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 newly approved medication 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 on reverse.

Brineura® (cerliponase alfa)

Brineura® (cerliponase alfa) Important Safety Information

INDICATION

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.

IMPORTANT SAFETY INFORMATION

Brineura is a prescription medicine. Before treatment with Brineura, 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. Your child's doctor will decide if Brineura is right for them. If you have questions or would like more information about Brineura, contact your child's doctor.

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. Intraventricular access device-related infections, including meningitis, were observed with Brineura treatment. 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 doctor should vigilantly be looking for signs and symptoms of infection, including meningitis, during treatment with Brineura.

Your child's intraventricular access device should be replaced prior to 4 years of single-puncture administration of Brineura, because the device may deteriorate due to repeated use.

Brineura should not be used in patients with active intraventricular access device-related complications (e.g., leakage, device failure, or device-related infection, including meningitis), symptom of acute, unresolved localized infection around the device insertion site (e.g. cellulitis or abscess), or and with shunts used to drain extra fluid around the brain. Your child's doctor should inspect the scalp and collect samples of your child's cerebrospinal fluid (CSF) prior to each infusion of Brineura, to check that there is no device failure or infections present.

Low blood pressure and/or slow heart rate may occur during and following the Brineura infusion. Contact your child's doctor immediately if these reactions occur.

Undesirable or hypersensitivity reactions related to Brineura treatment, including fever, vomiting, and irritability, may occur during treatment and as late as 24 hours after infusion. Your child may receive medication such as antihistamines before Brineura infusions to reduce the risk of reactions. Serious and severe allergic reactions (anaphylaxis) may occur. If a reaction occurs, the infusion will be stopped and your child may be given additional medication. If a severe reaction occurs, the infusion will be stopped and your child will receive appropriate medical treatment. If any signs of anaphylaxis occur, immediately seek medical care.

Safety and effectiveness in pediatric patients below 3 years of age have not been established.

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, hypersensitivity, collection of blood outside of blood vessels (hematoma), headache, irritability, and increased white blood cell count in the fluid of the brain, device-related infection, slow heart rate, feeling jittery, and low blood pressure. Intraventricular device-related side effects included infection, delivery system-related complications, and increased white blood cell count in fluid of the brain.

These are not all of the possible side effects with Brineura. Talk to your child's doctor if they have any symptoms that bother them or that do not go away.

Call your doctor for medical advice about side effects. You may report side effects to BioMarin Pharmaceutical Inc. at 1-866-906-6100, or the FDA at 1-800-FDA-1088 or go to www.fda.gov/medwatch.

Please see full Prescribing Information, or visit www.Brineura.com.

BIOMARIN

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.

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