

**MATERIAL SAFETY DATA SHEET****1. PRODUCT IDENTIFICATION**

Product name Leuprolide acetate Injection
1 mg/0.2 ml, 2.8 ml Multi Dose Vial

Company Name Sun Pharmaceutical Industries Ltd.
Acme Plaza, Andheri-Kurla Road, Andheri (E)
Mumbai – 400 059, INDIA

2. COMPOSITION AND INGREDIENTS

CHEMICAL NAME	Composition (mg/mL)
Leuprolide acetate (Equivalent to 4.75 mg free base)	5 mg
Benzyl alcohol NF (As preservative)	9 mg
Sodium chloride USP (For tonicity adjustment)	
Sodium Hydroxide NF (To adjust pH)	
Glacial acetic acid USP (To adjust pH)	
Water for Injection USP	

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.



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3. HAZARD IDENTIFICATION Cont...

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 as 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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4. FIRST-AID MEASURES

Skin Exposure: Remove contaminated shoes and clothing and cleanse affected area(s) thoroughly by washing with mild soap and water. If irritation or redness develops and persists, seek medical attention.

Eye Exposure: If irritation or redness develops, move victim away from exposure and into fresh air. Flush eyes with clean water and seek medical attention.

Inhalation: If respiratory symptoms develop, move victim away from source of exposure and into fresh air. If symptoms persist, seek medical attention. If victim is not breathing, clear airway and immediately begin artificial respiration. If breathing difficulties develop, oxygen should be administered by qualified personnel. Seek immediate medical attention.

Ingestion: If swallowed, seek emergency medical attention. If victim is drowsy or unconscious and vomiting, place on the left side with the head down and DO NOT give anything by mouth. If not vomiting and professional advice is not available, DO NOT induce vomiting. If possible, do not leave victim unattended and observe closely for adequacy of breathing.

Victims of chemical exposure must be taken for medical attention. Take a copy of the MSDS to the physician or health professional with victim. Physicians should refer to Section 11 (Toxicological Information) as well as the Physicians Desk Reference for additional treatment information.

5. FIRE-FIGHTING MEASURES

Flash Point: Not flammable Autoignition Temperature: Not applicable

Flammable Limits (in air by volume, %): Not applicable

Fire Extinguishing Equipment: The size and nature of this product is such that it will not contribute to the intensity of a fire. Use extinguishing agent suitable for type of surrounding fire.

Carbon Dioxide: OK

Halon: OK

Foam: OK

Water spray: OK

Dry Chemical: OK

Other: Any "ABC" Class



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5. FIRE-FIGHTING MEASURES Cont...

Unusual Fire and Explosion Hazards: When heated to decomposition, this product may emit toxic fumes.

Explosion Sensitivity to Mechanical Impact: Not sensitive

Explosion Sensitivity to Static Discharge: Not sensitive.

Special Fire Fighting Procedures: For fires beyond the incipient stage, emergency responders in the immediate hazard area should wear bunker gear. When the potential chemical hazard is unknown, in enclosed or confined spaces, or when explicitly required by DOT, a self-contained breathing apparatus should be worn. In addition, wear other appropriate protective equipment as conditions warrant (see Section 8). Isolate immediate hazard area and keep unauthorized personnel out. Contain spill if it can be done with minimal risk. Move undamaged containers from immediate hazard area if it can be done with minimal risk. Cool equipment exposed to fire with water, if it can be done with minimal risk.

NFPA HAZARD CLASS:

Health: 1 (Slight)

Flammability: 0 (Least)

Reactivity: 0 (Least)

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.



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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 77⁰F (25⁰C). 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

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



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8. EXPOSURE CONTROLS - PERSONAL PROTECTION Cont...

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		

**MATERIAL SAFETY DATA SHEET****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.

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.

**MATERIAL SAFETY DATA SHEET****11. TOXICOLOGICAL INFORMATION Cont..**

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 $\mu\text{g}/\text{kg}$ (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.

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



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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



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14. TRANSPORTATION INFORMATION Cont...

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