Abbreviated prescribing information (INTL)
BRINEURA®▼ (cerliponase alfa)

Refer to Summary of Product Characteristics for full 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:** Brineura (cerliponase alfa) 150 mg solution for infusion. **Presentation:** Each vial of Brineura 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:** Brineura is indicated for the treatment of neuronal ceroid lipofuscinosis type 2 (CLN2) disease, also known as tripeptidyl peptidase 1 (TPP1) deficiency. **Dosage and Administration:** Brineura 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. Brineura and the flushing solution must only be administered by the intracerebroventricular route. Each vial of Brineura and flushing solution are intended for single use only. Brineura 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 re-challenge is unsuccessful. CLN2 patients with ventriculo-peritoneal shunts. Brineura must not be administered as long as there are signs of acute intracerebroventricular access device leakage, device failure, or device-related infection. **Special Warnings and Precautions:** Brineura must be administered using aseptic technique to reduce the risk of infection. Intracerebroventricular access device-related infections, including sub-clinical infections and meningitis, have been observed in patients treated with Brineura. 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 Brineura 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 Brineura infusion. The signs and symptoms of device-related 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. Brineura 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 Brineura. Access device replacement should be considered prior to 4 years of regular administration of Brineura, 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 Brineura. As a precautionary measure, appropriate medical support should be readily available when Brineura 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 included upper respiratory tract infection, hypersensitivity, irritability, convulsion events, headache, CSF pleocytosis, vomiting, pyrexia, CSF protein increased, ECG abnormalities, CSF protein decreased and needle issue. Common adverse reactions include conjunctivitis, device-related infection, bradycardia, anaphylactic reaction, dropped head syndrome, abdominal pain, oral mucosal blistering, tongue blistering, gastrointestinal disorder, rash, urticaria, feeling jittery, pain, device leakage, and device occlusion. Meningitis and device dislocation were also reported at unknown frequency. Convulsions are a common manifestation of CLN2 disease and are expected to occur in this population. Overall, 23 (96%) subjects who received cerliponase alfa experienced an event that mapped to the Convulsions Standardized MedDRA Query. The most commonly reported convulsion events include seizure, epilepsy and generalized tonic-clonic seizure. Total convulsion events with a temporal relationship to cerliponase alfa administration was 17% and were mild to moderate, grade 1 to 2 in severity. Overall, 6% of all convulsion events were considered related to cerliponase alfa and ranged from mild to severe, (Common Terminology Criteria for Adverse Events (CTCAE) grade 1–4). Convulsions resolved with standard anti-convulsive therapies and did not result in discontinuation of Brineura treatment. Hypersensitivity reactions were reported in 14 out of 24 patients (58%) treated with Brineura. Severe CTCAE grade 3 hypersensitivity reactions occurred in three patients and no patients discontinued treatment. The most common manifestations included pyrexia with vomiting, pleocytosis, or irritability, which are inconsistent with classic immune-mediated hypersensitivity. These adverse reactions were observed during or within 24 hours after completion of the Brineura infusion and did not interfere with treatment. Symptoms resolved over time or with administration of antipyretics, antihistamines and/or glucocorticosteroids. **List of Excipients:** Sodium phosphate dibasic heptahydrate, sodium dihydrogen phosphate 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 Brineura and flushing solution should be used immediately. Product should only be withdrawn from the unopened vials immediately prior to use. If immediate use is not possible, unopened vials of Brineura or flushing solution should be stored at 2–8°C and used within 24 hours. **Preparation of Brineura 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 Revision of the Text:** February 2020. Brineura is a trademark of BioMarin Pharmaceutical Inc. from whom further information is available.

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