

SAFETY DATA SHEET

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

Contact information

General



Par Sterile Products
870 Parkdale Road, Rochester, M.I. 48307
T: +1 (800) 828-9393
F: +1 (201) 829-9222
E-mail: drugsafety@parpharm.com

Emergency telephone number

Chemtrec (24-hour availability):
+1 (800) 424-9300 (USA and Canada)
+1 (703) 527-3887 (International; collect calls accepted)

Product identifier	Vasopressin Injection, USP (20 units/ml)
Synonyms	For vasopressin: 8-Arginine vasopressin; argipressin
Trade names	Vasostrict®
Chemical family	Mixture - contains a synthetic peptide
Relevant identified uses of the substance or mixture and uses advised against	Bulk formulated pharmaceutical mixture/Formulated pharmaceutical product packaged in final form for patient use; indicated to treat residual hypotension in adults with vasodilatory shock.
Note	The physical, chemical, toxicological and ecological properties of this product/mixture has not been fully characterized. This SDS will be revisited as more data become available.

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 Vasopressin Injection.
Globally Harmonized System [GHS]	Not classified

SECTION 2 - HAZARDS IDENTIFICATION ...continued

Label elements

GHS hazard pictogram	None required
GHS signal word	None required
GHS hazard statements	None required
GHS precautionary statements	None required

Other hazards

Vasopressin is a potent antidiuretic and vasoconstricting agent. The most common adverse effects reported with use (up to ~100 µg/day) include marked pallor, pounding headache, vertigo, sweating, tremor, and gastrointestinal disturbances (nausea, vomiting, diarrhea, burping, cramps, and a desire to defecate). Women reported uterine cramps/contractions. A syndrome similar to water intoxication (characterized by listlessness, drowsiness, headache, and confusion, with subsequent seizures, coma, and death) has also been reported. Consistent with its activity, the drug may increase blood pressure, slow heart rate, and instigate other cardiovascular effects (*e.g.*, heart block, minor arrhythmias, coronary insufficiency, and heart attack). Hypersensitivity reactions have also occurred.

Based on its ability to cause uterine contractions and non-clinical study results described below, vasopressin may adversely affect pregnancy and/or a developing fetus.

Note

This mixture does not meet criteria for classification under GHS as implemented by Regulation EC No 1272/2008 (EU CLP) and Hazard Communication Standard No. 1910.1200 (US OSHA). Nevertheless, it should be handled with caution as it is pharmacologically active.

SECTION 3 - COMPOSITION/INFORMATION ON INGREDIENTS

<u>Ingredient</u>	<u>CAS #</u>	<u>EINECS/ ELINCS#</u>	<u>Amount</u>	<u>GHS Classification</u>
Chlorbutanol	57-15-8	200-317-6	≤ 0.5%	ATO4: H302
Vasopressin	113-79-1	204-035-4	≤ 0.005%	ATI3: H331; RT1B: H360Df

Note

The ingredient(s) listed above are considered hazardous. The remaining components are non-dangerous/not 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

SECTION 4 - FIRST AID MEASURES ...continued

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 vasopressin, a potent antidiuretic and vasoconstricting-agent. Medical conditions aggravated by exposure: cardiovascular diseases (especially of coronary arteries), renal disease, seizure disorders, migraine, and asthma. Treat symptomatically and supportively. If accidental exposure occurs to an individual who is also taking one or more concomitant medications, consult the respective 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, oxides of nitrogen and sulfur, nitric and sulfuric acid, hydrochloric acid, and other nitrogen-, sulfur-, and/or chlorine-containing compounds.
Flammability/Explosivity	No explosivity or flammability data identified. As product is an aqueous solution, it is not expected to be flammable or explosive.
Advice for firefighters	Wear full protective clothing and a self-contained breathing apparatus with a full facepiece operated in the pressure demand or other positive pressure mode. 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	If vials are crushed or broken, 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 (see Section 9).
Reference to other sections	See Sections 8 and 13 for more information.

SECTION 7 - HANDLING AND STORAGE

Precautions for safe handling	If vials are opened, crushed or broken, follow recommendations for handling bulk formulated pharmaceutical agents (i.e., use of engineering controls and/or other personal protective equipment if needed). Wash thoroughly after handling.
Conditions for safe storage including any incompatibilities	<p>Store refrigerated at 2-8°C, away from incompatible materials. Keep container upright. Discard unused portion. Do not freeze.</p> <p>Vials may be held up to 12 months upon removal from refrigeration to room temperature storage conditions (20°C to 25°C [68°F to 77°F], USP Controlled Room Temperature), anytime within the labeled shelf life. Once removed from refrigeration, unopened vials should be marked to indicate the revised 12 month expiration date. If the manufacturer's original expiration date is shorter than the revised expiration date, then the shorter date must be used. Do not use Vasostrict® beyond the manufacturer's expiration date stamped on the vial. Discard vial after 48 hours after the first puncture.</p>
Specific end use(s)	No information identified.

SECTION 8 - EXPOSURE CONTROLS/PERSONAL PROTECTION

Note	Dispose of broken vials in a sharps container.
-------------	------------------------------------------------

SECTION 8 - EXPOSURE CONTROLS/PERSONAL PROTECTION ...continued

**Control Parameters/
Occupational Exposure
Limit Values**

<u>Compound</u>	<u>Issuer</u>	<u>Type</u>	<u>OEL</u>
Chlorbutanol	--	--	--
Vasopressin	Par	Occupational Exposure Category/ Band	4 in a 4-band system. Consult the manufacturer for more details.

Exposure/Engineering controls None required for normal handling of packaged product. If handling bulk product or if vials are opened/crushed/broken: Selection and use of containment devices and personal protective equipment should be based on a risk assessment of exposure potential. Open handling must not be performed when handling potent substances, or substances of unknown toxicity. Material should be handled inside a closed process, ventilated enclosure, isolator or device of equivalent or better control that is suitable for dusts and/or aerosols.

Respiratory protection None required for normal handling of packaged product. If handling bulk product or if vials are opened/crushed/broken: Choice of respiratory protection should be appropriate to the task and the level of existing engineering controls. For routine handling tasks, an approved and properly worn powered air-purifying respirator equipped with appropriate HEPA filters or combination filters should provide ancillary protection based on the known or foreseeable limitations of existing engineering controls. Use a positive-pressure air-supplied respirator if there is any potential for an uncontrolled release, when exposure levels are not known, or in any other circumstances where air purifying respirators may not provide adequate protection.

Hand protection None required for normal handling of packaged product. Wear nitrile or other impervious gloves if skin contact is possible. Double gloves should be considered.

Skin protection Wear appropriate gloves, lab coat, or other protective overgarment if skin contact is likely. Base the choice of skin protection on the job activity, potential for skin contact and solvents and reagents in use.

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.

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 in vials
Color	Colorless
Odor	Faint, characteristic odor
Odor threshold	No information identified.
pH	3.4-3.6
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)	Not applicable.
Upper/lower flammability or explosive limits	No information identified.
Vapor pressure	No information identified.
Vapor density	No information identified.
Relative density	No information identified.
Water solubility	Soluble in water
Solvent solubility	No information identified.
Partition coefficient (<i>n</i>-octanol/water)	No information identified.
Auto-ignition temperature	No information identified.
Decomposition temperature	No information identified.
Viscosity	No information identified.
Explosive properties	No information identified.
Oxidizing properties	No information identified.

Other information

SECTION 9 - PHYSICAL AND CHEMICAL PROPERTIES ...continued

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

SECTION 10 - STABILITY AND REACTIVITY

Reactivity No information identified.
Chemical stability No information identified.
Possibility of hazardous reactions No information identified.
Conditions to avoid Avoid extreme temperatures.
Incompatible materials No information identified.
Hazardous decomposition products No information identified.

SECTION 11 - TOXICOLOGICAL INFORMATION

Note **No toxicology data for the product/mixture were identified. The following data describe the active ingredient, other individual ingredients, or comparator compounds, where applicable.**

Information on toxicological effects

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

Acute toxicity

<u>Compound</u>	<u>Type</u>	<u>Route</u>	<u>Species</u>	<u>Dose</u>
Chlorbutanol	LD ₅₀	Oral	Rat	510 mg/kg
	LD ₅₀	Oral	Mouse	150 mg/kg
Vasopressin	LD ₅₀	Intravenous	Mouse	220 units/kg (~528 µg/kg)*

Additional acute toxicity information *To err on the side of caution (due to the high potency of this substance), it is assumed that toxicity *via* inhalation may be comparable to the intravenous route.

Irritation/Corrosion No data available.

Sensitization No data available.

STOT-single exposure No data available.

STOT-repeated exposure/Repeat-dose toxicity No studies identified for vasopressin. No target organ effects were reported in rats and dogs treated subcutaneously with a synthetic analog (desmopressin) at low doses for up to 6 months.

SECTION 11 - TOXICOLOGICAL INFORMATION ...continued

Reproductive toxicity	No studies identified for vasopressin. In a repeat-dose toxicity study, decreased testicular weight and seminiferous tubule degeneration was reported in male rats receiving µg/kg-range IV doses of a mechanistically-similar compound (terlipressin). Based on these data, it is reasonable to predict that vasopressin may adversely affect reproduction.
Developmental toxicity	Vasopressin caused serious fetal toxicity (necrosis and amputation of digits, tail, nose, tongue, fetal death) and abortion in several species. These effects were believed to be secondary to peripheral vasoconstriction in the fetus. Parenteral doses ranged from 0.1-2 units/animal (~0.2-0.5 µg/animal).
Genotoxicity	No studies identified for vasopressin. Terlipressin was negative in the Ames bacterial mutagenicity assay, an <i>in vitro</i> chromosomal aberration test using Chinese hamster ovary cells and an <i>in vivo</i> mouse micronucleus test.
Carcinogenicity	No data available. None of the components present at levels greater than or equal to 0.1% are listed by NTP, IARC, ACGIH or OSHA as a carcinogen.
Aspiration hazard	No data available.
Human health data	See Section 2 - "Other hazards"

SECTION 12 - ECOLOGICAL INFORMATION

Toxicity

<u>Compound</u>	<u>Type</u>	<u>Species</u>	<u>Concentration</u>
Chlorbutanol	LC ₅₀ (time not specified)	<i>Pimephales promelas</i> (fathead minnow)	130-141 mg/L
Vasopressin	--	--	--

Persistence and Degradability No data identified.

Bioaccumulative potential No data identified.

Mobility in soil No data identified.

Results of PBT and vPvB assessment Not performed.

Other adverse effects No data identified.

Note The environmental characteristics of this mixture have not been fully investigated. The above data are for the active ingredient and/or any other ingredient(s) where applicable. Releases to the environment should be avoided.

SECTION 13 - DISPOSAL CONSIDERATIONS

Waste treatment methods Dispose of wastes in accordance to prescribed federal, state, and local guidelines, e.g., appropriately permitted chemical waste incinerator. Do not send down the drain or flush down the toilet. All wastes containing the material should be properly labeled. 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 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.

WHMIS classification Not classified.

TSCA status Drugs are exempt from TSCA.

SARA section 313 Not listed.

SECTION 15 - REGULATORY INFORMATION ...continued

California proposition 65 Not listed.
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. AT13 - Acute Toxicity (Inhalation) Category 3. H331 - Toxic if inhaled. RT1B - Reproductive toxicity Category 1B. H360Df - May damage the unborn child. Suspected of damaging fertility.

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; 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; WHMIS - Workplace Hazardous Materials Information System

Issue Date 27 June 2015

Revisions Updated formatting to comply with current regulations, contact information in Section 1, and storage information in Section 7.

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

SECTION 16 - OTHER INFORMATION ...continued

Disclaimer ...continued

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 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.