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Long-term data for cerliponase alfa▼ in children with CLN2 disease: A CLINICAL TRIAL UPDATE

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BMN 190-201/202 STUDY DESIGN:
Primary Phase I/II study and open-label extension

Primary Phase I/II study[1] (48 weeks*)
N=24
- Aged 3–16 years
- CLN2 CRS Motor-Language score ≥3

One patient discontinued (not due to AEs)†

Open-label extension[2] (Up to 240 weeks)
N=23
- 6 patients discontinued (not due to AEs)‡

Dosing[1,2] Cerliponase alfa was initiated at 30 mg, 100 mg or 300 mg; all participants then received a 300-mg dose every 2 weeks

Control group[1,2] Historical controls with untreated CLN2 disease included in the DEM-CHILD international registry

STUDY OUTCOMES:[1,2]

The Motor and Language domains of the CLN2 CRS were assessed every 8 weeks during the OLE study to monitor disease progression[2]

PRIMARY ENDPOINT
Time to unreversed 2-point decline,§ or score of 0 in the combined Motor-Language domains of the CLN2 CRS

CLN2 Motor-Language domains (combined score 0–6)

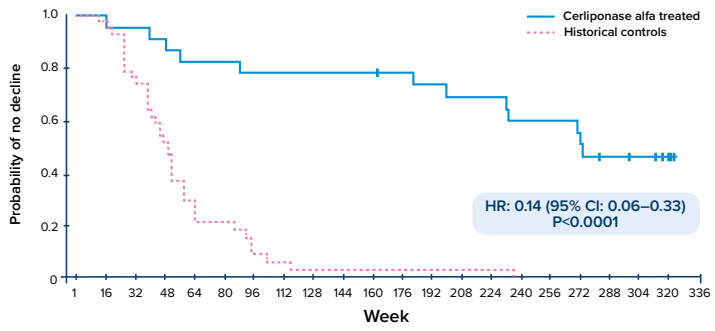
Motor	Score
Grossly normal gait, no prominent ataxia and no pathologic falls	3
Independent gait,¶ will have obvious instability and may have intermittent falls	2
External assistance to walk, or can crawl only	1
Can no longer walk or crawl	0

Language	Score
Apparently normal, intelligible and grossly age appropriate; no decline noted	3
Abnormal: some intelligible words; may form short sentences to convey concepts, requests or needs	2
Hardly understandable, few intelligible words	1
No intelligible words or vocalisations	0

EFFICACY RESULTS:
Primary Phase I/II study and OLE[2,3]

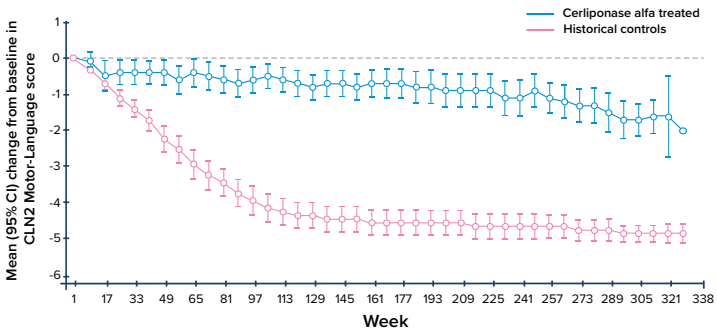
Cerliponase alfa significantly reduced the probability of decline in motor-language function

Treated patients were 86% less likely (P<0.0001) to experience a significant decline in motor-language function vs controls‖



‖Defined as the composite of an unreversed 2-point decline or score of 0 in the combined Motor-Language domains of the CLN2 CRS.

Combined Motor-Language score declined at a slower rate in the cerliponase alfa-treated group when compared with the historical controls



Abbreviations: AE, adverse event; CI, confidence interval; CLN2, neuronal ceroid lipofuscinosis type 2; CLN2 CRS, CLN2 Clinical Rating Scale; HR, hazard ratio; ICV, intracerebroventricular; OLE, open-label extension; TPP1, tripeptidyl peptidase 1.

*Stable-dose period (ICV 300 mg cerliponase alfa every other week). †One participant withdrew from the primary study at the parents' request after receiving one dose of the study drug due to an inability to comply with study procedures and was excluded from efficacy analyses.[1] ‡Four due to relocation or switch to commercial therapy; two due to meeting study-stopping criteria (having a score of 0 in the combined Motor-Language domains assessed at consecutive study visits). §An unreversed 2-point decline was defined as a decline that had not returned to within 1 point of baseline score by the last assessment. ¶Defined as ability to walk without support for 10 steps.

▼Cerliponase alfa is indicated in the EU for the treatment of neuronal ceroid lipofuscinosis type 2 (CLN2) disease, also known as tripeptidyl peptidase 1 (TPP1) deficiency. This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions.

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SAFETY PROFILE: Primary Phase I/II study and OLE[2,3]

Cerliponase alfa was generally well tolerated, demonstrating an acceptable safety profile, with no treatment discontinuations due to adverse events

ALL AEs

All participants experienced ≥1 AE, most of which were mild to moderate in severity

Most common drug-related AEs were:

- **Pyrexia**
- **Seizure**
- **Epilepsy**
- **Vomiting**
- **Hypersensitivity**

SAEs

21 participants (88%) experienced an SAE

8 participants (33%) experienced an SAE related to the study drug

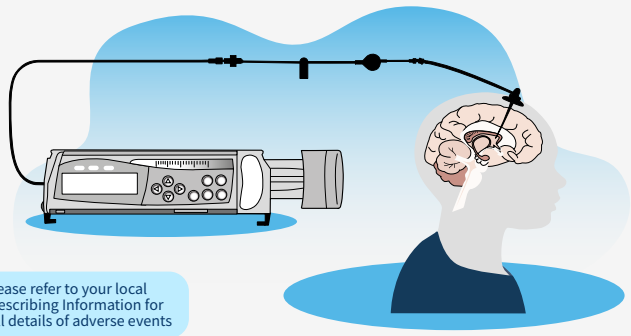
Most common drug-related SAEs were:

- **Hypersensitivity**
- **Pleocytosis**
- **Infusion-related reaction**

DEVICE-RELATED COMPLICATIONS

9 **Nine participants** experienced ICV device-related infections

6 **Six participants** required device replacement



Please refer to your local Prescribing Information for full details of adverse events

CONCLUSION: Primary Phase I/II study and OLE[2,3]

Over a period of >5 years, cerliponase alfa slowed the decline in motor and language function in children with CLN2 disease, with an acceptable safety profile

Abbreviations: AE, adverse event; CLN2, neuronal ceroid lipofuscinosis type 2; ICV, intracerebroventricular; OLE, open-label extension; SAE, serious adverse event.

References:
1. Schulz A, et al. Study of intraventricular cerliponase alfa for CLN2 disease. *N Engl J Med*. 2018;378(20):1898–1907.
2. Schulz A, et al. Safety and efficacy of cerliponase alfa in children with neuronal ceroid lipofuscinosis type 2 (CLN2 disease): an open-label extension study. *Lancet Neurol*. 2024;23(1):60–70.
3. ClinicalTrials.gov. BioMarin Pharmaceutical. A safety, tolerability, and efficacy study of BMN 190 in pediatric patients <18 years of age with CLN2 disease. NCT02678689. Available at: https://clinicaltrials.gov/study/NCT02678689 [Accessed 11 September 2026].

BioMarin does not recommend the use of any product in any manner other than that described in the approved Prescribing Information.
Regulatory status and approved indications may vary between countries. Please consult local Prescribing Information before prescribing.
Prescribing information and adverse event reporting information can be found here or at the end of this document.

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BIOMARIN®

Abbreviated prescribing information (INTL)
Cerliponase alfa® ▼

Refer to Summary of Product Characteristics for full prescribing information.

▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions.

Name of Product: Cerliponase alfa (cerliponase alfa) 150 mg solution for infusion. **Presentation:** Each vial of cerliponase alfa contains 150 mg cerliponase alfa in 5 ml of solution (30 mg/ml). Each presentation contains two vials of cerliponase alfa, and one vial of flushing solution. Cerliponase alfa is a recombinant form of human tripeptidyl peptidase 1 (rhTPP1). **Therapeutic indications:** Cerliponase alfa is indicated for the treatment of neuronal ceroid lipofuscinosis type 2 (CLN2) disease, also known as tripeptidyl peptidase 1 (TPP1) deficiency. **Dosage and administration:** Cerliponase alfa must only be administered by a trained healthcare professional knowledgeable in intracerebroventricular administration in a healthcare setting. The recommended dose is 300 mg cerliponase alfa administered once every other week by intracerebroventricular infusion. In patients less than 2 years of age, lower doses are recommended, see full Summary of Product Characteristics. Cerliponase alfa and the flushing solution must only be administered by the intracerebroventricular route. Each vial of cerliponase alfa and flushing solution are intended for single use only. Cerliponase alfa is administered to the cerebrospinal fluid (CSF) by infusion via a surgically implanted reservoir and catheter (intracerebroventricular access device). The intracerebroventricular access device must be implanted prior to the first infusion. The implanted intracerebroventricular access device should be appropriate for accessing the cerebral ventricles for therapeutic administration. **Contraindications:** Life-threatening anaphylactic reaction to the active substance or to any of the excipients, if rechallenge is unsuccessful. CLN2 patients with ventriculo-peritoneal shunts. Cerliponase alfa must not be administered if there are signs of acute intracerebroventricular access device leakage, device failure, or device-related infection. **Special Warnings and Precautions:** Cerliponase alfa must be administered using aseptic technique to reduce the risk of infection. Intracerebroventricular access devicerelated infections, including sub-clinical infections and meningitis, have been observed in patients treated with cerliponase alfa. Meningitis may present with the following symptoms: fever, headache, neck stiffness, light sensitivity, nausea, vomiting, and change in mental status. CSF samples should routinely be sent for testing to detect subclinical device infections. In clinical studies, antibiotics were administered, the intracerebroventricular access device was replaced, and cerliponase alfa treatment was continued. Healthcare professionals should inspect the scalp for skin integrity to ensure the intracerebroventricular access device is not compromised prior to each infusion. Common signs of device leakage and device failure include swelling, erythema of the scalp, extravasation of fluid, or bulging of the scalp around or above the intracerebroventricular access device. However, these signs may also occur in the context of device-related infections. Inspection of the infusion site and a patency check must be performed to detect intracerebroventricular access device leakage and/or failure prior to initiation of cerliponase alfa infusion. The signs and symptoms of devicerelated infections may not be apparent, therefore, CSF samples should routinely be sent for testing to detect subclinical device infections. Consultation with a neurosurgeon may be needed to confirm the integrity of the device. Cerliponase alfa treatment should be interrupted in cases of device failure and may require replacement of the access device prior to subsequent infusions. Material degradation of the intracerebroventricular access device reservoir occurs after long periods of use according to preliminary results of benchtop testing and as observed in clinical trials with approximately 4 years of use. In two clinical cases, the ICV access devices did not show signs of failure at the time of infusion; however, after removal, material degradation of the devices were apparent and consistent with data from benchtop testing of ICV access devices. The access devices were replaced and patients resumed treatment with cerliponase alfa. Access device replacement should be considered prior to 4 years of regular administration of cerliponase alfa, however, it must always be ensured that the intracerebroventricular access device is used in accordance with the provisions of the respective medical device manufacturer. In case of intracerebroventricular access device-related complications, refer to the manufacturer's labelling for further instruction. Caution should be taken in patients prone to complications from intracerebroventricular medicinal product administration, including patients with obstructive hydrocephalus. Anaphylactic reactions have been reported with cerliponase alfa. As a precautionary measure, appropriate medical support should be readily available when cerliponase alfa is administered. If anaphylactic reactions occur, immediately discontinue the infusion and initiate appropriate treatment. Observe patients closely during and after the infusion. If anaphylaxis occurs, caution should be exercised upon re-administration. **Undesirable Effects:** Very common adverse reactions: Device-related infection, hypersensitivity, irritability, convulsion events, headache, CSF pleocytosis, vomiting, pyrexia, CSF protein increased, ECG abnormalities, CSF protein decreased. Very common product issues: Device leakage, needle issue, device malfunction. Common adverse reactions include: bradycardia, anaphylactic reaction, gastrointestinal disorder, rash, urticaria, feeling jittery, medical device site irritation. Common product issues: Device occlusion and device breakage. Meningitis and device dislocation were also reported at unknown frequency. List of Excipients: Sodium phosphate dibasic monohydrate, sodium chloride, potassium chloride, magnesium chloride hexahydrate, calcium chloride dihydrate, water for injections. **Incompatibilities:** This medicinal product must not be mixed with other medicinal products. **Storage and Use:** Store upright in a freezer (-25°C to -15°C). Thawed cerliponase alfa and flushing solution should be used immediately. Product should only be withdrawn from the unopened vials immediately prior to use to protect from light. If immediate use is not possible, unopened vials of cerliponase alfa or flushing solution should be stored at 2–8°C and used within 24 hours. **Preparation of Cerliponase alfa Infusion:** See full Summary of Product Characteristics. **Legal Category:** Prescription only medicine **Marketing Authorisation Holder:** BioMarin International Limited, Shanbally, Ringaskiddy, County Cork, Ireland. **Marketing Authorisation Number(s):** EU/1/17/1192/001 **Date of First Authorisation:** 30 May 2017 **Date of API revision:** December 2023.

Healthcare professionals should report adverse events in accordance with their local requirements.

Adverse events should also be reported to BioMarin on +1 415 506 6179 or drugsafety@bmrn.com