



Teriparatide Injection

Effective Date: 28-Aug-2001

Eli Lilly and Company
Material Safety Data Sheet

Section 1 - Chemical Product and Company

Manufacturer:
Eli Lilly and Company
Lilly Corporate Center
Indianapolis, IN 46285

Manufacturer's Emergency Phone:
1-317-276-2000
CHEMTREC:
1-800-424-9300 (North America)
1-703-527-3887 (International)

Common Name: Teriparatide Injection

Chemical Name: L-Phenylalanine, L-seryl-L-valyl-L-seryl-L-alpha-glutamyl-L-isoleucyl-L-glutamyl-L-leucyl-L-methionyl-L-histidyl-L-asparaginyl-L-leucylglycyl-L-lysyl-L-histidyl-L-leucyl-L-asparaginyl-L-seryl-L-methionyl-L-alpha-glutamyl-L-arginyl-L-valyl-L-alpha-glutamyl-L-tryptophyl-L-leucyl-L-arginyl-L-lysyl-L-lysyl-L-leucyl-L-glutamyl-L-alpha-aspartyl-L-valyl-L-histidyl-L-asparaginyl-

Synonym(s): 1-34-Parathormone (human) Injection; 333334 Formulation; Human PTH(1-34) Injection; PTH(1-34) Injection; Recombinant Human Parathyroid Hormone (1-34) Injection; VL7641; rhPTH(1-34) Injection

Trademarks(s): Aphela; Forsteo; Forteo; Fortessa; Ophthia; Optia; Optiah; Zalectra; Zelletra

Lilly Item Code(s): AM0355; B02464; MS8971; MS8972; MS9513; VL7590; VL7591

See attached glossary for abbreviations.

Section 2 - Composition / Information on Ingredients

Ingredient	CAS	Concentration %
Teriparatide	52232-67-4	0.025 - 0.05
Mannitol	69-65-8	4.5
m-Cresol	108-39-4	0.3
Water	7732-18-5	95

Contains no hazardous components (one percent or greater) or carcinogens (one-tenth percent or greater) not listed above.

Exposure Guidelines:

Mannitol - Exposure Guideline 10 mg/m³ TWA for 8 or 12 hours.

m-Cresol - PEL 5 ppm (22 mg/m³) TWA (skin). TLV 5 ppm TWA (skin).

Ireland - Occupational Exposure Limit 5 ppm (22 mg/m³) TWA (skin).

Italy - Occupational Exposure Limit 5 ppm (22 mg/m³) TWA.

France - Occupational Exposure Limit 5 ppm (22 mg/m³) (VME) TWA.

Spain - Occupational Exposure Limit 5 ppm (22 mg/m³) (VLA-ED) TWA (skin).

Germany - TRGS 900 Limit Value 5 ppm (22 mg/m³) TWA (skin), 15 minute limit not to exceed MAK (skin).

Teriparatide - LEG 9 micrograms/m³ TWA (respirable) for 8 or 12 hours, 50 micrograms/m³ TWA (respirable) for 15 minutes STEG.

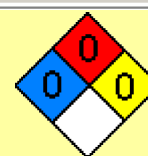
Section 3 - Hazards Identification

Appearance: Clear colorless solution

Physical State: Liquid

Odor: Faint phenol-like

Emergency Overview



Special
R = Reproductive

Emergency Overview Effective Date: 28-Aug-2001

Lilly Laboratory Labeling Codes:

Health 0

Fire 0

Reactivity 0

Special R

Primary Physical and Health Hazards: Reproductive, Heart, Blood and Kidney Effects.

Caution Statement: Effects of exposure to Teriparatide Injection may include decreased fetal survival, decreased blood pressure, increased blood levels of calcium, and kidney tissue changes.

Routes of Entry: Inhalation and skin contact.

Effects of Overexposure: The active ingredient teriparatide is not thought to be active by the oral route of exposure. Effects of overexposure may include headaches, dizziness, decreased blood pressure, decreased fetal survival, leg cramps, changes in clinical chemistry including increased in blood levels of calcium, decreased serum phosphorous, and increased urinary calcium and phosphorus.

Medical Conditions Aggravated by Exposure:

Teriparatide - Hyperparathyroidism, malignancy associated with hypercalcemia, vitamin D intoxication.

Carcinogenicity:

Mannitol - Not listed by IARC, NTP, ACGIH, or OSHA. Two-year dietary studies demonstrated no evidence of carcinogenicity in mice and rats.

m-Cresol - Not listed by IARC, NTP, ACGIH, or OSHA. Two- to three-month dermal application studies with cresols demonstrated evidence of tumor promotion in mice. The relevance of these

findings to humans is unknown.

Teriparatide - Not listed by IARC, NTP, ACGIH, or OSHA. In a carcinogenicity study in rats, an increased incidence of osteosarcoma (malignant bone tumor) was observed in animals given daily subcutaneous injections of 5, 30, or 75 micrograms/kg/day. The relevance of these findings to humans is uncertain. Teriparatide did not produce bone tumors in ovariectomized monkeys treated daily for 18 months.

Section 4 - First Aid Measures

Eyes: Flush eyes with plenty of water. Get medical attention.

Skin: Remove contaminated clothing and clean before reuse. Wash all exposed areas of skin with plenty of soap and water. Get medical attention if irritation develops.

Inhalation: Move individual to fresh air. Get medical attention if breathing difficulty occurs. If not breathing, provide artificial respiration assistance (mouth-to-mouth) and call a physician immediately.

Ingestion: Call a physician or poison control center. No first aid procedures are normally required.

Section 5 - Fire Fighting Measures

Flash Point: No applicable information found

UEL: No applicable information found

LEL: No applicable information found

Extinguishing Media: Use water, carbon dioxide, dry chemical, foam, or Halon.

Unusual Fire and Explosion Hazards: None known.

Hazardous Combustion Products: May emit toxic fumes when exposed to heat or fire.

Section 6 - Accidental Release Measures

Spills: Prevent further migration into the environment. Use absorbent/adsorbent material to solidify liquids. Sweep up or vacuum. Wear protective equipment, including eye protection, to avoid exposure (see Section 8 for specific handling precautions). m-Cresol is a CERCLA Hazardous Substance and a SARA 313 Toxic Chemical.

Section 7 - Handling and Storage

Storage Conditions: Do not freeze. Refrigerator: 2 to 8 C (36 to 46 F).

Section 8 - Exposure Controls / Personal Protection

See Section 2 for Exposure Guideline information.

Under normal use and handling conditions, no protective equipment is required. The following is recommended for a production setting:

Respiratory Protection: Use an approved respirator.

Eye Protection: Safety glasses.

Ventilation: Laboratory fume hood or local exhaust ventilation.

Other Protective Equipment: Chemical-resistant gloves and body covering to minimize skin contact. If handled in a ventilated enclosure, as in a laboratory setting, respirator and goggles or face shield may not be required. Safety glasses are always required.

Section 9 - Physical and Chemical Properties

Appearance: Clear colorless solution

Odor: Faint phenol-like

Boiling Point: No applicable information found

Melting Point: No applicable information found

Specific Gravity: No applicable information found

pH: 3.5 to 4.5

Evaporation Rate: No applicable information found

Water Solubility: Soluble

Vapor Density: No applicable information found

Vapor Pressure: No applicable information found

Section 10 - Stability and Reactivity

Stability: Stable at normal temperatures and pressures.

Incompatibility: May react with strong oxidizing agents (e.g., peroxides, permanganates, nitric acid, etc.).

Hazardous Decomposition: May emit toxic fumes when heated to decomposition.

Hazardous Polymerization: Will not occur.

Section 11 - Toxicological Information

Acute Exposure

No data available for mixture or formulation. Data for ingredient(s) or related material(s) are presented.

Oral: No applicable information found.

Skin: No applicable information found.

Inhalation:

Teriparatide - Monkey, 32 mg/m³ for 15 minutes, no deaths or toxicity, no irritation to eyes or respiratory tract.

Intravenous:

Teriparatide - Rat, 300 micrograms/kg, no deaths, redness of extremities.

Subcutaneous:

Teriparatide - Rat, 1000 micrograms/kg, no deaths, redness of extremities.

Skin Contact: No applicable information found.

Eye Contact:

Teriparatide - Nonirritant in monkeys following subchronic airborne exposure to 32 mg/m³.

Chronic Exposure

No data available for mixture or formulation. Data for ingredient(s) or related material(s) are presented.

Target Organ Effects:

Teriparatide - Blood effects (increased serum calcium, decreased white blood cell counts), circulatory effects (decreased blood pressure, vasodilation in extremities), kidney effects (tissue changes, mineralization), bone effects (increased bone formation).

Reproduction:

Teriparatide - No effect on fertility in male or female rats at subcutaneous doses up to 300 micrograms/kg. No teratogenic effects in rats, mice or rabbits, and no important adverse embryo/fetal development effects seen in rats or mice administered subcutaneous doses up to 1000 micrograms/kg. In rabbits, decreased embryo/fetal survival was reported at doses greater than or equal to 3 micrograms/kg. Mild growth retardation was reported in the offspring of rats administered 225 micrograms/kg.

Sensitization: No applicable information found.

Mutagenicity:

Teriparatide - Negative in Ames test, mouse lymphoma assay, chromosomal aberration assay, and the in vivo micronucleus test.

Section 12 - Ecological Information

No environmental data for the mixture or formulation. The environmental information for ingredient(s) or related material(s) are presented.

Environmental Fate:

Mannitol

Log Kow: -3.10
Log Koc: 0.7
Henry's Law constant (atm*m3/mole): 7.3×10^{-13}
Bioconcentration factor: 1
Biological oxygen demand (5-day): 1.15
Theoretical oxygen demand (5-day): 59%
Chemical oxygen demand (5-day) : 87%

Environmental Summary:

Mannitol - Material is not expected to be toxic to aquatic organisms. Material is expected to exist in the particulate phase if released into the air. Material is expected to have very high mobility in soil and is not expected to volatilize from aquatic environments. Material is not expected to bioconcentrate in aquatic organisms. Material is a simple sugar alcohol and should be readily biodegraded.

Section 13 - Disposal Considerations

Waste Disposal: Dispose of any cleanup materials and waste residue according to all applicable laws and regulations. This material contains m-cresol and may be regulated under 40 CFR 261.24 when disposed in bulk quantities or in a production setting. The finished product, e.g., vials, would not be regulated under 40 CFR 261 for disposal under normal use and handling conditions.

Section 14 - Transport Information

Regulatory Organizations:

DOT: Not Regulated

ICAO/IATA: Not Regulated

IMO: Not Regulated

Section 15 - Regulatory Information

Below is selected regulatory information chosen primarily for possible Eli Lilly and Company usage. This section is not a complete analysis or reference to all applicable regulatory information. Please consider all applicable laws and regulations for your country/state.

U.S. Regulations

Teriparatide

TSCA - No

CERCLA - Not on this list

SARA 302 - Not on this list

SARA 313 - Not on this list

OSHA Substance Specific - No

Remaining Ingredients

TSCA - Yes

CERCLA - Not on this list

SARA 302 - Not on this list

SARA 313 - Not on this list

OSHA Substance Specific - No

m-Cresol

TSCA - Yes

CERCLA - Name on list is m-cresol or m-cresylic acid or phenol, methyl-, or cresol, isomers and mixture. RQ = 100 pounds (45.4 kg)

SARA 302 - Not on this list

SARA 313 - Name on list is m-cresol. De minimis = 1%

OSHA Substance Specific - No

EU Regulations

EC Classification

Xn (Harmful)

Reproductive Category 3

Risk Phrases

R 62 - Possible risk of impaired fertility.

R 63 - Possible risk of harm to the unborn child.

Safety Phrases

S 36/37/39 - Wear suitable protective clothing, gloves and eye/face protection.

S 53 - Avoid exposure - obtain special instructions before use.

Section 16 - Other Information

MSDS Sections Revised: Section 1.

As of the date of issuance, we are providing available information relevant to the handling of this material in the workplace. All information contained herein is offered with the good faith belief that it is accurate. THIS MATERIAL SAFETY DATA SHEET SHALL NOT BE DEEMED TO CREATE ANY WARRANTY OF ANY KIND (INCLUDING WARRANTY OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE). In the event of an adverse incident associated with this material, this safety data sheet is not intended to be a substitute for consultation with appropriately trained personnel. Nor is this safety data sheet intended to be a substitute for product literature which may accompany the finished product.

For additional information contact:

Eli Lilly and Company

Hazard Communication

317-651-9533

GLOSSARY:

ACGIH = American Conference of Governmental Industrial Hygienists

AIHA = American Industrial Hygiene Association
BEI = Biological Exposure Index
CAS Number = Chemical Abstract Service Registry Number
CERCLA = Comprehensive Environmental Response Compensation and Liability Act (of 1980)
CHAN = Chemical Hazard Alert Notice
CHEMTREC = Chemical Transportation Emergency Center
DOT = Department of Transportation
EC = European Community
EINECS = European Inventory of Existing Chemical Substances
ELINCS = European List of New Chemical Substances
EPA = Environmental Protection Agency
HEPA = High Efficiency Particulate Air (Filter)
IARC = International Agency for Research on Cancer
ICAO/IATA = International Civil Aviation Organization/International Air Transport Association
IEG = Lilly Interim Exposure Guideline
IMO = International Maritime Organization
Kow = Octanol/Water Partition Coefficient
LEG = Lilly Exposure Guideline
LEL = Lower Explosive Limit
MSDS = Material Safety Data Sheet
MSHA = Mine Safety and Health Administration
NA = Not Applicable, except in Section 14 where NA = North America
NADA = New Animal Drug Application
NAIF = No Applicable Information Found
NCI = National Cancer Institute
NIOSH = National Institute for Occupational Safety and Health
NOS = Not Otherwise Specified
NTP = National Toxicology Program
OSHA = Occupational Safety and Health Administration
PEL = Permissible Exposure Limit (OSHA)
RCRA = Resource Conservation and Recovery Act
RQ = Reportable Quantity
RTECS = Registry of Toxic Effects of Chemical Substances
SARA = Superfund Amendments and Reauthorization Act
STEG = Lilly Short Term Exposure Guideline
STEL = Short Term Exposure Limit
TLV = Threshold Limit Value (ACGIH)
TPQ = Threshold Planning Quantity
TSCA = Toxic Substances Control Act
TWA = Time Weighted Average/8 Hours Unless Otherwise Noted
UEL = Upper Explosive Limit
UN = United Nations
WEEL = Workplace Environmental Exposure Level (AIHA)