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Version 1.1

SAFETY DATA SHEET

1. IDENTIFICATION OF THE SUBSTANCE/PREPARATION

Product Name Naloxone hydrochloride dihydrate

Synonyms Naloxone chlorhydrate
Morphinan-6-one, 4,5-epoxy-3,14-dihydroxy-17-(2-propenyl)-, hydrochloride, (5a)

Recommended Use Pharmaceutical Intermediate

Uses advised against No information available.

Manufacturer Address Rhodes Technologies L.P.
498 Washington Street
Coventry, RI 02816
Phone: 401-262-9200
Fax: 401-262-9201

24 Hour Emergency Phone Number Chemtrec (800) 424-9300
For all international transportation emergencies, call Chemtrec collect at (703) 527-3887.

2. HAZARDS IDENTIFICATION

This chemical is considered hazardous by the 2012 OSHA Hazard Communication Standard (29 CFR 1910.1200).

Combustible dust	Yes
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Emergency Overview

Signal Word	Warning	
Appearance Crystalline powder	Physical state Solid	Odor Odorless

Hazards Not Otherwise Classified (HNOC)

Not Applicable.

Other Information

No information available.

3. COMPOSITION/INFORMATION ON INGREDIENTS

Chemical Name	CAS No	Weight %
Naloxone Hydrochloride Dihydrate	51481-60-8	100

4. FIRST AID MEASURES

First aid measures

General advice	If symptoms persist, call a physician. Do not breathe dust/fume/gas/mist/vapors/spray. Do not get in eyes, on skin, or on clothing.
Eye contact	In case of eye contact, immediately flush eyes with fresh water for at least 15 minutes while holding the eyelids open. Remove contact lenses if worn. Get medical attention if irritation persists.
Skin contact	In case of contact, remove contaminated clothing. Immediately flush skin with copious amounts of water for at least 15 minutes. Obtain medical attention if skin reaction occurs.
Inhalation	In case of inhalation, remove to fresh air. If not breathing, provide artificial respiration. If breathing is difficult, administer oxygen. Seek medical attention immediately.
Ingestion	In case of accidental ingestion, wash out mouth with copious amounts of water. Seek medical attention immediately. Do not induce vomiting unless directed by medical personnel. Never give anything by mouth to an unconscious person.
Self-protection of the first aider	Do not use mouth-to-mouth method if victim ingested or inhaled the substance; give artificial respiration with the aid of a pocket mask equipped with a one-way valve or other proper respiratory medical device.
Most important symptoms and effects, both acute and delayed	
Symptoms	May cause abdominal or stomach cramps, body aches, convulsions, diarrhea, difficult or troubled breathing, excessive crying, fast, pounding, or irregular heartbeat or pulse, fever and goosebumps.
Indication of any immediate medical attention and special treatment needed	
Note to physicians	This material is an opioid agonist. For individuals with opioid dependency, this material will trigger withdrawal symptoms. Treat symptomatically.

5. FIRE-FIGHTING MEASURES

Suitable Extinguishing Media

Use extinguishing measures that are appropriate to local circumstances and the surrounding environment.

Unsuitable Extinguishing Media No information available.

Specific hazards arising from the chemical

Avoid generating dust; fine dust dispersed in air in sufficient concentrations, and in the presence of an ignition source is a potential dust explosion hazard.

Explosion Data

Sensitivity to Mechanical Impact None.

Sensitivity to Static Discharge See Section 9: PHYSICAL AND CHEMICAL PROPERTIES (Dust Values).

Protective equipment and precautions for firefighters

As in any fire, wear self-contained breathing apparatus pressure-demand, MSHA/NIOSH (approved or equivalent), and full protective gear.

6. ACCIDENTAL RELEASE MEASURES

Personal precautions, protective equipment and emergency procedures

Personal precautions Evacuate personnel to safe areas. Use personal protection recommended in Section 8.

Other Information Dust deposits should not be allowed to accumulate on surfaces, as these may form an explosive mixture if they are released into the atmosphere in sufficient concentration.

Environmental precautions

Environmental precautions Prevent entry into waterways, sewers, basements or confined areas. Do not flush into surface water or sanitary sewer system. See section 12 for additional Ecological Information.

Methods and material for containment and cleaning up

Methods for containment Prevent further leakage or spillage if safe to do so. Prevent dust cloud.

Methods for cleaning up Use personal protective equipment as required. Cover powder spill with plastic sheet or tarp to minimize spreading and keep powder dry. Clean up material with a HEPA filtered vacuum or wet mop. Do not create dust, place in appropriate container for disposal. Clean contaminated surface thoroughly.

7. HANDLING AND STORAGE

Precautions for safe handling

Advice on safe handling Avoid contact with skin, eyes or clothing. Use personal protective equipment as required. Wash contaminated clothing before reuse. Do not breathe dust/fume/gas/mist/vapors/spray. Do not eat, drink or smoke when using this product. Avoid generation of dust and accumulation. Routine housekeeping should be instituted to ensure that dusts do not accumulate on surfaces.

Conditions for safe storage, including any incompatibilities

Storage conditions Keep container tightly closed in a dry and well-ventilated place. Store at room temperature. Protect from sunlight. Dry powders can build static electricity charges when subjected to the friction of transfer and mixing operations. Provide adequate, such as electrical grounding and bonding, or inert atmospheres.

Incompatible materials None known based on available information.

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Exposure Guidelines

Chemical Name	Performance-Based Exposure Band (PBEB)	Company OEG (ug/m ³)
Naloxone Hydrochloride Dihydrate	3 (10-100 ug/m ³)	50

Engineering Controls Handle material under adequate ventilation (e.g., chemical fume hood, vented balance enclosure [VBE]). Keep container tightly closed.

It is recommended that all dust control equipment such as local exhaust ventilation and material transportation systems involved in handling of this product contain explosion relief vents, an explosion suppression system, or an oxygen-deficient environment.

Ensure that dust-handling systems (such as exhaust ducts, dust collectors, vessels, and processing equipment) are designed in a manner to prevent the escape of dust into the work area (i.e., there is no leakage from the equipment.)

Use only appropriately classified electrical equipment and powered industrial trucks.

Individual Protection Measures (Personal Protective Equipment)

Eye/face protection	Wear ANSI-approved safety glasses with side shields. Wear full-face protection when judged that the possibility exists for eye and face contact.
Skin and body protection	Disposable sleeve covers or longer gloves should be considered to ensure the wrist area is covered, and discard as contaminated PPE after use. In laboratories wear lab coat, safety shoes and gloves selected for chemicals in use. In large scale , i.e., pilot plant or manufacturing, wear impervious disposable clothing such as lab coat, shoe covers, apron, or jumpsuit, as appropriate, to prevent skin contact.
Respiratory protection	Use and selection of respiratory protection is based upon engineering controls in use and potential for aerosol generation. When engineering controls are not sufficient to control exposure select appropriate respiratory equipment. In a laboratory setting respirators are not required when handling substances in ventilated enclosures (hoods) that meet currently accepted airflow criteria for proper containment capture. In large scale settings , where appropriate, minimum of NIOSH-approved air purifying respirator when a respirator is judged appropriate to prevent inhalation.
General Hygiene Considerations	Handle in accordance with good industrial hygiene and safety practice. Clean and wet wipe the work area to prevent visible signs of dust or residue after each use, before moving to a new work area.

9. PHYSICAL AND CHEMICAL PROPERTIES

Physical and Chemical Properties

Physical state	Solid	
Appearance	Crystalline powder	
Odor	Odorless	
Color	White to Off-White	
Odor threshold	No information available.	
Property	Values	Remarks • Method
pH	No information available.	
Melting point / melting range	177-108 °C	
Boiling point / boiling range	No information available.	
Flash point	No information available.	
Evaporation rate	No information available.	
Flammability (solid, gas)	No information available.	
Flammability limits in air		
Upper flammability limits		
Lower flammability limits		
Vapor pressure	No information available.	
Vapor density	No information available.	
Specific gravity	No information available.	
Water solubility	Soluble in water	
Solubility in other solvents	No information available.	
Partition coefficient (n-octanol/water)	No information available.	
Autoignition temperature	No information available.	
Decomposition temperature	No information available.	
Kinematic viscosity	No information available.	
Dynamic viscosity	No information available.	
Explosive properties	No information available.	
Oxidizing properties	No information available.	

Other Information

Softening point No information available.
 Molecular weight No information available.
 VOC content; (%) No information available.
 Density No information available.
 Bulk density No information available.

Minimum ignition energy (MIE) 10-25
 Limiting Oxygen Concentration (% vol) 10-11

10. STABILITY AND REACTIVITY

Chemical stability Stable under recommended storage conditions.

Possibility of hazardous reactions No information available.
Hazardous polymerization Hazardous polymerization does not occur.
Conditions to avoid None known based on available information.
Incompatible materials None known based on available information.
Hazardous decomposition products None known based on available information.

11. TOXICOLOGICAL INFORMATION**Information on likely routes of exposure**

Product Information Studies detailed below support the classification for the purpose of hazard communication. The relevant data is summarized and is not a comprehensive list of all data collected. The toxicology data presented can be from the named material, the base, or alternative salt form of this material.

Inhalation May cause irritation of respiratory tract.

Eye contact No data available.

Skin contact No data available.

Ingestion May be harmful if swallowed.

Chemical Name	Oral LD50	Dermal LD50	Inhalation LC50
Naloxone Hydrochloride Dihydrate	>1000 Oral Rat	-	-

Information on toxicological effects

Symptoms May cause abdominal or stomach cramps, body aches, convulsions, diarrhea, difficult or troubled breathing, excessive crying, fast, pounding, or irregular heartbeat or pulse, fever and goosebumps.

Sensitization Did not cause sensitization in laboratory animals.

Delayed and immediate effects as well as chronic effects from short and long-term exposure

Germ cell mutagenicity The 4:1 combination of buprenorphine and naloxone was not mutagenic in a bacterial mutation assay (Ames test) using four strains of *S. typhimurium* and two strains of *E. coli*. The combination was not clastogenic in an in vitro cytogenetic assay in human lymphocytes, or in an intravenous micronucleus test in the rat.

Carcinogenicity In a carcinogenicity test(s) with rats, no evidence of carcinogenicity was observed at doses up to 100 mg/kg/day.

Reproductive toxicity Dietary administration of 4:1 combination of buprenorphine and naloxone in the rat at dose

levels of 47 mg/kg/day or greater produced a reduction in fertility demonstrated by reduced female conception rates. A dietary dose of 10 mg/kg/day had no adverse effect on fertility.

Effects on embryo-fetal development were studied in Sprague-Dawley rats and Russian white rabbits following oral (1:1) and intramuscular (3:2) administration of mixtures of buprenorphine and naloxone. Following oral administration to rats and rabbits, no teratogenic effects were observed at doses up to 250 mg/kg/day and 40 mg/kg/day, respectively. No definitive drug-related teratogenic effects were observed in rats and rabbits at intramuscular doses up to 30 mg/kg/day. Following oral administration to the rat, dose-related post-implantation losses, evidenced by increases in the numbers of early resorptions with consequent reductions in the numbers of fetuses, were observed at doses of 10 mg/kg/day or greater. In the rabbit, increased post-implantation losses occurred at an oral dose of 40 mg/kg/day. Following intramuscular administration in the rat and the rabbit, post-implantation losses, as evidenced by decreases in live fetuses and increases in resorptions, occurred at 30 mg/kg/day.

STOT-single exposure No information available.
STOT-repeated exposure No information available.
Chronic Toxicity No information available.
Target Organ Effects No information available.
Aspiration hazard No information available.

12. ECOLOGICAL INFORMATION

Ecotoxicity

Ecotoxicity Harmful to aquatic life with long lasting effects

Chemical Name	Algae/aquatic plants	Fish	Toxicity to microorganisms	Crustacea
Naloxone Hydrochloride Dihydrate	NOEC 13 mg/L (Growth and Yield)	NOEC 9.9 mg/L (P. promelus) Highest dose tested		NOEC 21 mg/L (D magna)

Persistence and degradability Not readily biodegradable.

Bioaccumulation No information available.

Chemical Name	Partition coefficient
Naloxone Hydrochloride Dihydrate	0.765

Other adverse effects No information available.

13. DISPOSAL CONSIDERATIONS

Waste treatment methods

Disposal of wastes Disposal should be in accordance with applicable regional, national, and local laws, and regulations.

Contaminated Packaging Do not reuse container.

14. TRANSPORT INFORMATION

DOT Not regulated.

IATA Not regulated.

15. REGULATORY INFORMATION

International Inventories

TSCA Not determined.
 DSL Not determined.

Legend:

TSCA - United States Toxic Substances Control Act Section 8 (b) Inventory
DSL/NDL - Canadian Domestic Substances List/Non-Domestic Substances List

US Federal Regulations

SARA 313

Section 313 of Title III of the Superfund Amendments and Reauthorization Act of 1986 (SARA). This product does not contain any chemicals which are subject to the reporting requirements of the Act and Title 40 of the Code of Federal Regulations, Part 372.

SARA 311/312 Hazard Categories

Acute Health Hazard	Yes
Chronic Health Hazard	Yes
Fire Hazard	No
Sudden Release of Pressure Hazard	No
Reactive Hazard	No

CWA (Clean Water Act)

This product does not contain any substances regulated as pollutants pursuant to the Clean Water Act (40 CFR 122.21 and 40 CFR 122.42).

CERCLA

This material, as supplied, does not contain any substances regulated as hazardous substances under the Comprehensive Environmental Response Compensation and Liability Act (CERCLA) (40 CFR 302) or the Superfund Amendments and Reauthorization Act (SARA) (40 CFR 355). There may be specific reporting requirements at the local, regional, or state level pertaining to releases of this material.

US State Regulations

California Proposition 65

This product does not contain any Proposition 65 chemicals.

US State Right-to-Know Regulations

US EPA Label Information

EPA Pesticide Registration Number Not Applicable.

16. OTHER INFORMATION

<u>NFPA</u>	Health Hazards 1	Flammability 1	Instability 0	Physical and Chemical Properties -
<u>HMIS</u>	Health Hazards 1*	Flammability 1	Physical Hazards 0	Personal protection X
<i>Chronic Hazard Star Legend</i>	<i>* = Chronic Health Hazard</i>			

General Information

In an industrial setting, refer to NFPA 654, Standard for the Prevention of Fire and Dust Explosions from the Manufacturing, Processing, and Handling of Combustible Particulate Solids, for Safe Handling.

Prepared By

This SDS was prepared by the Environmental, Health, and Safety & Toxicology Departments of Purdue Pharma L.P.

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Disclaimer

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End of Safety Data Sheet