

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.

Preparing for Brineura™ (cerliponase alfa) infusions

Next steps for you and your child

Brineura™
(cerliponase alfa)

Please see Important Safety Information on back cover.

Support throughout the Brineura™ (cerliponase alfa) treatment process

Now that your child is ready to begin Brineura™ (cerliponase alfa), it's helpful to understand more about the infusion process. Every hospital has its own policies and treatment procedures. This guide can give you a sense of what you and your child may experience before, during, and after their Brineura infusions.

Because you are a parent or caregiver, your child turns to you for support and comfort, so staying informed and preparing ahead of time may help your child feel more at ease. Keep in close contact with your healthcare team about how your child is doing and any instructions for your child's care. They are your partners in this, so don't hesitate to reach out to them with any questions or concerns you may have.

- Brineura is a type of treatment called an enzyme replacement therapy
  - Brineura helps replace an enzyme called TPP1 that is missing or not working properly in children who have CLN2 disease[1]
  - By helping to replace this enzyme, Brineura helps clear out the materials that build up in the cells of the brain as a result of CLN2 disease[1]

How is Brineura administered?

Brineura is administered every other week through intraventricular infusion[1]

Intraventricular drug delivery is an established method with clinical experience in other disease areas, including oncology.[2]

This method allows Brineura to be delivered directly to a ventricle in the brain, and then into the fluid surrounding the brain, known as the cerebrospinal fluid (CSF). Brineura is delivered into the CSF to help reach cells that are affected by CLN2 disease. Knowledgeable members of your healthcare team will give your child's Brineura infusions.[1]

To receive intraventricular infusions, your child will first need to have an intraventricular access device surgically implanted.[1] This procedure is commonly performed in pediatric neurosurgery.[2] The neurosurgeon will discuss the procedure with you and answer any additional questions you may have.

Before your child's first infusion:

MRI brain scans to help place the intraventricular access device[2]

- MRI (magnetic resonance imaging) scans are used to help the surgeon locate where the access device should be inserted, and to confirm placement after the surgery

Surgery to implant the intraventricular access device

- The access device is about the size of a penny, and is implanted just below the scalp[2]
- After the access device is placed, your healthcare team will work with you to schedule infusions. It is recommended that Brineura treatment begin at least 5 to 7 days after your child's access device is implanted[1]
- Over time, your child's access device may need to be replaced. Your healthcare team will advise you when this is needed[1]

Brineura should not be used in patients with active intraventricular access device-related complications (eg, leakage, device failure, or device-related infection) and with shunts used to drain extra fluid around the brain.

Preparing for infusion days

Below are important steps that will help prepare you and your child for infusion of Brineura™ (cerliponase alfa).

Talk with your child about the infusion process in a way that is comfortable for both of you. Your child may look to you for guidance, so it's important to stay positive and reassuring.

Plan ahead for any items you may need to bring. It may be helpful to talk with your child about special things you will do on infusion days, like watching their favorite TV show or reading a favorite book.

- Your child will have to sit relatively still during the infusion process, so consider bringing comforting items to keep your child engaged and entertained. Items can include tablets or similar devices, books, toys, snacks, music, games, or favorite items
- You may want to bring hair clips to hold back your child's hair, or a hat or scarf for your child to wear home

Update your healthcare team on any changes to your child's medications.

Carry the contact information of your healthcare team with you at all times in case any questions or concerns arise.

What to expect on infusion days

Below is an example of what you may expect on an infusion day. Your experience may be slightly different since each hospital has its own procedures.

Prepare by following your healthcare team's directions for what to do before the appointment. This may include:

- Washing your child's hair with a special shampoo
- Removing a small patch of your child's hair to prepare for accessing the intraventricular access device[2]
- Applying numbing cream to a small area of your child's head
- Giving your child medication 30 to 60 minutes before the infusion begins, to reduce the risk of reactions, like fever or hypersensitivity—your healthcare team will provide instructions[1]

Your child's healthcare team will use aseptic technique to help reduce the risk of infection. Each hospital will have its own procedures. Here are some things that may happen:

MAINTAINING A STERILE ENVIRONMENT

- You may be asked to wear a mask[2]
- The number of people in the room will be limited during the infusion, especially when accessing the intraventricular access device—ask your healthcare team who and what is allowed in the room[2]
- A healthcare team member may apply a numbing cream to the scalp before the infusion
- The skin over the port area will be cleaned by a healthcare team member[2]
- Please follow your healthcare team's instructions carefully—take care not to touch the skin over the access device once it is cleaned[2]

ACCESSING THE INTRAVENTRICULAR ACCESS DEVICE

- You may be asked to hold your child or sit behind them on the bed while the access needle is inserted to minimize movement during this part of the infusion
- Your child's head may be wrapped in gauze during or after the infusion process[2]
- Intraventricular access device-related infections were observed with Brineura treatment. If any signs of infection occur, contact your child's doctor immediately[1]

DURING THE INFUSION

- Your child can sit or lie down in a bed, chair, or stroller during the infusion and play with games or electronics[2]
  - Take care to minimize your child's movement during the infusion to avoid disconnecting the needle
- Plan to help keep your child entertained for about 4.5 hours[1]
- Your child's vital signs will be monitored regularly[1]

Possible side effects of Brineura™ (cerliponase alfa)[1]

Brineura™ (cerliponase alfa) can cause side effects. Talk to your healthcare team immediately if your child experiences any side effects.

The most common side effects reported during Brineura infusions included[1]:

- 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
- Increased white blood cell count in the fluid of the brain
- Device-related infection
- Slow heart rate
- Feeling jittery
- Low blood pressure

If your child is acting differently or if you have any concerns, talk to your healthcare team immediately.

What to watch for after infusion

After Brineura infusion, it is very important to watch for signs of infection or port leakage.[1]

Make sure that you have the emergency contact information for your healthcare team and keep it readily accessible at all times and in multiple places. Also be sure to provide this information to other family members and your child's day care or school.

Post-infusion care

Immediately after infusion

- Follow your hospital's instructions for care and bandage removal
- You and your child should avoid touching or putting direct pressure on the intraventricular access device and surrounding area

First few days following infusion

- Follow your healthcare team's instructions about wetting your child's head, shampooing, and using public pools or other areas that may expose the device to water
- Ask your healthcare team if your child can wear hats, caps, or bows

After your child's Brineura infusion, watch for signs of the following[1]:

- Intraventricular access device–related complications
  - There is a risk of device-related infections. There are steps the doctor can take to minimize this risk with every treatment. If you see any signs of infection, such as swelling or reddening of the skin, contact your healthcare team immediately
- Cardiovascular adverse reactions
  - Low blood pressure or slow heart rate may occur during and following Brineura infusion. Contact your healthcare team immediately if either occur
- Hypersensitivity
  - Hypersensitivity reactions related to Brineura treatment may occur, including fever, vomiting, and irritability. Some patients may experience anaphylaxis (severe allergic reactions to medicine). Talk to your healthcare team about signs and symptoms of anaphylaxis, and contact them immediately if any occur

Your healthcare team will help guide you with what activities are appropriate and safe for your child after infusion. Your child may be able to return to regular routines and activities after infusion.

Indication and 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 were observed with Brineura treatment. If any signs of infection occur, contact your child's doctor immediately. Your child's intraventricular access device may need to be replaced over time.

Brineura should not be used in patients with active intraventricular access device-related complications (e.g., leakage, device failure, or device-related infection) and with shunts used to drain extra fluid around the brain.

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 FDA at 1-800-FDA-1088.

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

Brineura™ (cerliponase alfa)

References: 1. Brineura [package insert]. Novato, CA: BioMarin Pharmaceutical Inc; 2017.
2. Cohen-Pfeffer JL, Gururangan S, Lester T, et al. Intracereboventricular delivery as a safe, long-term route of drug administration. *Pediatr Neurol.* 2017;67:23-35.

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