



MATERIAL SAFETY DATA SHEET

Product Name: Diazepam Injection, USP

1. CHEMICAL PRODUCT AND COMPANY INFORMATION

Manufacturer Name And Address Hospira, Inc.
275 North Field Drive
Lake Forest, Illinois 60045
USA

Emergency Telephone CHEMTREC: 800-424-9300
Hospira, Inc. 224 212-2055

Product Name Diazepam Injection, USP

Synonyms 7-Chloro-1,3-dihydro-1-methyl-5-phenyl-2H-1,4-benzodiazepin-2-one

2. COMPOSITION/INFORMATION ON INGREDIENTS

Active Ingredient Name Diazepam
Chemical Formula C₁₆H₁₃ClN₂O

Component	Approximate Percent by Weight	CAS Number	RTECS Number
Diazepam	0.5	439-14-5	DF1575000
Benzyl Alcohol	1.5	100-51-6	DN3150000
Propylene Glycol	40	57-55-6	TY2000000
Ethyl Alcohol	10	64-17-5	KQ6300000

Non-hazardous ingredients include water (48%, w/w). Five percent sodium benzoate and/or benzoic acid added as buffers to adjust the pH.

3. HAZARD INFORMATION

Emergency Overview Diazepam Injection, USP, contains diazepam, a benzodiazepine used to relieve anxiety and provide sedation. In the workplace, diazepam should be considered a potent drug, potentially irritating to the eyes and respiratory tract, and a potential occupational reproductive hazard. Possible target organs include the central nervous system, gastrointestinal system, genitourinary system, cardiovascular system, eyes, skin, and possibly the fetus.

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

Signs and Symptoms During occupational use, 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.

Medical Conditions Aggravated by Exposure Pre-existing hypersensitivity to diazepam or other ingredients in this product. Pre-existing central nervous system, gastrointestinal system, genitourinary system, cardiovascular system, eye, or skin ailments; pregnancy.

Carcinogen Lists: **IARC:** Group 3 – Not Classifiable **NTP:** Not listed **OSHA:** Not listed

4. FIRST AID MEASURES

Eye Contact	Remove from source of exposure. Flush with copious amounts of water. If irritation persists or signs of toxicity occur, seek medical attention. Provide symptomatic/supportive care as necessary.
Skin Contact	Remove from source of exposure. Flush with copious amounts of water. If irritation persists or signs of toxicity occur, seek medical attention. Provide symptomatic/supportive care as necessary.
Inhalation	Remove from source of exposure. If signs of toxicity occur, seek medical attention. Provide symptomatic/supportive care as necessary.
Ingestion	Remove from source of exposure. If signs of toxicity occur, seek medical attention. Provide symptomatic/supportive care as necessary. Manifestations of diazepam overdose include somnolence, confusion, coma and diminished reflexes. Respiration, pulse and blood pressure should be monitored, as in all cases of drug overdose, although, in general, these effects have been minimal following overdose. General supportive measures should be employed. Intravenous fluids should be administered and an adequate airway maintained. Hypotension may be managed by the use of Levophed® (levarterenol) or Aramine® (metaraminol). Dialysis is of limited value. Flumazenil, a specific benzodiazepine-receptor antagonist, is indicated for the complete or partial reversal of the sedative effects of benzodiazepines and may be used in situations when an overdose with a benzodiazepine is known or suspected. Prior to the administration of flumazenil, necessary measures should be instituted to secure airway, ventilation and intravenous access. Flumazenil is intended as an adjunct to, not as a substitute for, proper management of benzodiazepine overdose. Patients treated with flumazenil should be monitored for re sedation, respiratory depression and other residual benzodiazepine effects for an appropriate period after treatment. 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.

5. FIRE FIGHTING MEASURES

Flammability	Flash Point: 50°C (122°F).
Fire & Explosion Hazard	Combustible liquid. Keep away from flames, sparks, or other sources of ignition. When heated, product may produce combustible vapors due to the alcohol content.
Extinguishing Media	As with any fire, use extinguishing media appropriate for primary cause of fire. Dry chemical, foam, or carbon dioxide may be used for this product.
Special Fire Fighting Procedures	No special provisions required beyond normal fire fighting equipment such as flame and chemical resistant clothing and self contained breathing apparatus.

6. ACCIDENTAL RELEASE MEASURES

Spill Cleanup and Disposal	Isolate area around spill. Put on suitable protective clothing and equipment as specified by site spill procedures. Absorb the liquid with suitable material and clean affected area with soap and water. Dispose of spill materials according to the applicable federal, state, or local regulations.
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7. HANDLING AND STORAGE

- Handling** No special handling required under conditions of normal product use. Protect from light by retaining in carton until contents have been used.
- Storage** No special storage required for hazard control. For product protection, follow USP controlled room temperature storage recommendations noted on the product case label, the primary container label, or the product insert.
- Special Precautions** Protect from freezing, light, and extreme heat.

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Exposure Guidelines

Component	OSHA-PEL	ACGIH-TLV	AIHA WEEL	Hospira EEL
Diazepam	8 hr TWA: Not Established	8 hr TWA: Not Established	8-hr TWA: Not Established	8 hr TWA: 8 mcg/m ³ STEL: Not Established
Benzyl Alcohol	8 hr TWA: Not Established	8 hr TWA: Not Established	8-hr TWA: 10 ppm	8 hr TWA: Not Established STEL: Not Established
Propylene Glycol	8 hr TWA: Not Established	8 hr TWA: Not Established	8-hr TWA: 10 mg/m ³	8 hr TWA: Not Established STEL: Not Established
Ethyl Alcohol	8 hr TWA: 1000 ppm; 1900 mg/m ³	8 hr TWA: 1000 ppm	8-hr TWA: Not Established	8 hr TWA: Not Established STEL: Not Established

Notes: OSHA PEL: US Occupational Safety and Health Administration – Permissible Exposure Limit
 ACGIH TLV: American Conference of Governmental Industrial Hygienists – Threshold Limit Value.
 AIHA WEEL : American Industrial Hygiene Association - Workplace Environmental Exposure Level
 EEL: Employee Exposure Limit.
 TWA: 8 hour Time Weighted Average.
 STEL: 15-minute Short Term Exposure Limit.

- Respiratory Protection** Respiratory protection is not needed during the normal use of this product. However, if the generation of aerosols is likely, and engineering controls are not adequate to control potential airborne exposures, the use of an approved air-purifying respirator with a HEPA cartridge (P100 or equivalent) and an organic vapor cartridge may be needed if excess volatiles are generated. Personnel who wear respirators should be fit tested and approved for respirator use as required.
- Skin Protection** If skin contact with the product formulation is likely, the use of latex or nitrile gloves is recommended.
- Eye Protection** Eye protection is normally not required during intended product use. However, if eye contact is likely to occur, the use of chemical safety goggles (as a minimum) is recommended.
- Engineering Controls** Engineering controls are normally not needed during the anticipated use of this product.

9. PHYSICAL/CHEMICAL PROPERTIES

Appearance/Physical State	Solution may appear clear, colorless to slightly yellow
Odor	NA
Odor Threshold:	NA
pH:	6.2 – 6.9
Melting point/Freezing point:	Not determined.
Initial Boiling Point/Boiling Point Range	98°C
Evaporation Rate:	NA
Flammability (solid, gas):	NA
Upper/Lower Flammability or Explosive Limits:	LEL: 3.3% based on ethanol UEL: 19% based on ethanol
Vapor Pressure	43 mm Hg at 23°C for ethyl alcohol; 0.07 mm Hg at 20°C for propylene glycol; 1.0 mm Hg at 58°C for benzyl alcohol.
Vapor Density (Air =1)	1.59 for ethyl alcohol; 2.6 for propylene glycol; 3.72 for benzyl alcohol.
Evaporation Rate	Not determined
Specific Gravity	1.0349
Solubility	Water; slightly soluble in alcohol
Partition coefficient: n-octanol/water:	NA
Auto-ignition temperature	NA
Decomposition temperature	NA

10. STABILITY AND REACTIVITY

Reactivity	Not determined.
Chemical Stability	Stable under standard use and storage conditions.
Hazardous Reactions	Not determined
Conditions to avoid	Not determined
Incompatibilities	Strong oxidizers, acids.
Hazardous Decomposition Products	Not determined. During thermal decomposition, it may be possible to generate irritating vapors and/or toxic fumes of carbon oxides (COx), nitrogen oxides (NOx), and hydrogen chloride.
Hazardous Polymerization	Not anticipated to occur with this product.

11. TOXICOLOGICAL INFORMATION

Acute Toxicity – Oral:

Not determined for the product formulation. Information for the ingredients is as follows:

Ingredient(s)	Percent	Test Type	Value	Units	Species
Diazepam	100	LD50	249, 352, 710, 1240	mg/kg	Rat
Diazepam	100	LD50	48, 278, 720	mg/kg	Mouse
Diazepam	100	LD50	328	mg/kg	Rabbit
Benzyl Alcohol	100	LD50	1040 - 2500	mg/kg	Rat, Mouse, Rabbit, Guinea Pig
Propylene Glycol	100	LD50	10,400 – 29,536	mg/kg	Rat, Mouse, Rabbit, Dog, Guinea Pig
Ethyl Alcohol	100	LD50	3450 – 11,500	mg/kg	Guinea Pig, Rat, Mouse, Dog

LD 50: Dosage that produces 50% mortality.

Acute Toxicity – Dermal:

Not determined for the product formulation. Information for the ingredients is as follows:

Ingredient(s)	Percent	Test Type	Value	Units	Species
Diazepam	100	LD50	800	mg/kg	Mice
Benzyl Alcohol	100	LD50	2000	mg/kg	Rabbit
Propylene Glycol	100	LD50	20,800	mg/kg	Rabbit

LD50(dermal) is the dosage that produces 50% mortality when applied to the skin.

Acute Toxicity – Inhalation:

Not determined for the product formulation. Information for the ingredients is as follows:

Ingredient(s)	Percent	Test Type	Value	Units	Species
Benzyl Alcohol	100	LC50(8 hr)	1000	ppm	Rat
Ethyl Alcohol	100	LC50 (10h)	20,000	ppm	Rat
Ethyl Alcohol	100	LD50 (4h)	39,000	mg/m3	Mouse

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

Aspiration Hazard

None anticipated from normal handling of this product.

Dermal Irritation/Corrosion

None anticipated from normal handling of this product. Ethanol may produce mild skin irritation with redness and dryness.

Ocular Irritation/Corrosion

None anticipated from normal handling of this product. Inadvertent contact of this product with eyes may produce irritation. Exposure to ethanol has produced severe eye irritation in studies in animals.

Dermal or Respiratory Sensitization

None anticipated from normal handling of this product.

Reproductive Effects

A series of reproduction studies was conducted in rats with diazepam at oral dosages of 1, 10, 80 and 100 mg/kg given for periods ranging from 60–228 days prior to mating. At 100 mg/kg, there was a decrease in the number of pregnancies and surviving offspring in these rats. These effects were attributed to prolonged sedative activity, resulting in lack of interest in mating and lessened maternal nursing and care of the young. Neonatal survival of rats at dosages lower than 100 mg/kg was within normal limits. Several neonates in both controls and treated groups showed skeletal or other defects. Further studies in rats at doses up to and including 80 mg/kg/day did not reveal significant teratological effects on the offspring. Rabbits were given dosages of 1, 2, 5 and 8 mg/kg from day 6 through day 18 of gestation. No adverse

11. TOXICOLOGICAL INFORMATION: continued

Reproductive Effects: continued	<p>effect on reproduction and no teratological changes were noted. In another study, no evidence of teratogenicity was observed in the offspring of rabbits treated with oral doses up to 30 mg/kg/day during gestation days 7 through 19. In other studies, Swiss-Webster mice were treated orally with 50, 100, 140, or 500 mg/kg diazepam daily for three days on gestation days 8-10 or days 11-13, or for one day only between days 8 and 15 or with 280 or 400 mg/kg for one day only between days 11 and 14. The highest dosage was associated with a maternal mortality rate of 50%. When 140 mg/kg diazepam was administered on day 13, there was 21% fetal resorption. The incidence of cleft palate was significantly increased in the offspring of mice treated with 140 mg/kg diazepam on days 11, 12, and 13, and with single-day administration of 400 mg/kg on days 11-14 and 500 mg/kg on days 9 and 11-15. In another study in hamsters, exencephaly, cleft palate, and limb defects were detected after a single oral dose of 30, 50, 70, or 100 mg on days 8 and 10, or single iv injections of 10 mg diazepam on day 11. There was no dose-related effect. Ethanol has been shown to produce fetotoxicity in the embryo or fetus of laboratory animals. Chronic prenatal exposure to ethanol has been associated with a distinct pattern of congenital malformations that have collectively been termed the "fetal alcohol syndrome".</p>
Mutagenicity	<p>Diazepam is generally negative in the Ames test for mutagenicity. It produced chromosomal aberrations in an in vitro micronucleus assay in V79 cells. It also produced chromosomal aberrations in an in vivo micronucleus assay and sister chromatid exchange assay in mice.</p>
Carcinogenicity	<p>No statistically significant evidence of tumorigenicity was observed in rats when administered as a dietary admix at doses of 1, 15, and 100 mg/kg/day, rising to 225 mg/kg/day by week 13, over a period of 2 years.</p>
Target Organ Effects	<p>Based on clinical use, possible target organs include the central nervous system, gastrointestinal system, genitourinary system, cardiovascular system, eyes, skin, and possibly the fetus.</p>

12. ECOLOGICAL INFORMATION

Aquatic Toxicity	<p>Not determined for the product. Information for ingredients is provided below:</p> <p>*LC50(96 hr) = 84 mg/L in rainbow trout for diazepam *EC50(24 hr) = 4.3 - 14 mg/L in Daphnia magna for diazepam *EC50(72 hr) = 3.11 - 11.9 mg/L in algae for diazepam</p> <p>LC50(24 hr) = 12,900 - 15,300 mg/L in rainbow trout for ethanol LC50 (24 hr) = 11,200 mg/L in fingerling trout for ethanol LC50(48 hr) = 9,268 - 14,221 mg/L in Daphnia magna for ethanol EC50 = 9310 mg/L in Chlorella pyrenoidosa (green algae) for ethanol</p> <p>LC50(96 hr) = 460 mg/L in Pimephales promelas for benzyl alcohol LC50 = 640 mg/L in Leuciscus idus for benzyl alcohol EC50(24 hr) = 400 mg/L in Daphnia magna for benzyl alcohol EC50 = 95 mg/L in Chlorella pyrenoidosa for benzyl alcohol</p> <p>LC50(96 hr) = 51,600 mg/L in rainbow trout for propylene glycol LC50(48 hr) = 34,400 - 43,500 mg/L in Daphnia magna for propylene glycol EC50(14 day) = 19,000 mg/L in algae for propylene glycol</p>
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12. ECOLOGICAL INFORMATION: continued

Persistence/Biodegradability Not determined for the product. Information for ingredients is provided below:

*Diazepam is not inherently biodegradable; it degraded less than 5% in an 84-day biodegradation assay. Diazepam degraded approximately 25% in 120 hours in an abiotic degradation assay.

Ethanol was reported to be degraded between 45% and 74% in five days in two aqueous biodegradation assays.

Benzyl alcohol was degraded over 90% in a 28-day biodegradation assay in sewage sludge.

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

Bioaccumulation Not determined for the product. Because of its low octanol:water partition coefficient, ethanol is not anticipated to bioaccumulate.

Mobility in Soil Not determined.

* Hoffmann- La Roche, Inc.

Notes:

1. LC50: Concentration in water that produces 50% mortality in fish or Daphnia.
2. EC50: Concentration in water that produces 50% inhibition of growth in algae or immobilization in Daphnia.

13. DISPOSAL CONSIDERATIONS

Waste Disposal Disposal should be performed in accordance with the federal, state or local regulatory requirements. Product is classified as hazardous waste (D001) based on flashpoint testing.

Container Handling and Disposal Dispose of container and unused contents in accordance with federal, state and local regulations.

14. TRANSPORTATION INFORMATION

DOT STATUS: Not Regulated
Proper Shipping Name: NA
Hazard Class: NA
UN Number: NA
Packing Group: NA
Reportable Quantity: NA

ICAO/IATA STATUS Not Regulated
Proper Shipping Name: NA
Hazard Class: NA
UN Number: NA
Packing Group: NA
Reportable Quantity: NA

IMDG STATUS Not Regulated
Proper Shipping Name: NA
Hazard Class: NA
UN Number: NA
Packing Group: NA
Reportable Quantity: NA

Notes: DOT - US Department of Transportation Regulations




15. REGULATORY INFORMATION

TSCA Status	Exempt
CERCLA Status	Not listed
SARA 302 Status	Not listed
SARA 313 Status	Not listed
RCRA Status	Classified as D001 hazardous waste based on ignitability.
PROP 65 (Calif.)	This product is, or contains chemical(s) known to the State of California to cause developmental toxicity.

Notes: TSCA, Toxic Substance Control Act; CERCLA, US EPA law, Comprehensive Environmental Response, Compensation, and Liability Act; SARA, Superfund Amendments and Reauthorization Act; RCRA, US EPA, Resource Conservation and Recovery Act; Prop 65, California Proposition 65

U.S. OSHA Classification Possible Irritant
 Reproductive Toxin
 Target Organ Toxin
 Combustible Liquid

GHS Classification

Hazard Class	Acute Oral Toxicity	Eye Irritation	Toxic to Reproduction	Target Organ Toxicity	Flammable Liquid
Hazard Category	Unclassified	2B	2	2	3
Symbol	NA				
Signal Word	NA	Warning	Warning	Warning	Warning
Hazard Statement	NA	Causes eye irritation	Suspected of damaging the unborn child	May cause damage to the central nervous system, gastrointestinal system, genitourinary system, cardiovascular system, eyes, and skin through prolonged or repeated exposure.	Flammable liquid and vapor

Prevention: Obtain special instructions before use.
 Do not handle until all safety precautions have been read and understood.
 Use personal protective equipment as required.
 Keep container tightly closed
 Keep away from ignitions sources such as heat/sparks/open flame – No smoking
 Wear protective gloves and eye/face protection
 Take precautionary measures against static discharge.

Response: If exposed or concerned: Get medical attention.




In case of fire, use media appropriate for the primary cause of the fire for extinction
 IF ON SKIN: Remove/take off immediately all contaminated clothing. Rinse skin with water/shower.

IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. If eye irritation persists, get medical attention.
 Wash hands after handling.

15. REGULATORY INFORMATION: continued

EU Classification*

*Medicinal products are exempt from the requirements of the EU Dangerous Preparations Directive. Information provided below is for the pure drug substance diazepam.

Classification(s):	Harmful	Irritant	Toxic to Reproduction Category 2
Symbol:			
Indication of Danger:	Xn	Xi	T
Risk Phrases:	R22 – Harmful if swallowed R36/37 - Irritating to eyes and respiratory system R61 – May cause harm to the unborn child		
Safety Phrases:	S24: Avoid contact with the skin S25: Avoid contact with eyes S37/39 Wear suitable gloves and eye/face protection.		

16. OTHER INFORMATION

Notes:

ACGIH TLV	American Conference of Governmental Industrial Hygienists – Threshold Limit Value
CAS	Chemical Abstracts Service Number
CERCLA	US EPA law, Comprehensive Environmental Response, Compensation, and Liability Act
DOT	US Department of Transportation Regulations
EEL	Employee Exposure Limit
IATA	International Air Transport Association
LD ₅₀	Dosage producing 50% mortality
NA	Not applicable/Not available
NE	Not established
NIOSH	National Institute for Occupational Safety and Health
OSHA PEL	US Occupational Safety and Health Administration – Permissible Exposure Limit
Prop 65	California Proposition 65
RCRA	US EPA, Resource Conservation and Recovery Act
RTECS	Registry of Toxic Effects of Chemical Substances
SARA	Superfund Amendments and Reauthorization Act
STEL	15-minute Short Term Exposure Limit
TSCA	Toxic Substance Control Act
TWA	8-hour Time Weighted Average

MSDS Coordinator: Global Occupational Toxicology
 Date Prepared: September 15, 2005
 Revision Date: July 10, 2008

Disclaimer:

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