

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

Adrenalin® (epinephrine injection, USP);
Adrenalin® Chloride Nasal Solution (epinephrine nasal solution, USP)

Synonyms

Epinephrine chloride solution;
For epinephrine: 4-[1-hydroxy-2-(methylamino)ethyl]1,2 benzenediol

Trade names

Adrenalin®

Chemical family

Mixture - contains benzenediol derivative

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 for the emergency treatment of severe acute allergic reactions, asthma, and chronic pulmonary disease.

Note

This SDS is written to address potential worker health and safety issues associated with the handling of the formulated product. This SDS will be revisited if 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 Epinephrine Solution.**

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

Epinephrine (*i.e.*, adrenaline) is an endogenous neurotransmitter hormone and its primary effects are vasoconstriction, cardiac stimulation, and smooth muscle relaxation. The most common adverse effects reported with therapeutic use include transient/moderate anxiety, feelings of over stimulation, restlessness, headache, tremor, weakness, shakiness, dizziness, sweating, increased heart rate, palpitations, paleness, nausea, vomiting, and difficulty breathing. Other symptoms, such as high blood pressure, cardiac arrhythmias, and cerebral bleeding, have occurred. As epinephrine can cross the placenta, it may adversely affect the fetus (*e.g.*, reduce fetal oxygen levels due to constriction of blood vessels).

Note

This mixture does not meet criteria for classification 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). Nevertheless, it should be handled with caution as it has not yet been fully tested.

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 |
| Epinephrine | 51-43-4 | 200-098-7 | ≤ 0.1 % | ATO2: H300; ATD2: H310; ATI2: H330; STOT-R1: H372; RT1B: H360Df; CA3: H412 |
| Sodium bisulfite | 7631-90-5 | 231-548-0 | ≤ 0.05% | ATO4: H302; EUH031 |

Note

The ingredient(s) listed above are considered hazardous. GHS classifications for sodium bisulfite are based on EU - CLP Annex VI - Table 3.1. 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 epinephrine, a potent vasoconstricting-agent. Medical conditions aggravated by exposure: cardiovascular diseases, hypertension, and hypersensitivity. Rapidly acting vasodilators can counteract the the marked pressor effects of epinephrine. 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 | Store between 20 to 25°C (68 to 77°F). (See USP Controlled Room Temperature.) Epinephrine is light sensitive. Protect from light and freezing. Keep container upright. Discard unused portion. |
| Specific end use(s) | No information identified. |

SECTION 8 - EXPOSURE CONTROLS/PERSONAL PROTECTION

Note Dispose of broken vials in a sharps container.

Control Parameters/ Occupational Exposure Limit Values

| <u>Compound</u> | <u>Issuer</u> | <u>Type</u> | <u>OEL</u> |
|------------------|---------------|-------------|---------------------|
| Chlorbutanol | -- | -- | -- |
| Epinephrine | -- | -- | -- |
| Sodium bisulfite | ACGIH | 8-hour TWA | 5 mg/m ³ |

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

| | |
|--|--|
| 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 |

SECTION 9 - PHYSICAL AND CHEMICAL PROPERTIES ...continued

| | |
|---|----------------------------|
| Odor | Odorless |
| Odor threshold | No information identified. |
| pH | 3.3-4.2 |
| 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 | |
| Molecular formula | Not applicable (Mixture) |
| Molecular weight | 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 or other individual ingredients, 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 |
| Epinephrine | LD ₅₀ | Intravenous | Rat | 150 µg/kg* |
| | LD ₅₀ | Intravenous | Mouse | 217 µg/kg |
| | LD ₅₀ | Intravenous | Dog | 100 µg/kg |
| | LD ₅₀ | Dermal | Rat | 62 mg/kg |
| | LD _{LO} | Oral | Mouse | 50 mg/kg |
| | LD _{LO} | Oral | Rat | 30 mg/kg |
| Sodium bisulfite | LD ₅₀ | Oral | Rat | 2150-3160 mg/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 In 13-week inhalation studies, increased respiratory rate, changes in respiratory epithelium, and increased heart/adrenal gland weight were observed in rats and mice exposed to 40 mg/m³ epinephrine (duration not specified). Additionally, degenerative lesions of the laryngeal muscle were seen in rats exposed to concentrations ≥20 mg/m³. In mice, inflammation of the glandular stomach and uterine atrophy were observed at concentrations ≥10 and 40 mg/m³, respectively.

SECTION 11 - TOXICOLOGICAL INFORMATION ...continued

| | |
|-------------------------------|--|
| Reproductive toxicity | In hamsters, epinephrine caused a decrease in reproductive success at 500 µg/kg (route of administration not specified). In mice, epinephrine decreased sexual receptivity in female mice at subcutaneous (SC) doses of 40 µg (~1.6 mg/kg), but implantation success was not affected. |
| Developmental toxicity | Adverse developmental effects have been reported in rabbits, mice, and hamsters at SC doses as low as 1.2, 1 and 0.5 mg/kg, respectively. Uterine vasoconstriction and impaired fetal gas exchange were observed in pregnant monkeys treated with intravenous (IV) doses of 0.5-20 µg/kg/min for 1 to 18 minutes. Fetal asphyxia was observed after epinephrine administration to pregnant monkeys at doses similar to those used in humans. |
| Genotoxicity | Epinephrine was negative in the Ames bacterial mutagenicity assay and an <i>in vivo</i> micronucleus assay (species not specified). Although both negative and equivocal effects were observed in a chromosomal aberration assay with Chinese hamster ovary cells in the presence and absence of metabolic activation, respectively, the overall weight of evidence suggests a low genotoxicity potential. |
| Carcinogenicity | Epinephrine was not carcinogenic in rats and mice exposed by inhalation to concentrations up to 5 and 3 mg/m ³ , respectively. 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 |
| Epinephrine | EC ₅₀ /24h | <i>Daphnia magna</i> | 40.0 mg/L |
| | EC ₅₀ /48h | <i>Daphnia magna</i> | 31.7 mg/L |
| Sodium bisulfite | NOEC (34d) | <i>Danio rerio</i> (Zebrafish) | ≥316 mg/L (sodium sulfite) |
| | EC ₅₀ /48h | <i>Daphnia magna</i> (crustacea) | 89 mg/L (disodium disulfite) |
| | NOEC (21 days) | <i>Daphnia magna</i> (crustacea) | >10 mg/L (disodium disulfite) |
| | EC ₅₀ /72h | <i>Desmodesmus subspicatus</i> (algae, green) | 43.8 mg/L (disodium disulfite) |

Persistence and Degradability No data identified.

Bioaccumulative potential No data identified.

SECTION 12 - ECOLOGICAL INFORMATION ...continued

| | |
|---|--|
| 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 | 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 | 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. ATO2 - Acute Toxicity (Oral) Category 2. H300 - Fatal if swallowed. ATD2 - Acute Toxicity (Dermal) Category 2. H310 - Fatal in contact with skin. STOT-R1 - Specific Target Organ Toxicity Following Repeat Exposure Category 1. H372 - Causes damage to the cardiovascular system through prolonged or repeated exposure. RT1B - Reproductive toxicity Category 1B. H360Df - May damage the unborn child. Suspected of damaging fertility. EUH031 - Contact with acids liberates very toxic gas. (Specific concentration limit: $\geq 5\%$) |
| 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 - |

SECTION 16 - OTHER INFORMATION ...continued

**Abbreviations
...continued** Transportation of Dangerous Goods; TSCA - Toxic Substances Control Act; TWA - Time Weighted Average; WHMIS - Workplace Hazardous Materials Information System

Issue Date 21 July 2017

Revisions Updated product identifier in Section 1; ingredient list in Section 3; and storage information in Section 7. Updated general format for compliance with most recent regulatory requirements in the US, EU, and Canada.

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 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.