

SAFETY DATA SHEET

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

Contact information

General

Æterna Zentaris

Aeterna Zentaris GmbH
Weismullerstraße 50, D-60314 Frankfurt/Main, GERMANY
Main: +49 (0) 69-42602-0
Fax: +49 (0) 69-42602-3444
E-mail: msds@aezsinc.com
Internet: <http://www.aeternazentaris.com>

Emergency telephone number

POISON CENTER, Mainz, GERMANY
+49 (0) 6131-19240 (24-hour availability)

Product identifier

Macimorelin acetate (AEZS-130)

Synonyms

ARD-07; EPO1572; SP001572; D-87575; H-Aib-D-Trp-gD-Trp-CHO; D-Tryptophanamide, 2-methylalanyl-N-[(1R)-1-(formylamino)-2-(1H-indol-3-yl)ethyl]acetate

Trade names

None identified

Chemical family

Synthetic polypeptide (a ghrelin mimetic)

Relevant identified uses of the substance or mixture and uses advised against

Active pharmaceutical ingredient; under investigation as a diagnostic tool for adult growth hormone deficiency (AGHD).

Note

This SDS is written to address potential worker health and safety issues associated with the handling of the active pharmaceutical ingredient. The physical, chemical, toxicological and ecological properties of this substance have not been fully characterized. This SDS will be revisited as more data become available.

SECTION 2 - HAZARDS IDENTIFICATION

Classification of the substance or mixture

Globally Harmonized System [GHS]

Not classified

Other/Supplemental

Substance not yet fully tested

SECTION 2 - HAZARDS IDENTIFICATION ...continued

Label elements

GHS hazard pictogram	None required
GHS signal word	None required
GHS hazard statements	None required
GHS precautionary statements	None required

Other hazards Macimorelin acetate (AEZS-130) is a synthetic ghrelin mimetic, and growth hormone (GH) secretagogue. In clinical trials to date oral doses of 5 mg/kg were pharmacologically efficacious, effectively and transiently increasing GH levels for approximately 3 hours. The most common adverse effects reported, and believed to be drug-related, were mild, including upset stomach, headache, and diarrhea.

Note This substance does not meet criteria for classification under GHS as implemented by Regulation EC No 1272/2008 (EU CLP) and Hazard Communication Standard No. 1910.1200 (US OSHA). Nevertheless, it should be handled with caution as it has not yet been fully tested and is pharmacologically active.

SECTION 3 - COMPOSITION/INFORMATION ON INGREDIENTS

<u>Ingredient</u>	<u>CAS #</u>	<u>EINECS/ ELINCS#</u>	<u>Amount</u>	<u>GHS Classification</u>
Macimorelin acetate (AEZS-130)	945212-59-9	N/A	~100 %	Not classified

Note The substance listed above is not classified, but is listed because its toxicological and ecological properties have not yet been fully characterized. See Section 16 for full text of GHS classifications.

SECTION 4 - FIRST AID MEASURES

Description of first aid measures

Immediate Medical Attention Needed	Yes
Eye Contact	If easy to do, remove contact lenses, if worn. Immediately flush eyes with copious quantities of water for at least 15 minutes. 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.

SECTION 4 - FIRST AID MEASURES ...continued

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	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	Macimorelin acetate is a synthetic ghrelin mimetic. 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.
Specific hazards arising from the substance or mixture	No information identified. May emit carbon monoxide, carbon dioxide, and oxides of nitrogen.
Flammability/Explosivity	No explosivity or flammability data identified. High concentrations of finely divided airborne organic particles can potentially explode if ignited.
Advice for firefighters	Wear full protective clothing and a self-contained breathing apparatus with a full facepiece operated in the pressure demand or other positive pressure mode. 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. Do not breathe dust.
Environmental precautions	Do not empty into drains. Avoid release to the environment.

SECTION 6 - ACCIDENTAL RELEASE MEASURES ...continued

Methods and material for containment and cleaning up	DO NOT RAISE DUST. Surround spill or powder with absorbents and place a damp cloth or towel over the area to minimize entry of powder into the air. Add excess liquid to allow the material to enter solution. Capture remaining liquid onto spill absorbents. Place spill materials into a leak-proof container suitable for disposal in accordance with applicable waste disposal regulations (see Section 13). Decontaminate the area twice.
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 pharmaceutical agents (i.e., use of engineering controls and/or other personal protective equipment if needed). Avoid breathing dust. Wash thoroughly after handling.
Conditions for safe storage including any incompatibilities	Store at refrigerated at 2-8°C away from incompatible materials. Protect from light and atmospheric moisture (compound is hygroscopic). Storage group 13 (see TRGS 510, German National Regulation)
Specific end use(s)	No information identified.

SECTION 8 - EXPOSURE CONTROLS/PERSONAL PROTECTION

Note Wash hands, face and other potentially exposed areas immediately in the event of physical contact.

Control Parameters/Occupational Exposure Limit Values

<u>Compound</u>	<u>Issuer</u>	<u>Type</u>	<u>OEL</u>
Macimorelin acetate (AEZS-130)	Aeterna Zentaris	8-hour TWA	300 µg/m ³

Exposure/Engineering controls Control exposures to below the OEL (if available). Otherwise, 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 dust-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.

SECTION 8 - EXPOSURE CONTROLS/PERSONAL PROTECTION ...continued

Respiratory protection	Choice of respiratory protection should be appropriate to the task and the level of existing engineering controls. For routine powder 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 substance, 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).

SECTION 9 - PHYSICAL AND CHEMICAL PROPERTIES

Information on basic physical and chemical properties

Appearance	Powder
Color	Off-white to pale yellow
Odor	Acidic
Odor threshold	No information identified.
pH	6.1 (as 0.1% w/w water solution)
Melting point/freezing point	No information identified.

SECTION 9 - PHYSICAL AND CHEMICAL PROPERTIES ...continued

Initial boiling point and boiling range	Not applicable.
Flash point	No information identified.
Evaporation rate	Not applicable.
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 (300 mg/mL; pH 1-8)
Solvent solubility	Soluble in ethanol (260 mg/mL) and acetonitrile (40 mg/mL) at 25 °C
Partition coefficient (<i>n</i>-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	
Molecular weight	474.5 g/mol (base)
Molecular formula	C ₂₆ H ₃₀ N ₆ O ₃

SECTION 10 - STABILITY AND REACTIVITY

Reactivity	No information identified.
Chemical stability	Stable at 2-8 °C, as recommended (protected from light and atmospheric moisture). Substance is unstable with strong oxidizing agents.
Possibility of hazardous reactions	Not expected to occur.

SECTION 10 - STABILITY AND REACTIVITY ...continued

Conditions to avoid	Do not use/handle at temperatures >25 °C. Protect from light and atmospheric moisture.
Incompatible materials	Strong oxidizing agents, strong acids and alkalies.
Hazardous decomposition products	No information identified.

SECTION 11 - TOXICOLOGICAL INFORMATION

Information on toxicological effects

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

Acute toxicity

<u>Compound</u>	<u>Type</u>	<u>Route</u>	<u>Species</u>	<u>Dose</u>
Macimorelin acetate (AEZS-130)	LD ₅₀	Oral	Rat	>2000 mg/kg (extrapolated from subacute study)
	Minimum Lethal Dose	IV	Rat	>60 mg/kg

Irritation/Corrosion No data available.

Sensitization No data available.

STOT-single exposure Macimorelin acetate was administered as single IV doses to rats at 30, 45, and 60 mg/kg to 5 males and 5 females. Increased sedation and shallow breathing was noted at the highest dose immediately after injection, followed by hypoactivity, piloerection (hair standing on end), hunched posture, and blood in the urine. Some sedation, hypoactivity, and piloerection were also noted at 45 mg/kg. All effects were reversible with one week of treatment. NOAEL = 30 mg/kg.

STOT-repeated exposure/Repeat-dose toxicity Repeated oral dose toxicity studies up to 28 days in duration were conducted with rats and dogs. No adverse effects were noted at any dose tested in either species. Accordingly, NOAELs of 1000 and 100 mg/kg/day (the highest doses tested), respectively, were identified.

In a 2-week repeated IV dose toxicity study in rats, some clinical signs (sedation/hypoactivity, ear redness and blood in the urine) and slight increases in pituitary weights (at necropsy) were noted at 10 and 30 mg/kg/day (NOAEL = 3 mg/kg/day). No mortality occurred at any dose level.

Reproductive toxicity No data available.

Developmental toxicity No data available for macimorelin acetate. Treatment (presumably *via* parenteral injection) with a similar GH secretagogue only produced minor skeletal variations in the offspring of rats and rabbits treated with low to moderate doses.

SECTION 11 - TOXICOLOGICAL INFORMATION ...continued

Genotoxicity	Macimorelin acetate was negative for genotoxicity in a bacterial Ames assay, an <i>in vitro</i> mouse lymphoma cell assay, and an <i>in vitro</i> micronucleus assay using Chinese Hamster Ovary-K1 cells.
Carcinogenicity	No data available.
Aspiration hazard	No data available.
Human health data	See "Section 2 - Other Hazards"
Additional information	The toxicological properties of this substance have not been fully characterized.

SECTION 12 - ECOLOGICAL INFORMATION

Toxicity

<u>Compound</u>	<u>Type</u>	<u>Species</u>	<u>Concentration</u>
Macimorelin acetate (AEZS-130)	--	--	--

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 Ecological characteristics of this substance were not available. Releases to the environment should be avoided.

SECTION 13 - DISPOSAL CONSIDERATIONS

Waste treatment methods Dispose of wastes in accordance to prescribed federal, state, and local guidelines, e.g., appropriately permitted chemical waste incinerator. Do not send down the drain or flush down the toilet. All wastes containing the material should be properly labeled. 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 substance is not regulated as a hazardous material/ dangerous good under EU ADR/RID, US DOT, Canada TDG, IATA, or IMDG.

SECTION 14 - TRANSPORT INFORMATION ...continued

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 substance 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.
WHMIS classification	Not classified.
TSCA status	Drugs are exempt from TSCA.
SARA section 313	Not listed.
California proposition 65	Not listed
Additional information	No other information identified.

SECTION 16 - OTHER INFORMATION

Full text of H phrases and GHS classifications	Not applicable.
Sources of data	Information from published literature and internal company data.

SECTION 16 - OTHER INFORMATION ...continued

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

Issue Date 17 February 2016

Revisions Updated with new data; Updated general format for compliance with most recent regulatory requirements in the US, EU, and Canada.

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.