Prior approval is required for some or all procedure codes listed in this Corporate Drug Policy.

OVERVIEW
Brineura is indicated to slow the loss of ambulation in symptomatic pediatric patients ≥ 3 years of age with late infantile neuronal ceroid lipofuscinosis type 2 (CLN2), also known as tripeptidyl peptidase 1 (TPP1) deficiency. Brineura is recombinant human TPP1 produced using recombinant DNA technology in a Chinese hamster ovary (CHO) cell line. The recommended dose of Brineura is 300 mg administered once every other week (QOW) via intracerebroventricular (ICV) infusion. Following Brineura administration, the patient must also receive an infusion of intraventricular electrolytes. The drug is administered into the CSF via a surgically implanted reservoir and catheter and should only be administered by or under the direction of a physician who is knowledgeable in ICV administration. Brineura is available as single-dose vials, each containing 150 mg/5ml (30 mg/mL). Brineura is supplied in two packages. Package 1 contains two 5 mL vials of Brineura solution and one 5 mL vial of intraventricular electrolytes. Package 2 is the administration kit for use with Brineura; it contains two 20 mL syringes, two syringe needles, one extension line, one infusion set with a 0.2 micron inline filter, and one port needle. Brineura and the intraventricular electrolytes should be stored upright in a freezer (-25° to -15°C [-13° to 5°F]), in the original packaging protected from light. The administration kit should not be frozen. Thawed Brineura and intraventricular electrolytes should be used immediately. If not used immediately, they may be stored unopened in the original vials in the refrigerator (2° to 8° C [36° to 46°F]) for up to 24 hours. If product is drawn up into labeled syringes, it should be used immediately. If not used immediately, it may be stored in the labeled syringes in the refrigerator for up to 4 hours prior to infusion.

POLICY STATEMENT
This policy involves the use of Brineura. Prior authorization is recommended for medical benefit coverage of Brineura. Approval is recommended for those who meet the conditions of coverage in the Initial Approval and Renewal Criteria, Preferred Drug (when applicable), Dosing/Administration, Length of Authorization, and Site of Care (when applicable) for the diagnosis provided. The requirement that the patient meet the Criteria and Preferred Drug for coverage of the requested medication applies to the initial authorization only. All approvals for initial therapy are provided for the initial approval duration noted below; if reauthorization is allowed, a response to therapy is required for continuation of therapy.

Recommended Authorization Criteria
Coverage of Brineura is recommended in those who meet the following criteria:
I. Length of Authorization

Coverage will be provided for 6 months and may be renewed.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC unit]:
   - Brineura 150 mg/5 mL single dose vial: 2 vials every 14 days

B. Max Units (per dose and over time) [HCPCS Unit]:
   - 300 billable units (two kits) every 14 days

III. Initial Approval Criteria

Coverage is provided in the following conditions:

Universal Criteria
- Patient is 3 years of age or older; AND
- Patient must not have acute intraventricular access device-related complications (e.g., leakage, extravasation of fluid, or device-related infection); AND
- Patient must not have ventriculoperitoneal shunts; AND
- Patient has no sign or symptom of acute, unresolved localized infection on or around the device insertion site (e.g. cellulitis or abscess); or a suspected or confirmed CNS infection; AND
- Late infantile neuronal ceroid lipofuscinosis type 2 (CLN2); tripeptidyl peptidase 1 (TPP1) deficiency†
  - Patient must have a definitive diagnosis of late infantile CLN2 confirmed by deficiency of the lysosomal enzyme tripeptidyl peptidase-1 (TPP1) and/or molecular analysis indicating dysfunctional mutation of the TPP1 gene on chromosome 11p15.4; AND
  - Patient has mild to moderate disease documented by a two-domain score of 3 to 6 on the motor and language domains of the Hamburg CLN2 Clinical Rating Scale, with a score of at least 1 in each of these two domains; AND
  - Patient is ambulatory; AND
  - Patients with a history of bradycardia, conduction disorder, or with structural heart disease must have electrocardiogram (ECG) monitoring performed during the infusion

† FDA-labeled indication(s)
IV. Renewal Criteria\textsuperscript{1,5,7}

- Patient continues to meet universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in section III; \textbf{AND}

- Absence of unacceptable toxicity from the drug or complications from the device. Examples of unacceptable toxicity or complications include: meningitis and other intraventricular access device-related infections, intraventricular access device-related complications, severe hypersensitivity reactions, severe cardiovascular reactions, severe hypotension; etc.; \textbf{AND}

- Patient had a 12-lead ECG evaluation performed within the last 6 months (those with cardiac abnormalities require an ECG during each infusion); \textbf{AND}

- Patient has responded to therapy compared to pretreatment baseline with stability/lack of decline in motor function/milestones on the Motor domain of the Hamburg CLN2 Clinical Rating Scale [Decline is defined as having an unreversed (sustained) 2-category decline or an unreversed score of 0].

V. Dosage/Administration\textsuperscript{1,2,5,7}

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dose</th>
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<tbody>
<tr>
<td>CLN2</td>
<td>300 mg administered once every other week by intraventricular infusion. Administer Brineura first followed by infusion of the Intraventricular Electrolytes each at an infusion rate of 2.5 mL/hr. The complete Brineura infusion, including the required infusion of Intraventricular Electrolytes, is approximately 4.5 hours.</td>
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- Aseptic technique must be strictly observed during preparation and administration
- Brineura should be administered by, or under the direction of a physician knowledgeable in intraventricular administration
- Brineura is administered into the cerebrospinal fluid (CSF) by infusion via a surgically implanted reservoir and catheter (intraventricular access device). Brineura is intended to be administered via the Codman\textsuperscript{\textregistered} HOLTER RICKHAM Reservoirs with the Codman\textsuperscript{\textregistered} Ventricular Catheter. The intraventricular access device must be implanted prior to the first infusion. It is recommended that the first dose be administered at least 5 to 7 days after device implantation.
- Brineura is intended to be administered with the B Braun Perfusor\textsuperscript{\textregistered} Space Infusion Pump System.
- Pre-treatment of patients with antihistamines with or without antipyretics or corticosteroids is recommended 30 to 60 minutes prior to the start of infusion.
Store upright in freezer (-25°C to -15°C); thaw at room temperature for ~60 minutes prior to administration

VI. Billing Code/Availability Information

HCPCS Code:

- J0567 – Injection, cerliponase alfa, 1 mg: 1 billable unit = 1 mg (effective 1/1/19)

NDC:

- Brineura 150 mg/5 mL (30 mg/mL) solution, two single-dose vials per carton co-packaged with Intraventricular Electrolytes Injection 5 mL in a single-dose vial: 68135-0811-xx

VII. References


Documentation Requirements:

The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the drug provided or services performed were not medically necessary, investigational or experimental, not within the scope of benefits afforded to the member and/or a pattern of billing or other practice has been found to be either inappropriate or excessive. Additional documentation supporting medical necessity for the services provided must be made available upon request to the Company. Documentation requested may include patient records, test results and/or credentials of the provider ordering or performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.
FOR MEDICAL BENEFIT COVERAGE REQUESTS:

Prior approval is required for HCPCS Codes J0567