SAFETY DATA SHEETS

This SDS packet was issued with item:

078940890

N/A

SAFETY DATA SHEET

Product Name: Diazepam Injection, USP

1. CHEMICAL PRODUCT AND COMPANY IDENTIFICATION

Name, Address, and Telephone of the Responsible Party Company	Dash Pharmaceuticals LLC 2 Park Way, 2nd Floor Upper Saddle River, NJ 07458 USA
Emergency Telephone	Dash Pharmaceuticals LLC Customer Service: 877-245-9739
Product Name Synonyms	Diazepam Injection, USP 7-Chloro-1,3-dihydro-1-methyl-5-phenyl-2H-1,4-benzodiazepin-2-one

2. HAZARD(S) IDENTIFICATION

Emergency Overview

Diazepam Injection, USP, is a solution containing diazepam, a benzodiazepine used to relieve anxiety and provide sedation. Diazepam is a Schedule IV controlled substance. In the workplace, this product should be considered a flammable liquid, potentially irritating to the eyes and respiratory tract, a potential occupational reproductive hazard, and a potent drug. Based on clinical use, possible target organs include the central nervous system, gastrointestinal system, genitourinary system, liver and cardiovascular system.

U.S. OSHA GHS Classification

Physical Hazards	**Hazard Class**	**Hazard Category**
	Flammable Liquid	3

Health Hazards	**Hazard Class**	**Hazard Category**
	Eye Damage/Irritation	2A
	Toxic to Reproduction	2
	STOT - RE	2

Label Element(s)

Pictogram

Signal Word

Warning

Hazard Statement(s)

Flammable liquid and vapor
Causes serious eye irritation
Suspected of damaging fertility and the unborn child
May cause damage to organs through prolonged or repeated exposure

2. HAZARD(S) IDENTIFICATION: continued

Precautionary Statement(s)

Prevention

Keep away from heat/sparks/open flames/hot surfaces.– No smoking
Keep container tightly closed
Ground/Bond container and receiving equipment
Use explosion-proof equipment
Use only non-sparking tools
Take precautionary measures against static discharge
Obtain special instructions before use
Do not handle until all safety precautions have been read and understood
Wear protective gloves/protective clothing/eye protection/face protection
Do not breathe vapor or spray
Wash hands thoroughly after handling

Response

Get medical attention if you feel unwell.

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.

IF ON SKIN (OR HAIR): Take off immediately all contaminated clothing. Rinse skin with water/shower.

IN CASE OF FIRE: For small fires, use water fog or fire extinguishing media suitable for Class B fires (e.g. dry chemical, carbon dioxide or foam). For large fires, apply water from as far away as possible; use very large quantities of water applied as a mist or spray.

3. COMPOSITION/INFORMATION ON INGREDIENTS

Active Ingredient Name	Diazepam	Benzyl Alcohol	Propylene Glycol	Ethyl Alcohol
Chemical Formula	$C_{16}H_{13}ClN_2O$	C_7H_8O	$C_3H_8O_2$	C_2H_6O

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 for Injection (48%, w/w). Five percent sodium benzoate and/or benzoic acid added as buffers.

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.

4. FIRST AID MEASURES: continued

Ingestion	Remove from source of exposure. If signs of toxicity occur, seek medical attention. Provide symptomatic/supportive care as necessary. Manifestations of diazepam overdosage include somnolence, confusion, coma and diminished reflexes. Respiration, pulse and blood pressure should be monitored, as in all cases of drug overdosage, although, in general, these effects have been minimal following overdosage. 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 resedation, 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	GHS Flammable liquid – Category 3. 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 such as carbon dioxide, dry chemical extinguishing powder or foam.
Special Fire Fighting Procedures	No special provisions required beyond normal firefighting 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. Remove potential sources of ignition in the spill area. 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. Dispose of spill materials according to the applicable federal, state, or local regulations.

7. HANDLING AND STORAGE

Handling	No special handling required for hazard control under conditions of normal product use. Keep away from flames or other sources of ignition. Diazepam is a Schedule IV controlled substance. Additional training and procedures may be required when handling this material.
Storage	No special storage required for hazard control. For product protection, follow storage recommendations noted on the product case label, the primary container label, or the product insert.
Special Precautions	No special precautions required for hazard control.

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Exposure Guidelines

	Exposure Limits			
Component	**OSHA-PEL**	**ACGIH-TLV**	**AIHA WEEL**	**Dash EEL**
Diazepam	8 hr TWA: Not Established	8 hr TWA: Not Established	8-hr TWA: Not Established	8 hr TWA: Not Established
Benzyl Alcohol	8 hr TWA: Not Established	8 hr TWA: Not Established	8-hr TWA: 10 ppm	8 hr TWA: Not Established
Propylene Glycol	8 hr TWA: Not Established	8 hr TWA: Not Established	8-hr TWA: 10 mg/m3	8 hr TWA: Not Established
Ethyl Alcohol	8 hr TWA: 1000 ppm; 1900 mg/m3	8 hr TWA: 1000 ppm	8-hr TWA: Not Established	8 hr TWA: 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.

Respiratory Protection

Respiratory protection is normally not needed during intended product use. However, if the generation of aerosols or vapors 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) with an organic vapor cartridge is recommended under conditions where airborne aerosol or vapor 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.

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	NA
Initial Boiling Point/Boiling Point Range	98°C
Flash Point	50°C (122°F)
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
Relative Density	1.0349
Solubility	Water; slightly soluble in alcohol
Partition Coefficient: n-octanol/water	NA
Auto-ignition Temperature	NA
Decomposition Temperature	NA
Viscosity	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 – Not determined for the product formulation. Information for the ingredients is as follows:

Ingredient(s)	Percent	Test Type	Route of Administration	Value	Units	Species
Diazepam	100	LD50	Oral	249, 352, 710, 1240 48, 278, 720 328	mg/kg mg/kg mg/kg	Rat Mouse Rabbit
Diazepam	100	LD50	Dermal	800	mg/kg	Mouse
Benzyl Alcohol	100	LD50	Oral	1040 - 2500	mg/kg	Rat, Mouse, Rabbit, Guinea Pig
Benzyl Alcohol	100	LD50	Dermal	2000	mg/kg	Rabbit
Benzyl Alcohol	100	LC50(8 hr)	Inhalation	1000	ppm	Rat
Ethyl Alcohol	100	LD50	Oral	3450 – 11,500	mg/kg	Rat, Mouse, Dog, Guinea Pig,
Ethyl Alcohol	100	LC50 (10h)	Inhalation	20,000	ppm	Rat
Ethyl Alcohol	100	LC50 (4h)	Inhalation	39,000	mg/m3	Mouse
Propylene Glycol	100	LD50	Oral	10,400 – 29,536	mg/kg	Rat, Mouse, Rabbit, Dog, Guinea Pig
Propylene Glycol	100	LD50	Dermal	20,800	mg/kg	Rabbit

LD 50(oral): Dosage that produces 50% mortality. LD50 (dermal) is the dosage that produces 50% mortality when applied to the skin. 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 have indicated that diazepam has some potential to be absorbed through intact skin. Avoid liquid aerosol generation and skin contact.

Signs and Symptoms

None anticipated from normal handling of this product. In the workplace, 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.

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

None anticipated from normal handling of this product. 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.

11. TOXICOLOGICAL INFORMATION: continued

Reproductive Effects: continued

No adverse 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. Ethyl alcohol 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".

Mutagenicity

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.

Carcinogenicity

No statistically significant evidence of tumorigenicity was observed in rats when administered as a dietary admix at doses o f 1, 15, and 100 mg/kg/day, rising t o 225 mg/kg/day by week 13, over a period o f 2 years.

Carcinogen Lists

IARC: Group 3 – Not Classifiable for diazepam **NTP:** Not listed **OSHA:** Not listed

Specific Target Organ Toxicity – Single Exposure

NA

Specific Target Organ Toxicity – Repeat Exposure

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

12. ECOLOGICAL INFORMATION

Aquatic Toxicity

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

*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

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

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

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

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 biodegradaton 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	All waste materials must be properly characterized. Further, disposal should be performed in accordance with the federal, state or local regulatory requirements. Follow requirements for Schedule IV controlled substances. Product is classified as hazardous waste (D001) based on ignitability.
Container Handling and Disposal	Dispose of container and unused contents in accordance with federal, state and local regulations.

14. TRANSPORTATION INFORMATION

ADR/ADG/ 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
IMDG STATUS	Not regulated
Proper Shipping Name	NA
Hazard Class	NA
UN Number	NA
Packing Group	NA
Notes:	DOT - US Department of Transportation Regulations
Transport Comments:	DOT: 49 CFR, 173.150(e) excepts aqueous solutions of alcohol containing no more than 24% ethanol and more than 50% water. 173.150(f) excepts combustible liquids having a flash point of 100ºF or higher in non-bulk packagings of 119 gallons or less which also meet no other hazard class. 173.150(g) excepts retail products containing less than 70% ethanol in 8 oz bottles or less. IATA: A58 excepts aqueous solutions of no more than 24% ethanol. IMDG: Special provision 144 excepts aqueous solutions of no more than 24% ethanol.

15. REGULATORY INFORMATION

US TSCA Status	Exempt. However, ethyl alcohol is listed on the TSCA inventory.
US CERCLA Status	Not listed
US SARA 302 Status	Not listed
US SARA 313 Status	Not listed
US RCRA Status	Classified as D001 hazardous waste based on ignitability
US 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

GHS/CLP Classification*

*In the EU, classification under GHS/CLP does not apply to certain substances and mixtures, such as medicinal products as defined in Directive 2001/83/EC, which are in the finished state, intended for the final user.

Hazard Class	Hazard Category	Pictogram	Signal Word	Hazard Statement
NA	NA	NA	NA	NA

Prevention

Keep away from heat/sparks/open flames/hot surfaces.– No smoking
Keep container tightly closed
Ground/Bond container and receiving equipment
Use explosion-proof equipment
Use only non-sparking tools
Take precautionary measures against static discharge
Obtain special instructions before use
Do not handle until all safety precautions have been read and understood
Wear protective gloves/protective clothing/eye protection/face protection
Do not breathe vapor or spray
Wash hands thoroughly after handling

Response

Get medical attention if you feel unwell.

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.

IF ON SKIN (OR HAIR): Take off immediately all contaminated clothing. Rinse skin with water/shower.

IN CASE OF FIRE: For small fires, use water fog or fire extinguishing media suitable for Class B fires (e.g. dry chemical, carbon dioxide or foam). For large fires, apply water from as far away as possible; use very large quantities of water applied as a mist or spray.

EU Classification*

*Medicinal products are exempt from the requirements of the EU Dangerous Preparations Directive.

Classification(s)	NA
Symbol	NA
Indication of Danger	NA
Risk Phrases	NA
Safety Phrases	S16: Keep away from sources of ignition - No smoking. S23: Do not breathe vapor/spray 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
STOT - SE	Specific Target Organ Toxicity – Single Exposure
STOT - RE	Specific Target Organ Toxicity – Repeated Exposure
TSCA	Toxic Substance Control Act
TWA	8-hour Time Weighted Average

MSDS Coordinator: Global Occupational Toxicology
Date Prepared: June 02, 2014
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