Brineura (cerliponase alfa)

NEW PRODUCT SLIDESHOW

MPR

Introduction

- **Brand name:** Brineura
- **Generic name:** Cerliponase alfa
- **Pharmacological class:** Hydrolytic lysosomal N-terminal tripeptidyl peptidase
- **Strength and Formulation:** 30mg/mL; soln for intraventricular infusion
- **Manufacturer:** BioMarin Pharmaceuticals
- **How supplied:** Single-dose vial (5mL)—2 (w. Intraventricular Electrolytes 5mL vial) + Administration Kit—1 (infusion supplies)
- **Legal Classification:** Rx

BRINEURA


Brineura™
(cerliponase alfa)
Injection
150 mg/5 mL
(30 mg/mL)
For Intraventricular Infusion Only
Use before Intraventricular Electrolytes
Brineura™
(cerliponase alfa)
Injection
150 mg/5 mL
(30 mg/mL)
For Intraventricular Infusion Only
Use before Intraventricular Electrolytes
Intraventricular Electrolytes
Injection
Use after Brineura (cerliponase alfa)
5 mL
For Intraventricular Infusion Only

Indications

- To slow the loss of ambulation in late infantile neuronal ceroid lipofuscinosis type 2 (CLN2), also known as **tripeptidyl peptidase 1 (TPP1) deficiency**

Dosage & Administration

- **Adult: not applicable**
- See full labeling
- Give by intraventricular infusion via implanted access device; administer first dose at least 5–7 days post-implantation

Dosage & Administration

- **Pre-treat** with antihistamines ± antipyretics or corticosteroids 30–60mins prior to infusion
- **Infuse Brineura first**, followed by Intraventricular Electrolytes each at a rate of 2.5mL/hr
- **≥3yrs**: 300mg once every other week

Considerations for Special Populations

- **Adults:** Not applicable
- **Pregnancy:** No available data
- **Nursing mothers:** No available data
- **Pediatric:** <3yrs: not established

Contraindications

- Patients with acute intraventricular access device-related complications (eg, leakage, device failure, infection) or ventriculoperitoneal shunts

Warnings/Precautions

- Should be administered by trained healthcare providers
- **Inspect** the scalp to ensure access device is not compromised prior to each infusion
- **Discontinue** if access device-related complications develop
- **Routinely test** CSF samples to detect subclinical device infections

Warnings/Precautions

- **Monitor** BP and HR before starting, during, and post-infusion
- History of bradycardia, conduction disorder, structural heart disease: perform ECG during infusion; without cardiac abnormalities: **perform ECG** every 6 months

Warnings/Precautions

- Have appropriate medical treatment available
- **Discontinue** immediately if anaphylaxis or severe hypersensitivity reactions occur

Interactions

- **Do not mix** with other drugs

Adverse Reactions

- Pyrexia
- ECG abnormalities
- CSF protein increase/decrease
- Vomiting
- Seizures
- Hypersensitivity
- Hematoma
- Headache
- Irritability
- Pleocytosis
- Device-related infection
- Bradycardia
- Feeling jittery
- Hypotension
- Cardiovascular events

Mechanism of Action

- **Cerliponase alfa** (rhTTP1) is a proenzyme taken up by target cells in the CNS and is translocated and activated in the lysosome
- Activated cerliponase alfa cleaves tripeptides from the N-terminus of proteins

Clinical Studies

- A 96-week non-randomized, single-arm, dose escalation clinical study (n=23) with extension evaluated the efficacy of Brineura in symptomatic pediatric patients aged 3–8 with CLN2 disease
- Treated patients were compared to untreated patients from a natural history cohort

Clinical Studies

- Patients were given Brineura 300mg every other week for 48 weeks and continued during extension period
  - 1 patient withdrew after Week 1
- Evaluated patients had combined Motor plus Language CLN2 Clinical Rating Scale score < 6

Clinical Studies

- Patients were assessed for primary endpoint of decline in the Motor domain of CLN2 Clinical Rating Scale at Weeks 48, 72, and 96
- Decline in Motor domain was defined as having unreversed (sustained) 2-category decline or an unreversed score of 0

Clinical Studies

- 22 treated patients were compared with 42 untreated patients who satisfied inclusion criteria
- Brineura-treated patients were **13 times less likely** to have a decline at Week 96 than natural history cohort patients (odds ratio [OR] 13.1, 95% CI: 1.2, 146.9)

Clinical Studies

- 21 of 22 (95%) treated patients did not decline in the Motor domain at Week 96
  - Only 1 patient who terminated early had a decline
- In the natural history cohort, 21 of 42 (50%) of patients experienced a decline in Motor domain over study period

Clinical Studies

- Additionally, 22 treated patients were matched with 42 natural history cohort patients based on the following covariates:
  - Baseline age at screening within 3 months
  - Genotype (0, 1, or 2 key mutations)
  - Baseline Motor domain CLN2 score at screening
- Decline was defined as unreversed 2-category decline or unreversed score of 0

Clinical Studies

- Follow-ups were performed at Weeks 48, 72, and 96 in 17 matched pairs
- At **Week 48**, there was no decline in **16** (94%) Brineura-treated pairs vs. **13** (76%) natural history pairs (OR 4.0, 95% CI: 0.4, 200)

Clinical Studies

- At **Week 72**, there was no decline in **16** (94%) Brineura-treated pairs vs. **11** (65%) natural history pairs (OR 5.9, 95% CI: 0.7, 250)
- At **Week 96**, there was no decline in **16** (94%) Brineura-treated pairs vs. **6** (35%) natural history pairs (OR 11, 95% CI 1.6, 500)
- For more clinical trial data, see full labeling

New Product Monograph

- For more information view the product monograph available at:

  http://www.empr.com/brineura/drug/34682/