

SAFETY DATA SHEET

1. Identification

Product Identifier: Lorazepam Injection, USP CIV

Synonyms: 7-Chloro-5-(2-chlorophenyl)-1,3-dihydro-3-hydroxy-2H-1,4-benzodiazepin-2-one

National Drug Code (NDC): 17478-040-01

Recommended Use: Pharmaceutical.

Company: Akorn, Inc.
1925 West Field Court, Suite 300
Lake Forest, Illinois 60045

Contact Telephone: 1-800-932-5676

E mail: customer.service@akorn.com

Emergency Phone Number: CHEMTREC 1-800-424-9300 (U.S. and Canada)

2. Hazard(s) Identification

Physical Hazards: Not classifiable.

Health Hazards: Eye Damage / Irritation Category 2B
Toxic to Reproduction Category 2

Symbol(s):



Signal Word:

Warning.

Hazard Statement(s):

H320 Causes eye irritation.

H361 Suspected of damaging fertility or the unborn child.

Precautionary Statement(s):

P201 Obtain special instructions before use.

P202 Do not handle until all safety precautions have been read and understood.

P280 Wear protective gloves/protective clothing/eye protection/face protection.

P260 Do not breathe vapor or spray.

P264 Wash hands thoroughly after handling.

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P308 If exposed or concerned: Get medical advice/attention.
+
P313

P314 Get medical attention if you feel unwell.

P305 IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
+
P351
+
P338

P337 If eye irritation persists, get medical advice/attention.
+
P313

Hazards Not Otherwise Classified: None.
Supplementary Information: None.

3. Composition/Information on Ingredients

Chemical Name	CAS Number	Synonyms	Chemical Formula	Molecular Weight	Percentage
Lorazepam	846-49-1	7-Chloro-5-(2-chlorophenyl)-1,3-dihydro-3-hydroxy-2H-1,4-benzodiazepin-2-one	C ₁₅ H ₁₀ Cl ₂ N ₂ O ₂	321.16	2.0 mg

*The formula also contains Polyethylene Glycol 400, 203 mg; and Benzyl Alcohol, 2.0%.

4. First Aid Measures

Ingestion:

Remove from source of exposure. If signs of toxicity occur, seek medical attention. Provide symptomatic/supportive care as necessary. Overdosage is manifested by varying degrees of central-nervous-system depression, ranging from drowsiness to coma. In mild cases, symptoms include drowsiness, mental confusion, and lethargy. In more serious cases, symptoms may include ataxia, hypotonia, hypotension, hypnosis, stages one (1) to three (3) coma, and very rarely, death. Treatment of overdosage is mainly supportive until the drug is eliminated from the body. Vital signs and fluid balance should be carefully monitored in conjunction with close observation of the patient. An adequate airway should be maintained and assisted respiration used as needed. With normally functioning kidneys, forced diuresis with intravenous fluids and electrolytes may accelerate elimination of benzodiazepines from the body. In addition, osmotic diuretics, such as mannitol, may be effective as adjunctive measures. In more critical situations, renal dialysis and exchange blood transfusions may be indicated. Lorazepam does not appear to be removed in significant quantities by dialysis, although lorazepam glucuronide may be highly dialyzable. The value of

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dialysis has not been adequately determined for lorazepam. The benzodiazepine antagonist flumazenil may be used in hospitalized patients as an adjunct to, not as a substitute for, proper management of benzodiazepine overdose. The prescriber should be aware of a risk of seizure in association with flumazenil treatment, particularly in long-term benzodiazepine users and in cyclic antidepressant overdose.

Eye Contact:

Remove from source of exposure. Flush with copious amounts of water for at least 15 minutes. If irritation persists or signs of toxicity occur, seek medical attention. Provide symptomatic/supportive care as necessary. Ensure that medical personnel are aware of the material(s) involved and are aware of precautions to protect themselves.

Skin Contact:

Remove from source of exposure. Remove and isolate contaminated clothing and shoes. Flush with copious amounts of water for at least 20 minutes. If irritation persists or signs of toxicity occur, seek medical attention. Provide symptomatic/supportive care as necessary. Ensure that medical personnel are aware of the material(s) involved and are aware of precautions to protect themselves.

Inhalation:

Remove from source of exposure. Move individual(s) to fresh air. Give artificial respiration if individual(s) are not breathing and call emergency medical service. If signs of toxicity occur, seek medical attention. Provide symptomatic/supportive care as necessary. Ensure that medical personnel are aware of the material(s) involved and are aware of precautions to protect themselves.

Protection of First-Aiders:

Use personal protective equipment (see section 8).

Signs and Symptoms:

None anticipated from normal handling of this product. This product should be considered potentially irritating to the eyes and respiratory tract. In clinical use, common adverse effects include drowsiness, sedation, muscle weakness, and ataxia. Less frequent adverse effects include vertigo, headache, confusion, depression, slurred speech or dysarthria, changes in libido, tremor, visual disturbances, urinary retention or incontinence, gastrointestinal disturbances, decreased blood pressure, changes in salivation, and amnesia. An increased risk of congenital malformations associated with the clinical use of minor tranquilizers (chlordiazepoxide, diazepam, and meprobamate) during the first trimester of pregnancy has been reported.

Medical Conditions Aggravated by Exposure:

Not determined.

Notes to Physician:

Treat supportively and symptomatically.

5. **Firefighting Measures**

- Flammability:** None anticipated for this product. However, when heated, this product may produce combustible vapors.
- Suitable Extinguishing Media:** Use water, carbon dioxide, dry chemical or foam as necessary.
- Unsuitable Extinguishing Media:** Not determined.
- Special Fire Fighting Procedures:** No special provisions required beyond normal firefighting equipment such as flame and chemical resistant clothing and self-contained breathing apparatus.

Specific Hazards Arising from the Chemical:

- Hazardous Combustion Products:** Not determined.
- Other Specific Hazards:** Not determined.
- Special Protective Equipment/Precautions for Firefighters:** No special provisions required beyond normal firefighting equipment such as flame and chemical resistant clothing and self-contained breathing apparatus.

6. **Accidental Release Measures**

- Personal Precautions:** Use personal protective equipment recommended in Section 8 of this document and isolate the hazard area.
- Personal Protective Equipment:** For personal protection see section 8.
- Methods for Cleaning Up:** Isolate area around spill. Put on suitable protective clothing and equipment as specified by site spill control procedures. Absorb the liquid with suitable material and clean affected area with soap and water.
- Environmental Precautions:** No data available.
- Reference to Other Sections:** Refer to Sections 8, 12 and 13 for further information.

7. **Handling and Storage**

- Precautions for Safe Handling:** Handle in accordance with product label and/or product insert information. However, Lorazepam is a Schedule IV controlled substance. Additional training and procedures may be required when handling this material. Handle in accordance with good industrial hygiene and safety practices.
- Conditions for Safe Storage, Including Any Incompatibilities:** Store according to label and/or product insert information. Store away from oxidizing agents and acids.
- Specific End Use:** Pharmaceuticals.

8. Exposure Controls/Personal Protection

Occupational Exposure Guidelines:

Common or Chemical Name	Employee Exposure Limits
Lorazepam	Not established.
Polyethylene Glycol 400	AIHA WEEL: 10 mg/m ³ , 8 Hour TWA
Propylene Glycol	AIHA WEEL: 10 mg/m ³ , 8 Hour TWA
Benzyl Alcohol	AIHA WEEL: 10 ppm, 8 Hour TWA

Engineering Controls:

Engineering controls should be used as the primary means to control exposures.

Respiratory Protection:

Respiratory protection is normally not needed during intended product use. However, if the generation of aerosols is likely, and engineering controls are not considered adequate to control potential airborne exposures, the use of an approved air-purifying respirator with a HEPA cartridge (N95 or equivalent) and an organic vapor cartridge is recommended under conditions where airborne aerosol concentrations are not expected to be excessive. For uncontrolled release events, or if exposure levels are not known, provide respirators that offer a high protection factor such as a powered air purifying respirator or supplied air. A respiratory protection program that meets OSHA's 29 CFR 1910.134 and ANSI Z88.2 requirements must be followed whenever workplace conditions require respirator use. Personnel who wear respirators should be fit tested and approved for respirator use as required.

Eyes Protection:

Not required for the normal use of this product. Safety glasses with side shields are recommended. Face shields or goggles may be required if splash potential exists or if corrosive materials are present. Approved eye protection (e.g., bearing the ANSI Z87 or CSA stamp) is preferred. Maintain eyewash facilities in the work area.

Hand Protection:

Not required for the normal use of this product. Chemically compatible gloves. For handling solutions, ensure that the glove material is protective against the solvent being used. Use handling practices that minimize direct hand contact. Employees who are sensitive to natural rubber (latex) should use nitrile or other synthetic non-latex gloves. Use of powdered latex gloves should be avoided due to the risk of latex allergy.

Skin Protection:

Not required for the normal use of this product. Wear protective laboratory coat, apron, or disposable garment when working with large quantities.

9. Physical and Chemical Properties

Physical State/Color:	Clear colorless solution.
Odor:	No data available.
Odor Threshold:	No data available.
pH:	No data available.
Melting Point:	No data available.
Freezing Point:	No data available.
Boiling Point:	No data available.
Flash Point:	No data available.
Evaporation Rate:	No data available.
Flammability (solid, gas):	No data available.
Flammability Limit - Lower:	No data available.
Flammability Limit - Upper:	No data available.
Vapor Pressure:	No data available.
Vapor Density:	No data available.
Relative Density:	No data available.
Solubility(ies):	Lorazepam is a nearly white powder almost insoluble in water.
Partition Coefficient (n-octanol/water):	No data available.
Auto-Ignition Temperature:	No data available.
Decomposition Temperature:	No data available.
Viscosity:	No data available.

10. Stability and Reactivity

Reactivity:	No data available.
Chemical Stability:	Stable under recommended storage conditions.
Possibility of Hazardous Reactions:	No data available.
Conditions to Avoid (e.g., static discharge, shock, or vibration):	No data available.
Incompatible Materials:	Strong oxidizers, acids.
Hazardous Decomposition Products:	No data available.
Hazardous Polymerization:	Not anticipated to occur with this product.

11. Toxicological Information**Information on the Likely Routes of Exposure:**

Inhalation:	No data available.
Ingestion:	No data available.
Skin Contact:	No data available.
Eye Contact:	No data available.

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Symptoms Related to the Physical, Chemical and Toxicological Characteristics:

See Section 4. To the best of our knowledge, the chemical, physical and toxicological properties have not been thoroughly investigated.

Delayed and Immediate Effects of Exposure:

No data available.

Acute Toxicity:

Compound	Percent	Species	Route	Test Type	Dose
Lorazepam	100%	Rat	Oral	LD ₅₀	4,500 mg/kg
Lorazepam	100%	Mouse	Oral	LD ₅₀	1,850 mg/kg
Lorazepam	100%	Dog	Oral	LD ₅₀	>2000 mg/kg
Benzyl Alcohol	100%	Rat, Mouse, Rabbit, Guinea Pig	Oral	LD ₅₀	1,040 – 2,500 mg/kg
Benzyl Alcohol	100%	Rabbit	Dermal	LD ₅₀	2,000 mg/kg
Propylene Glycol	100%	Rat, Mouse, Rabbit, Dog, Guinea Pig	Oral	LD ₅₀	10,400 – 29,536 mg/kg
Propylene Glycol	100%	Rabbit	Dermal	LD ₅₀	20,800 mg/kg
Polyethylene Glycol	100%	Rat, Mouse, Rabbit, Guinea Pig	Oral	LD ₅₀	15,700 – 30,200 mg/kg
Polyethylene Glycol	100%	Rabbit	Dermal	LD ₅₀	>20,000 mg/kg

LD₅₀: Dosage that produces 50% mortality. LC₅₀ is the concentration in air that produces 50% mortality when inhaled.

Occupational Exposure Potential:

Information on the absorption of this product via inhalation or skin contact is not available. Published reports indicate that some benzodiazepines have the potential to be absorbed through intact skin. Avoid liquid aerosol generation and skin contact.

Acute Toxicity – Dermal:

No data available.

Acute Toxicity – Inhalation:

No data available.

Corrosivity:

No data available.

Dermal Irritation:

None anticipated from normal handling of this product.

Eye Irritation:

None anticipated from normal handling of this product. However, inadvertent contact of this product with eyes may produce irritation with redness and tearing.

Dermal or Respiratory

Sensitization:

None anticipated from normal handling of this product.

Toxicokinetics/Metabolism:

No data available.

Specific Target Organ Toxicity

– Single Exposure:

No data available.

Specific Target Organ Toxicity

– Repeat Exposure:

Based on clinical use, possible target organs include the central nervous system, gastrointestinal system, genitourinary system, and cardiovascular system.

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Reproductive Effects: None anticipated from normal handling of this product. In a preimplantation study in rats, oral administration of lorazepam at a dosage of 20 mg/kg did not impair fertility. Reproductive studies have been conducted in mice, rats, and two strains of rabbits. Occasional anomalies (reduction of tarsals, tibia, metatarsals, malrotated limbs, gastroschisis, malformed skull, and microphthalmia) were noted in rabbits. At dosages of 40 mg/kg orally or 4 mg/kg intravenously and higher, there was evidence of fetal resorption and increased fetal loss in rabbits.

Carcinogenicity: No evidence of carcinogenic potential was noted in rats and mice during an 18-month oral study with lorazepam.

National Toxicology Program (NTP): Not considered to be a carcinogen.

International Agency for Research on Cancer (IARC): Not considered to be a carcinogen.

Occupational Safety and Health Administration (OSHA): Not considered to be a carcinogen.

Mutagenicity: No mutagenicity studies have been conducted.

Aspiration Hazard: None anticipated from normal handling of this product.

12. Ecological Information

Ecotoxicity

Aquatic:

Compound	Species	Test Type	Dose
Polyethylene Glycol	Carassius auratus (goldfish)	LC ₅₀ (24hr)	>5,000 mg/L
Polyethylene Glycol	Oncorhynchus mykiss (rainbow trout)	LC ₅₀ (24hr)	>20,000 mg/L
Benzyl Alcohol	Pimephales promelas	LC ₅₀ (96hr)	460 mg/L
Benzyl Alcohol	Leuciscus idus	LC ₅₀ (96hr)	640 mg/L
Benzyl Alcohol	Daphnia magna	EC ₅₀ (24hr)	400 mg/L
Benzyl Alcohol	Chlorella pyrenoidosa	EC ₅₀ (24hr)	95 mg/L
Propylene glycol	Rainbow trout	LC ₅₀ (96hr)	51,600 mg/L
Propylene glycol	Daphnia magna	LC ₅₀ (48hr)	34,400 – 43,500 mg/L
Propylene glycol	Algae	EC ₅₀ (14day)	19,000 mg/L

Terrestrial: No data available.

Persistence and Degradability: Not determined for the product. Information for ingredients is provided below:
Benzyl Alcohol was degraded over 90% in 28-day biodegradation assay in sewage sludge.

Propylene Glycol was reported to be 100% biodegradable after 24-hours in activated sludge.

Bioaccumulative Potential: No data available.

Mobility in Soil: No data available.
Mobility in Environment: No data available.
Other Adverse Effects: No data available.

13. Disposal Considerations

Dispose of all waste in accordance with Federal, State and Local regulations.

14. Transport Information

UN Number: Not applicable.
UN Proper Shipping Name: Not applicable.
Transport Hazard Class(es): Not applicable.
Packing Group: Not applicable.

Department of Transportation: Not regulated as a hazardous material.

International Air Transport Association (IATA): Not regulated as a dangerous good.

International Maritime Dangerous Good (IMDG): Not regulated as a dangerous good.

15. Regulatory Information**US Federal Regulations:**

Toxic Substance Control Act (TSCA): Polyethylene glycol is listed.

CERCLA Hazardous Substance and Reportable Quantity: Not listed.

SARA 313: Not listed.
SARA 302: Not listed.

State Regulations

California Proposition 65: This product is, or contains chemical(s) known to the State of California to cause developmental toxicity.

16. Other Information

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