

Eligard[®] 7.5 MG

1. CHEMICAL PRODUCT AND COMPANY IDENTIFICATION

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PRODUCT NAME: Eligard[®] 7.5 mg
SYNONYMS: Leuprolide acetate for injectable suspension

2. HAZARDS IDENTIFICATION

APPEARANCE: ELIGARD[®] 7.5 mg is available in a single use kit. The kit consists of a two-syringe mixing system, a 19-gauge 5/8-inch needle, a silicone desiccant pouch to control moisture uptake, and a package insert for constitution and administration procedures. Each syringe is individually packaged. One contains the ATRIGEL[®] Delivery System (including N-methyl-pyrrolidone) and the other contains the active ingredient leuprolide acetate.

EMERGENCY OVERVIEW: Warning: Leuprolide acetate is a potent drug, and sex hormones may be reduced in both men and women who are exposed. Leuprolide acetate may be harmful if swallowed, inhaled or absorbed through skin. Risk of fetal harm. May cause irritation to skin and eyes.

INHALATION: N-Methyl-2-pyrrolidone: May cause pallor, nausea, anesthetic or narcotic effects.

SKIN AND EYE EFFECTS: N-Methyl-2-pyrrolidone: Irritant.

3. COMPOSITION/INFORMATION ON INGREDIENTS

ELIGARD[®] 7.5 mg is prefilled and supplied in two separate, sterile syringes whose contents are mixed immediately prior to administration. The two syringes are joined and the single dose product is mixed until it is homogenous.

One syringe contains the ATRIGEL[®] Delivery System and the other contains leuprolide acetate. ATRIGEL[®] is a polymeric (non-gelatin containing) delivery system consisting of a biodegradable poly (DL-lactide-co-glycolide) (PLG) polymer formulation dissolved in a biocompatible solvent, N-methyl-2-pyrrolidone (NMP).

The second syringe contains leuprolide acetate and the constituted product is designed to deliver 7.5 mg of leuprolide acetate at the time of subcutaneous injection.

ACTIVE INGREDIENT: Leuprolide acetate
CAS NUMBER: 74381-53-6

INACTIVE INGREDIENTS:

<u>INGREDIENT</u>	<u>CAS NUMBER</u>
N-methyl-2-pyrrolidone (NMP)	872-50-4
ATRIGEL [®] (1,4 Dioxane-2, 5-dione; 3,6-dimethyl-1,4-dioxane-2, 5-dione, polymer and copolymer (PLG))	26780-50-7

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4. FIRST AID MEASURES

EYES

In case of contact with liquid, flush eyes with water for at least 15 minutes. Seek medical attention if irritation develops.

SKIN

If liquid comes in contact with skin and clothing, remove contaminated clothing and wash thoroughly with running water for at least 15 minutes. Use soap if available. Seek medical attention if irritation develops.

INGESTION

In case of acute overdose by ingestion, seek immediate medical attention.

INHALATION

Remove to fresh air, seek immediate medical attention.

NOTE TO PHYSICIAN

Treat symptomatically and supportively.

5. FIRE FIGHTING MEASURES

N-Methyl-2-pyrrolidone:

FLASH POINT: 187 F (86 C) (CC)

LOWER FLAMMABLE LIMIT: 1.3%

UPPER FLAMMABLE LIMIT: 9.5%

AUTOIGNITION: 655 F (346 C)

FIRE AND EXPLOSION HAZARDS

This formulation is aqueous based and does not present any significant fire and explosion hazards.

EXTINGUISHING MEDIA

Use any extinguishing agent which is suitable for the surrounding fire.

FIRE FIGHTING INSTRUCTIONS

As in any fire, wear pressure demand self-contained breathing apparatus (SCBA), NIOSH approved or equivalent, and full protective gear.

6. ACCIDENTAL RELEASE MEASURES

Personal protective equipment should be worn when cleaning up a spill [See Section 8].

Soak up contents of spilled liquid with an absorbent material. Carefully collect materials and place in a properly labeled waste container for disposal. Wash area of spill to remove from surfaces. Wash thoroughly after handling.

7. HANDLING AND STORAGE

HANDLING AND STORAGE PRECAUTIONS

Store product at 2-8 °C (35.6-46.4 °F).

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WORK/HYGIENE PRACTICES

Avoid contact with eyes, skin, and clothing. Use local exhaust ventilation, supplementary ventilation or respiratory protection for operations which generate aerosols. Wash thoroughly after handling.

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

A risk assessment should be performed on operations which generate aerosols.

EXPOSURE LIMITS

Leuprolide acetate: Sanofi-aventis Occupational Exposure Band 4 (1-10 mcg/m³). 8-hour TWA.

N-METHYL-2-PYRROLIDONE:

10 ppm AIHA WEEL recommended TWA (cutaneous absorption danger)

25 ppm (103 mg/m³) UK WEL TWA (skin)

75 ppm (309 mg/m³) UK WEL STEL (skin)

ATRIGEL[®]: Not available.

ENGINEERING CONTROLS

Normal ventilation. However, if aerosols are generated, local exhaust ventilation may be required.

EYE/FACE PROTECTION

Avoid eye contact with liquid and aerosol. Wear safety glasses with side shields or goggles where risk of eye exposure exists.

SKIN PROTECTION

Avoid skin contact with liquid and aerosol. Impervious gloves should be worn.

RESPIRATORY PROTECTION

None normally required. However, a respiratory protection program that meets OSHA 29 CFR 1910.134 and ANSI Z88.2 requirements must be followed whenever workplace conditions warrant respirator usage, such as operations which generate aerosols.

9. PHYSICAL AND CHEMICAL PROPERTIES

ELIGARD:

APPEARANCE

Clear, colorless to pale yellow liquid.

BASIC PHYSICAL PROPERTIES

pH: 3.2 - 4.0

N-Methyl-2-pyrrolidone:

PHYSICAL STATE: liquid

COLOR: colorless to yellow

ODOR: fishy odor

MOLECULAR WEIGHT: 99.13

MOLECULAR FORMULA: C₅H₉N-O

BOILING POINT: 396-399 F (202-204 C)

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FREEZING POINT: -11 to -9 F (-24 to -23 C)
VAPOR PRESSURE: 0.29 mmHg @ 20 C
VAPOR DENSITY (air=1): 3.4
SPECIFIC GRAVITY (water=1): 1.026-1.033
WATER SOLUBILITY: miscible
PH: 7.7-8.0 (10% solution)

Leuprolide acetate:

PHYSICAL STATE: Solid, fluffy powder.
COLOR: White to off-white.
ODOR: Slight odor.
CHEMICAL FORMULA: C₅₉ H₈₄ N₁₆ O₁₂ – C₂ H₄ O₂
MOL. WT.: 1269.65.

10. STABILITY AND REACTIVITY

STABILITY

Stable

HAZARDUS DECOMPOSITION PRODUCTS

Carbon monoxide and oxides of nitrogen emitted when heated to decomposition.

INCOMPATIBLE MATERIALS

Strong oxidizers and reducing agents.

HAZARDOUS POLYMERIZATION

Will not occur.

11. TOXICOLOGICAL INFORMATION

ELIGARD/Leuprolide acetate:

Acute toxicity: Oral LD₅₀ (rat) > 5,000 mg/kg

Carcinogenesis, Mutagenesis, Impairment of Fertility: Two-year carcinogenicity studies were conducted with leuprolide acetate in rats and mice. In rats, a dose-related increase of benign pituitary hyperplasia and benign pituitary adenomas was noted at 24 months when the drug was administered subcutaneously at high daily doses (0.6 to 4 mg/kg). There was a significant but not dose-related increase of pancreatic islet-cell adenomas in females and of testicular interstitial cell adenomas in males (highest incidence in the low dose group). In mice, no leuprolide acetate-induced tumors or pituitary abnormalities were observed at a dose as high as 60 mg/kg for two years. No carcinogenicity studies have been conducted with ELIGARD[®].

Mutagenicity studies have been performed with leuprolide acetate using bacterial and mammalian systems and with ELIGARD[®] in bacterial systems. These studies provided no evidence of a mutagenic potential.

Leuprolide acetate can cause fetal harm when administered to a pregnant woman. Major fetal abnormalities were observed in rabbits but not in rats after administration of leuprolide acetate throughout gestation. There were increased fetal mortality and decreased fetal weights in rats and rabbits. The effects on fetal mortality are expected consequences of the alterations in hormonal levels brought about by this drug. The possibility exists that spontaneous abortion may occur.

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N-Methyl-2-pyrrolidone:**INHALATION:****ACUTE EXPOSURE:**

Inhalation of very high vapor concentrations may cause mucous membrane irritation, headache, giddiness, mental confusion, and nausea. Inhalation of 180-200 mg/m³ for 2 hours, and a 6 hour exposure to saturated vapors caused no deaths in mice and rats.

Inhalation LC50 (rat) > 400 ppm

CHRONIC EXPOSURE:

Prolonged exposure to very high vapor concentrations may cause headache, giddiness, mental confusion and nausea. In one case study, a 23 year old laboratory technician experienced a stillbirth after occupational exposure in the first trimester of pregnancy. Inhalation studies in laboratory animals failed to show any gross or histopathological abnormalities when exposed to concentrations of 50 ppm/8 hours/day for 20 days or 370 ppm/6 hours/day for 10 days.

SKIN CONTACT:**ACUTE EXPOSURE:**

Contact may cause mild irritation. Skin absorption may occur.

Dermal LD50 (rabbit) = 8,000 mg/kg

CHRONIC EXPOSURE:

Prolonged contact has been reported to cause severe dermatitis with redness, cracking, swelling, blisters and edema. Reproductive effects have been reported in animals.

EYE CONTACT:**ACUTE EXPOSURE:**

Exposure to vapors may cause irritation. Contact with the liquid may cause painful burning or stinging of eyes and lids, watering of the eyes, inflammation of conjunctiva and temporary corneal clouding.

CHRONIC EXPOSURE:

Repeated or prolonged exposure to irritants may cause conjunctivitis.

INGESTION:**ACUTE EXPOSURE:**

Ingestion may cause gastrointestinal disturbances.

Oral LD50 (rat) = 4,500 mg/kg

CHRONIC EXPOSURE:

Ninety day feeding studies in laboratory animals at concentrations up to 1% of their diet failed to demonstrate any toxicologically relevant effect. Mice fed 2500 ppm for three months produced significantly increased mean absolute and relative liver weights and 7500 ppm produced centrilobular hypertrophy of the liver cells. At 7500 and 18,000 ppm rats developed neurobehavioral changes. It has been demonstrated to be embryotoxic to rats and mice in very high doses.

12. ECOLOGICAL INFORMATION

N-Methyl-2-pyrrolidone:

Elimination information (persistence and degradability):

Biodegradability Result: 90 % - Readily biodegradable.

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Ecotoxicity effects

Toxicity to fish:

LC50 - other fish - 4,000 mg/l - 96 h

LC50 - Leuciscus idus (Golden orfe) > 500 mg/l - 96 h

Toxicity to aquatic invertebrates:

EC50 - Daphnia magna (Water flea) > 1,000 mg/l – 24

No data available for other constituents.

13. DISPOSAL CONSIDERATIONS

Dispose of in accordance with local, state and federal regulations.

14. TRANSPORT INFORMATION

This product is not regulated by US DOT as a hazardous material.

This product is not regulated by ICAO/IATA as a dangerous good.

N-Methyl-2-pyrrolidone is regulated by US DOT as a Class 3 Combustible Liquid (NA 1993) in bulk quantities only (> 119 gallons).

15. REGULATORY INFORMATION

U.S. FEDERAL REGULATORY INFORMATION

N-Methyl-2-pyrrolidone is subject to reporting under section 313 of EPCRA (SARA Title III).

STATE REGULATIONS:

California Proposition 65: This product contains chemicals known to the state of California to cause birth defects or other reproductive harm:

N-METHYL-2-PYRROLIDONE

LEUPROLIDE ACETATE

16. OTHER INFORMATION

N/A = Not Applicable N/D = Not Determined ~ = Approximately Equal To

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