SAFETY DATA SHEET

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

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Product identifier	Dexmedetomidine Hydrocholoride 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

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

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

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 See Sections 2 and 11.

Indication of immediate medical attention and special treatment needed, if necessary 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.

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
Sodium chloride	Latvia, Lithuania, Russia	TWA-8 HR	5 mg/m³

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

Information on basic physical and chemical properties

Appearance	Lyophilized powder
Color	White
Odor	Odorless
Odor threshold	No information identified.
pH	pH when dissolved in water is 4.5 to 7
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	No information identified.
Water solubility	Freely soluble in water
Solvent solubility	No information identified.
Partition coefficient (*n-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.

SECTION 9 - PHYSICAL AND CHEMICAL PROPERTIES …continued

Other information

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 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

Compound	Type	Route	Species	Dose
Dexmedetomidine hydrochloride	Highest non-lethal dose	IV	mice, rats, and dogs	1 mg/kg
	LD_{50}	IV	Dog	2 mg/kg
Sodium chloride	LD_{50}	Oral	Rat	3000 mg/kg
	LD_{50}	Dermal	Rabbit	>10,000 mg/kg
	LC_{50}	Inhalation	Rat	>42 g/m³ (1-hr)
	LD_{50}	Oral	Mouse	4000 mg/kg

Irritation/Corrosion No information identified.

Sensitization No information identified.

STOT-single exposure No information identified.

SECTION 11 - TOXICOLOGICAL INFORMATION …continued

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 abberations (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

Toxicity

Compound	Type	Species	Concentration
Dexmedetomidine hydrochloride	--	--	--
Sodium chloride	EC_{50}/96h	Fish (various species)	>4,700 mg/L
	EC_{50}/48h	Daphnia magna	340-1000 mg/L

Persistence and Degradability

No data identified.

SECTION 12 - ECOLOGICAL INFORMATION …continued

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	Ecological characteristics of this product/mixture were not available. 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 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 -

SECTION 16 - OTHER INFORMATION …continued

Abbreviations …continued	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.