Brineura®
(cerliponase alfa)

COVERAGE AUTHORIZATION GUIDE

BIOMARIN Rare Connections™

Uncommon Support for Rare Disease
1-866-906-6100 or
support@biomarin-rareconnections.com
BioMarin-RareConnections.com

Please see page 2 for Important Safety Information, including Boxed Warning for risk of anaphylaxis, and full Prescribing Information.

INDICATION AND IMPORTANT SAFETY INFORMATION

Brineura® (cerliponase alfa) injection for intraventricular use is indicated to slow the loss of ambulation in pediatric patients with neuronal ceroid lipofuscinosis type 2 (CLN2 disease), also known as tripeptidyl peptidase 1 (TPP1) deficiency.

WARNING: HYPERSENSITIVITY REACTIONS INCLUDING ANAPHYLAXIS

Patients treated with enzyme replacement therapies have experienced life-threatening hypersensitivity reactions, including anaphylaxis. These reactions have occurred during and up to 24 hours after completion of the Brineura infusion. Anaphylaxis has occurred during the early course of enzyme replacement therapy and after extended duration of therapy.

Administration of Brineura should be supervised by a healthcare provider knowledgeable in the management of hypersensitivity reactions including anaphylaxis. Initiate Brineura in a healthcare setting with appropriate medical monitoring and support measures, including access to cardiopulmonary resuscitation equipment. If a severe hypersensitivity reaction (e.g., anaphylaxis) occurs, discontinue Brineura and immediately initiate appropriate medical treatment, including use of epinephrine. Inform patients of the symptoms of life-threatening hypersensitivity reactions, including anaphylaxis and to seek immediate medical care should symptoms occur.

Patients less than 3 years of age may be at increased risk for developing hypersensitivity reactions with Brineura use compared to patients 3 years of age and older.

Observe patients closely during and after the infusion. The management of hypersensitivity reactions should be based on the severity of the reaction and may include temporarily interrupting the infusion, and/or treatment with antihistamines, antipyretics, and/or corticosteroids. Consider the risks and benefits of readministration of Brineura following an anaphylactic reaction. If the decision is made to readminister Brineura after the occurrence of anaphylaxis, ensure appropriately trained personnel and equipment for emergency resuscitation (including epinephrine and other emergency medicines) are readily available during infusion. Initiate subsequent infusion at approximately one-half the initial infusion rate at which the anaphylactic reaction occurred.

Contraindications

Brineura is contraindicated in patients with:

- any sign or symptom of acute, unresolved localized infection on or around the device insertion site (e.g., cellulitis or abscess); or suspected or confirmed CNS infection (e.g., cloudy CSF or positive CSF gram stain, or meningitis)
- any acute intraventricular access device-related complications (e.g., leakage, extravasation of fluid, or device failure)
- ventriculoperitoneal shunts

Recommendations Prior to Brineura Treatment

Premedication of patients with antihistamines with or without antipyretics or corticosteroids is recommended 30–60 minutes prior to the start of infusion. Brineura must only be administered via the intraventricular route using aseptic technique to reduce the risk of infection. Administer Brineura and the Intraventricular Electrolytes using the provided Administration Kit for use with Brineura components. Prior to each infusion, inspect the scalp for signs of intraventricular access device leakage or failure and for potential infection. Prior to each infusion of Brineura and when clinically indicated, send cerebrospinal fluid (CSF) samples for testing of cell count and culture. Replace the intraventricular access device reservoir prior to 4 years of single-puncture administrations.

Special Populations

Brineura is not recommended in patients less than 37 weeks post-menstrual age (gestational age at birth plus post-natal age) or those weighing less than 2.5 kg.

Brineura has not been studied in pregnancy or lactation.

WARNINGS AND PRECAUTIONS

Meningitis and Other Intraventricular Access Device-Related Infections

Bacterial meningitis requiring antibiotic treatment and removal of the device was reported during postmarketing use of Brineura. The signs and symptoms of infections may not be readily apparent in patients with CLN2 disease. To reduce the risk of infectious complications, Brineura should be administered by, or under the supervision of, a physician experienced in intraventricular administration.

Intraventricular Access Device-Related Complications

During the clinical trials and in postmarketing reports, intraventricular access device-related complications were reported (e.g., device leakage, device failure, extravasation of CSF fluid, or bulging of the scalp around or above the intraventricular access device). In case of intraventricular access device-related complications, discontinue the Brineura infusion and refer to the device manufacturer's labeling for further instructions.

Material degradation of the intraventricular access device reservoir was reported after approximately 4 years of administration, which may impact the effective and safe use of the device. The intraventricular access device should be replaced prior to 4 years of single-puncture administrations, which equates to approximately 105 administrations of Brineura.

Cardiovascular Adverse Reactions

Monitor vital signs before infusion starts, periodically during infusion, and post-infusion in a healthcare setting. Perform electrocardiogram (ECG) monitoring during infusion in patients with a history of bradycardia, conduction disorder, or with structural heart disease. In patients without cardiac abnormalities, regular 12-lead ECG evaluations should be performed every 6 months.

Infusion Associated Reactions (IAR) such as vomiting, seizure, rash, pyrexia, hypersensitivity, and anaphylactic reaction have been observed in patients treated with Brineura. If an IAR occurs, decreasing the infusion rate, temporarily stopping the infusion, and/or administering antihistamines and/or antipyretics may ameliorate the symptoms. Closely monitor patients who have experienced IARs when re-administering Brineura.

ADVERSE REACTIONS

In clinical trials, the most frequently reported adverse reactions (≥8%) were pyrexia, ECG abnormalities, decreased CSF protein, vomiting, seizures, device-related complications, hypersensitivity, increased CSF protein, hematoma, headache, irritability, pleocytosis, device-related infection, bradycardia, feeling jittery, and hypotension. The most frequent adverse reactions reported in patients < 3 years of age treated with Brineura were similar to those observed in patients > 3 years of age except for hypersensitivity reactions, which were reported in 5 of 8 (63%) in patients < 3 years of age at baseline compared with 0 of 6 in patients > 3 years of age at baseline. The most common manifestations of hypersensitivity were fever and vomiting. Such symptoms resolved over time or with administration of antipyretics, antihistamines and/or corticosteroids.

To report SUSPECTED ADVERSE REACTIONS, contact BioMarin Pharmaceutical Inc. at 1-866-906-6100, or FDA at 1-800-FDA-1088, or go to www.fda.gov/medwatch.

Please see accompanying full **Prescribing Information**, with Boxed Warning for risk of anaphylaxis or visit **www.Brineura.com**.

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For access-related questions regarding BRINEURA® (cerliponase alfa) payment or reimbursement, call **1-866-906-6100** or email support@biomarin-rareconnections.com.

Please see page 2 for Important Safety Information, including Boxed Warning for risk of anaphylaxis, and full Prescribing Information.

Brineura® (cerliponase alfa)

I. Introduction and Disclaimer

BRINEURA® (cerliponase alfa) injection for intraventricular use is indicated to slow the loss of ambulation in pediatric patients with neuronal ceroid lipofuscinosis type 2 (CLN2), also known as tripeptidyl peptidase 1 (TPP1) deficiency.[1] As an enzyme replacement therapy (ERT), BRINEURA helps replace the lysosomal enzyme TPP1, which is deficient in individuals with CLN2 disease. The efficacy of BRINEURA was assessed in a non-randomized single-arm dose escalation clinical study with extension. BRINEURA-treated patients were compared to untreated patients from a natural history cohort. The Motor domain of a CLN2 Clinical Rating Scale was used to assess disease progression. Over 96 weeks, Brineura helped maintain children's ability to walk, with or without assistance. BRINEURA'S efficacy was also assessed in an open label clinical study designed to enroll symptomatic and pre-symptomatic CLN2 patients less than 18 years of age, including patients younger than age 3. At week 169, patients younger than 3 years of age showed no decline in their motor domain score. BRINEURA has a well characterized safety profile. The most common adverse reactions in patients treated with BRINEURA include pyrexia, ECG abnormalities including bradycardia, hypersensitivity, decrease or increase in CSF protein, vomiting, seizures, hematoma, headache, irritability, pleocytosis, device-related infection, feeling jittery and hypotension. The most frequent adverse reactions in patients younger than 3 were similar to those observed in older patients except for hypersensitivity reactions. Patients younger than 3 may be at a higher risk for developing hypersensitivity reactions. BRINEURA is administered via intraventricular infusion every other week.[1]

BioMarin, the manufacturer of BRINEURA, wants to help every patient who is medically appropriate for the product have access to it. Therefore, BioMarin has compiled this guide with information gathered from third-party sources and experienced insurance reimbursement experts to serve as a source of information to assist your institution in obtaining approval and ongoing authorization for BRINEURA.

BioMarin provides this information as a convenience; it does not constitute legal advice or a recommendation regarding medical practice. Medical coding and billing may vary among payers, and are subject to change without notice because of frequently changing guidelines, laws, rules, and regulations. BioMarin makes no guarantee that the use of this information will prevent denials, delays, or differences of opinion with payers as to the correct form of billing that will expedite payment to providers of service.

For access-related questions regarding BRINEURA® (cerliponase alfa) payment or reimbursement, call **1-866-906-6100** or email **support@biomarin-rareconnections.com**.
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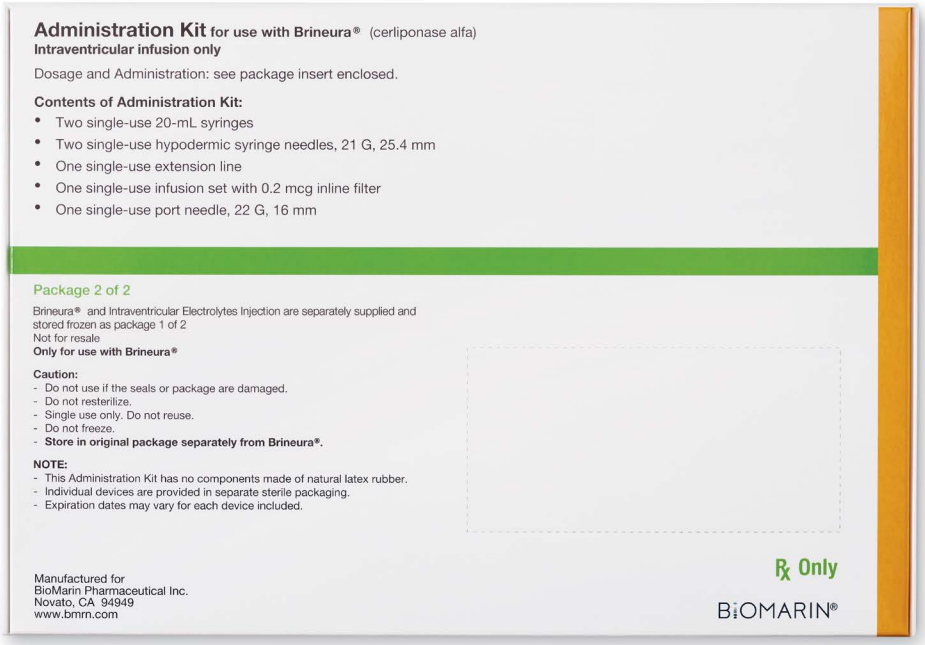
Please contact each applicable payer source for counsel when interpreting coding, coverage, and payment policies. This document provides assistance for FDA-approved indications that are documented in the Package Insert (see link below). Where reimbursement is sought for prescribed use and/or administration of this product that may be inconsistent with, or not expressly specified in, the FDA-cleared or -approved labeling outlined in the Package Insert, consult with your billing advisers or payers on handling such issues.



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Brineura® (cerliponase alfa)

II. Tips for Insurance Verification for BRINEURA® (cerliponase alfa)

Patient's benefits should be verified prior to the first dose of BRINEURA® (cerliponase alfa). Even if the patient has been under the care of your facility for a long time, you may not have gathered all of the information you may need for full coverage of BRINEURA. This is because different information is often necessary for payment of infused specialty drugs as compared with diagnostic tests, surgery, or an inpatient stay.

The tips below may assist your organization in verifying all benefits that may be necessary to ensure payment throughout the course of BRINEURA therapy. When you investigate the patient's benefits, these may be necessary for full coverage:

- Ascertain which parent's insurance is primary for the patient in the setting of care where BRINEURA is administered
- Determine whether a second opinion is required for any aspects of BRINEURA therapy
- Find the correct organization and its telephone numbers for prior approval or pre-certification (if prior authorization is not required) for drug, surgery, and setting of service care
- Know the plan type (HMO/PPO/other), and determine whether or not your institution is in-network for that specific plan
- Determine whether or not the payer allows rate negotiation for medically necessary and appropriate tertiary care
- Calculate possible deductibles impacting care delivered in the hospital inpatient or outpatient setting, eg, IV drugs, radiology, laboratory tests, chemotherapy administration, or surgery

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II. Tips for Insurance Verification for BRINEURA® (cerliponase alfa)

- Determine if there is episodic patient cost sharing for care delivered in the inpatient or outpatient setting, eg:
  - Flat copays for drugs; coinsurance payments
  - Coinsurance for surgery (if verifying for it), drugs, drug administration, and/or patient stay
  - Differing patient responsibility by tier for specialty drugs and amount of out-of-pocket costs for the applicable drug tier for BRINEURA® (cerliponase alfa)
- Determine if the plan has a lifetime, annual, or episodic out-of-pocket maximum
- Determine if the plan has catastrophic coverage (yes/no); if yes, what is the dollar figure where this coverage begins? Calculate the patient's current progress toward qualifying for catastrophic coverage
- Assess whether there are benefit "caps" (limits): lifetime or periodic
- If possible, determine the patient's current status regarding deductibles and out-of-pocket maximums, and current progress toward caps
- Document the specific insurer requirements:
  - Prior authorization/authorization renewal time frame
  - Re-certification of therapy, patient stay, or site of service
  - Case management parameters
  - Appeal guidelines

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III. Tips for Prior Authorization

Here are the common health plan forms and documents that may be needed in order to obtain prior authorization.

- **Request for Prior Authorization** (see Section IV) or health plan prior authorization form, if there is one
- Statement of Medical Necessity (see Section V)
- Copy of patient's health plan card
- Supporting documentation:
  - Patient history and physical findings or consultation report(s) discussing the patient's diagnosis and medical necessity for BRINEURA® (cerliponase alfa) therapy
  - Physicians' chart notes
  - Testing and laboratory results pertinent to a diagnosis of TPP1 deficiency
  - Any hospital admission or emergency room documents/notes
  - Any shared decision-making notes from multidisciplinary discussions or case conferences
  - ICD-10-CM codes pertinent to the diagnosis of TPP1 deficiency, BRINEURA administration, the placement of the reservoir, and/or secondary diagnoses for the patient. The authorizing body may also request the procedure codes for the reservoir and catheter (intraventricular access device) placement and/or the infusion. Possible codes that may be pertinent to BRINEURA treatment are in Section VI

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III. Tips for Prior Authorization

Health Plan Guidelines

- Understand each plan's specific guidelines for submitting prior authorization
  - Determine if the plan has a specific website where information can be completed online
  - Check if a specific form is necessary; otherwise, see the **Request for Prior Authorization** in Section IV
- Query if the health plan covers infusion therapies only in a particular setting, such as a doctor's office, an outpatient hospital, or inpatient hospital settings such as NICU, PICU, or regular floor or observation unit

Correct ID Numbers

- It is important to indicate the individual provider ID number versus the group practice/facility provider tax ID number on the Statement of Medical Necessity
- Patient ID number should be taken directly from the patient's health insurance card

Statement of Medical Necessity

- This form may need to be updated and resubmitted, as it is typically valid for only 6 to12 months. *Check with the authorizing entity to ascertain when renewal is required*

Deadlines

- Be sure to know and meet all deadlines for submitting the prior authorization request and other required documents
- Make sure you have clearly documented the date and time that the authorization was received
- Make sure to note the dates for renewal and any other reporting that the plan or utilization management company approving treatment requires

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III. Tips for Prior Authorization

Complete Records

- Keep a copy of everything that is submitted to the health plan. Log all calls, and document the date, time, and with whom you spoke in case you need to escalate within the health plan

Out-of-Network/Out-of-State Medical Exception

- BRINEURA® (cerliponase alfa) is currently offered at a limited number of US institutions, increasing the likelihood that a patient receiving BRINEURA will seek treatment at a site both geographically located outside of the patient's home state and outside of the patient's in-network, contracted health insurance benefits. As such, prior to administering BRINEURA, it may be important to obtain an out-of-network medical exception for a patient whose coverage does not have in-network benefits contracted with your institution.

- When seeking an out-of-network medical exception for the patient, it may be useful to (1) emphasize factors unique to the patient case, including whether the healthcare provider(s) place any urgency on access to treatment and (2) describe your healthcare provider(s) and/or institution's expertise with treating Batten disease, and experience or preparedness treating with BRINEURA.

Site of Service Justification

- There are various settings where BRINEURA and/or the associated procedures can be administered. It is important to explain in the prior authorization request the intended site of service and the justification for using that site of service for surgery and/or treatment

- In addition, a prior authorization can often be obtained for the product, site of service, and any associated procedure at the same time; conversely, you may find that authorizations for these have to be obtained separately

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IV. An Example Prior Authorization Request

Prior Authorization Request

Date: _____ Time: _____

Contact Person: _____

Telephone Number of Contact Person: _____

Email of Contact Person: _____

Insurance Company Name and Address: _____

Patient's Legal First Name and Last Name*: _____

Date of Birth: _____

Subscriber Name: _____

Subscriber ID Number: _____

Subscriber Group Number: _____

Subscriber Plan Number (if applicable): _____

Effective Date of Coverage: _____

Treating Physician(s): _____

Provider (NPI) Number: _____

Provider Tax ID Number (TIN): _____

*Patient's name must be **exactly** the way it appears on the insurance card.

RE: Authorization for BRINEURA® (cerliponase alfa)

Dear [Payer Contact],

Please see the enclosed documentation to support the request for prior authorization for my patient [Patient Name], who has been diagnosed with tripeptidyl peptidase 1 (TPP1) deficiency. The patient will be treated with BRINEURA® (cerliponase alfa) for TPP1 deficiency. On April 27, 2017, the FDA first approved BRINEURA and currently it is indicated to slow the loss of ambulation in pediatric patients with neuronal ceroid lipofuscinosis type 2 (CLN2), also known as tripeptidyl peptidase 1 (TPP1) deficiency. CLN2 disease is a rare, rapidly progressing neurodegenerative disease. We request the most expedited review of the prior authorization request along with enclosed information. Please provide authorization of surgical placement of the ICV access device necessary for the therapy and for the ongoing intraventricular treatment with BRINEURA.

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IV. An Example Prior Authorization Request

Clinical History

- *Provide brief description of:*
  - *Patient age*
  - *Test results verifying diagnosis*
  - *Functional status*
  - *Treatments to date*
- *Include underlying health issues, symptoms, developmental history, and any disabilities or other factors that impact the treatment decision*
- *Include supporting medical records such as:*
  - *Clinical notes/history and physical/consultation(s), medication records, relevant laboratory reports/results*

Rationale for BRINEURA® (cerliponase alfa) Therapy

On April 27, 2017, the FDA first approved BRINEURA and currently it is indicated to slow the loss of ambulation in pediatric patients with neuronal ceroid lipofuscinosis type 2 (CLN2), also known as tripeptidyl peptidase 1 (TPP1) deficiency.

Each infusion consists of 3.3 to 10 mL of BRINEURA followed by 2 mL of Intraventricular Electrolytes. The intraventricular electrolytes solution is used to fully administer BRINEURA and to maintain patency of the intraventricular access device.

- *Include benefits of BRINEURA for the treatment of TPP1 deficiency in this patient*
- *Provide patient's prognosis without treatment*
- *Note site of care and rationale (NICU, PICU, outpatient)*
- *Please see Section VI for potential billing codes for the proposed treatment, if required for prior authorization*

Rationale for Placement of intraventricular access device (ICV device)

BRINEURA is administered to the cerebrospinal fluid (CSF) by infusion via a surgically implanted reservoir and intraventricular catheter (intraventricular access device). The intraventricular access device must be implanted prior to the first infusion. The implanted intraventricular access device is for accessing the cerebral ventricles for therapeutic drug administration.

Therefore, if the payer requires codes for approval, please refer to your institution's reservoir placement coding policies, or contact the specified device manufacturer. Section VI of this guide contains some possible codes for the placement of the ICV access device

The recommended reservoirs and catheter below have been tested and are compatible with the provided needle.[2]*

- *Codman®-branded HOLTER RICKHAM reservoirs: part numbers 82-1625, 82-1621, 82-1616*

* These specific reservoirs have been evaluated for administration of BRINEURA. Other types and brands of reservoirs may not be appropriately cleared for drug administration.

Gauthier-Campbell C, Lester T, Sluzky V. Regulatory challenges of brain delivered therapies: a combination product perspective. *Pharmaceut Reg Affairs*. 2018;7:1-7.

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IV. An Example Prior Authorization Request

- *Codman®-branded ventricular catheter: part number 82-1650*
- *Note site of care for procedure and rationale (NICU, PICU, outpatient, observation)*

Rationale for Out-of-Network/Out-of-State Medical Exception

- *If your institution requests an out-of-network or out-of-state medical exception, include rationale here.*

Conclusion

My patient [Patient Name] has [patient diagnosis]. [He/She] has been diagnosed with TPP1 deficiency. The patient experienced [history of neurological symptoms and deficits, developmental history]. TPP1 deficiency was affirmatively diagnosed via [include laboratory and genetic testing]. Please review this information for expedited prior authorization of BRINEURA® (cerliponase alfa) therapy, site of service, and (as appropriate) the placement of the ICV access device.

Thank you for your time and immediate attention to this request.

Sincerely,

[Physician's name, contact information, and credentials]

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IV. An Example Prior Authorization Request

Suggested enclosures by HCP:

- Package Insert
- Medical records
  - History and physical or consultation report
  - Laboratory reports verifying the diagnosis

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V. An Example Statement of Medical Necessity

Statement of Medical Necessity

Date: _____

Contact Person: _____

Telephone Number of Contact Person: _____

Email of Contact Person:_____

Insurance Company Name and Address: _____

_____

Patient's Legal First Name and Last Name: _____

Subscriber Name: _____

Relationship to Patient: _____

Subscriber ID Number:_____

Subscriber Group Number: _____

Subscriber Plan Number (if applicable): _____

Effective Date of Coverage:_____

Re: BRINEURA® (cerliponase alfa) therapy

To Whom It May Concern:

I am writing on behalf of my patient [Patient Name] to request that [Insurance Company Name] approve coverage and appropriate payment for BRINEURA® (cerliponase alfa) through expedited review. BRINEURA is a medically necessary treatment for [Patient Name], who has been diagnosed with tripeptidyl peptidase 1 (TPP1) deficiency. This letter provides information about my patient's medical history, diagnosis, and details regarding the appropriateness and medical necessity of the treatment plan with BRINEURA.

Patient History and Diagnosis

- *Provide brief description of patient's age, functional status, and developmental history*
- *Include laboratory and genetic history verifying the diagnosis*
- *Include underlying health issues, symptoms, and any disabilities or other factors that impact the treatment decision*
- *Include supporting medical records such as:*
  - *Clinical notes/history and physical/consultation(s), medication records, relevant laboratory reports/results*

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V. An Example Statement of Medical Necessity

Disease and Treatment Information

BRINEURA® (cerliponase alfa) injection is FDA approved to slow the loss of ambulation in pediatric patients with neuronal ceroid lipofuscinosis type 2 (CLN2), also known as tripeptidyl peptidase 1 (TPP1) deficiency.

BRINEURA is administered to the cerebrospinal fluid (CSF) by infusion via a surgically implanted reservoir and catheter (intraventricular access device). The intraventricular access device must be implanted prior to the first infusion. The implanted intraventricular access device is for accessing the cerebral ventricles for therapeutic drug administration.

Each infusion consists of 3.3 to 10 mL of BRINEURA followed by 2 mL of Intraventricular Electrolytes. The intraventricular electrolytes solution is used to fully administer BRINEURA and to maintain patency of the intraventricular access device. BRINEURA patients should also be observed by clinicians following therapy.

- *Include benefits of BRINEURA for the treatment of this particular patient*
- *Provide patient's prognosis without treatment*
- *Note site of care (NICU, PICU, outpatient) for BRINEURA treatment and surgery for the ICV access device reservoir placement*
- *See example prior authorization request—If your institution requests an out-of-network or out-of-state medical exception, include rationale here.*

We are requesting that you approve treatment with BRINEURA for this child, [Patient Name]. Should you require additional information, please contact me.

Sincerely,

[Physician's name, contact information, and credentials]

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V. An Example Statement of Medical Necessity

Suggested enclosures:

- Package Insert
- Clinical notes, eg, history and physical, consultation reports
- Relevant laboratory reports

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VI. Possible Coding Scenarios for BRINEURA® (cerliponase alfa) in All Settings

DIAGNOSIS CODES FOR THE DRUG THERAPY INDICATION (USED IN ALL SETTINGS)

DRUG INDICATION	ICD-10-CM CODE 2021	CODE DESCRIPTION
BRINEURA is a hydrolytic lysosomal N-terminal tripeptidyl peptidase indicated for patients with CLN2 disease, also known as tripeptidyl peptidase 1 (TPP1) deficiency.[a]	E75.4	Neuronal Ceroid Lipofuscinosis[a]

[a] While this is not an exact code for TPP1 deficiency, it is the closest descriptor in the ICD-10-CM Tabular List of codes.

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VI. Possible Coding Scenarios for BRINEURA® (cerliponase alfa) in All Settings

POSSIBLE SECONDARY DIAGNOSIS WHILE PATIENT ON BRINEURA® (CERLIPONASE ALFA) THERAPY

DRUG INDICATION	ICD-10-CM CODE 2021	CODE DESCRIPTION
Medical necessity for drug therapy biweekly for life	Z79.899	Other long-term drug therapy (Z codes represent reasons for encounters. A corresponding procedure code must accompany a Z code if a procedure is performed)

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VI. Possible Coding Scenarios for BRINEURA® (cerliponase alfa) in All Settings

POSSIBLE PROCEDURE CODES FOR ICV ACCESS DEVICE PLACEMENT

CODE FAMILY	ICD-10-PCS CODE 2021	CODE DESCRIPTION
Insertion of Infusion Device Into the Brain	00H003Z	Insertion of Infusion Device, Open Approach
	00H033Z	Insertion of Infusion Device, Percutaneous Approach
	00H043Z	Insertion of Infusion Device, Percutaneous Endoscopic Approach
	00H603Z	Insertion of Infusion Device Into Cerebral Ventricle, Open Approach
	00H633Z	Insertion of Infusion Device Into Cerebral Ventricle, Percutaneous Approach
	00H643Z	Insertion of Infusion Device Into Cerebral Ventricle, Percutaneous Endoscopic Approach

Outpatient Procedures

CODE FAMILY	CPT CODE 2021	CODE DESCRIPTION
Implantation of ventricular, catheter, reservoir, or other device	61210	Burr hole(s); for implanting ventricular catheter, reservoir, EEG electrode(s), pressure recording device, or other cerebral monitoring device (separate procedure)
	61215	Insertion of subcutaneous reservoir, pump, or continuous infusion system for connection to ventricular catheter

The following are recommended ICV access device components, which have tested and are compatible with the provided needle: Codman®-branded HOLTER RICKHAM reservoirs: part numbers 82-1625, 82-1621, 82-1616; Codman®-branded ventricular catheter: part number 82-1650

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Please see page 2 for Important Safety Information, including Boxed Warning for risk of anaphylaxis, and full Prescribing Information.

VI. Possible Coding Scenarios for BRINEURA® (cerliponase alfa) in All Settings

BIWEEKLY DRUG INFUSION PROCEDURE

Inpatient Procedures

CODE FAMILY	ICD-10-PCS CODE 2021	CODE DESCRIPTION
Introduction of a substance	3E0Q3GC	Introduction of Other Substance Into Cranial Cavity and Brain, Percutaneous Approach
Irrigation and exploration	3E1Q38Z	Irrigation of Cranial Cavity and Brain Using Irrigating Substance, Percutaneous Approach **OR**
Introduction of a substance	3E0Q37Z	Introduction of Other Substance Into Cranial Cavity and Brain, Percutaneous Approach, Electrolytes and Water Balance Substance

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Brineura® (cerliponase alfa)

VI. Possible Coding Scenarios for BRINEURA® (cerliponase alfa) in All Settings

OUTPATIENT PROCEDURES AND PROFESSIONAL FEES

There are no definitive codes for a therapeutic infusion of 2 to 4.5 hours (depending on dose and volume administered) and an INTRAVENTRICULAR irrigation in the brain. The codes listed below represent possibilities only. You may choose the one(s) that best matches the documentation in the chart or employ a different code identified in your own research or through discussions with your patient's payer. Please note: The patient may also have charges for outpatient observation room and board, plus professional fee

CODE FAMILY	CPT CODE 2021	CODE DESCRIPTION
Injection, Drainage, or Aspiration Procedures on the Skull, Meninges, and Brain	61026	Ventricular puncture through previous burr hole, fontanelle, suture, or implanted ventricular catheter/ reservoir; with injection of medication or other substance for diagnosis or treatment
Injection, Drainage, or Aspiration Procedures on the Skull, Meninges, and Brain	61070	Puncture of shunt tubing or reservoir for aspiration or injection procedure
Chemotherapy Administration	96542	Chemotherapy injection, subarachnoid or intraventricular via subcutaneous reservoir, single or multiple agents
Chemotherapy Administration	96549	Unlisted chemotherapy administration
Neurology Procedures	64999	Unlisted nervous system procedure
Medicine Procedure	95990	Refilling and maintenance of implantable pump or reservoir for drug delivery, spinal (intrathecal, epidural) or brain (intraventricular), includes electronic analysis of pump, when performed
Medicine Procedure	95991	Refilling and maintenance of implantable pump or reservoir for drug delivery, spinal (intrathecal, epidural) or brain (intraventricular), includes electronic analysis of pump, when performed; requiring skill of a physician or other qualified healthcare professional
Modifiers	-22	Unusual services
Modifiers	-51	Multiple services

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VI. Possible Coding Scenarios for BRINEURA® (cerliponase alfa) in All Settings

DRUG BILLING FOR BRINEURA® (CERLIPONASE ALFA)

CODE FAMILY	CODE 2021	CODE DESCRIPTION
National Drug Codes (NDC) Please use HIPAA 5-4-2 format[a]	**68135-0811-02 (Carton),**[b] which contains: 68135-0500-00 (2 BRINEURA® [cerliponase alfa] vials) 68135-0495-04 (Intraventricular Electrolytes vial)	Specific codes to BRINEURA and to the intraventricular electrolytes infusate
HCPCS Code	J0567	Injection, cerliponase alfa, 1mg
Revenue Codes[c]	0250	Pharmacy: General
Revenue Codes	0258	Pharmacy: IV solutions
Revenue Codes	0261	IV Therapy: Infusion pump
Revenue Codes	0262	IV Therapy: IV therapy/pharmacy services
Revenue Codes	0263	IV Therapy: IV therapy/drug/supply/delivery
Revenue Codes	0636	Pharmacy: Drugs requiring detailed coding

[a] Not all payers require the HIPAA format of 5-4-2 numbers.
[b] The carton National Drug Code most likely will be used for billing.
[c] Revenue codes reference: https://med.noridianmedicare.com/web/jea/topics/claim-submission/revenue-codes.

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Brineura® (cerliponase alfa)

VII. An Example Appeal Letter for BRINEURA® (cerliponase alfa)

Appeal Letter

Date: _____

Contact Person: _____

Re: [Patient First Name] [Patient Last Name]

Subscriber Name: _____

Subscriber ID Number: _____

Subscriber Group Number: _____

Subscriber Plan Number (if applicable): _____

Insurance Company Name and Address: _____

_____

Diagnosis and/or Procedure Code(s): _____

Date of Denial: _____

Dear [Name of Contact]:

This letter serves as a formal appeal for the most expedited review of coverage for [BRINEURA® (cerliponase alfa) and/or the related procedure to place the ICV access device], which was originally denied to [Patient Name] on [Date of Service] for [insert denial reason].

[Patient Name] has been under treatment for [Diagnosis and/or Procedure Code—see Section VI] since [Date of Initial Treatment]. [Insurance Company Name] has stated that [BRINEURA and/or the procedure for the ICV access device insertion] is not covered because [denial reason].

Treatment Information

On April 27, 2017, the FDA first approved BRINEURA and currently it is indicated to slow the loss of ambulation in pediatric patients with neuronal ceroid lipofuscinosis type 2 (CLN2), also known as tripeptidyl peptidase 1 (TPP1) deficiency. CLN2 disease is a rapidly progressive neurodegenerative disease, and it's critical that treatment begin for this patient as soon as possible.

Appeal for BRINEURA and/or the placement of the ICV access device

On [Date], [Patient Name] was infused with [insert volume of Brineura solution] of BRINEURA followed by 2 mL of intraventricular electrolytes solution at [insert site of service: eg, PICU, outpatient]. The product was administered at [insert site of care: eg, PICU, inpatient bed, or hospital outpatient]. A catheter was inserted into the [right/left] ventricle of the brain, and a reservoir was accessed to infuse BRINEURA at [insert infusion rate]. The infusion takes approximately 2 to 4.5 hours. Then a proprietary intraventricular electrolytes solution was used to fully administer all the BRINEURA solution and to maintain patency of the intraventricular access device.

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VII. An Example Appeal Letter for BRINEURA® (cerliponase alfa)

BRINEURA® (cerliponase alfa) must only be administered via the intraventricular route. It's critical that treatment begin for this patient as soon as possible.

In summary, BRINEURA was administered to the cerebrospinal fluid (CSF) by infusion via a surgically implanted reservoir and catheter (intraventricular access device) that was done in the [insert site of care: eg, PICU, outpatient] on [Date]. The intraventricular access device was implanted prior to the first infusion, which was administered on [Date]. The implanted intraventricular access device is necessary to access the cerebral ventricles for therapeutic drug administration.

Patient History and Diagnosis
[Patient Name] is a [Age]-year-old [male/female], who has been under treatment for CLN2 disease, also known as tripeptidyl peptidase 1 (TPP1) deficiency, since [Date]. BRINEURA is the only known treatment for this deficiency.

For Denial of Product
[Insurance Company Name] should provide adequate coverage for BRINEURA because it is medically necessary for CLN2 disease, also known as TPP1 deficiency, and clinically appropriate for this patient, [Name].

- *Insert justification for site of service if applicable*

For Denial of Procedure
[Insurance Company Name] should provide adequate coverage for the procedure to implant the ICV access device because it is medically necessary for the administration of BRINEURA for TPP1 deficiency. According to its FDA approval, BRINEURA may only be administered via the intraventricular route. It's critical that treatment begin for this patient as soon as possible.

- *Insert justification for site of service if applicable*
- *Include underlying health issues, symptoms, developmental history, and any disabilities or other factors that impacted the treatment decision*
- *Include supporting medical records such as:*
  - *Clinical notes, medication records, relevant laboratory reports/results*
- *Include site of care justification depending on denial reason*
- *Reference applicable product and procedure codes as needed depending on denial reason. (See Section VI for relevant product and procedure codes)*

On behalf of [Patient Name], we would appreciate your reconsideration of coverage for BRINEURA and/or the procedure to insert the ICV access device. Please call me at [Primary Treating Site Phone Number] if I can be of further assistance or you require additional information.

Sincerely,

[Treating Provider Name], [Treating Provider Title], [Contact Information], [Provider Number]

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Brineura® (cerliponase alfa)

VII. An Example Appeal Letter for BRINEURA® (cerliponase alfa)

Suggested enclosures by HCP:

- Package Insert
- FDA approval letter
- Clinical notes
- Medication records and any relevant laboratory reports

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Reference: 1. BRINEURA® [package insert]. Novato, CA: BioMarin Pharmaceutical Inc; 2024. **2.** Gauthier-Campbell C, Lester T, Sluzky V. Regulatory challenges of brain delivered therapies: a combination product perspective. *Pharmaceut Reg Affairs*. 2018;7:1-7.

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