loss of ambulation. Brineura is the only enzyme replacement therapy to address the cause of CLN2 disease, a form of Batten disease. This approval marks the first time that a treatment is available for any type of Batten disease. Hospital planning and setup for a medicine like Brineura can take time, and this roadmap is meant to give you an overview of the path toward ongoing treatment. Your family may have a similar path, or your path may vary.

1 DOCTOR'S APPOINTMENT

You'll consult with your child's doctor and, together, determine whether Brineura is right for your child.

Your child's doctor may consult with other experts more familiar with CLN2 disease. You and your child may need to travel every other week to one of these experts at a different hospital to receive treatment.

2 REGISTER YOUR CHILD WITH BIOMARIN RARECONNECTIONS™ TODAY

Beyond the therapeutic support provided to children with CLN2 disease, BioMarin is committed to supporting family members and caregivers. BioMarin RareConnections provides a variety of personalized support services at no cost, including education on CLN2 disease and Brineura, and support to coordinate additional services, such as information about financial assistance programs.

COMPLETE THE PATIENT REGISTRATION FORMS FOR YOUR CHILD TODAY
Registration forms are available at Brineura.com.
Contact BioMarin RareConnections at 1-866-906-6100 or support@biomarin-rareconnections.com, or visit www.biomarin-rareconnections.com.

3 HOSPITAL TREATMENT PLAN

Brineura is a unique therapy, so creating a treatment plan specific to your child's needs may take some time.

Brineura requires a multidisciplinary team—that means many people from different departments in the hospital will be involved. The hospital will work with your insurance provider to establish reimbursement for Brineura therapy.

As a caregiver, you're the most important part of your child's team. You are your child's advocate and a key source of information, whether it's medical records or insights into your child's well-being.

4 TREATMENT WITH BRINEURA

Brineura is an enzyme replacement therapy that is administered through intraventricular infusion—a method that allows Brineura to be directly delivered into the fluid surrounding the brain, known as the cerebrospinal fluid.

- Once all the details have been worked out to begin treatment, you and your child will travel to the hospital every other week for treatment administration
- Before starting Brineura, your child will need to have an intraventricular device surgically implanted—an established procedure in pediatric neurology. The device is about the size of a penny and is implanted just below the scalp. It's recommended that Brineura treatment begin at least 5 to 7 days after your child's device is implanted
- Pre-infusion and post-infusion care instructions will be provided by your healthcare team

This visual is an example illustrating the general path toward Brineura treatment. The actual timing and process will be different for each hospital and each family.

Please see Important Safety Information throughout, and full Prescribing Information.

Brineura® (cerliponase alfa)

Brineura® (cerliponase alfa) Important Safety Information

What is Brineura?

Brineura® (cerliponase alfa) is a prescription medication used to slow loss of ability to walk or crawl (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.

Who should not take Brineura?

- Patients with active intraventricular access device-related complications (eg, leakage, device failure, or device-related infection, including meningitis)
- Patients with any sign or symptom of acute or unresolved localized infection around the device insertion site (eg, cellulitis or abscess) or suspected or confirmed central nervous system (CNS) infection (eg, cloudy cerebrospinal fluid [CSF] or positive CSF gram stain, or meningitis)
- Patients with shunts used to drain extra fluid around the brain

What is the most important information I should know about Brineura?

Administration: Brineura is only given by infusion into the fluid of the brain (known as an intraventricular injection) and using sterile technique to reduce the risk of infection. An intraventricular access device or port must be in place at least 5 to 7 days prior to the first infusion.

- Prior to administration, it is important to discuss your child's medical history with their doctor
- Tell the doctor if they are sick or taking any medication and if they are allergic to any medicines

Meningitis and other device-related infections: Intraventricular access device-related infections, including meningitis, were observed with Brineura treatment. Infections required treatment with antibiotics and removal of the access device. If any signs of infection or meningitis occur, contact your child's doctor immediately. The signs and symptoms of infections may not be readily apparent in patients with CLN2 disease.

- Your child's doctor should vigilantly be looking for signs and symptoms of infection, including meningitis, during treatment with Brineura
- Your child's doctor should inspect the scalp and collect samples of your child's CSF prior to each infusion of Brineura, to check for infections and that there is no device failure
- Signs of infection on or around the device insertion site may include redness, tenderness, or discharge

Device-related complications such as device leakage, device failure, extravasation of CSF fluid, or bulging of the scalp around or above the intraventricular access device have occurred. In case of intraventricular access device-related complications, Brineura infusions may be discontinued.

Material degradation of the intraventricular access device reservoir was reported after approximately 4 years of administration, which may impact the effective and safe use of the device. During testing such material degradation was recognized after approximately 105 perforations of the intraventricular access device. The intraventricular access device should be replaced prior to 4 years of single-puncture administrations, which equates to approximately 105 administrations of Brineura.

Cardiovascular side effects: Low blood pressure and/or slow heart rate may occur during and following the infusion of Brineura. Contact your child's healthcare provider immediately if these reactions occur. As part of the infusion, the healthcare provider will monitor vital signs (blood pressure, heart rate) before infusion starts, periodically during infusion, and post-infusion, and assess the patient's status after administration to determine if continued observation may be necessary. Additional monitoring is required for patients with a history of cardiac abnormalities. In patients without cardiac abnormalities, regular 12-lead electrocardiogram (ECG) evaluations should be performed every 6 months.

Hypersensitivity reactions including serious and severe allergic reactions (anaphylaxis) may occur. Symptoms of anaphylaxis may include fever, respiratory distress, rash, vomiting, and irritability, and may occur during treatment or within several hours of Brineura infusion. Seek immediate medical care should signs and symptoms of anaphylaxis occur. Your child may receive medication such as antihistamines before Brineura infusions to reduce the risk of reactions.

If anaphylaxis occurs, you and your child's healthcare providers should consider the risks and benefits of readministration of Brineura. If the decision is made to readminister Brineura after the occurrence of anaphylaxis, the healthcare providers should ensure appropriately trained personnel and equipment for emergency resuscitation (including epinephrine and other emergency medicines) are readily available during infusion and will start the subsequent infusion at approximately one-half the initial infusion rate at which the anaphylactic reaction occurred.

The most common side effects reported during Brineura infusions included:

- Fever, problems with the electrical activity of the heart, decreased or increased protein in the fluid of the brain, vomiting, seizures, device-related complications, hypersensitivity, collection of blood outside of blood vessels (hematoma), headache, irritability, increased white blood cell count in the fluid of the brain, device-related infection, slow heart rate, feeling jittery, and low blood pressure

The risk information provided here is not comprehensive. Talk to your healthcare provider to learn more or for medical advice about any side effects.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1–800-FDA-1088.

Please click here to see full Prescribing Information or visit www.Brineura.com.

REGISTER YOUR CHILD WITH BIOMARIN RARECONNECTIONS™ TODAY

Complete the Patient Registration Forms to get started. BioMarin provides a wide variety of support services, offered at no cost, including:

- Education on CLN2 disease and Brineura
- Personalized support to coordinate additional services, including information about financial assistance programs

Registration forms are available at Brineura.com.

Contact BioMarin RareConnections at 1-866-906-6100 or support@biomarin-rareconnections.com, or visit www.biomarin-rareconnections.com.

Brineura® (cerliponase alfa)

BIOMARIN