SAFETY DATA SHEET

SECTION 1 - IDENTIFICATION OF THE SUBSTANCE/MIXTURE AND OF THE COMPANY/UNDERTAKING

Contact information

General

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Product identifier	Diazepam nasal spray
Synonyms	For diazepam: 2H-1,4-Benzodiazepin-2-one, 7-chloro-1,3-dihydro-1-methyl-5-phenyl-
Trade names	VALTOCO®
Chemical family	Mixture - contains diazepam; a benzodiazepine
Relevant identified uses of the substance or mixture and uses advised against	Bulk formulated pharmaceutical product/ Formulated pharmaceutical product packaged in final form for patient use; indicated for short-term/symptomatic treatment of anxiety, alcohol withdrawal, musculoskeletal disorders, and epileptic seizures.
Note	This SDS is written to address potential worker health and safety issues associated with the handling of the formulated product.

SECTION 2 - HAZARDS IDENTIFICATION

Classification of the substance or mixture	**Drugs in the finished state and intended for the final user are not subject to labeling in the US, EU or Canada.** Please consult the prescribing/packaging information. **The classification and labeling listed below is for bulk formulated product.**
Globally Harmonized System [GHS]	Acute Toxicity (Oral) Category 4. Irritant (eye) - Category 2. Reproductive Toxicity - Category 2. Specific Target Organ Toxicity (single exposure) - Category 3.

Label elements

SECTION 2 - HAZARDS IDENTIFICATION …continued

GHS hazard pictogram



GHS signal word Warning

GHS hazard statements H302 - Harmful if swallowed. H336 - May cause drowsiness or dizziness. H361d - Suspected of damaging the unborn child.

GHS precautionary statements P201 - Obtain special instructions before use. P261 - Avoid breathing mist or vapor. P264 - Wash hands thoroughly after handling. P270 - Do not eat, drink or smoke when using this product. P271 - Use only outdoors or in a well-ventilated area. P281 - Use personal protective equipment as required. P304 + P340 - IF INHALED: Remove victim to fresh air and keep at rest in a position comfortable for breathing. P308 + P313 - IF exposed or concerned: get medical advice/ attention. P312 - Call a Poison Center or doctor/physician if you feel unwell. P403 + P233 - Store in a well-ventilated place. Keep container tightly closed. P405 - Store locked up. P501 - Dispose of contents/container to location in accordance with local/regional/national/international regulations.

Other hazards Diazepam is a long-lasting benzodiazepine, with anticonvulsant, antianxiety, sedative, and muscle relaxant properties. Commonly reported adverse events include fatigue, drowsiness, muscle weakness, and lack of voluntary muscle coordination.

Infants exposed to diazepam *in utero* may exhibit withdrawal symptoms characterized by the "floppy baby syndrome," which is manifested by poor muscle tone, decreased suckling, bluish coloring, and impaired temperature maintenance. The recommended oral and intravenous (IV) doses are 2-10 mg, which may be administered several times a day (~4-60 mg/day).

Note This mixture is classified as hazardous under GHS as implemented by Regulation EC No 1272/2008 (EU CLP), WHMIS 2015 (Health Canada), and Hazard Communication Standard No. 1910.1200 (US OSHA).

SECTION 3 - COMPOSITION/INFORMATION ON INGREDIENTS

Ingredient	CAS #	EINECS/ELINCS#	Amount	GHS Classification
Diazepam	439-14-5	2071225	5-15%	CA3:H412; ATO4:H302, RT2:H361d; STOT-S3:H336
Benzyl alcohol	100-51-6	202-859-9	10-15%	ATO4: H302; ATD4: H302; ATI4: H332
Vitamin E	1406-18-4	606-803-8	59-61%	Not classified

SECTION 3 - COMPOSITION/INFORMATION ON INGREDIENTS …continued

Note	The ingredient(s) listed above are considered hazardous and/or are the active ingredient. Vitamin E is not classified, but is included as it is a major component of the formulated mixture. The remaining components are non-hazardous and/or present at amounts below reportable limits. See Section 16 for full text of GHS classifications.

SECTION 4 - FIRST AID MEASURES

Description of first aid measures

Immediate Medical Attention Needed	Yes
Eye Contact	If easy to do, remove contact lenses, if worn. Immediately flush eyes with copious quantities of water for at least 15 minutes. If irritation occurs or persists, notify medical personnel and supervisor.
Skin Contact	Wash exposed area with soap and water and remove contaminated clothing/shoes. If irritation occurs or persists, notify medical personnel and supervisor.
Inhalation	Immediately move exposed subject to fresh air. If not breathing, give artificial respiration. If breathing is labored, administer oxygen. Immediately notify medical personnel and supervisor.
Ingestion	Do not induce vomiting unless directed by medical personnel. Do not give anything to drink unless directed by medical personnel. Never give anything by mouth to an unconscious person. Notify medical personnel and supervisor.
Protection of first aid responders	See Section 8 for Exposure Controls/Personal Protection recommendations.

Most important symptoms and effects, both acute and delayed	See Sections 2 and 11.
Indication of immediate medical attention and special treatment needed, if necessary	Contains diazepam. Medical conditions aggravated by exposure: None known or reported. Treat symptomatically and supportively. If accidental exposure occurs to an individual who is also taking other medication(s), consult the corresponding package or prescribing information for potential drug interactions.

SECTION 5 - FIREFIGHTING MEASURES

Extinguishing media	Use water spray (fog), foam, dry powder, or carbon dioxide, as appropriate for surrounding fire and materials.
Specific hazards arising from the substance or mixture	No information identified. May emit carbon monoxide, carbon dioxide, and oxides of chloride and nitrogen.

SECTION 5 - FIREFIGHTING MEASURES …continued

Flammability/Explosivity No explosivity or flammability data identified.

Advice for firefighters	In case of fire in the surroundings: use the appropriate extinguishing agent. Wear full protective clothing and an approved, positive pressure, self-contained breathing apparatus. Decontaminate all equipment after use.

SECTION 6 - ACCIDENTAL RELEASE MEASURES

Personal precautions, protective equipment and emergency procedures	If product is released or spilled, take proper precautions to minimize exposure by using appropriate personal protective equipment (see Section 8). Area should be adequately ventilated. Do not breathe mist/spray.
Environmental precautions	Do not empty into drains. Avoid release to the environment.
Methods and material for containment and cleaning up	DO NOT CAUSE MATERIAL TO BECOME AIRBORNE. For small spills, soak up material with absorbent, e.g., paper towels. For large spills, cordon off spill area and minimize the spreading of spilled material. Soak up material with absorbent. Collect spilled material, absorbent, and rinse water into suitable containers for proper disposal in accordance with applicable waste disposal regulations (see Section 13). Decontaminate the area twice with an appropriate solvent.
Reference to other sections	See Sections 8 and 13 for more information.

SECTION 7 - HANDLING AND STORAGE

Precautions for safe handling	Follow recommendations for handling potent pharmaceutical agents (i.e., use of engineering controls and/or other personal protective equipment if needed). Avoid contact with eyes, skin and other mucous membranes. Avoid breathing vapor/mist/ spray. Wash thoroughly after handling.
Conditions for safe storage including any incompatibilities	Store at room temperature between 59° F to 77° F (15° C to 25° C). Excursions between 15° and 30° C (59° and 86° F) permitted.
Specific end use(s)	No information identified.

SECTION 8 - EXPOSURE CONTROLS/PERSONAL PROTECTION

Note	Wash hands, face and other potentially exposed areas immediately in the event of physical contact.

Control Parameters/Occupational Exposure Limit Values

Compound	Issuer	Type	OEL
Diazepam	--	--	--
Benzyl alcohol	AIHA	TWA-8 HR	10 ppm
	Bulgaria, Latvia	TWA-8 HR	5 mg/m³
	Czech Republic	TWA-8 HR	40 mg/m³
	Czech Republic	Ceiling	80 mg/m³
	Lithuania	TWA-8 HR	5 mg/m³ (skin)
	Poland	TWA-8 HR	240 mg/m³
Vitamin E	--	--	--

Exposure/Engineering controls

None required for normal handling of packaged product. If handling bulk product or if vials are opened/crushed/broken: Control exposures to below the OEL (for the active ingredient(s) if available). Selection and use of containment devices and personal protective equipment should be based on a risk assessment of exposure potential. Utilize closed and sealed systems whenever possible. Solutions used for procedures where aerosolization may occur (e.g., spraying, pumping, open transfers,) must be handled using an engineered local exhaust ventilation (LEV) and/or enclosure or isolator system. Control the potential for spills and leaks by securing all connections. Use clean-in-place systems.

Respiratory protection

None required for normal handling of packaged product. Choice of respiratory protection should be appropriate to the task and the level of existing engineering controls. A powered air-purifying respirator (PAPR) with HEPA filters and head cover is required when performing aerosol generating operations. An airline respirator or self-contained breathing apparatus (SCBA) and disposable outerwear is required for spill cleanup.

Hand protection

Wear nitrile or other impervious gloves if skin contact is possible. Double gloves should be considered.

Skin protection

Wear disposable coveralls appropriate to the task, booties, two pairs of gloves and safety glasses with side shields. Protective garments (coveralls, disposable coveralls, lab coats) are not to be worn in common areas (e.g., cafeterias) or out-of- doors. Employees must be trained in proper gowning and degowning practices. An anteroom or transition area must be used for gowning and degowning.

Eye/face protection

Wear safety glasses with side shields, chemical splash goggles, or full face shield, if necessary. Base the choice of protection on the job activity and potential for contact with eyes or face. An emergency eye wash station should be available.

SECTION 8 - EXPOSURE CONTROLS/PERSONAL PROTECTION …continued

Environmental Exposure Controls	Avoid release to the environment and operate within closed systems wherever practicable. Air and liquid emissions should be directed to appropriate pollution control devices. In case of spill, do not release to drains. Implement appropriate and effective emergency response procedures to prevent release or spread of contamination and to prevent inadvertent contact by personnel.
Other protective measures	Wash hands in the event of contact with this mixture, especially before eating, drinking or smoking. Protective equipment is not to be worn outside the work area (e.g., in common areas or out-of-doors).

SECTION 9 - PHYSICAL AND CHEMICAL PROPERTIES

Information on basic physical and chemical properties

Appearance	Liquid
Color	Clear to pale amber to amber
Odor	No information identified.
Odor threshold	No information identified.
pH	No information identified.
Melting point/freezing point	No information identified.
Initial boiling point and boiling range	No information identified.
Flash point	No information identified.
Evaporation rate	No information identified.
Flammability (solid, gas)	No information identified.
Upper/lower flammability or explosive limits	No information identified.
Vapor pressure	No information identified.
Vapor density	No information identified.
Relative density	Approx. 0.9
Water solubility	No information identified.
Solvent solubility	No information identified.

SECTION 9 - PHYSICAL AND CHEMICAL PROPERTIES …continued

Partition coefficient (*n-octanol/water*)	No information identified.
Auto-ignition temperature	No information identified.
Decomposition temperature	No information identified.
Viscosity	30-100cps.
Explosive properties	No information identified.
Oxidizing properties	No information identified.

Other information

Molecular formula	Not applicable (Mixture)
Molecular weight	Not applicable (Mixture)

SECTION 10 - STABILITY AND REACTIVITY

Reactivity	No information identified.
Chemical stability	Stable at controlled room temperature.
Possibility of hazardous reactions	Not expected to occur.
Conditions to avoid	Do not freeze, protect from light and high (> 40 °C) temperatures.
Incompatible materials	No information identified.
Hazardous decomposition products	None identified.

SECTION 11 - TOXICOLOGICAL INFORMATION

Note	No data for this product/mixture were identified. The following data describe the active ingredient and/or the individual ingredients where applicable.

Information on toxicological effects

Route of entry	May be absorbed by inhalation, skin contact and ingestion.

SECTION 11 - TOXICOLOGICAL INFORMATION …continued

Acute toxicity

Compound	Type	Route	Species	Dose
Diazepam	LD_{50}	Oral	Rat	352 mg/kg
	LD_{50}	Oral	Mouse	48 mg/kg
	LD_{50}	Dermal	Mouse	800 mg/kg
Benzyl alcohol	LC_{50}	Inhalation	Rat	8.8 mg/L/4 hours
	LD_{50}	Oral	Rat	1230 - 3100 mg/kg
	LD_{50}	Dermal	Rabbit	2000 mg/kg
	LD_{50}	Oral	Mouse	1150 - 1580 mg/kg
Vitamin E	--	--	--	--

Irritation/Corrosion Benzyl alcohol is highly irritating to the rabbit eye.

Sensitization Benzyl alcohol produced equivocal sensitization results guinea pigs (positive in Freund's complete adjuvant test and open epicutaneous test; negative in Draize test and Guinea pig Maximization test)

STOT-single exposure No information identified.

STOT-repeated exposure/Repeat-dose toxicity 42 week administration of diazepam at oral doses of 240 mg/kg/day did not result in abnormalities in growth, food consumption, blood counts, gross and microscopic findings in rats.

No notable changes were observed in mice following oral gavage administration of benzyl alcohol at doses up to 200 mg/kg/day for two-years.

Reproductive toxicity Diazepam did not adversely affect reproductive function in rats at oral doses up to 300 mg/kg/day (0.38% of diet).

Developmental toxicity Diazepam is teratogenic in mice and hamsters at oral doses of ≥45 and 280 mg/kg/day, respectively, but is not teratogenic in rats and rabbits at oral doses of 80 and 50 mg/kg/day, respectively. Oral administration of ≥100 mg/kg/day throughout mating, gestation, and lactation resulted in in developmental toxicity (*e.g.*, smaller offspring size, fewer offspring).

Genotoxicity Diazepam was not genotoxic in a battery of *in vitro* (bacterial reverse mutation assay) or *in vivo* (mouse chromosome aberration assay, mouse micronucleus test, and rat direct DNA damage test) tests. It tested positive in an *in vitro* mouse micronucleus test. The weight of evidence suggests that diazepam is not genotoxic.

Benzyl alcohol is not genotoxic *in vitro* (bacterial reverse mutation assay, chromosome aberration assay in Chinese hamster ovary cells) or *in vivo* (mouse micronucleus test).

Carcinogenicity Increased incidence of liver tumors was observed in male mice and rats orally administered 75 mg/kg/day diazepam for 80 and 104 weeks, respectively. Given the high dose and the fact that liver tumors are common in rodents, diazepam is unlikely to pose a carcinogenic concern in an occupational setting.

Benzyl alcohol was not carcinogenic in mice and rats at oral doses up to 200 and 400 mg/kg/day, respectively, in two-year studies.

SECTION 11 - TOXICOLOGICAL INFORMATION …continued

Carcinogenicity …continued: Diazepam is listed as a group 3 (not classifiable as to its carcinogenicity in humans) by IARC. No other components of the product present at levels greater than or equal to 0.1% are listed by NTP, IARC, ACGIH or OSHA as a carcinogen.

Aspiration hazard: No studies identified

Human health data: See "Section 2 - Other Hazards"

SECTION 12 - ECOLOGICAL INFORMATION

Toxicity

Compound	Type	Species	Concentration
Diazepam	EC_{50} (48 h)	Daphnia Magna (Water Flea)	4.27 mg/L
	LC_{50} (96 h)	Gambusia holbrooki (fish)	12.7 mg/L
	LC_{50} (24h)	Streptophalus proboscideus (shrimp)	37.3 mg/L
Benzyl alcohol	LC_{50}/48h	Leuciscus idus (freshwater fish)	646 mg/L
	LC_{50}/96h	Fathead minnow	460 mg/L
	EC_{50}/48h	Daphnia magna	23 mg/L
	EC_{50}/48h	Bacteria (E.coli)	1000 mg/L
	LC_{50}	Lepomis macrochirus	10 mg/mL
Vitamin E	--	--	--

Persistence and Degradability: No data available.

Bioaccumulative potential: No data available.

Mobility in soil: No data available.

Results of PBT and vPvB assessment: Not performed.

Other adverse effects: No data available.

Note: The environmental characteristics of the formulated product have not been fully investigated. Releases to the environment should be avoided.

SECTION 13 - DISPOSAL CONSIDERATIONS

Waste treatment methods	Used product should be disposed of according to local, state, and federal regulations. All wastes containing the material should be properly labeled. Dispose of wastes in accordance to prescribed federal, state, and local guidelines, e.g., appropriately permitted chemical waste incinerator. Rinse waters resulting from spill cleanups should be discharged in an environmentally safe manner, e.g., appropriately permitted municipal or on-site wastewater treatment facility.

SECTION 14 - TRANSPORT INFORMATION

Transport	Based on the available data, this product/mixture is not regulated as a hazardous material/ dangerous good under EU ADR/RID, US DOT, Canada TDG, IATA, or IMDG.
UN number	None assigned.
UN proper shipping name	None assigned.
Transport hazard classes and packing group	None assigned.
Environmental hazards	Based on the available data, this product/mixture is not regulated as an environmental hazard or a marine pollutant.
Special precautions for users	Due to lack of data, avoid release to the environment.
Transport in bulk according to Annex II of MARPOL73/78 and the IBC Code	Not applicable.

SECTION 15 - REGULATORY INFORMATION

Safety, health and environmental regulations/legislation specific for the substance or mixture	This SDS generally complies with the requirements listed under current guidelines in the US, EU and Canada. Consult your local or regional authorities for more information.
Chemical safety assessment	Not conducted.
TSCA status	Drugs are exempt from TSCA.
SARA section 313	Not listed.
California proposition 65	Diazepam is listed as a developmental toxicant.
Additional information	No other information identified.

SECTION 16 - OTHER INFORMATION

Full text of H phrases and GHS classifications	ATO4 - Acute Toxicity (Oral) Category 4. H302 - Harmful if swallowed. ATD4 - Acute Toxicity (Dermal) Category 4. H312 - Harmful in contact with skin. ATI4 - Acute Toxicity (Inhalation) Category 4. H332 - Harmful if inhaled. STOT-S3 - Specific Target Organ Toxicity Following Single Exposure Category 3. H336 - May cause drowsiness or dizziness. RT2 - Reproductive toxicity Category 2. H361d - Suspected of damaging the unborn child. CA3 - Chronic Aquatic Toxicity Category 3. H412 - Harmful to aquatic life with long lasting effects.
Sources of data	Information from published literature and internal company data.
Abbreviations	ACGIH - American Conference of Governmental Industrial Hygienists; ADR/RID - European Agreement Concerning the International Carriage of Dangerous Goods by Road/Rail; AIHA - American Industrial Hygiene Association; CAS# - Chemical Abstract Services Number; CLP - Classification, Labelling, and Packaging of Substances and Mixtures; DNEL - Derived No Effect Level; DOT - Department of Transportation; EINECS - European Inventory of New and Existing Chemical Substances; ELINCS - European List of Notified Chemical Substances; EU - European Union; GHS - Globally Harmonized System of Classification and Labeling of Chemicals; IARC - International Agency for Research on Cancer; IDLH - Immediately Dangerous to Life or Health; IATA - International Air Transport Association; IMDG - International Maritime Dangerous Goods; LOEL - Lowest Observed Effect Level; LOAEL - Lowest Observed Adverse Effect Level; NIOSH - The National Institute for Occupational Safety and Health; NOEL - No Observed Effect Level; NOAEL - No Observed Adverse Effect Level; NTP - National Toxicology Program; OEL - Occupational Exposure Limit; OSHA - Occupational Safety and Health Administration; PBT - Persistent, Bioaccumulative, and Toxic; PNEC - Predicted No Effect Concentration; SARA - Superfund Amendments and Reauthorization Act; STOT - Specific Target Organ Toxicity; STEL - Short Term Exposure Limit; TDG - Transportation of Dangerous Goods; TSCA - Toxic Substances Control Act; TWA - Time Weighted Average; vPvB - Very Persistent and Very Bioaccumulative; WHMIS - Workplace Hazardous Materials Information System
Issue Date	25 February 2020
Revisions	This is the second version of this SDS.
Disclaimer	The above information is based on data available to us and is believed to be correct. Since the information may be applied under conditions beyond our control and with which we may be unfamiliar, we do not assume any responsibility for the results of its use and all persons receiving it must make their own determination of the effects, properties and protections which pertain to their particular conditions. No representation, warranty, or guarantee, express or implied (including a warranty of fitness or merchantability for a particular purpose), is made with respect to the materials, the accuracy of this information, the results to be obtained from the use thereof, or the hazards connected with the use of the material. Caution should be used in the handling and use of the material because it is a potent pharmaceutical product. The above information is offered in good faith and with the belief that it is accurate. As of the date of issuance, we are providing all information relevant to the foreseeable handling of the material. However, in the event of an adverse incident associated with this product, this Safety Data Sheet is not, and is not intended to be, a substitute for consultation with appropriately trained personnel.