

Leuprolide Acetate Injection

1. PRODUCT IDENTIFICATION

Product Name Leuprolide Acetate Injection
Product Use Medical Treatment; Prostate Cancer, Central Precocious Puberty
Manufacturer Teva Parenteral Medicines, Inc.
Address 11 Hughes
 Irvine, CA 92618-1902

Chemtrec Emergency No. 1-800-424-9300 (United States)
 1-202-483-7617 (International Collect)

Business Phone 1-800-729-9991
Website Address <http://www.newsicor.com>

Common Names Lupron®
Chemical Name 5-Oxo-L-propyl-L-histidyl-L-tryptophyl-L-seryl-L-tyrosyl-D-leucyl-L-leucyl-L-arginyl-N-ethyl-L-prolinamide acetate (salt)

Chemical Formula C₅₉H₈₄N₁₆O₁₂•C₂H₄O₂
Chemical Family Nonapeptide

How Supplied 5 mg/mL, 2.8 mL in a 6 mL vial

Date of Preparation: December 11, 2005

2. COMPOSITION AND INGREDIENTS

CHEMICAL NAME	CAS#	EXPOSURE LIMITS IN AIR					
		Wt%	ACGIH		OSHA		Other
			TLV	STEL	PEL	STEL	
Leuprolide Acetate	74381-53-6	0.5	NE	NE	NE	NE	20 ng/m3 TWA
Benzyl Alcohol	500-51-6	0.9	NE	NE	NE	NE	NE
Sodium Chloride	7647-14-5	0.63	NE	NE	NE	NE	NE
Sodium Hydroxide and/or Glacial Acetic Acid	1310-73-2 64-19-7	Trace	2 (C) ppm 10 ppm	NE	NE 10 ppm	2 mg/m3 NE	NE
Water (for injection)	7732-18-5	Balance	NE	NE	NE	NE	NE

NE - Not Established C - Ceiling Limit *Innovators exposure limit

NOTE: All WHMIS required information is included. It is located in appropriate sections based on the ANSI Z400.1 format

CHEMTREC NUMBER: Use only in the event of a chemical emergency involving a spill, leak, fire, exposure or accident involving this drug.



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3. HAZARD IDENTIFICATION

EMERGENCY OVERVIEW: Material is clear, colorless, odorless liquid. May cause damage to the cardiovascular, nervous and reproductive systems. Harmful to the fetus. Avoid contact with eyes, skin and clothing. Avoid exposure during pregnancy and while breastfeeding. Do not taste or swallow. Wash thoroughly after handling.

Symptoms of Overexposure by Route of Exposure: This material is intended for subcutaneous injection under the supervision of physicians.

Inhalation: Inhalation of significant amounts of the product is not anticipated to occur because of the small size of individual containers.

Contact with Skin or Eyes: Contact may cause mild irritation. Effects may include stinging, watering, and redness of the eyes and redness and a burning sensation of the skin. May cause an allergic skin reaction.

Ingestion: Ingestion is not an anticipated route of occupational exposure. The active ingredient, Leuprolide Acetate, is not acutely toxic if swallowed. Symptoms similar to those identified under injection may occur.

Injection: Local redness and pain are the primary symptoms of accidental injection in an occupational setting. Medical personnel are not anticipated to experience over-exposures to the therapeutic doses of this product. However, effects including headaches, hot flashes, and mood changes, constipation, nausea, vomiting, stomach pains and disturbances of the digestive system, joint pain, bone and muscle pain, muscle spasms, blurred vision, itching rashes, fever, chills, dry skin and skin pigmentation changes, hair loss, and incontinence may occur. See package insert for other adverse reactions associated with therapeutic doses of this product.

Health Effects or Risks From Exposure (An explanation in lay terms):

Acute: The primary health effects anticipated in an occupational setting include irritation of eyes and skin as well as redness and local swelling after accidental injection. In case of over-exposure by injection, effects such headaches, hot flashes, and mood changes, constipation, nausea, vomiting, stomach pains and disturbances of the digestive system, joint pain, bone and muscle pain, muscle spasms, blurred vision, itching rashes, fever, chills, dry skin and skin pigmentation changes, hair loss, and incontinence may occur.

Cancer: Leuprolide Acetate has been tested for cancer (see Section 11 for additional information).

Chronic: Leuprolide Acetate is considered a potential developmental and reproductive toxicant (see Section 11).

Target Organs: Potential hazard to the cardiovascular, nervous and reproductive systems (see Section 11).

Other: This product contains benzyl alcohol which is potentially toxic when administered locally to neural tissues. Benzyl alcohol has been reported to be associated with fatal "gaspings syndrome" in premature infants.

Pre-Existing Medical Conditions: Pre-existing nervous, reproductive and cardiovascular disorders may be aggravated by exposure to this material.



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6. ACCIDENTAL RELEASE MEASURES

Spill and Leak Response:

For small releases of this product, wear latex or nitrile gloves and safety glasses. Absorb spilled liquid and rinse area thoroughly with soap and water.

For large or uncontrolled releases, stay away from spill. Isolate immediate hazard area and keep unauthorized personnel out. Contain spill if it can be done with minimal risk. Wear appropriate protective equipment including respiratory protection as conditions warrant (see Section 8). Prevent spilled material from entering sewers, storm drains, other unauthorized treatment drainage systems, and natural waterways. Dike far ahead of spill for later recovery or disposal. Spilled material may be absorbed into an appropriate absorbent material. Notify appropriate federal, state, and local agencies. Immediate cleanup of any spill is recommended.

7. HANDLING and STORAGE

Work and Hygiene Practices: As with all chemicals, avoid getting this product ON YOU or IN YOU. Do not eat, drink, smoke or apply cosmetics while handling the product. Wash hands thoroughly after handling.

Particular care in working with this product must be practiced in pharmacies and other preparation areas, during manufacture of this product, and during patient administration. Precautions should be taken during the following activities:

- Withdrawal of needles from drug vials.
- Drug transfers using syringes and needles or filter straws.
- Expulsion of air from drug-filled syringes.

Storage and Handling Practices: Employees must be trained to properly use the product. Ensure vials are properly labeled. Store only in approved containers. Keep away from any incompatible materials or conditions (see Section 10). Store containers below 77°F (25°C). Do not freeze. Protect from light. Store vial in carton until used.

Protective Practices During Maintenance of Contaminated Equipment: When cleaning non-disposable equipment, wear latex or nitrile gloves (double gloving is recommended), goggles, and lab coat. Wash equipment with soap and water. All needles, syringes, vials and other disposable items contaminated with this product should be disposed of properly.



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8. EXPOSURE CONTROLS - PERSONAL PROTECTION

Ventilation and Engineering Controls: Use with adequate ventilation. Follow standard medical product handling procedures.

Respiratory Protection: Not normally required for routine, medical administration of this product. A NIOSH certified air-purifying respirator with a type 95 filter may be used under conditions where airborne concentrations are expected to be excessive. Protection provided by air purifying respirators is limited (see manufacturer's respirator selection guide). Use a positive pressure air supplied respirator if there is potential for uncontrolled release, exposure levels are not known, or any other circumstances where air-purifying respirators may not provide adequate protection. A respiratory protection program that meets OSHA's 29 CFR 1910.134 and ANSI Z88.2 requirements must be followed whenever workplace conditions warrant a respirator's use.

Eye Protection: Approved eye protection to safeguard against potential eye contact, irritation or injury is recommended. Depending on conditions of use, a face shield may be necessary.

Hand Protection: Use latex, nitrile, or rubber gloves. Check gloves for leaks. Wash hands before and after using gloves.

Body Protection: No special body protection required for routine, medical administration of this product. Wear lab coat, gown, or smock, as appropriate for procedure.

Product Preparation Instructions for Medical Personnel: Follow standard procedure for handling pharmaceutical materials and recommendations presented on the Package Insert.

9. PHYSICAL and CHEMICAL PROPERTIES

Relative Vapor Density (air = 1):	Not determined	Evaporation Rate (n-BuAc=1):	>1
Specific Gravity (water = 1):	Approx. 1	Melting/Freezing Point:	Not determined
Solubility in Water:	Soluble	Boiling Point:	Approx 100°C
Vapor Pressure, mm Hg @	Not determined	pH:	5.5-6.5
Odor Threshold: Odorless			
Appearance and Color: Clear, colorless, odorless liquid			

10. STABILITY and REACTIVITY

Stability: Stable under normal conditions of storage and handling.

Materials With Which Substance is Incompatible: This product is generally compatible with other common materials in a medical facility. This product would not be compatible with strong oxidizers.

Hazardous Polymerization: Will not occur.

Hazardous Combustion Products: Heat may cause product to decompose, destroying the product or producing carbon oxides as well as oxides of nitrogen.



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11. TOXICOLOGICAL INFORMATION

Toxicity Data: The following information is for Leuprolide Acetate, the active ingredient

Oral LD50(rat) >5 g/kg	IV LD50(rat) =29900 ug/kg	IP LD50(rat) >5 g/kg
Oral LD50(Mouse) > 5 g/kg	IV LD50(mouse) = 137 mg/kg	IP LD50(mouse) >5 g/kg
SubQ(mouse) >5 g/kg	SubQ(rat) >5 g/kg	IM LD50(rat) >2 g/kg
IM LD50(mouse) >2 g/kg		

Suspected Cancer Agent: Sex steroid hormone-type compounds generally can promote cell growth and may “promote” tumor production although they are generally not considered to be carcinogenic. This is likely to be the case for Leuprolide Acetate. A dose-dependent increase in benign pituitary tumors was produced at subcutaneous doses ranging from 0.6 to 4 mg/kg/day for 24 months in rats while no increase in tumors was found in mice treated up to 60 mg/kg/day for 24 months or in patients treated up to 10 mg/day for 3 years or 20 mg/day for 2 years. The doses that caused an increase in endocrine organ tumors in laboratory animals are much higher than doses used in patients therapeutically. It is not listed as carcinogenic by NTP, IARC or OSHA.

Irritancy of Product: This product is expected to be mildly irritating to contaminated skin, eyes and other tissues.

Sensitization to the Product: No data is available to indicate it is a sensitizer.

Target Organ(s): May cause nervous and cardiovascular disorders.

Reproductive Toxicity Information: Leuprolide Acetate has rating of Pregnancy Category X (Contra-indicated in Pregnancy) and is a human reproductive toxin, based on both human and animal data. Listed below is information concerning the effects of Leuprolide Acetate, the active ingredient on this product, on the human reproductive system.

Mutagenicity: Sex steroid hormone-type compounds generally do not affect genetic material directly. These compounds usually test negative in various short-term screening tests for genetic damage. This is the case for Leuprolide. There was no evidence that leuprolide possessed genotoxicity potential in these tests.

Embryotoxicity/Teratogenicity/Reproductive Toxicity: When administered subcutaneously on day 6 of pregnancy to rabbits at a dose of 0.24, 2.4, or 24 µg/kg (1/300, 1/30, and 1/3 the recommended human dose), leuprolide produced a dose-related increase in major fetal abnormalities. Similar studies failed to demonstrate an increase in fetal malformations in rats. An increased in fetal mortality occurred at the two higher doses in rabbits and at the highest dose in rats. The effects on fetal mortality are logical consequences of the alterations in hormonal levels caused by this drug.

As a result of its pharmacological actions on sex steroid hormones, leuprolide clearly impairs fertility in animals and humans. Leuprolide can reduce male and female sex steroid hormones in humans to castrate levels at the therapeutic dose, either as daily 1 mg subcutaneous injections or as monthly 3.75 or 7.5 mg depot injections. This reduction in sex steroid hormones and inhibition of fertility is reversible upon cessation of drug exposure.



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11. TOXICOLOGICAL INFORMATION cont..

ACGIH Biological Exposure Indices: Currently there are no Biological Exposure Indices (BEIs) associated with the components of this product.

12. ECOLOGICAL INFORMATION

All work practices must be aimed at eliminating environmental contamination.

Environmental Stability: This product will be relatively stable under ambient environmental conditions.

Effect of Materials on Plants or Animals: No specific information is available on the effect on plants or animals in the environment. This product may be harmful to contaminated plant and animal life. Refer to Section 11 (Toxicological Information) for additional information on Leuprolide Acetate and its effects on test animals.

Effect of Chemicals on Aquatic Life: No specific information is available on the effect on plants or animals in the aquatic environment. This product may be harmful to aquatic plant and animal life in contaminated bodies of water, especially in large quantities.

13. DISPOSAL CONSIDERATIONS

Preparing Wastes for Disposal: This material, if discarded as produced, is not a RCRA "listed" hazardous waste. Use resulting in chemical or physical change or contamination may subject it to regulation as a hazardous waste. Along with properly characterizing all waste materials consult state and local regulations regarding the proper disposal of this material.

U.S. EPA Waste Number: None

14. TRANSPORTATION INFORMATION

This Materials is not Hazardous as Defined by 49 CFR 172.101 by the U. S. Department of Transportation

Proper Shipping Name: Not applicable

Hazard Class Number and Description: Not applicable

UN Identification Number: Not applicable

Packing Group: Not applicable

DOT Label(s) Required: Not applicable

North American Emergency Response Guidebook Number (1996): Not applicable.

MARINE POLLUTANT: No component of this product is listed as a Marine Pollutant (49 CFR 172.101, Appendix B)

Transport Canada Transportation of Dangerous Goods Regulations: Not applicable



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15. REGULATORY INFORMATION

U.S. REGULATIONS

U.S. SARA Reporting Requirements: The components of this product are not subject to the reporting requirements of Sections 302, 304 and 313 of Title II of the Superfund Amendments and Reauthorization Act.

U.S. SARA Threshold Planning Quantity: Not applicable

U.S. TSCA Inventory Status: Leuprolide Acetate is a "drug" as defined by the Federal Food, Drug and Cosmetic Act and is therefore not a chemical substance under TSCA.

California Safe Drinking Water and Toxic Enforcement Act (Proposition 65): Leuprolide Acetate is a chemical known to the State of California to cause developmental and reproductive effects.

Other U.S. Federal Regulations: Based on this product's use, the requirements of the OSHA Bloodborne Pathogen Standard (29 CFR 1910.1030) are applicable.

CANADIAN REGULATIONS

Canadian DSL/NDSL Status: Leuprolide Acetate is regulated by the Food and Drug Administration of Health Canada and is therefore exempt from the requirements of CEPA.

ANSI Labeling (Based on 129.1, Provided to Summarize Occupational Exposure Hazards): Harmful to the Fetus. May Cause Damage to the Cardiovascular, Nervous and Reproductive Systems. Leuprolide Acetate should be administered under the supervision of a qualified physician. Avoid over-exposure. Avoid contact with eyes, skin and clothing. Avoid exposure during pregnancy and while breastfeeding. Avoid accidental injection. Do not eat, drink or smoke when handling. Do not taste or swallow. Wash thoroughly after handling. Clean up spills promptly.

16. OTHER INFORMATION

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