Purdue Pharma L.P.

Material Safety Data Sheet

Dilaudid® Injectable 1, 2, 4 mg/mL
(Hydromorphone Hydrochloride) **Version: 13-October-2009**

1. CHEMICAL PRODUCT/COMPANY IDENTIFICATION

Material Identification: Dilaudid® Injectable 1, 2, 4 mg/mL

Chemical Name: Mixture, not applicable

Active Ingredient: 4, 5α-epoxy-3-hydroxy-17-methylmorphinan-6-one hydrochloride

Synonyms: Dihydromorphinone hydrochloride

Molecular Formula: Mixture
Active Ingredient: $C_{17}H_{19}NO_3 \cdot HCl$

Molecular Weight: Mixture
Active Ingredient: 321.80

CAS Number: Mixture, N/A
Active Ingredient: 71-68-1

Product Use: Opioid analgesic

Company Identification:

Responsible Party
Purdue Pharma L.P.
One Stamford Forum
201 Tresser Boulevard
Stamford, CT 06901-3431
Telephone: (888) 726-7535

EMERGENCY CONTACT
Chemtrec (800) 424- 9300. For all international transportation emergencies, call Chemtrec collect at (703) 527-3887.

2. HAZARDOUS COMPONENTS

Material	CAS Number	%
hydromorphone hydrochloride (1 mg/ml)	71-68-1	0.1
hydromorphone hydrochloride (2 mg/ml)	71-68-1	0.2
hydromorphone hydrochloride (4 mg/ml)	71-68-1	0.4

3. HAZARDS IDENTIFICATION

Emergency Overview

Colorless liquid.
May be fatal if ingested.
Harmful by inhalation.
Harmful by skin contact.
May cause skin and eye irritation.
May cause skin and respiratory allergies.
Causes pinpoint pupils.
Target organs: central nervous system, gastrointestinal tract, cardiovascular system.
Serious overdose produces respiratory depression, extreme somnolence, stupor or coma, skeletal muscle flaccidity, cold and clammy skin, bradycardia and hypotension.
Severe overdose produces apnea, circulatory collapse, cardiac arrest and death.

Potential Health Effects

Hydromorphone hydrochloride is an orally active opioid analgesic with potency approximately 8 times that of morphine.

Hydromorphone hydrochloride may cause eye irritation and mild skin irritation.

Repetitive exposure to hydromorphone hydrochloride may cause skin and/or respiratory allergies. Hydromorphone hydrochloride may be absorbed through the skin.

Overdose may cause dizziness, euphoria, flushing, itching, hypotension, pinpoint pupils, nausea/vomiting, constipation and reduced urination.

Serious overdose produces respiratory depression, extreme somnolence, stupor or coma, skeletal muscle flaccidity, cold and clammy skin, bradycardia and hypotension.

Severe overdose produces apnea, circulatory collapse, cardiac arrest and death.

Maternal exposure to hydromorphone hydrochloride during pregnancy may cause respiratory depression in the neonate. Repeated maternal exposure to hydromorphone hydrochloride during pregnancy may produce respiratory depression and/or withdrawal in the neonate.

Conditions that may be aggravated by exposure include significant chronic obstructive lung disease, asthma and hypotension.

Carcinogenicity Information

Hydromorphone hydrochloride is not listed by IARC, NTP, OSHA, or ACGIH as a carcinogen.

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4. FIRST AID MEASURES

First Aid

INHALATION

If inhaled, remove to fresh air. If not breathing, give artificial respiration. If breathing is difficult, give oxygen. Call a physician (see notes to physician below). If allergic reactions occur (e.g., stuffy, runny or itchy nose, itchy throat, sneezing, watery/itchy eyes, etc.) see a physician.

SKIN CONTACT

Remove contaminated clothing. Flush skin with plenty of water and wash thoroughly with soap and water. If irritation (redness, itching, swelling) develops, seek medical attention. Wash contaminated clothing before reuse.

EYE CONTACT

In case of contact, immediately flush eyes with plenty of water for at least 15 minutes. If easy to do, remove contact lenses. See a physician.

INGESTION

If swallowed, immediately give 2 glasses of water and induce vomiting under the direction of medical personnel. Never give anything by mouth to an unconscious person. Call a physician.

Notes to Physicians

Hydromorphone hydrochloride is a pure opioid agonist with an analgesic potency about 8 times that of morphine. Naloxone is a specific antidote against respiratory depression from opioid overdose. Opioid antagonists should not be administered in the absence of clinically significant respiratory or circulatory depression secondary to hydromorphone hydrochloride overdose.

In cases of overdose, primary attention should be given to the re-establishment of a patent airway and institution of assisted or controlled ventilation. Supportive measures (including oxygen and vasopressors) should be employed in the management of circulatory shock and pulmonary edema accompanying overdose as indicated. Cardiac arrest or arrhythmias may require cardiac massage or defibrillation.

If ingested and the patient is conscious, induction of emesis may be indicated. Gastric lavage may be indicated if the patient is unconscious.

5. FIRE FIGHTING MEASURES

Flammable Properties

Hydromorphone hydrochloride is not considered flammable.

Extinguishing Media

Water spray, carbon dioxide, dry chemical powder, or foam as appropriate for the surrounding material.

Fire Fighting Instructions

Evacuate personnel to a safe area. Keep personnel removed and upwind of fire. Wear self-contained breathing apparatus. Wear full protective equipment.

6. ACCIDENTAL RELEASE MEASURES

Safeguards (Personnel)

NOTE: Review FIRE FIGHTING MEASURES and HANDLING (PERSONNEL) sections before proceeding with clean-up. Use appropriate PERSONAL PROTECTIVE EQUIPMENT during clean-up to minimize exposure to this material. Evacuate personnel from the area.

Initial Containment

Prevent material from entering sewers, waterways, or low areas. Dike area for later disposal.

Spill Clean-up

Hydromorphone hydrochloride is a Schedule II controlled substance. Wear suitable protective clothing and equipment. Mop up the spill, and place collected material into a suitable container for reclamation or disposal. Thoroughly wash area with detergent and water. All clean up operations should be witnessed by more than one individual. The amount of material collected should be assessed and documented. Dispose of all solid waste and wash and rinse water in accordance with federal, state, and local regulations.

7. HANDLING AND STORAGE

Handling (Personnel)

Avoid contact with eyes, skin, or clothing. Wash thoroughly after handling. Wash contaminated clothing after use.

Handling (Physical Aspects)

Avoid generation of aerosols.

Storage

Hydromorphone hydrochloride is a Schedule II controlled substance. Protect from light. To maintain potency, store at 25°C (77°F) and control temperature excursions to between 15-30°C (59-86°F).

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Engineering Controls

Handle material under adequate ventilation.

Personal Protective Equipment

Wear safety glasses with side shields if exposure to liquid or aerosols is possible. Wear full-face protection when judged that the possibility exists for eye and face contact.

Wear impervious clothing such as gloves, lab coat, shoe covers, apron, or jumpsuit, as appropriate, to prevent skin exposure to liquid or aerosols. Consult the site safety professional for additional guidance, as needed.

Exposure Guidelines

Exposure Limits

Hydromorphone hydrochloride

PEL (OSHA): None established.
TLV (ACGIH): None established.
Occupational Exposure Guideline (Purdue Pharma L.P.): 10 $\mu g/m^3$ (hydromorphone free base).

Exposure Guideline Comments

May be absorbed through skin; may cause skin or respiratory sensitization.

9. PHYSICAL AND CHEMICAL PROPERTIES

Physical Data

Odor: Odorless.
Form: Liquid.
Color: Colorless.
Vapor Pressure: No information available.
Melting Point: No information available.
pKa (25 °C): No information available.
Solubility: No information available.

10. STABILITY AND REACTIVITY

Chemical Stability

Low stability hazard expected at normal operating temperatures.

Incompatibility with Other Materials

Strong oxidizers, acids, bases.
Oxidizing materials will increase the risk or fire and explosion (e.g., potassium perchlorate, potassium nitrate).

Conditions to Avoid

Not applicable.

Decomposition

Will not decompose under conditions of usual handling.

Polymerization

Material will not polymerize.

11. TOXICOLOGICAL INFORMATION

Relevant Data

Except where otherwise noted, the following data for hydromorphone hydrochloride are reflected as hydromorphone free base.

Skin/Eyes

Hydromorphone hydrochloride has not been evaluated in skin and eye irritation studies in animals. It is expected that hydromorphone hydrochloride may produce mild skin irritation and may cause eye irritation.

Acute

Hydromorphone hydrochloride

LD_{50}: IV: 55 mg/kg (mouse).
LDL: IV: 51 mg/kg (rat).
Approximate Lethal Dose: oral: 500 mg/kg (female rat).
Approximate Lethal Dose: oral: 175 mg/kg (female rabbit).

Subchronic

Hydromorphone hydrochloride

In a 12-day oral range finding study in female rats with hydromorphone hydrochloride, mortality was observed at each of the dosages tested (50-200 mg/kg/day) within the first six days of treatment. Abnormalities observed after dosing included reduced activity, incoordination, rigidity, ocused gaze, unresponsivenesss to external stimuli, increased heart rate and decreased body weight. Microscopic evaluation of tissues from animals in the study was not performed.

In a 30-day oral range finding study in male and female rats with hydromorphone hydrochloride, 50 mg/kg/day (highest dosage tested) produced mortality. At 1, 5, 20, and 50 mg/kg/day hydromorphone hydrochloride reduced food consumption and body weight (5, 20, 50 mg/kg/day groups) and produced stereotypic effects such as increased/decreased activity, impaired righting reflex, clonic convulsion, excessive salivation, etc. in a dose-and time-dependent manner. The number of estrous stages in female rats in the 20 and 50 mg/kg/day groups was reduced in the 30-day study and consecutive days of diestrus were increased in female rats in the 50 mg/kg/day group. Microscopic evaluation of tissues from animals in the study was not performed.

In a 13-day oral range finding study in female rabbits with hydromorphone hydrochloride, 100 mg/kg/day (highest dosage tested) produced reduced activity and muscle tone, recumbency and mortality during the first three days of treatment; no mortality, but similar effects were observed in rabbits that received 50 mg/kg/day. No treatment-related effects were observed in female rabbits that received 25 mg/kg/day. Microscopic evaluation of tissues from animals in the study was not performed.

Chronic Toxicity

Hydromorphone hydrochloride

No information available.

Carcinogenicity

Hydromorphone hydrochloride

No information available.

Mutagenicity/Genotoxicity

Hydromorphone hydrochloride

Bacterial mutagenicity: negative.
Mouse micronucleus: negative.
Mouse lymphoma: positive.

Developmental/Reproductive Toxicity

Hydromorphone hydrochloride

Oral administration of hydromorphone hydrochloride had no effect on reproductive performance of male or female rats at dosages as high as 5 mg/kg/day.

Hydromorphone hydrochloride was not teratogenic in rats treated orally with as high as 10 mg/kg/day or in rabbits treated with as high as 50 mg/kg/day. In a separate study, hydromorphone hydrochloride administered orally at dosages of 2 and 5 mg/kg/day to pregnant rats over the last third of the gestation period to the weaning of pups produced an increased incidence of peri/postnatal pup deaths and reduced pup body weight. These effects were not observed at a dosage of 0.5 mg/kg/day.

In early studies in the literature, hydromorphone hydrochloride had been reported to be teratogenic in hamsters (20 mg/kg, subcutaneous) and in mice (5 mg/kg, subcutaneous infusion). However, in these studies profound sedation and hypoxia/hypercarbia in the pregnant animals is believed to be the cause of the teratogenic effects, not the direct effect of hydromorphone on the fetus.

Repetitive maternal exposure to opioids has been associated with respiratory depression and/or withdrawal symptoms in neonates.

Although testing has not been conducted to determine if hydromorphone hydrochloride is present in breast milk, other opioids have been found in breast milk and it is expected hydromorphone hydrochloride will be present in breast milk of women treated with hydromorphone hydrochloride.

12. ECOLOGICAL INFORMATION

Ecotoxicological Information

Hydromorphone hydrochloride

No information available.

Chemical Fate Information

Hydromorphone hydrochloride

No information available.

13. DISPOSAL CONSIDERATIONS

Disposal

This material is not listed under US RCRA. It is a Schedule II drug. Disposal of this material must be in accordance with federal, state/provincial, and local regulations.

14. TRANSPORTATION INFORMATION

Shipping Information

This material is non-hazardous under US DOT.

15. REGULATORY/STATUATORY INFORMATION

US Federal

Hydromorphone hydrochloride preparations are subject to control under the US Federal Controlled Substances Act of 1970 as schedule II (C-II) drugs.

16. OTHER INFORMATION

The information contained in this Material Safety Data Sheet is believed to be accurate and represents the best information available at the time of preparation. However, no warranty, express or implied, with respect to such information, is made. The data in this Material Safety Data Sheet relate only to the specific material designated herein and does not relate to use in combination with any other material. The data in this Material Safety Data Sheet are subject to revision as additional knowledge and experience are gained.

This MSDS was prepared for Purdue Pharma L.P. by the Occupational and Environmental Assessment Section of Purdue Pharma L.P.