SAFETY DATA SHEET

Issue Date 26-May-2009 **Revision Date** 15-Jun-2017 **Version** 2

1. IDENTIFICATION OF THE SUBSTANCE/PREPARATION

Product Name MS Contin® (morphine sulfate extended-release tablets) C-II

Synonyms MS Contin® 15, 30, 60, 100, 200 mg tablets

Other Information **This is a controlled substance under Schedule II of the Controlled Substances Act.**

Recommended Use Opioid analgesic

Uses advised against This product is not for use in patients for whom alternative treatment options are effective, tolerated, or would be otherwise adequate to provide sufficient management of pain, nor for use as an as-needed (prn) analgesic.

Manufacturer Address Purdue Pharma L.P.
One Stamford Forum
201 Tresser Boulevard
Stamford, Connecticut 06901-3431
(888) 726-7535

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

2. HAZARDS IDENTIFICATION

Drugs when in solid final form (e.g. capsules, tablets or pills) are considered exempt under the criteria of the Federal OSHA Hazard Communication Standard, 29 CFR 1910.1200. However, in an industrial setting where a component's occupational exposure limits may be surpassed, it can be considered hazardous.

Emergency Overview

Appearance Film-coated tablet **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 %
Morphine sulfate	6211-15-0	5-70
Lactose	63-42-3	0-60
Cetostearyl alcohol	67762-27-0	20-30
Talc	14807-96-6	1-5
Magnesium stearate	557-04-0	1-5

4. FIRST AID MEASURES

First aid measures

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 Overexposure may cause dizziness, euphoria, flushing, itching, hypotension, pinpoint pupils, nausea/vomiting, constipation, reduced urination, respiratory depression, extreme somnolence, stupor or coma, skeletal muscle flaccidity, cold and clammy skin, bradycardia, hypotension, apnea, circulatory collapse, cardiac arrest, and eventually death.

Indication of any immediate medical attention and special treatment needed

Note 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 case of an overdosage, primary attention should be given to the reestablishment 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

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 None.

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. Avoid dispersal of dust in the air (i.e., clearing dust surfaces with compressed air). Nonsparking tools should be used.

Environmental precautions

Environmental precautions	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	Pick up and transfer to properly labeled containers.

7. HANDLING AND STORAGE

Precautions for safe handling

Advice on safe handling	Avoid contact with skin, eyes or clothing. Wash thoroughly after handling. Wash contaminated clothing before reuse. 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	Morphine is a Schedule II controlled substance and requires DEA-compliant storage. 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 15-20°C (59-86°F).
Incompatible materials	Strong oxidizers, acids, bases. Oxidizing materials will increase the risk of fire and explosion (e.g., potassium perchlorate, potassium nitrate).

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Exposure Guidelines

Chemical Name	ACGIH TLV	OSHA PEL	NIOSH IDLH
Talc 14807-96-6	TWA: 2 mg/m^3 particulate matter containing no asbestos and <1% crystalline silica, respirable particulate matter	<1% Crystalline silica, containing no asbestos TWA: 20 mppcf if 1% quartz or more, use quartz limit	IDLH: 1000 mg/m^3 TWA: 2 mg/m^3 containing no asbestos and <1% quartz respirable dust
Magnesium stearate 557-04-0	TWA: 10 mg/m^3 except stearates of toxic metals, A4	-	-

Chemical Name	Performance-Based Exposure Band (PBEB)	Company OEG (ug/m^3)
Morphine sulfate	None	44

Engineering Controls Handle material under adequate ventilation (e.g., chemical fume hood, vented balance enclosure [VBE]). Keep container tightly closed. Minimize the amount of material handled at any one time

Individual Protection Measures (Personal Protective Equipment)

Eye/face protection None required for consumer use. In laboratory, medical or industrial settings, safety glasses with side shields are recommended. The use of goggles or full face protection may be required depending on the industrial exposure setting or possibility of splashing. Contact a health and safety professional for specific information.

Skin and body protection None required for consumer use. In laboratory, medical or industrial settings, gloves and lab coats are recommended. Contact a health and safety professional for specific information.

Respiratory protection Respirators may be required for certain laboratory and manufacturing tasks if engineering controls do not maintain airborne concentrations below recommended exposure limits (where applicable) or to an acceptable level (where the exposure limits have not been established). Workplace risk assessments should be completed before specifying and implementing respirator usage. In the United States of America, if respirators are used, they are to be NIOSH-approved and part of a respiratory protection program instituted to assure compliance with OSHA Standard 29 CFR 1910.134. Contact a health and safety professional or manufacturer for specific information.

General Hygiene Considerations Handle in accordance with good industrial hygiene and safety practice.

9. PHYSICAL AND CHEMICAL PROPERTIES

Physical and Chemical Properties

Physical state Solid
Appearance Film-coated tablet
Odor Odorless
Color Blue 15 mg, lavender 30 mg, orange 60 mg, gray 100 mg, green 200 mg
Odor threshold No information available.

Property	Values	Remarks • Method
pH	No information available.	
Melting point / melting range	~ 250 °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	1 gm/15.5 mL @ 25°C
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.

10. STABILITY AND REACTIVITY

Chemical stability	Low stability hazard expected at normal operating temperatures.
Possibility of hazardous reactions	No information available.
Hazardous polymerization	Hazardous polymerization does not occur.
Conditions to avoid	Static charge, sparks, generation of dust, and temperatures above 200°C.
Incompatible materials	Strong oxidizers, acids, bases. Oxidizing materials will increase the risk of fire and explosion (e.g., potassium perchlorate, potassium nitrate).
Hazardous decomposition products	Will not decompose under conditions of usual handling.

11. TOXICOLOGICAL INFORMATION

Information on likely routes of exposure

Product Information	No data available.
Inhalation	No data available.
Eye contact	No data available.
Skin contact	No data available.
Ingestion	No data available.

Chemical Name	Oral LD50	Dermal LD50	Inhalation LC50
Cetostearyl alcohol	10000 mg/kg (Rat)	8000 mg/kg (Rabbit)	-
Morphine sulfate	973 mg/kg (Rat) 1125 mg/kg (Mouse)	-	-
Talc	920 mg/kg (Rat)	-	-
Lactose	10 g/kg (Rat)	-	-

Information on toxicological effects

Symptoms

Overexposure may cause dizziness, euphoria, flushing, itching, hypotension, pinpoint pupils, nausea/vomiting, constipation, reduced urination, respiratory depression, extreme somnolence, stupor or coma, skeletal muscle flaccidity, cold and clammy skin, bradycardia, apnea, circulatory collapse, cardiac arrest, and eventually death

Skin corrosion/irritation

Neither morphine sulfate nor MS Contin® has been evaluated in skin irritation studies in animals. It is expected that morphine may produce mild skin irritation.

Talc is not a primary skin irritant, but talc particles are physical irritants which may cause inflammatory changes such as skin rash.

Serious eye damage/eye irritation

Neither morphine sulfate nor MS Contin® has been evaluated in eye irritation studies in animals. It is expected that morphine sulfate may cause eye irritation.

Talc particles are physical irritants which can cause serious eye damage.
Talc Draize (human): 300 µg/3D mild reaction.

Irritation

Morphine sulfate: Possible respiratory irritant.

Sensitization

Morphine sulfate tested negative for sensitization in an animal study. Repeated or prolonged contact may cause allergic reactions in very susceptible persons. Talc does not cause sensitization.

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

Germ cell mutagenicity

Morphine:
Bacterial mutagenicity: negative
Human lymphocyte chromosome aberration: negative
Mouse micronucleus: positive
Drosophila melanogaster lethal mutation: positive

Talc:
Bacterial mutagenicity: negative

Carcinogenicity

Rats exposed to talc aerosols for 6 hours a day for 5 days a week for 2 years exhibited a concentration-time related increase in lung talc burden and impairment of lung function (total and vital lung capacities, compliance, gas exchange efficiency). Inhalation exposure produced inflammatory, reparative, and proliferative processes in the lungs. Female rats exposed to 18 mg/m^3 of talc aerosols exhibited clear evidence of carcinogenic activity in the lungs. Male rats exposed to 18 mg/m^3 of talc aerosols exhibited some evidence of carcinogenic activity in the adrenal glands (increased incidence of pheochromocytomas).

Mice exposed to talc aerosols for 6 hours a day for 5 days a week for 2 years exhibited a concentration-time related increase in lung talc burden; lung function was not measured in this study. Talc inhalation was associated with chronic active inflammation in the lungs, but not the proliferative changes that were observed in rats. There was no evidence of carcinogenic activity in male or female mice.

Chemical Name	ACGIH	IARC	NTP	OSHA
Talc 14807-96-6		Group 2B Group 3		X

IARC (International Agency for Research on Cancer)
Group 3 - Not classifiable as a human carcinogen

Reproductive toxicity

Morphine was not teratogenic in rats at dosages as high as 35 mg/kg/day. In mice, morphine administered on day 8 or 9 of gestation produced exencephaly at dosages of 100-500 mg/kg. 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.

Talc was not teratogenic or embryotoxic in studies with mice, rats, hamsters, or rabbits.

STOT-single exposure

No information available.

STOT-repeated exposure

No information available.

Subchronic toxicity

In a 5-day oral study of morphine 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. Food consumption was decreased among rats in the 15, 150, 450 mg/kg/day groups. Male body weights were decreased in the 50, 150, and 450 mg/kg/day groups. No abnormalities in behavior or appearance were observed at 5, 15, or 50 mg/kg/day. The no-effect level was 5 mg/kg/day.

In a 3-month oral toxicity study of morphine in rats, observations similar to those in the 5-day study, as well as 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 of morphine in dogs, a dosage of 1 mg/kg/day was associated with emesis and reduced fecal output; dosages of 4, 8, and 12 mg/kg/day were associated with hind limb 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 of morphine 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 gate, hind limb weakness, and were occasionally immobile and unresponsive to external stimuli. The no-adverse effect level in the study was 0.3 mg/kg/day.

Aspiration hazard

No information available.

12. ECOLOGICAL INFORMATION

Ecotoxicity

Chemical Name	Algae/aquatic plants	Fish	Toxicity to microorganisms	Crustacea
Cetostearyl alcohol				EC50 48 h = 1666 mg/L (Daphnia magna)
Talc		LC50 96 h > 100 g/L (Brachydanio rerio - semi-static)		

Persistence and degradability No information available.

Bioaccumulation No information available.

Chemical Name	Partition coefficient
Cetostearyl alcohol	6.65

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

Morphine is a DEA Scheduled II controlled substance.

International Inventories

TSCA Not determined.
DSL Not determined.

Legend:

TSCA - United States Toxic Substances Control Act Section 8 (b) Inventory
DSL/NDSL - 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	No
Chronic Health Hazard	No
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

NFPA	**Health Hazards**	1	**Flammability**	0	**Instability** 0	**Physical and Chemical Properties**	-
HMIS	**Health Hazards**	1	**Flammability**	0	**Physical Hazards** 0	**Personal protection**	X

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.

Issue Date 26-May-2009
Revision Date 15-Jun-2017
Revision Note SDS reformated for OSHA (GHS) 2012.

Disclaimer
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End of Safety Data Sheet