Cerliponase alfa

Targets (1) Biointeractions (1)

IDENTIFICATION

Name

Cerliponase alfa

Accession Number

DB13173

Type

Biotech

Groups

Approved, Investigational

Biologic Classification

Protein Based Therapies
Recombinant Enzymes

Description

Cerliponase alfa is an enzyme replacement treatment for a specific form of Batten disease. It was the first FDA-approved treatment to slow loss of walking ability (ambulation) in symptomatic pediatric patients 3 years of age and older with late infantile neuronal ceroid lipofuscinosis type 2 (CLN2), also known as tripeptidyl peptidase-1 (TPP1) deficiency. Intraventricular administration of the drug allows significant uptake into the brain. Cerliponase alfa was approved in April, 2017 (as Brineura).

Protein chemical formula

Not Available

Protein average weight

SYSPEPDQRRTLPPGWVSLGRADPEEELSLTFALRQQNVERLSELVQAVSDPSSPQYGKY
LTLENVADLVRPSPLTLHTVQKWLLAAGAQKCHSVITQDFLTCWLSIRQAELLLPGAEFH
HYVGGPTETHVVRSPHPYQLPQALAPHVDFVGGLHRFPPTSSLRQRPEPQVTGTVGLHLG
VTPSVIRKRYNLTSQDVGSGTSNNSQACAQFLEQYFHDSDLAQFMRLFGGNFAHQASVAR
VVGQQGRGRAGIEASLDVQYLMSAGANISTWVYSSPGRHEGQEPFLQWLMLLSNESALPH
VHTVSYGDDEDSLSSAYIQRVNTELMKAAARGLTLLFASGDSGAGCWSVSGRHQFRPTFP
ASSPYVTTVGGTSFQEPFLITNEIVDYISGGGFSNVFPRPSYQEEAVTKFLSSSPHLPPS
SYFNASGRAYPDVAALSDGYWVVSNRVPIPWVSGTSASTPVFGGILSLINEHRILSGRPP
LGFLNPRLYQQHGAGLFDVTRGCHESCLDEEVEGQGFCSGPGWDPVTGWGTPNFPALLKT
LLNP

Download FASTA Format

Synonyms

Immature cell growth-inhibiting gene 1 protein

Immature human tripeptidyl-peptidase 1

Immature lysosomal pepstatin-insensitive protease

Immature tripeptidyl-peptidase I

External IDs

BMN 190 / BMN-190

Prescription Products

Search

NAME	DOSAGE	STRENGTH	ROUTE	LABELLER	MARKETING START	MARKETING END		
Brineura	Kit	150 mg/5mL	Intraventricular	Biomarin International Limited	2017-04-27	Not applicable		

Showing 1 to 1 of 1 entries

‹ ›

Categories

Hydrolytic Lysosomal N-terminal Tripeptidyl Peptidase

P-glycoprotein/ABCB1 Substrates

X8R2D92QP1

CAS number

151662-36-1

PHARMACOLOGY

Indication

Cerliponase alfa is a treatment for late infantile neuronal ceroid lipofuscinosis type 2 (CLN2) disease to decelerate the progressive motor function decline in patients 3 years of age and older. CLN2 disease is a form of Batten disease, a rare inherited neurodegenerative disorder and is associated with seizures, ataxia, rapid loss of language and motor functions, blindness, and early death [4]. It is caused by the lack the lysosomal enzyme tripeptidyl peptidase-1 (TPP1) and subsequent accumulation of lysosomal storage materials normally metabolized by this enzyme in the central nervous system.

Associated Conditions

Neuronal ceroid lipofuscinosis type 2

Pharmacodynamics

Cerliponase alfa contains the active substance tripeptidyl peptidase-1 (rhTPP1), a recombinant human lysosomal exopeptidase which cleaves the N-terminal of tripeptides with a broad substrate specificity. Cerliponase alfa slows the progressive decline in motor function caused by abnormal motor signalling in the brain by restoring the normal levels and activity of TPP1.

Mechanism of action

The mature form of enzyme contains 5 consensus N-glycosylation sites with high mannose, phosphorylated high mannose and complex glycosylation structures. It is taken up by LINCL fibroblasts and translocated to the lysosomes through the Cation Independent Mannose-6-Phosphate Receptor (CI-MPR, also known as M6P/IGF2 receptor). Cerliponase alfa is activated in the lysosome under low pH conditions and the activated proteolytic form of rhTPP1 cleaves tripeptides from the N-terminus of stored proteins.

U	Cation-independent mannose-6-phosphate receptor
ligand	
Human	

Volume of distribution

The estimated CSF volume of distribution of cerliponase alfa following intraventricular infusion of 300mg of Brineura (median Vss = 245 mL) exceeds the typical CSF volume (100 mL) [Label].

Protein binding

Not Available

Metabolism

Predicted to be metabolized through peptide hydrolysis.

Route of elimination

Not Available

Half life

Refer to FDA Label

Clearance

Refer to FDA Label

Toxicity

No data from carcinogenicity, genotoxicity, and fertility studies. Unwanted effects of cerliponase alfa treatment include pyrexia, ECG abnormalities, decreased CSF protein, seizure and hypersensitivity.

Affected organisms

Humans and other mammals

Pathways

Not Available

Pharmacogenomic Effects/ADRs

Not Available

INTERACTIONS

INVESTIGATIONAL EXPERIMENTAL

Search

DRUG	INTERACTION
Acetaminophen	The serum concentration of Cerliponase alfa can be increased when it is combined with Acetaminophen.
Albendazole	The serum concentration of Cerliponase alfa can be increased when it is combined with Albendazole.
Amiodarone	The serum concentration of Cerliponase alfa can be increased when it is combined with Amiodarone.
Amlodipine	The serum concentration of Cerliponase alfa can be increased when it is combined with Amlodipine.
Amoxapine	The serum concentration of Cerliponase alfa can be increased when it is combined with Amoxapine.
Amsacrine	The serum concentration of Cerliponase alfa can be increased when it is combined with Amsacrine.
Azelastine	The serum concentration of Cerliponase alfa can be increased when it is combined with Azelastine.
Azithromycin	The serum concentration of Cerliponase alfa can be increased when it is combined with Azithromycin.
Benzyl alcohol	The serum concentration of Cerliponase alfa can be increased when it is combined with Benzyl alcohol.
Bepridil	The serum concentration of Cerliponase alfa can be increased when it is combined with Bepridil.

Showing 1 to 10 of 127 entries

‹ ›

Food Interactions

Not Available

REFERENCES

General References

10.1073/pnas.1217733110. Epub 2013 Mar 18. [PubMed:23509301]
3. Pal A, Kraetzner R, Gruene T, Grapp M, Schreiber K, Gronborg M, Urlaub H, Becker S, Asif AR, Gartner J, Sheldrick GM, Steinfeld R: Structure of tripeptidyl-peptidase I provides insight into the molecular basis of late infantile neuronal ceroid lipofuscinosis. J Biol Chem. 2009 Feb 6;284(6):3976-84. doi: 10.1074/jbc.M806947200. Epub 2008 Nov 26. [PubMed:19038966]
4. Intracerebroventricular Cerliponase Alfa (BMN 190) in Children with CLN2 Disease: Interim Results from a Phase 1/2, Open-Label, Dose-Escalation Study [Link]

External Links

KEGG Drug

D10813

PubChem Substance

347911440

ChEMBL

CHEMBL3544921

Wikipedia

Cerliponase_alfa

FDA label

Download (793 KB)

CLINICAL TRIALS

Clinical Trials

Search

PHASE	STATUS	PURPOSE	CONDITIONS	COUNT
1, 2	Active Not Recruiting	Treatment	CLN2 Disease / CLN2 Disorder / Jansky-Bielschowsky Disease / Juvenile Neuronal Ceroid Lipofuscinosis / Late-Infantile Neuronal Ceroid Lipofuscinosis Type 2	1
1, 2	Completed	Treatment	CLN2 Disease / Jansky-Bielschowsky Disease / Juvenile Neuronal Ceroid Lipofuscinosis / Late-Infantile Neuronal Ceroid Lipofuscinosis Type 2	1

Showing 1 to 3 of 3 entries

PHARMACOECONOMICS

Manufacturers

Not Available

Packagers

Not Available

Dosage forms

Search

FORM	ROUTE	STRENGTH
Kit	Intraventricular	150 mg/5mL

Showing 1 to 1 of 1 entries

Prices

Not Available

Patents

Not Available

PROPERTIES

State

Liquid

Experimental Properties

Not Available

Not Available

Kingdom

Organic Compounds

Super Class

Organic Acids

Class

Carboxylic Acids and Derivatives

Sub Class

Amino Acids, Peptides, and Analogues

Direct Parent

Peptides

Alternative Parents

Not Available

Substituents

Not Available

Molecular Framework

Not Available

External Descriptors

Not Available

TARGETS

1. Cation-independent mannose-6-phosphate receptor

Kind

Pharmacological action

Unknown

Actions

Ligand

General Function

Transporter activity

Specific Function

Transport of phosphorylated lysosomal enzymes from the Golgi complex and the cell surface to lysosomes. Lysosomal enzymes bearing phosphomannosyl residues bind specifically to mannose-6-phosphate r...

Gene Name

IGF2R

Uniprot ID

P11717

Uniprot Name

Cation-independent mannose-6-phosphate receptor

Molecular Weight

274372.42 Da

References

1. Meng Y, Sohar I, Wang L, Sleat DE, Lobel P: Systemic administration of tripeptidyl peptidase I in a mouse model of late infantile neuronal ceroid lipofuscinosis: effect of glycan modification. PLoS One. 2012;7(7):e40509. doi: 10.1371/journal.pone.0040509. Epub 2012 Jul 6. [PubMed:22792360]

Drug created on April 28, 2017 13:55 / Updated on October 01, 2018 15:27

Support

FAQ

Help

Email Support

Commercial Products

API Pricing

API Docs

Data Licenses

Support

This project is supported by the **Canadian Institutes of Health Research** (award #111062), **Alberta Innovates - Health Solutions**, and by **The Metabolomics Innovation Centre (TMIC)**, a nationally-funded research and core facility that supports a wide range of cutting-edge metabolomic studies. TMIC is funded by **Genome Alberta**, **Genome British Columbia**, and **Genome Canada**, a not-for-profit organization that is leading Canada's national genomics strategy with funding from the federal government. Maintenance, support, and commercial licensing is provided by **OMx Personal Health Analytics, Inc.** Designed by **Educe Design & Innovation Inc.**