

Purdue Pharma L.P.

Material Safety Data Sheet

MS Contin[®] (morphine sulfate controlled-release) 15, 30, 60, 100, 200 mg Tablets **Version: 26-May-09**

1. CHEMICAL PRODUCT/COMPANY IDENTIFICATION

Material Identification: MS Contin[®] (morphine sulfate controlled-release) 15, 30, 60, 100, 200 mg Tablets

Chemical Name: Mixture, not applicable.
Active Ingredient: 7,8-didehydro-4,5 α -epoxy-17-methylmorphinan-3,6 α -diol sulfate (2:1) (salt) pentahydrate

Synonyms: None known.
Active Ingredient: Morphine sulfate, morphine

Molecular Formula: Mixture **Molecular Weight:** Mixture
Active Ingredient: C₃₄H₄₀N₂O₁₀S•5H **Active Ingredient:** 758.81

CAS Number: Mixture, not applicable.
Active Ingredient: 6211-15-0

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.

Purdue Pharma L.P.

2. HAZARDOUS COMPONENTS

| <u>Material</u> | <u>CAS Number</u> | <u>%</u> |
|------------------|-------------------|---------------|
| Morphine sulfate | 6211-15-0 | 9.7 (15 mg) |
| | | 19.3 (30 mg) |
| | | 38.7 (60 mg) |
| | | 64.5 (100 mg) |
| | | 64.5 (200 mg) |
| Talc USP | 14807-96-6 | 1.9 |

3. HAZARDS IDENTIFICATION

Emergency Overview

Round, film coated tablets (15 mg blue; 30 mg lavender; 60 mg orange; 100 mg gray). Capsule-shaped, film coated tablets (200 mg green).

MS Contin[®] tablets do not pose a significant workplace hazard unless tablets are broken or crushed. The following information is provided for those circumstances where uncontrolled exposure to morphine sulfate may occur due to breakage or crushing of MS Contin[®] tablets.

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 overdosage produces apnea, circulatory collapse, cardiac arrest, and death.

Repeated maternal exposure may cause neonatal respiratory depression and/or withdrawal syndrome.

Intact, broken or crushed tablets may be fatal if ingested.

Broken or crushed tablets may be harmful by inhalation or skin contact.

Contact with broken or crushed tablets, may cause eye and skin irritation and pinpoint pupils.

Repetitive skin contact with broken or crushed tablets may cause allergic skin reactions.

Potential Health Effects

The active ingredient of MS Contin[®] is morphine sulfate, an orally active opioid analgesic. MS Contin[®] is designed to provide controlled release of morphine in the body. If MS Contin[®] tablets are broken or crushed, workplace exposure to morphine sulfate may occur. The following information is provided for those circumstances where uncontrolled exposure to the hazardous components in MS Contin[®] may occur due to breakage or crushing of the tablet.

Purdue Pharma L.P.

Morphine sulfate

Morphine may cause eye irritation and mild skin irritation.

Repetitive exposure to morphine may cause skin and/or respiratory allergies. Systemic absorption may occur through skin.

Overdosage 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 overdosage produces apnea, circulatory collapse, cardiac arrest, and death.

Maternal exposure to MS Contin[®] may cause respiratory depression in the neonate. Repeated maternal exposure to morphine may produce respiratory depression and/or withdrawal in the neonate.

Talc

If MS Contin[®] is crushed, exposure to talc may occur and can cause eye, skin, nose, throat, and lung irritation resulting in coughing, wheezing and shortness of breath. Long term inhalation overexposure to talc is associated with talc pneumoconiosis. Symptoms include shortness of breath, clubbing of fingers, coughing with sputum, changes in lung x-rays, chronic lung disease with impaired lung function, and can cause right-sided heart failure.

Conditions that may be aggravated by exposure to broken or crushed MS Contin[®] tablets include significant chronic obstructive lung disease, asthma, and hypotension.

Carcinogenicity Information

Neither MS Contin[®] nor its components are listed by IARC, NTP, OSHA, or ACGIH as a carcinogen.

4. FIRST AID MEASURES

First Aid

INHALATION

If dusts are inhaled, remove to fresh air. If not breathing, give artificial respiration. If breathing is difficult, give oxygen. Call a physician (see notes to

Purdue Pharma L.P.

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

MS Contin[®] is an opioid agonist analgesic. The extended release of morphine sulfate from MS Contin[®] tablets should be taken into account when treating an overdose due to ingestion of intact tablets. 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 morphine overdose.

In cases of overdosage, 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

MS Contin[®] tablets are not considered flammable. However, concentrated dust from broken or crushed tablets may pose a dust explosion hazard. Eliminate sources of ignition. Bond and ground as necessary. Use non-sparking tools.

Extinguishing Media

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

Purdue Pharma L.P.

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

Wear suitable protective clothing and equipment. Sweep up intact tablets or vacuum up broken or crushed tablets and place collected material into a suitable container for reclamation or disposal. Thoroughly wash area with detergent and water. Morphine is a Schedule II controlled substance. All clean up operations should be witnessed by more than one individual. The amount of material collected should be assessed and documented. Notify appropriate company regulatory personnel. Dispose of all solid waste and wash and rinse water in accordance with federal, state, and local regulations.

7. HANDLING and STORAGE

Handling (Personnel)

Do not break or crush tablets. Avoid procedures that will generate dust. Local exhaust is recommended to avoid generation of significant airborne dust levels. Avoid contact with eyes, skin, or clothing. Wash thoroughly after handling. Wash contaminated clothing after use.

Handling (Physical Aspects)

Close container after each use. Do not generate dust.

Storage

Morphine is a Schedule II controlled substance. Keep containers of MS Contin[®] tightly closed. Protect from light. To maintain potency, store at 25°C (77°F) and control temperature excursions to between 15-30°C (59-86°F).

Purdue Pharma L.P.

8. EXPOSURE CONTROLS /PERSONAL PROTECTION

Engineering Controls

Handle material under adequate ventilation. Keep container tightly closed.

Personal Protective Equipment (PPE)

Wear chemical goggles if exposure to dust is possible. Wear impervious clothing such as gloves, lab coat, shoe covers, apron, or jumpsuit, as appropriate, to prevent skin exposure to broken or crushed tablets, powder, and dust. Wear approved respiratory protection when the possibility exists for respiratory exposure. Consult the site safety professional for additional guidance, as needed

Exposure Guidelines

Exposure Limits

None for MS Contin[®]

Morphine sulfate

PEL (OSHA): None established.

TLV (ACGIH): None established.

Purdue L.P. (Occupational Exposure Guideline): 80 $\mu\text{g}/\text{m}^3$ (free base).

Talc

TLV (ACGIH): 2 mg/m^3 , as respirable fraction containing no asbestos fibers and <1% crystalline silica; A4 (not classifiable as a human carcinogen).

PEL (OSHA): 20 mppcf, as respirable dust containing no asbestos fibers and <1% quartz mg/m^3 .

NIOSH (REL): 2 mg/m^3 , as respirable dust containing no asbestos fibers.

NIOSH (IDLH): 1,000 mg/m^3 , as respirable dust containing no asbestos fibers.

California (OEL): 2 mg/m^3 , containing < 1% crystalline silica.

Exposure Guideline Comments

Morphine sulfate may be absorbed through skin (crushed tablets); may cause skin or respiratory sensitization.

9. PHYSICAL and CHEMICAL PROPERTIES

Physical Data

Morphine Sulfate

Odor: odorless

Form: powder (solid)

Color: white to off-white

Vapor Pressure: no information available

Melting Point: ~ 250°C

Purdue Pharma L.P.

Solubility: 1gm/15.5mL @ 25°C (water)

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 of fire and explosion (e.g., potassium perchlorate, potassium nitrate).

Conditions to Avoid

Static charge, sparks, generation of dust, and temperatures above 200°C.

Decomposition

Will not decompose under conditions of usual handling.

Polymerization

Material will not polymerize.

11. TOXICOLOGICAL INFORMATION

Relevant Data

The following data for morphine are reflected as morphine free base. The information for talc is for non-asbestos containing material.

Skin/Eyes

Morphine

Neither morphine sulfate nor MS Contin[®] have been evaluated in skin or eye irritation studies in animals. It is expected that morphine may produce mild skin irritation and may cause eye irritation.

Talc

Draize (human): 300 µg/3D mild reaction

Talc is not a primary skin irritant and it does not cause sensitization. Talc particles are physical irritants which may cause inflammatory changes such as skin rash and can cause serious eye damage.

Acute

Morphine

| Species | Oral LD50 Values (mg/kg) | IV LD50 Values (mg/kg) |
|---------|--------------------------|------------------------|
| Mouse | 423-524 | 135 |

Purdue Pharma L.P.

| | | |
|-----|---------|-----|
| Rat | 335-336 | 140 |
| Dog | | 133 |

Talc

Rat oral LD₅₀: 920 mg/kg

Subchronic

Morphine

In a 5-day oral study in rats, mortality was observed after three days at 450 mg/kg/day; 150 and 450 mg/kg/day produced decreased activity, unkempt appearance, rigidity on handling, and stereotypic behavior. No abnormalities in behavior or appearance were observed at 5, 15, or 50 mg/kg/day. Male, but not female, rat body weights were decreased in the 50, 150, and 450 mg/kg/day groups. Food consumption was decreased among rats in the 15, 50, 150, and 450 mg/kg/day groups. The no-effect level was 5 mg/kg/day.

In a 3-month oral toxicity study in rats, observations similar to those in the 5-day study and including increased activity were observed at dosages of 3 – 125 mg/kg/day. The no-adverse effect level in the study was 3 mg/kg/day for male rats and < 7.5 mg/kg/day for female rats (lowest dosage tested in females).

In a 2-week oral study in dogs, a dosage of 1 mg/kg/day was associated with emesis and reduced fecal output; doses of 4, 8, and 12 mg/kg/day were associated with hindlimb weakness, emesis, reduced fecal output and salivation. Lateral recumbency was also observed among dogs in the 12 mg/kg/day group.

In a 3-month oral study in dogs, 0.3 mg/kg/day (lowest dose tested) produced a low incidence of emesis. Dosages of 1 – 10 mg/kg/day produced a higher incidence and frequency of emesis; dogs in the 4 and 10 mg/kg/day groups also exhibited wobbly gait, hindlimb weakness, and were occasionally immobile and unresponsive to external stimuli. The no-adverse effect level in the study was 0.3 mg/kg/day.

Chronic Toxicity

Morphine: No information available.

Talc: No information available.

Carcinogenicity

Morphine: No information available.

Talc:

Inhalation Studies

Rats were exposed to non-asbestiform talc aerosols (0, 6, or 18 mg/m³) for 6 hours a day for 5 days a week for as long as 113 weeks for males and 122 weeks for females. Rats exhibited a concentration-time related increase in lung talc burden and impairment of lung function (total and vital lung capacities, compliance, gas exchange efficiency). Lung weights for rats in the 18mg/m³

Purdue Pharma L.P.

group were greater than control values during and at the end of the study. Inhalation exposure produced inflammatory, reparative, and proliferative processes in the lungs. Female, but not male, rats in the 18 mg/m³ group exhibited clear evidence of carcinogenic activity in the lungs. Male, but not female, rats in the 18 mg/m³ group exhibited some evidence of carcinogenic activity in the adrenal gland (increased incidence of pheochromocytomas).

Mice were exposed to non-asbestiform talc aerosols (0, 6, 18 mg/m³) for 6 hours a day for 5 days a week for up to 104 weeks. The mice in the study exhibited a concentration-time increase in lung talc burden; lung function was not measured in this study. Talc inhalation was associated with chronic active inflammation in the lung but the proliferative changes observed in rats were not observed in the mice. There was no evidence of carcinogenic activity in the male or female mice.

Mutagenicity/Genotoxicity

Morphine

Bacterial mutagenicity: negative

Human lymphocyte chromosome aberration: negative

Mouse micronucleus: positive

Drosophila melanogaster lethal mutation: positive

Talc

Bacterial mutagenicity: negative

Developmental/Reproductive Toxicity

Morphine

Morphine was not teratogenic in rats at dosages as high as 35 mg/kg/day. In mice, morphine at dosages of 100 to 500 mg/kg administered on day 8 or 9 of gestation was reported to produce exencephaly. In hamsters, morphine produced exencephaly and cranioschisis at a dose of 35 mg/kg.

Morphine administered subcutaneously to maternal rats at 0.4 mg/kg/day during the last trimester of pregnancy has been reported to cause reversible reductions in brain and spinal cord volume, reduced testes size, decreased female offspring fertility, and decreased postnatal body weight. In another study, morphine administered orally at maternally toxic dosages (10 mg/kg/day) caused an increase in pup mortality and growth retardation. Treatment of male rats with about 8 mg/kg/day, 10 days prior to mating with untreated females, reduced litter size and pup viability.

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

Morphine has been detected in breast milk.

Purdue Pharma L.P.

Talc

Mice and rats were fed up to 1,600 mg/kg/day during pregnancy. Hamsters received 1,200 mg/kg/day during pregnancy and rabbits received 9.0-900 mg/kg/day orally during pregnancy. There was no evidence of teratogenicity or embryotoxicity in these species at these dosages.

12. ECOLOGICAL INFORMATION

Ecotoxicological Information: No information available.

Chemical Fate Information: 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/STATUTORY INFORMATION

US Federal: MS Contin[®] (Morphine preparations) is subject to control under the US Federal Controlled Substances Act of 1970 as schedule II (C-II) drugs.

California Hazardous Substance List: Talc (exempt if no inhalable dust is present or can be generated through use).

Illinois Toxic Substance Disclosure to Employees Act: Talc, as a nuisance dust.

Indiana OSHA Approved Implementation Plan: Talc, as a nuisance dust.

Kentucky OSHA Approved Implementation Plan: Talc, as a nuisance dust.

Massachusetts Right-to-Know Substance List: Talc (exempt if encapsulated or if particulates are not present or cannot be generated through use of this product).

Minnesota Hazardous Substance List: Talc, as a nuisance dust.

New Jersey Right-to-Know Substance List: Talc.

North Carolina: Talc, as a nuisance dust.

Pennsylvania Right-to-Know Hazardous Substance List: Talc (1% or greater).

Rhode Island Hazardous Substances Right-to-Know Act: Talc.

Purdue Pharma L.P.

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 and the Environment, Health and Safety Sections of Purdue.