

SAFETY DATA SHEET

SECTION 1 - IDENTIFICATION OF THE SUBSTANCE/MIXTURE AND OF THE COMPANY/UNDERTAKING

Contact information

General



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Product identifier	rhTPP1 enzyme (BMN 190) formulated product
Synonyms	Cerliponase alfa, Recombinant human tripeptidyl peptidase-1 formulated product
Trade names	Brineura [®]
Chemical family	Mixture
Relevant identified uses of the substance or mixture and uses advised against	Commercial bulk formulated pharmaceutical product/mixture used in treatment of CLN2 disease (tripeptidyl peptidase-1 enzyme deficiency).
Note	This SDS is written to address potential worker health and safety issues associated with the handling of the formulated product.

SECTION 2 - HAZARDS IDENTIFICATION

Classification of the substance or mixture

Globally Harmonized System [GHS] Respiratory sensitizer - Category 1.

Label elements

SECTION 2 - HAZARDS IDENTIFICATION ...continued

GHS hazard pictogram**GHS signal word** Danger**GHS hazard statements** H334 - May cause allergy or asthma symptoms or breathing difficulties if inhaled.**GHS precautionary statements** P261 - Avoid breathing mist or vapor. P285 - In case of inadequate ventilation wear respiratory protection. P304 + P341 - IF INHALED: If breathing is difficult, remove victim to fresh air and keep at rest in a position comfortable for breathing. P342 + P311 - If experiencing respiratory symptoms: Call a POISON CENTER or doctor/physician. P501 - Dispose of contents/container to location in accordance with local/regional/national/international regulations.**Other hazards**

In human clinical studies, common adverse effects associated with doses of 300 mg BMN 190 administered every 14 days (over a period of 91 weeks) and with a mean duration of exposure of 63 weeks were consistent with CLN2 disease, the pediatric population, and enzyme replacement therapy, and included pyrexia, seizure, vomiting, upper respiratory tract infections, epilepsy, and hypersensitivity. Adverse effects leading to interruption, incompleteness, or discontinuation of infusions occurred rarely. Subjects who experienced infusion changes (interrupted, incomplete, or missed infusions) secondary to adverse effects received and tolerated subsequent infusions without recurrence of the events. The most commonly reported serious adverse effect was hypersensitivity.

As a recombinant human protein and enzyme, BMN 190 has the potential to cause an allergic skin or respiratory reaction (e.g., potential to cause anaphylaxis from repeated exposure).

Note This mixture is classified as hazardous under GHS as implemented by Regulation EC No 1272/2008 (EU CLP), WHMIS 2015 (Health Canada), and Hazard Communication Standard No. 1910.1200 (US OSHA).

SECTION 3 - COMPOSITION/INFORMATION ON INGREDIENTS

<u>Ingredient</u>	<u>CAS #</u>	<u>EINECS/ELIN CS#</u>	<u>Amount</u>	<u>GHS Classification</u>
BMN 190	151662-36-1	N/A	2-4%	RS1: H334

SECTION 3 - COMPOSITION/INFORMATION ON INGREDIENTS ...continued

Note The ingredient listed above is considered hazardous. The remaining components are non-hazardous and/or present at amounts below reportable limits. See Section 16 for full text of GHS classifications. The GHS classifications are based on Regulation (EC) 1272/2008, WHMIS 2015 and Hazard Communication Standard No. 1910.1200.

SECTION 4 - FIRST AID MEASURES

Description of first aid measures

Immediate Medical Attention Needed	Yes
Eye Contact	In the event of a chemical exposure, immediately irrigate eyes with copious quantities of water for at least 15 minutes. Remove contact lenses as soon as practical. Do not delay irrigation while waiting for contact lens removal. If irritation occurs or persists, notify medical personnel and supervisor.
Skin Contact	Wash exposed area with soap and water and remove contaminated clothing/shoes. If irritation occurs or persists, notify medical personnel and supervisor.
Inhalation	Immediately move exposed subject to fresh air. If not breathing, give artificial respiration. If breathing is labored, administer oxygen. Immediately notify medical personnel and supervisor.
Ingestion	If swallowed, call a physician immediately. Do not induce vomiting unless directed by medical personnel. Do not give anything to drink unless directed by medical personnel. Never give anything by mouth to an unconscious person. Notify medical personnel and supervisor.
Protection of first aid responders	See Section 8 for Exposure Controls/Personal Protection recommendations.
Most important symptoms and effects, both acute and delayed	See Sections 2 and 11
Indication of immediate medical attention and special treatment needed, if necessary	Medical conditions aggravated by exposure: None known or reported. Treat symptomatically and supportively.

SECTION 5 - FIREFIGHTING MEASURES

Extinguishing media Use water spray (fog), foam, dry powder, or carbon dioxide, as appropriate for surrounding fire and materials.

SECTION 5 - FIREFIGHTING MEASURES ...continued

Specific hazards arising from the substance or mixture No information identified. May emit toxic gases of carbon monoxide and carbon dioxide, phosphorus-containing compounds, and chlorine-containing compounds.

Flammability/Explosivity No explosivity or flammability data identified. As product is an aqueous solution, it is not expected to be flammable or explosive.

Advice for firefighters In case of fire in the surroundings: use the appropriate extinguishing agent. Wear full protective clothing and an approved, positive pressure, self-contained breathing apparatus. Decontaminate all equipment after use.

SECTION 6 - ACCIDENTAL RELEASE MEASURES

Personal precautions, protective equipment and emergency procedures If product is released or spilled, take proper precautions to minimize exposure by using appropriate personal protective equipment (see Section 8). Area should be adequately ventilated.

Environmental precautions Do not empty into drains. Avoid release to the environment.

Methods and material for containment and cleaning up DO NOT CAUSE MATERIAL TO BECOME AIRBORNE. For small spills, soak up material with absorbent, e.g., paper towels. For large spills, cordon off spill area and minimize the spreading of spilled material. Soak up material with absorbent. Collect spilled material, absorbent, and rinse water into suitable containers for proper disposal in accordance with applicable waste disposal regulations (see Section 13). Decontaminate the area twice with an appropriate solvent (see Section 9).

Reference to other sections See Sections 8 and 13 for more information.

SECTION 7 - HANDLING AND STORAGE

Precautions for safe handling Follow recommendations for handling bulk formulated/packaged pharmaceutical agents (i.e., use of engineering controls and/or other personal protective equipment if needed). Wash thoroughly after handling. Avoid contact with eyes, skin and other mucous membranes. Avoid breathing vapor or mist.

Conditions for safe storage including any incompatibilities Store BMN 190 drug product vials frozen between -15 °C to -50 °C, away from incompatible materials. Keep container upright. Protect product from light.

Specific end use(s) No information identified.

SECTION 8 - EXPOSURE CONTROLS/PERSONAL PROTECTION

**Control
Parameters/Occupational
Exposure Limit Values**

<u>Compound</u>	<u>Issuer</u>	<u>Type</u>	<u>OEL</u>
BMN 190	--	--	--

**Exposure/Engineering
controls**

Selection and use of containment devices and personal protective equipment should be based on a risk assessment of exposure potential. Use local exhaust and/or enclosure at aerosol-generating points. Emphasis is to be placed on closed material transfer systems and process containment, with limited open handling of powders. High-energy operations such as milling, particle sizing, spraying or fluidizing should be done within an approved emission control or containment system.

Respiratory protection

Choice of respiratory protection should be appropriate to the task and the level of existing engineering controls. For routine handling tasks, an approved and properly fitted air-purifying respirator with HEPA filters should provide ancillary protection based on the known or foreseeable limitations of existing engineering controls. Use a powered air-purifying respirator equipped with HEPA filters or combination filters or a positive-pressure air-supplied respirator if there is any potential for an uncontrolled release, when exposure levels are not known, or in any other circumstances where a lower level of respiratory protection may not provide adequate protection.

Hand protection

Wear nitrile or other impervious gloves if skin contact is possible. When the material is dissolved or suspended in an organic solvent, wear gloves that provide protection against the solvent.

Skin protection

Wear appropriate gloves, lab coat, or other protective overgarment if skin contact is likely. Base the choice of skin protection on the job activity, potential for skin contact and solvents and reagents in use.

Eye/face protection

Wear safety glasses with side shields, chemical splash goggles, or full face shield, if necessary. Base the choice of protection on the job activity and potential for contact with eyes or face. An emergency eye wash station should be available.

**Environmental Exposure
Controls**

Avoid release to the environment and operate within closed systems wherever practicable. Air and liquid emissions should be directed to appropriate pollution control devices. In case of spill, do not release to drains. Implement appropriate and effective emergency response procedures to prevent release or spread of contamination and to prevent inadvertent contact by personnel.

**Other protective
measures**

Wash hands in the event of contact with this product/mixture, especially before eating, drinking or smoking. Protective equipment is not to be worn outside the work area (e.g., in common areas or out-of-doors). Decontaminate all protective equipment following use.

SECTION 9 - PHYSICAL AND CHEMICAL PROPERTIES

Information on basic physical and chemical properties

Appearance	Clear to slightly opalescent liquid
Color	Colorless to pale yellow
Odor	No information identified.
Odor threshold	No information identified.
pH	6 - 7
Melting point/freezing point	No information identified.
Initial boiling point and boiling range	~100 °C
Flash point	No information identified.
Evaporation rate	No information identified.
Flammability (solid, gas)	No information identified.
Upper/lower flammability or explosive limits	No information identified.
Vapor pressure	No information identified
Vapor density	No information identified.
Relative density	No information identified.
Water solubility	Soluble in water
Solvent solubility	No information identified.
Partition coefficient (n-octanol/water)	No information identified.
Auto-ignition temperature	No information identified.
Decomposition temperature	No information identified.
Viscosity	No information identified.
Explosive properties	No information identified.
Oxidizing properties	No information identified.

Other information

SECTION 9 - PHYSICAL AND CHEMICAL PROPERTIES ...continued

Molecular weight 59.31kDa
Molecular formula C₂₆₅₇H₄₀₄₂N₇₃₄O₇₉₃S₁₁

SECTION 10 - STABILITY AND REACTIVITY

Reactivity No information identified.
Chemical stability Stable under normal handling and storage conditions.
Possibility of hazardous reactions Not expected to occur.
Conditions to avoid No information identified.
Incompatible materials No information identified.
Hazardous decomposition products No information identified.

SECTION 11 - TOXICOLOGICAL INFORMATION

Information on toxicological effects

Route of entry May be absorbed by inhalation and skin contact.

Acute toxicity

<u>Compound</u>	<u>Type</u>	<u>Route</u>	<u>Species</u>	<u>Dose</u>
BMN 190	--	--	--	--

Irritation/Corrosion No studies identified.

Sensitization No studies identified. As the product contains a recombinant human protein, there is potential for the mixture to cause an allergic response in humans.

STOT-single exposure In a single dose toxicity study in monkeys administered intracerebroventricular (ICV) doses of up to 20 mg BMN 190 with a recovery period of up to 14 days, there were no BMN 190-related findings in the central nervous system (CNS) or other organs.

STOT-repeated exposure/Repeat-dose toxicity In repeated dose studies conducted in dogs, ICV doses of up to 48 mg administered every other week over a period of up to 18 months were associated with hypersensitivity reactions, as well as detection of anti-BMN 190 antibodies in plasma and cerebrospinal fluid (CSF), and a drop in plasma exposures following repeat dosing with BMN 190 (with no effect on CSF BMN 190 concentrations or CNS tissue distribution). No findings of systemic target organ toxicity were observed.

In TPP1-null dogs, pharmacodynamic effects of BMN 190 observed after ICV administration included: reduction of lysosomal storage material, maintenance of cognitive and motor function, delay in or prevention of neurodegenerative clinical signs and extension of lifespan (e.g., BMN 190-treatment extended lifespan in a dose-dependent manner).

SECTION 11 - TOXICOLOGICAL INFORMATION ...continued

Reproductive toxicity	No studies identified.
Developmental toxicity	No studies identified.
Genotoxicity	No studies identified.
Carcinogenicity	No studies identified. None of the components of the mixture present at levels greater than or equal to 0.1% are listed by NTP, IARC, ACGIH or OSHA as a carcinogen.
Aspiration hazard	No studies identified
Human health data	See "Section 2 - Other Hazards"
Additional information	The toxicological properties of this mixture have not been fully characterized.

SECTION 12 - ECOLOGICAL INFORMATION

Toxicity

<u>Compound</u>	<u>Type</u>	<u>Species</u>	<u>Concentration</u>
BMN 190	--	--	--

Persistence and Degradability No data available.

Bioaccumulative potential No data available.

Mobility in soil No data available.

Results of PBT and vPvB assessment Not performed.

Other adverse effects No data available.

Note The environmental characteristics of this product/mixture have not been fully investigated. Releases to the environment should be avoided.

SECTION 13 - DISPOSAL CONSIDERATIONS

Waste treatment methods Used product should be disposed of according to local, state, and federal regulations. Do not send down the drain or flush down the toilet. All wastes containing the material should be properly labeled. Dispose of wastes in accordance to prescribed federal, state, and local guidelines, e.g., appropriately permitted chemical waste incinerator. Rinse waters resulting from spill cleanups should be discharged in an environmentally safe manner, e.g., appropriately permitted municipal or on-site wastewater treatment facility.

SECTION 14 - TRANSPORT INFORMATION

Transport Based on the available data, this product/mixture is not regulated as a hazardous material/dangerous good under EU ADR/RID, US DOT, Canada TDG, IATA, or IMDG.

UN number None assigned.

UN proper shipping name None assigned.

Transport hazard classes and packing group None assigned.

Environmental hazards Based on the available data, this product/mixture is not regulated as an environmental hazard or a marine pollutant.

Special precautions for users Due to lack of data, avoid release to the environment.

Transport in bulk according to Annex II of MARPOL73/78 and the IBC Code Not applicable.

SECTION 15 - REGULATORY INFORMATION

Safety, health and environmental regulations/legislation specific for the substance or mixture This SDS generally complies with the requirements listed under current guidelines in the US, EU and Canada. Consult your local or regional authorities for more information.

Chemical safety assessment Not conducted.

TSCA status Drugs are exempt from TSCA.

SARA section 313 Not listed.

California proposition 65 Not listed.

SECTION 15 - REGULATORY INFORMATION ...continued

Additional information No other information identified.

SECTION 16 - OTHER INFORMATION

Full text of H phrases and GHS classifications RS1 - Respiratory Sensitizer Category 1. H334 - May cause allergic or asthmatic symptoms or breathing difficulty if inhaled.

Sources of data Information from published literature and internal company data.

Abbreviations ACGIH - American Conference of Governmental Industrial Hygienists; ADR/RID - European Agreement Concerning the International Carriage of Dangerous Goods by Road/Rail; AIHA - American Industrial Hygiene Association; CAS# - Chemical Abstract Services Number; CLP - Classification, Labelling, and Packaging of Substances and Mixtures; DNEL - Derived No Effect Level; DOT - Department of Transportation; EINECS - European Inventory of New and Existing Chemical Substances; ELINCS - European List of Notified Chemical Substances; EU - European Union; GHS - Globally Harmonized System of Classification and Labeling of Chemicals; IARC - International Agency for Research on Cancer; IDLH - Immediately Dangerous to Life or Health; IATA - International Air Transport Association; IMDG - International Maritime Dangerous Goods; LOEL - Lowest Observed Effect Level; LOAEL - Lowest Observed Adverse Effect Level; NIOSH - The National Institute for Occupational Safety and Health; NOEL - No Observed Effect Level; NOAEL - No Observed Adverse Effect Level; NTP - National Toxicology Program; OEL - Occupational Exposure Limit; OSHA - Occupational Safety and Health Administration; PNEC - Predicted No Effect Concentration; SARA - Superfund Amendments and Reauthorization Act; STOT - Specific Target Organ Toxicity; STEL - Short Term Exposure Limit; TDG - Transportation of Dangerous Goods; TSCA - Toxic Substances Control Act; TWA - Time Weighted Average; WHMIS - Workplace Hazardous Materials Information System

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Revisions This is the third version of this SDS.

Disclaimer The above information is based on data available to us and is believed to be correct. Since the information may be applied under conditions beyond our control and with which we may be unfamiliar, we do not assume any responsibility for the results of its use and all persons receiving it must make their own determination of the effects, properties and protections which pertain to their particular conditions. No representation, warranty, or guarantee, express or implied (including a warranty of fitness or merchantability for a particular purpose), is made with respect to the materials, the accuracy of this information, the results to be obtained from the use thereof, or the hazards connected with the use of the material. Caution should be used in the handling and use of the material because it is a pharmaceutical product. The above information is offered in good faith and with the belief that it is accurate. As of the date of issuance, we are providing all information relevant to the foreseeable handling of the material. However, in the event of an adverse incident associated with this product, this Safety Data Sheet is not, and is not intended to be, a substitute for consultation with appropriately trained personnel.