SAFETY DATA SHEET

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

Contact information

General

Leucadia Pharmaceuticals
2325 Camino Vida Roble, Suite A
Carlsbad, CA 92011
Main: +1 (844) 538-2231 (Mon-Fri 8:00 AM - 6:00 PM Central)
Email: info.sds@leucadiapharma.com

Emergency telephone number

Chemtrec *(24-hour availability)*:
+1 (800) 424-9300 (USA and Canada)
+1 (703) 527-3887 (International; collect calls accepted)

Product identifier

Calcitonin Salmon, Injection, USP, Synthetic (200 I.U. per mL)

Synonyms

L-cysteinyl-L-seryl-L-asparaginyl-L-leucyl-L-seryl-L-threonyl-L-cysteinyl-L-valyl-L-leucylglycyl-L-lysyl-L-leucyl-L-seryl-L-glutaminyl-L-glutamyl-L-leucyl-L-histidyl-L-lysyl-L-leucyl-L-glutaminyl-L-threonyl-L-tyrosyl-L-prolyl-L-arginyl-L-threonyl-L-asparaginyl-L-threonyl-glycyl-L-seryl-glycyl-L-threonyl-L-prolineamide [Disulfide bond: cysteinyl 1- cysteinyl 7]

Trade names

Not applicable

Chemical family

Peptide

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

Active pharmaceutical ingredient, used in treatment of postmenopausal osteoporosis in women, Paget's disease, and hypercalcemia.

Note

This SDS is written to address potential worker health and safety issues associated with the handling of the product/mixture.

SECTION 2 - HAZARDS IDENTIFICATION

Classification of the substance or mixture

Globally Harmonized System [GHS]

Not classified

Label elements

SECTION 2 - HAZARDS IDENTIFICATION …continued

GHS hazard pictogram	None required
GHS signal word	None required
GHS hazard statements	None required
GHS precautionary statements	None required
Other hazards	Calcitonin is a hormone important for the regulation of calcium metabolism. Administration of calcitonin-salmon, which is more potent than endogenous calcitonin, reduces bone resorption, decreases serum calcium, and increases renal excretion of phosphate, calcium, sodium, magnesium, and potassium by decreasing tubular resorption. The most commonly reported adverse effects include nasal effects (runny nose, nasal dryness with crusting, non-severe nosebleeds, and sinusitis), nausea, facial flushing, loss of appetite, metallic taste, and tingling of the hands.
Note	This product/mixture is classified as not 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

Ingredient	CAS #	EINECS/ ELINCS#	Amount	GHS Classification
Calcitonin, salmon (recombinant)	47931-85-1	256-342-8	≤0.1%	LAC: H362; RT2: H361d
Acetic acid (glacial)	64-19-7	200-580-7	≤0.5%	FL3: H226; SC1A: H314
Phenol	108-95-2	203-632-7	≤0.5%	SC1B: H314; ATI3: H331; ATD3: H311; ATO3: H301; STOT-R2: H373; GCM2: H341

Note The substances listed above are considered hazardous or are listed because they are the active pharmaceutical ingredient. The remaining ingredients are primarily water, and are non-hazardous and/or are present at levels below the reportable limits. See Section 16 for full text of GHS classifications.

SECTION 4 - FIRST AID MEASURES

Description of first aid measures

Immediate Medical Attention Needed	No. If exposed or concerned: Get medical advice/attention.

SECTION 4 - FIRST AID MEASURES …continued

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: 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, oxides of nitrogen, and other nitrogen-containing compounds.
Flammability/ Explosivity	No explosivity or flammability data identified. High airborne concentrations of finely divided 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 mist/spray.

SECTION 6 - ACCIDENTAL RELEASE MEASURES …continued

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	Patients should adhere to the instructions provided within the product information insert or product label for appropriate consumer-specific information about this product when used according to the physician's directions. This SDS is for a pharmaceutical agent - Handling of this product in its final form presents minimal occupational exposure risk. In an occupational setting, handle in accordance with good industrial hygiene and safety procedures. Avoid contact with eyes, skin and clothing. Avoid breathing vapor or mist. Use appropriate personal protective equipment when handling and observe good personal hygiene measures after handling. Wash thoroughly after handling.
Conditions for safe storage including any incompatibilities	Store in a dry, cool and well-ventilated place. Protect from heat and direct sunlight. Store in refrigerator between 2°C-8°C (36°F-46°F).
Specific end use(s)	Pharmaceutical.

SECTION 8 - EXPOSURE CONTROLS/PERSONAL PROTECTION

Control Parameters/ Occupational Exposure Limit Values

Compound	Issuer	Type	OEL
Calcitonin, salmon (recombinant)	--	--	--
Acetic acid (glacial)	ACGIH	TWA-8 HR	10 ppm

Control Parameters/ Occupational Exposure Limit Values

…continued

Compound	Issuer	Type	OEL
	Austria, Belgium, Cyprus, Denmark, Estonia, Germany, Greece, Ireland, Italy, Malta, Latvia, Lithuania, Luxembourg	TWA-8 HR	10 ppm
	Finland, Sweden	TWA-8 HR	5 ppm
	Belgium, Greece, Ireland, Italy	STEL	15 ppm
	ACGIH	TLV-STEL	15 ppm
	Austria	STEL	20 ppm
	Estonia, Finland, France, Sweden	STEL	10 ppm
	Czech Republic	Ceiling	35 mg/m³
	Germany	Ceiling	20 ppm
	Bulgaria	STEL	37 mg/m³
	Hungary	STEL	25 mg/m³
	Bulgaria, Czech Republic, Hungary	TWA-8 HR	25 mg/m³
	Poland	TWA-8 HR	15 mg/m³
	Poland	STEL	30 mg/m³
	Portugal, Romania, Slovak Republic, Slovenia, Spain	TWA-8 HR	10 ppm
	Portugal, Spain	STEL	15 ppm

Control Parameters/ Occupational Exposure Limit Values

…continued

Compound	Issuer	Type	OEL
	U.S. OSHA	PEL-TWA 8-Hr	10 ppm
Phenol	ACGIH	TLV-TWA (8-Hr)	5 ppm (skin)
	OSHA	PEL	5 ppm (skin)
	NIOSH	REL-TWA	5 ppm (skin)
	NIOSH	REL-Ceiling	15.6 ppm
	Alberta, British Columbia, Ontario	TWA (8-hour)	5 ppm (skin)
	Denmark, Sweden	TWA (8-hour)	1 ppm (skin)
	Belgium, Finland, United Kingdom	TWA (8-hour)	2 ppm (skin)
	Austria	MAK-TMW	2 ppm
	France	VME (8-Hour)	2 ppm (skin)
	Poland	MAC-TWA (8-Hr)	10 mg/m³
	Poland	MAC-STEL (15 min)	20 mg/m³
	Hungary, Netherlands	MAC-TWA (8-Hr)	8 mg/m³ (skin)

Exposure/Engineering controls

Selection and use of containment devices and personal protective equipment should be based on a risk assessment of exposure potential. Utilize closed and sealed systems whenever possible. Solutions used for procedures where aerosolization may occur (e.g., spraying, pumping, open transfers,) must be handled using an engineered local exhaust ventilation (LEV) and/or enclosure or isolator system. Control the potential for spills and leaks by securing all connections. Use clean-in-place systems.

Respiratory protection

Choice of respiratory protection should be appropriate to the task and the level of existing engineering controls. A powered air-purifying respirator (PAPR) with HEPA filters and head cover is required when performing aerosol generating operations. An airline respirator or self-contained breathing apparatus (SCBA) and disposable outerwear is required for spill cleanup.

Hand protection

Wear nitrile or other impervious gloves if skin contact is possible. Double gloves should be considered.

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.

SECTION 8 - EXPOSURE CONTROLS/PERSONAL PROTECTION …continued

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).

SECTION 9 - PHYSICAL AND CHEMICAL PROPERTIES

Information on basic physical and chemical properties

Appearance	Liquid
Color	Clear
Odor	No information identified.
Odor threshold	No information identified.
pH	No information identified.
Melting point/ freezing point	No information identified.
Initial boiling point and boiling range	No information identified.
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	No information identified.

SECTION 9 - PHYSICAL AND CHEMICAL PROPERTIES …continued

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

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

SECTION 10 - STABILITY AND REACTIVITY

Reactivity	No information identified.
Chemical stability	No information identified.
Possibility of hazardous reactions	Not expected to occur.
Conditions to avoid	Avoid extreme temperatures.
Incompatible materials	No information identified.
Hazardous decomposition products	No information identified.

SECTION 11 - TOXICOLOGICAL INFORMATION

Note	No data for this product/mixture were identified. The following data describe the active ingredient and/or the individual ingredients where applicable.

Information on toxicological effects

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

Acute toxicity

Compound	Type	Route	Species	Dose
Calcitonin, salmon (recombinant)	LD_{50}	Oral	Rat	>72.8 mg/kg
Acetic acid (glacial)	LD_{50}	Oral	Mouse	4960 mg/kg
	LD_{50}	Oral	Rat	3310 mg/kg
	LD_{50}	Oral	Rabbit	1200 mg/kg
Phenol	LD_{50}	Oral	Rodents	300-600 mg/kg
	LD_{50}	Dermal	Rat/Rabbit	670-1400 mg/kg
	LC_{50} (8 hour)	Inhalation	Rat	>900 mg/m^3

Irritation/Corrosion Phenol and acetic acid are corrosive to skin.

Sensitization Calcitonin was not sensitizing in guinea pigs.

STOT-single exposure No information identified.

STOT-repeated exposure/Repeat-dose toxicity No effects were observed in dogs administered up to 200 IU/day calcitonin-salmon intranasally (equivalent to 30 µg/day) for 4 weeks. In animal studies, calcitonin-salmon caused development of neutralizing antibodies against calcitonin when complexed with a larger protein or combined with an adjuvant, however, these antibodies have not caused systemic allergic or anaphylactic reactions.

Inhalation of phenol at moderate doses (0.02 to 1 ppm) for 2 months produced changes in blood enzyme activity and adverse lung effects (including pneumonia and hyperplasia) in rats. In two additional rat studies, NOAELs of 40 and 60 mg/kg/day (details not specified) were identified. A NOAEL of 140 mg/kg/day (details not specified) was also identified in a mouse study.

In animals (species not identified) given a 3% acetic acid solution via intragastric administration over a period of six months, chronic inflammation of the esophagus was observed.

Reproductive toxicity No information identified.

Developmental toxicity In a peri- and postnatal studies in rats, subcutaneous (SC) doses of 20-80 IU/kg/day calcitonin-salmon (equivalent to 3-12 µg/kg/day) from gestation through lactation resulted in reduced fetal weight, increased incidence of stillbirth, reduced pup weight, and partial to complete lactation failure in the dams. Microscopic and macroscopic kidney effects were also observed in some dams. No kidney effects were observed at 5 IU/kg/day (equivalent to 0.75 µg/kg/day). No teratogenicity was reported in testing with acetic acid in mice, rats, rabbits, hamsters, and guinea pigs.

SECTION 11 - TOXICOLOGICAL INFORMATION …continued

Genotoxicity Calcitonin-salmon was negative in an Ames assay, an *in vitro* chromosome aberration assay in Chinese hamster cells, and an *in vivo* mouse micronucleus test. Phenol was not mutagenic in bacterial cells, but has caused mutations, chromosomal damage, and DNA effects in mammalian cells. It was also positive in some *in vivo* mouse micronucleus assays at high doses. Acetic acid was negative for mutagenic effects with or without metabolic activation in the Ames bacterial cell mutagenicity assay.

Carcinogenicity In a two year study in rats administered 1.25-80 IU/kg/day calcitonin-salmon (equivalent to 0.187-12 µg/kg/day), an increased incidence of non-functioning pituitary adenomas was observed in male rats at ≥20 IU/kg/day (equivalent to 3 µg/kg/day), and in female rats to a lesser extent (dose not identified). These effects were determined to be species-specific due to triggering spontaneous proliferative lesions in aged laboratory rats. No carcinogenicity was observed in mice administered up to 800 IU/kg/day (equivalent to 120 µg/kg/day) SC for 2 years, nor in dogs treated with up to 80 IU/kg/day (equivalent to 12µg/day) for 16 weeks. Overall, the carcinogenic potential of calcitonin-salmon is considered to be low.

Aspiration hazard No information identified.

Human health data See "Section 2 - Other Hazards"

SECTION 12 - ECOLOGICAL INFORMATION

Toxicity

Compound	Type	Species	Concentration
Calcitonin, salmon (recombinant)	--	--	--
Acetic acid (glacial)	LC_{50}/96h	*Pimephales promelas*(Fathead minnow)	79 mg/L [static]
	LC_{50}/96h	*Lepomis macrochirus*(bluegill sunfish)	75 mg/L [static]
	EC_{50}/24h	*Daphnia magna*(water flea)	47 mg/L
	EC_{50}/48h	*Daphnia magna* (water flea)	65 mg/L [static]
Phenol	LC_{50} (24-48 hours)	*Daphnia magna* (water flea)	17 mg/L
	LC_{50} (24h)	*Lepomis macrochirus* (bluegill sunfish)	19-160 mg/L
	LC50 (24 h)	*Oncorhynchus mykiss* (rainbow trout)	5.6-11 mg/L
	LC_{50} (48-96 hours)	*Pimephales promelas*(Fathead minnow)	36-41 mg/L
	LC50 (24 h)	*Carassius auratus*(fresh water fish)	60-200 mg/L

Persistence and Degradability Calcitonin-salmon is readily biodegradable.

SECTION 12 - ECOLOGICAL INFORMATION …continued

Bioaccumulative potential	As a protein, calcitonin is not expected to persist in the environment. The Log Pow for Acetic Acid is -0.31 (at 20 °C). The Log Pow for Phenol is 1.47.
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	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	GCM2 - Germ Cell Mutagenicity Category 2. H341 - Suspected of causing genetic defects. STOT-R2 - Specific Target Organ Toxicity Following Repeated Exposure Category 2. H373 - May cause damage to lungs through prolonged or repeated exposure. ATO3 - Acute Toxicity (Oral) Category 3. H301 - Toxic if swallowed. ATD3 - Acute Toxicity (Dermal) Category 3. H311 - Toxic in contact with skin. ATI3 - Acute Toxicity (Inhalation) Category 3. H331 - Toxic if inhaled. SC1 - Skin corrosion Category 1. H314 - Causes severe skin burns and eye damage. FL3 - Flammable Liquid Category 3. H226 - Flammable liquid and vapor. RT2 - Reproductive toxicity Category 2. H362 - May cause harm to breast-fed children. H361d - Suspected of damaging the unborn child. Effects via lactation.
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; PBT - Persistent, Bioaccumulative, and Toxic; PNEC - Predicted No Effect Concentration; SARA -

SECTION 16 - OTHER INFORMATION …continued

Abbreviations …continued	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; vPvB - Very Persistent and Very Bioaccumulative; WHMIS - Workplace Hazardous Materials Information System
Issue Date	12 September 2019
Revisions	This is the first 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 potent 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.