SAFETY DATA SHEET

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

Contact information

General

ACHAOGEN

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Product identifier	Plazomicin Injection 50 mg/mL
Synonyms	Plazomicin Injection 500 mg/10mL
Trade names	ZEMDRI ™
Chemical family	Mixture; contains an aminoglycoside antibacterial
Relevant identified uses of the substance or mixture and uses advised against	Bulk formulated pharmaceutical mixture/Formulated pharmaceutical product/ mixture packaged in final form for patient use.
Note	This SDS is written to address potential worker health and safety issues associated with the handling of the formulated drug product. This product is intended for therapeutic use only when prescribed by a physician.

SECTION 2 - HAZARDS IDENTIFICATION

Classification of the substance or mixture	**Drugs in the finished state and intended for the final user are not subject to labeling in the US, EU or Canada. The classification and labeling listed below is for bulk drug product.**
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 Plazomicin injection contains plazomicin sulfate, an aminoglycoside antibiotic indicated for intravenous (IV) treatment of bacterial infections. Common adverse effects associated with use in clinical trials for the treatment of complicated urinary tract infection or acute pyelonephritis include gastrointestinal (GI) upset (diarrhea, nausea, vomiting), decreased renal function, and headache. The aminoglycoside class is associated with kidney damage. High acute IV exposures of aminoglycosides have been associated with neuromuscular blockade. High repeat-dose IV exposures of aminoglycosides have been associated with damage to hearing and/or balance. Clinical cases of respiratory sensitization following inhalation of similar aminoglycosides have been reported. May cause adverse effects on the developing fetus. Serious allergic reactions, including anaphylaxis, have been reported for aminoglycosides.

Note This mixture is classified as hazardous according to Regulation EC No 1272/2008 (EU CLP) and Hazard Communication Standard No. 1910.1200 (US OSHA). The ecological properties of this mixture have not been fully characterized.

SECTION 3 - COMPOSITION/INFORMATION ON INGREDIENTS

Ingredient	CAS #	EINECS/ELINCS#	Amount	GHS Classification
Plazomicin sulfate	1380078-95-4	N/A	5-9%	STOT-S2: H371; STOT-R2: H373; RS-1: H334

Note The ingredients listed above are considered hazardous or are the active ingredient. The remaining components are non-hazardous and/or present at amounts below reportable limits. Amounts are listed as ranges; the exact percentage of composition is withheld as a trade secret.

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.
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	Medical conditions aggravated by exposure: Serious hypersensitivity or serious toxic reactions to aminoglycosides. Treat symptomatically and supportively. If accidental exposure occurs to an individual who is also taking one or more concomitant medications, consult the respective package or prescribing information for potential drug interactions.

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 sulphur or nitrogen.
Flammability/Explosivity	As product is an aqueous solution, it is not expected to be flammable or explosive.
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/mist/vapors/spray.

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.

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). Wash thoroughly after handling. Take extra care should be taken to minimize direct contact.

Conditions for safe storage including any incompatibilities — Store refrigerated between 2 to 8° C.

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

Compound	Issuer	Type	OEL
Plazomicin sulfate	Achaogen, Inc.	8-hour TWA	670 µg/m^3

Exposure/Engineering controls — None required for normal handling of packaged product. Control exposures to below the OEL. 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 aerosol/mist-generating points. Emphasis is to be placed on closed material transfer systems and process containment, with limited open handling. High-energy operations should be done within an approved emission control or containment system.

SECTION 8 - EXPOSURE CONTROLS/PERSONAL PROTECTION …continued

Respiratory protection	None required for normal handling of packaged product. Choice of respiratory protection should be appropriate to the task and the level of existing engineering controls. An approved and properly fitted air purifying respirator 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	None required for the normal handling of packaged product. Wear nitrile or other impervious gloves if skin contact is possible. When the material is diluted 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 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	Liquid.
Color	Colorless to yellow.
Odor	Odorless.
Odor threshold	Not applicable.
pH	6.5
Melting point/freezing point	No information identified.
Initial boiling point and boiling range	No information identified.

SECTION 9 - PHYSICAL AND CHEMICAL PROPERTIES …continued

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	Freely soluble in water.
Solvent solubility	Insoluble in most organic solvents.
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

Molecular formula	Not applicable (Mixture).
Molecular weight	Not applicable (Mixture).

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

Toxicology summary The information included in this section describes the potential hazards of the active substance.

Information on toxicological effects

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

Acute toxicity

Compound	Type	Route	Species	Dose
Plazomicin sulfate	Approximate Lethal Dose	IV	Rat	150 mg/kg

Irritation/Corrosion No data available.

Sensitization No data available.

STOT-single exposure Single IV doses of plazomicin in rats at doses ≥100 mg/kg caused abnormal clinical signs consistent with neuromuscular blockade (*e.g.*, uncoordinated movement, altered respiration, decreased activity), leading to death. Kidney toxicity was also seen at ≥150 mg/kg.

STOT-repeated exposure/Repeat-dose toxicity Reversible kidney toxicity was reported in 14- and 28-day studies with plazomicin at IV doses ≥30 mg/kg/day in rats and ≥10 mg/kg/day in dogs, respectively. Plazomicin did not cause hearing impairment in a guinea pig study administered IV doses of plazomicin up to 80 mg/kg/day. One of 8 animals at 80 mg/kg/day had a unilateral loss of hearing hair cells outside the normal range of variation without hearing impairment.

Reproductive toxicity Plazomicin had no adverse effects on fertility in male rats at up to 50 mg/kg/day. In female rats, there were no effects on estrous cyclicity or reproductive performance. At 25 and 50 mg/kg/day, female rats had fewer corpora lutea, leading to fewer uterine implantation sites, and viable embryos per dam. The no observed effect level (NOEL) for fertility and reproductive performance in female rats was 8 mg/kg/day (parental toxicity observed at ≥ 8 mg/kg/day)

Developmental toxicity Plazomicin was not teratogenic and did not cause developmental toxicity in rats or rabbits at IV doses of up to 50 mg/kg/day (doses which were maternally toxic). Plazomicin did not cause adverse effects on offspring's pre- or postnatal development and reproductive capability at up to the highest tested dose of 30 mg/kg/day.

Genotoxicity Plazomicin was negative for mutagenicity in an Ames test and did not induce chromosome aberrations in cultured human peripheral blood lymphocytes. In vivo, a mouse bone marrow micronucleus assay showed no evidence of clastogenic potential.

Carcinogenicity	No data available. 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 data available.
Human health data	See "Section 2 - Other Hazards"

SECTION 12 - ECOLOGICAL INFORMATION

Toxicity

Compound	Type	Species	Concentration
Plazomicin sulfate	--	--	--

SECTION 12 - ECOLOGICAL INFORMATION …continued

Persistence and Degradability	No data available.
Bioaccumulative potential	No data available.
Mobility in soil	No data available.
Results of PBT and vPvB assessment	No data available.
Other adverse effects	No data available.
Note	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 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	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.
Additional information	No other information identified.

SECTION 16 - OTHER INFORMATION

Full text of H phrases and GHS classifications	STOT-S2 - Specific Target Organ Toxicity Following Single Exposure Category 2. H371 - May cause damage to neuromuscular system STOT-R2 - Specific Target Organ Toxicity Following Repeated Exposure Category 2. H373 - May cause damage to kidneys through prolonged or repeated exposure. 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; 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	
Revisions	This is the second version of this SDS. Updated synonyms, Other Hazards, and Toxicology Information.

SECTION 16 - OTHER INFORMATION …continued

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.