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

Par Sterile Products
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drugsafety@parpharm.com

Emergency telephone number (Chemtrec):
1-(800) 424-9300 (US and Canada)
1-(703) 527-3887 (collect calls accepted)

Product identifier
Dexmedetomidine Hydrochloride Injection

Synonyms
None identified

Trade names
None identified

Chemical family
Mixture

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 as a sedative

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.

Issue Date
7 May 2014

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 labelling listed below is for bulk dexmedetomidine hydrochloride for injection.

Regulation (EC) 1272/2008 [GHS]
Specific Target Organ Toxicity (single exposure) - Category 3.

Directive 67/548/EEC or 1999/45/EC
Not classified
SECTION 2 - HAZARDS IDENTIFICATION

Label elements

CLP/GHS hazard pictogram

CLP/GHS signal word

Warning

CLP/GHS hazard statements

H336 - May cause drowsiness or dizziness.

CLP/GHS precautionary statements

P260 - Do not breathe dust. P264 - Wash hands thoroughly after handling. P281 - Use personal protective equipment as required. P308 + P313 - If exposed or concerned: get medical advice/attention. P405 - Store locked up. P501 - Dispose of contents/container to location in accordance with local/regional/national/international regulations.

EU symbol/indication of danger

None required

Risk (R) Phrase(s)

None required

Safety Advice

None required

Other hazards

Dexmedetomidine is a potent sedative effective at very low doses. The initial clinical dose is 1 µg/kg, given intravenously (IV). The most common adverse effects reported with use of mixtures containing dexmedetomidine are hypotension, bradycardia, and dry mouth. Other adverse effects include transient hypertension, fever, hypoxia, and anemia, and tachycardia episodes. Symptoms of withdrawal (e.g., nausea, vomiting, and agitation) have been reported following discontinuation after 7 days of repeated administration.

US Signal word

Attention!

US Hazard overview

Contains dexmedetomidine, a potent sedative.

Note

This mixture is classified as dangerous/hazardous according to directive 1999/45/EC, Regulation (EC) No 1272/2008 (EU CLP) and applicable US regulations. The EU symbol/indicator of danger, R Phrases and Safety Advice are based on Directive 67/548/EEC or 1999/45/EC. The GHS classifications are based on Regulation (EC) 1272/2008. See Section 16 for full text of EU and GHS classifications.
SECTION 3 - COMPOSITION/INFORMATION ON INGREDIENTS

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>CAS #</th>
<th>EINECS/ELINCS#</th>
<th>Amount</th>
<th>EU Classification</th>
<th>GHS Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dexmedetomidine hydrochloride</td>
<td>145108-58-8</td>
<td>N/A</td>
<td>1-5%</td>
<td>Harmful - Xn: R63</td>
<td>STOT-S3: H336; RT2: H361d</td>
</tr>
<tr>
<td>Sodium chloride</td>
<td>7647-14-5</td>
<td>231-598-3</td>
<td>&gt; 95%</td>
<td>Not classified</td>
<td>Not classified</td>
</tr>
</tbody>
</table>

Note

The ingredient(s) listed above are considered dangerous/hazardous. Sodium chloride is included because it has an OEL. See Section 16 for full text of EU and GHS classifications. The EU classification is based on Directive 67/548/EEC and the GHS classification is based on Regulation (EC) 1272/2008.

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

Contains dexmedetomidine, a potent sedative. Medical conditions aggravated by exposure: None known or reported. Treat symptomatically and supportively. Refer to current prescribing information or to local poison control information centers.

SECTION 5 - FIREFIGHTING MEASURES

Extinguishing media

Use water spray (fog), foam, dry powder, or carbon dioxide, as appropriate for surrounding fire and materials.
SECTION 5 - FIREFIGHTING MEASURES …continued

Specific hazards arising from the substance or mixture
No information identified. May emit toxic fumes of carbon monoxide, carbon dioxide, oxides of nitrogen or chloride and sodium-containing compounds.

Flammability/Explosivity
No specific information identified for the product/mixture. High concentrations of finely divided airborne particles can potentially explode if ignited.

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 dust.

Environmental precautions
Do not empty into drains. Avoid release to the environment.

Methods and material for containment and cleaning up
DO NOT RAISE DUST. Surround spill or powder with absorbents and place a damp cloth or towel over the area to minimize entry of powder into the air. Add excess liquid to allow the material to enter into solution. Capture remaining liquid onto spill absorbents. Place spill materials into a leak-proof container for 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
When handling, use proper personal protective equipment as specified in Section 8. Follow recommendations for handling potent pharmaceutical agents (i.e., use of engineering controls and/or other personal protective equipment if needed).

Conditions for safe storage including any incompatibilities
Store at controlled room temperatures (20-25°C). Protect from light.

Specific end use(s)
No information identified.
Note

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

Control Parameters/
Occupational Exposure

Limit Values

<table>
<thead>
<tr>
<th>Compound</th>
<th>Issuer</th>
<th>Type</th>
<th>OEL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium chloride</td>
<td>Latvia, Lithuania, Russia</td>
<td>TWA-8 HR</td>
<td>5 mg/m³</td>
</tr>
</tbody>
</table>

Exposure/Engineering controls

Control exposures to below the OEL (if available). Otherwise, 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

Choice of respiratory protection should be appropriate to the task and the level of existing engineering controls. For routine powder handling tasks, an approved and properly worn powered air-purifying respirator equipped with 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

Wear nitrile or other impervious gloves if skin contact is possible. Double gloves should be considered. When the material is dissolved or suspended in an organic solvent, wear gloves that provide protection against the solvent.

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

<table>
<thead>
<tr>
<th>Information on basic physical and chemical properties</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Appearance</td>
<td>Lyophilized powder</td>
</tr>
<tr>
<td>Color</td>
<td>White</td>
</tr>
<tr>
<td>Odor</td>
<td>Odorless</td>
</tr>
<tr>
<td>Odor threshold</td>
<td>No information identified.</td>
</tr>
<tr>
<td>pH</td>
<td>pH when dissolved in water is 4.5 to 7</td>
</tr>
<tr>
<td>Melting point/ freezing point</td>
<td>No information identified.</td>
</tr>
<tr>
<td>Initial boiling point and boiling range</td>
<td>No information identified.</td>
</tr>
<tr>
<td>Flash point</td>
<td>No information identified.</td>
</tr>
<tr>
<td>Evaporation rate</td>
<td>No information identified.</td>
</tr>
<tr>
<td>Flammability (solid, gas)</td>
<td>No information identified.</td>
</tr>
<tr>
<td>Upper/lower flammability or explosive limits</td>
<td>No information identified.</td>
</tr>
<tr>
<td>Vapor pressure</td>
<td>No information identified.</td>
</tr>
<tr>
<td>Vapor density</td>
<td>No information identified.</td>
</tr>
<tr>
<td>Relative density</td>
<td>No information identified.</td>
</tr>
<tr>
<td>Water solubility</td>
<td>Freely soluble in water</td>
</tr>
<tr>
<td>Solvent solubility</td>
<td>No information identified.</td>
</tr>
<tr>
<td>Partition coefficient ( (n\text{-octanol}/water) )</td>
<td>No information identified.</td>
</tr>
<tr>
<td>Auto-ignition temperature</td>
<td>No information identified.</td>
</tr>
<tr>
<td>Decomposition temperature</td>
<td>No information identified.</td>
</tr>
<tr>
<td>Viscosity</td>
<td>No information identified.</td>
</tr>
<tr>
<td>Explosive properties</td>
<td>No information identified.</td>
</tr>
<tr>
<td>Oxidizing properties</td>
<td>No information identified.</td>
</tr>
</tbody>
</table>
### SECTION 9 - PHYSICAL AND CHEMICAL PROPERTIES …continued

**Other information**

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight</td>
<td>Not applicable (Mixture)</td>
</tr>
<tr>
<td>Molecular formula</td>
<td>Not applicable (Mixture)</td>
</tr>
</tbody>
</table>

### 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 and/or the individual ingredients where applicable.

**Information on toxicological effects**

**Route of entry**

May be absorbed by inhalation, skin contact and ingestion.

**Acute toxicity**

<table>
<thead>
<tr>
<th>Compound</th>
<th>Type</th>
<th>Route</th>
<th>Species</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dexmedetomidine hydrochloride</td>
<td>LD&lt;sub&gt;50&lt;/sub&gt;</td>
<td>IV</td>
<td>Dog</td>
<td>2 mg/kg</td>
</tr>
<tr>
<td>Sodium chloride</td>
<td>LD&lt;sub&gt;50&lt;/sub&gt;</td>
<td>Oral</td>
<td>Rat</td>
<td>3000 mg/kg</td>
</tr>
<tr>
<td></td>
<td>LD&lt;sub&gt;50&lt;/sub&gt;</td>
<td>Dermal</td>
<td>Rabbit</td>
<td>&gt;10,000 mg/kg</td>
</tr>
<tr>
<td></td>
<td>LC&lt;sub&gt;50&lt;/sub&gt;</td>
<td>Inhalation</td>
<td>Rat</td>
<td>&gt;42 g/m³ (1-hr)</td>
</tr>
<tr>
<td></td>
<td>LD&lt;sub&gt;50&lt;/sub&gt;</td>
<td>Oral</td>
<td>Mouse</td>
<td>4000 mg/kg</td>
</tr>
</tbody>
</table>

**Irritation/Corrosion**

No information identified.

**Sensitization**

No information identified.

**STOT-single exposure**

No information identified.
STOT-repeated exposure/Repeat-dose toxicity

Dexmedetomidine given IV to rats caused sedation, piloerection (hair standing up), and exophthalmos (abnormal eyeball protrusion) 160 µg/kg/day. Small changes in thymus and body weights were reported at lower doses. A NOAEL of 40 µg/kg/day was identified.

Reproductive toxicity

No effects on fertility were reported in rats given subcutaneous (SC) dexmedetomidine at doses up to 54 µg/kg/day. The NOAEL for systemic toxicity was 6 µg/kg/day.

Developmental toxicity

Dexmedetomidine was administered SC to rats and IV to rabbits during gestation at doses up to 200 and 96 µg/kg/day, respectively. Increased post-implantation loss and a reduced number of live pups were noted in rats (NOAEL = 20 µg/kg/day). No developmental/maternal toxicity was seen in rabbits (NOAEL = 96 µg/kg/day).

In a multi-generational study, SC dexmedetomidine was administered to pregnant rats from gestational day 16 through nursing. Decreased pup weights were noted at doses ≥ 8 µg/kg/day. When pups born to mothers treated with 32 µg/kg/day were allowed to mature and mate, elevated embryo-fetal toxicity and delayed motor development was noted in their offspring. The NOAEL was 2 µg/kg/day.

Genotoxicity

Dexmedetomidine was negative for mutagenicity in the Ames assay, an in vitro forward mutation assay with mouse lymphoma cells, and was negative for chromosomal aberrations (in human lymphocytes). However, it was positive for chromosomal aberrations with rat S9 metabolic activation, and was positive in vivo in the mouse micronucleus test with NMRI mice, but not with CD-1 mice. Overall, the mutagenicity data are difficult to interpret.

Carcinogenicity

No studies identified. None of the components of this mixture 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

<table>
<thead>
<tr>
<th>Toxicity</th>
<th>Compound</th>
<th>Type</th>
<th>Species</th>
<th>Concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Toxicity</td>
<td>Dexmedetomidine hydrochloride</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Persistence and Degradability</td>
<td>Sodium chloride</td>
<td>EC₅₀/96h</td>
<td>Fish (various species)</td>
<td>&gt;4,700 mg/L</td>
</tr>
<tr>
<td></td>
<td></td>
<td>EC₅₀/48h</td>
<td>Daphnia magna</td>
<td>340-1000 mg/L</td>
</tr>
</tbody>
</table>
SECTION 12 - ECOLOGICAL INFORMATION

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bioaccumulative potential</td>
<td>No data identified.</td>
</tr>
<tr>
<td>Mobility in soil</td>
<td>No data identified.</td>
</tr>
<tr>
<td>Results of PBT and vPvB assessment</td>
<td>Not performed.</td>
</tr>
<tr>
<td>Other adverse effects</td>
<td>No data identified.</td>
</tr>
<tr>
<td>Note</td>
<td>Ecological characteristics of this product/mixture were not available. Releases to the environment should be avoided.</td>
</tr>
</tbody>
</table>

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 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 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 complies with the requirements under US, EU and GHS (EU CLP - Regulation EC No 1272/2008) guidelines. Consult your local/regional authorities for more information. |
| Chemical safety assessment | Not conducted. |
| OSHA Hazardous | Contains dexmedetomidine, a potent sedative. |
| WHMIS classification | Not required. Drugs are not subject to WHMIS. This product has been classified in accordance with the hazard criteria of the Controlled Products Regulations and the SDS contains all of the information required by those regulations. |
| 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 R phrases and EU Classifications | Xn - Harmful. Repr. Cat. 3 - Toxic for Reproduction Category 3. R63 - Possible risk of harm to the unborn child. |
| Full text of H phrases, P phrases and GHS classification | 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. |
| 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; STEL - |
Abbreviations

Short Term Exposure Limit; TDG - Transportation of Dangerous Goods; TSCA - Toxic Substances Control Act; TWA - Time Weighted Average; WHMIS - Workplace Hazardous Materials Information System

Revisions

Updated contact information in Section 1.

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.