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

Buprenorphine Hydrochloride (HCl) for Injection

Synonyms

For buprenorphine HCl: 21-Cyclopropyl-7alpha-((S)-1-hydroxy-1,2,2-trimethylpropyl)-6,14-endo-ethano-6,7,8,14-tetrahydrooripavine hydrochloride

Trade names

Generic brand

Chemical family

Mixture - contains an oripavine derivative

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 the treatment of pain.

Note

This SDS is written to address potential worker health and safety issues associated with the handling of the formulated drug 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 drug product, packaged in vials.**

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

Buprenorphine hydrochloride ("Buprenorphine") is an opioid analgesic compound. Common adverse effects reported with clinical use include gastrointestinal (GI) (nausea, vomiting, constipation, dry mouth) and CNS (*e.g.* drowsiness, lightheadedness, headaches, confusion, euphoria, hallucinations, blurred vision) effects. Skin rash and irritation were reported following transdermal patch use. Severe effects on the cardiovascular (heart attack) and respiratory (respiratory depression) systems have also occurred, usually with overdose. Hypersensitivity (allergic) reactions were also reported.

Buprenorphine is a narcotic. Although it has a lower potential for dependence than morphine, its use can lead to some psychological dependence and abuse, and minor withdrawal symptoms may occur upon abrupt cessation of a prolonged exposure. Neonatal withdrawal symptoms were reported in infants born to mothers treated with buprenorphine during pregnancy.

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

Ingredient	CAS #	EINECS/ ELINCS#	Amount	GHS Classification
Buprenorphine hydrochloride	53152-21-9	258-396-8	0.03-0.05 %	STOT-S3:H336; RT2:H361d

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	Medical conditions aggravated by exposure: none identified. 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.
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 material is released or spilled, cordon off spill area. 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 pharmaceutical agents (i.e., use of engineering controls and/or other personal protective equipment if needed). Avoid breathing mist/spray. Wash thoroughly after handling.
Conditions for safe storage including any incompatibilities	Store at controlled room temperature (20-25°C or 68-77 °F) (See USP Controlled Room Temperature) away from incompatible materials. Keep container upright. Protect from light. Discard unused portion.
Specific end use(s)	Pain reliever

SECTION 8 - EXPOSURE CONTROLS/PERSONAL PROTECTION

Note	Wash hands, face and other potentially exposed areas immediately in the event of physical contact. Dispose of broken vials/syringes in a sharps container.

Control Parameters/ Occupational Exposure Limit Values

Compound	Issuer	Type	OEL
Buprenorphine hydrochloride	--	--	--

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 should 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 the 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 substance, 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	Clear, colorless

SECTION 9 - PHYSICAL AND CHEMICAL PROPERTIES …continued

Odor	Odorless
Odor threshold	No information identified.
pH	4.0-7.0
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
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	Aqueous solution; not anticipated to be explosive.
Oxidizing properties	No information identified.

Other information

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

SECTION 10 - STABILITY AND REACTIVITY

Reactivity No information identified.

Chemical stability Chemically stable; pharmacological stability not guaranteed beyond expiration date imprinted on package.

Possibility of hazardous reactions Not expected to occur.

Conditions to avoid Avoid extreme temperatures.

Incompatible materials No information identified.

Hazardous decomposition products No information identified.

SECTION 11 - TOXICOLOGICAL INFORMATION

Note No data for the mixture were identified. Data below are for the active ingredient and/or other 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
Buprenorphine hydrochloride	LD_{50}	Oral	Rat	>600 mg/kg
	LD_{50}	Oral	Mouse	260 mg/kg
	LD_{50}	Intravenous (IV)	Rat	31 mg/kg
	LD_{50}	Intravenous (IV)	Mouse	24 mg/kg
	LD_{50}	Dermal	Rat	>100 mg/kg
	LC_{50}	Inhalation	Rat	>0.93 mg/L

Irritation/Corrosion Buprenophine was mildly irritating to rabbit skin, but was not phototoxic.

Sensitization Buprenophine was not a sensitizer in guinea pigs.

STOT-single exposure Signs associated with single buprenophine exposure usually consist of convulsions and changes in motor activity (*e.g.*, ataxia), similar to other opioid agonists.

STOT-repeated exposure/Repeat-dose toxicity No mortality or target organ effects were reported in 90-day toxicity studies in rats and dogs treated with buprenorphine doses up to 5 and 25 mg/kg/day, respectively (route not specified).

Reproductive toxicity No fertility impairment was observed in rats treated with buprenorphine at oral or parenteral doses of 80 and 5 mg/kg/day, respectively. Labor difficulties were noted at doses as low as 0.8 and 0.1 mg/kg/day, respectively, in a perinatal rat study.

SECTION 11 - TOXICOLOGICAL INFORMATION …continued

Developmental toxicity	An increase in neonatal mortality was observed at the doses mentioned above in the perinatal rat study. Increases in pre- and post-implantation loss were noted in rabbits treated orally and intravenously with doses as low as 1 and 0.2 mg/kg/day buprenorphine. Skeletal abnormalities were also reported in rats and rabbits at buprenorphine doses as low as 1 mg/kg/day by several routes.
Genotoxicity	Results from several *in vitro* studies with buprenorphine using bacteria, yeasts, and mammalian cells were equivocal.
Carcinogenicity	In a 27-month study with rats, an oral dose of 56 mg/kg/day buprenorphine produced a dose-related increase in benign Leydig cell (testicular) tumors. No evidence of tumorgenicity was noted in mice treated orally with up to 100 mg/kg/day. Overall, buprenorphine has a low carcinogenic potential. None of the 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 data available.
Human health data	See "Section 2 - Other Hazards"

SECTION 12 - ECOLOGICAL INFORMATION

Toxicity

Compound	Type	Species	Concentration
Buprenorphine hydrochloride	--	--	--

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 this product/mixture have not been fully investigated. 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.
WHMIS classification	Not classified.
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	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.

SECTION 16 - OTHER INFORMATION …continued

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	10 July 2015
Revisions	This is the first 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 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.