

Purdue Pharma L.P.

Material Safety Data Sheet

OxyContin[®] (Oxycodone HCl Controlled Release) Tablets, 10 mg

(NDC 59011-410-10, NDC 59011-410-20)

Version: 16-Sep-10

1. CHEMICAL PRODUCT/COMPANY IDENTIFICATION

Material Identification: OxyContin[®] 10 mg Tablets.

Chemical Name: Mixture, N/A.

Active Ingredient: Oxycodone hydrochloride.

Synonyms:

Active Ingredient: 4, 5 α -epoxy-14-hydroxy-3-methoxy-17-methylmorphinan-6-one hydrochloride.

Molecular Formula: Mixture.

Molecular Weight:

Mixture.

Active Ingredient: C₁₈H₂₁NO₄·HCl.

Molecular Weight:

351.83

CAS Number: N/A (mixture).

Active Ingredient: 124-90-3.

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	%
Oxycodone Hydrochloride	124-90-3	6.7

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3. HAZARDS IDENTIFICATION

Emergency Overview

White unscored, film-coated, tablet.

OxyContin[®] 10 mg Tablets do not pose a significant workplace hazard unless tablets are cut, broken or crushed. The following information is provided for those circumstances where uncontrolled exposure to oxycodone may occur due to cutting, breakage or crushing of the OxyContin[®] 10 mg Tablets.

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

Cut, broken or crushed tablets may be harmful by inhalation or skin contact.

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

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

Target organs: central nervous system, gastrointestinal tract, cardiovascular system, respiratory tract.

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.

Warning! Powder may form combustible dust concentrations in air. 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.

Potential Health Effects

OxyContin[®] 10 mg Tablets are a film-coated, tablet product which does not pose a hazard under normal workplace handling conditions.

The active ingredient of OxyContin[®] 10 mg Tablets is oxycodone hydrochloride, an orally active opioid analgesic approximately twice the potency of morphine. OxyContin[®] 10 mg Tablets are designed to provide controlled release of oxycodone in the body. If OxyContin[®] 10 mg Tablets are cut, broken or crushed, workplace exposure to oxycodone may occur. The following information is provided for those circumstances where uncontrolled exposure to oxycodone hydrochloride in OxyContin[®] 10 mg Tablets may occur due to cutting, breakage or crushing of the

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tablet.

Oxycodone

Oxycodone hydrochloride may cause eye irritation and mild skin irritation.

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

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.

Maternal exposure to oxycodone may cause respiratory depression in the neonate. Repeated maternal exposure to oxycodone hydrochloride 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

OxyContin[®] 10 mg Tablets and its components are not 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.

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. Seek medical attention.

INGESTION

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

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Notes to Physicians

OxyContin[®] 10 mg Tablets contain oxycodone hydrochloride. Oxycodone is a pure opioid agonist with an analgesic potency about twice that of morphine. Naloxone is a specific antidote against respiratory depression from opioid overexposure. Opioid antagonists should not be administered in the absence of clinically significant respiratory or circulatory depression secondary to oxycodone overexposure.

In cases of oxycodone overexposure, 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 overexposure 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

OxyContin[®] 10 mg Tablets are not considered flammable. However, concentrated dust from cut, broken or crushed tablets may pose a dust explosion hazard. Eliminate sources of ignition. Bond and ground as necessary. Use non-sparking tools.

For OxyContin[®] 10 mg Tablets

No information available.

For Oxycodone Hydrochloride

Minimum ignition energy: 10-25 mJ

Minimum ignition temperature – dust cloud: 420-440°C

Minimum ignition temperature – dust layer: 225 °C

Maximum explosion pressure (20 L sphere): 9.4 bar

Maximum rate of pressure rise: 779 bar/sec

K_{st}: 212 bar·m/sec

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.

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NFPA

H=1;F=1;R=0

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.

Spill Clean-up

Wear suitable protective clothing and equipment. Sweep up intact tablets or vacuum up cut, broken or crushed tablets and place collected material into a suitable container for reclamation or disposal. Thoroughly wash area with detergent and water. Oxycodone hydrochloride 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 cut, 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

Oxycodone hydrochloride is a Schedule II controlled substance. Keep container 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).

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8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Engineering Controls

Handle material under adequate ventilation (e.g., chemical fume hood).
Keep container tightly closed.

Personal Protective Equipment (PPE)

Wear safety glasses with side shields. Wear full-face protection when judged that the possibility exists for eye and face contact.

Wear an appropriate NIOSH-approved air purifying respirator or positive pressure air-supplied respirator in situations where a respirator is judged appropriate to prevent inhalation.

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

Exposure Guidelines

Exposure Limits

Oxycodone hydrochloride

PEL (OSHA):	None established.
TLV (ACGIH):	None established.
Occupational Exposure Guideline (Purdue Pharma L.P.):	40 $\mu\text{g}/\text{m}^3$ (free base).

Exposure Guideline Comments

Purdue Pharma L.P. has established a workplace exposure limit of 40 $\mu\text{g}/\text{m}^3$ for oxycodone (free base) for internal use.

9. PHYSICAL AND CHEMICAL PROPERTIES

Physical Data

Form: Film-coated, controlled-release tablet.
Color: White unscored.

Physical Data for Oxycodone hydrochloride

Form:	Solid.
Color:	White.
Vapor Pressure:	No information available.
Melting Point:	270-272°C.
log P_{ow} :	-1.55 (pH 4); 1.18 (pH 9).
Solubility:	10 g in 100g of water.

10. STABILITY AND REACTIVITY

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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. Heating to decomposition may release acrid smoke and fumes.

Polymerization

Material not expected to be subject to polymerization.

11. TOXICOLOGICAL INFORMATION

Relevant Data

OxyContin[®] 10 mg Tablets have not been tested in animals. The following data are for oxycodone hydrochloride reflected as oxycodone free base.

Skin/Eyes

Oxycodone

Oxycodone has not been evaluated in skin and eye irritation studies in animals. It is expected that oxycodone and/or dust from cut, broken or crushed OxyContin[®] 10 mg Tablets may produce mild skin irritation and may cause eye irritation. Oxycodone has not been evaluated in skin sensitization studies in animals; based on structure activity relationships, oxycodone may cause skin sensitization and/or respiratory sensitization.

Acute

<u>Species</u>	<u>Oral LD₅₀</u> <u>(mg/kg)</u>	<u>I.P. LD₅₀</u> <u>(mg/kg)</u>
Mouse	482 (oxycodone)	250 (oxycodone)
Rat	20 (LDL) (oxycodone)	

Subchronic Toxicity

Oxycodone

In a 10-day oral study in rats, 4.5 mg/kg/day (lowest dose tested) produced stereotypic behavior and increased activity only after 5 days of

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treatment. At 45 mg/kg/day, stereotypic behavior, body rigidity, and labored breathing were observed on the first day of dosing. Animals that received ≥ 90 mg/kg/day did not survive past two days of dosing.

In a 28-day oral study in rats, 10 and 25 mg/kg/day produced clinical signs, including rigidity, ocular discharge, chewing on the forelimbs and hyper-reactivity, decreased body weight, and decreased food intake. The no-observed-adverse-effect level (NOAEL) in this study was considered to be 4.0 mg/kg/day.

In a 3-month oral toxicity study in rats, 1.6 mg/kg/day (lowest dose tested) and 4.0 mg/kg/day produced stereotypic behavior and increased and/or decreased activity; these changes were observed after 2-6 weeks of treatment. Prior to that time, no effects were observed. Dosages of 10 and 25 mg/kg/day were associated with stereotypic behavior, increased activity, postural rigidity, and pale color of the extremities. One rat that received 25 mg/kg/day did not survive past 22 days of dosing.

In a 12-day oral study in rabbits, no effects were observed at 4.5 mg/kg/day; ≥ 22 mg/kg/day was associated with decreased activity, reduced fecal output, and convulsions. An animal that received 269 mg/kg/day did not survive six doses.

In a 28-day oral study in dogs, a dosage of 1 mg/kg/day was associated with minimal effects including excessive salivation and slow capillary refill in the oral mucosa; dosages of 4, 8, or 20 mg/kg/day were associated with decreased activity, sedation, ataxia, pale color, and slow capillary refill of the oral mucosa. One dog given 20 mg/kg/day did not survive past 3 days of dosing and one animal given 20 mg/kg/day had convulsions. The no-observed-adverse-effect level (NOAEL) in male dogs was considered to be 1 mg/kg/day; slight effects on food consumption and body weights in females at 1 mg/kg/day might indicate a NOAEL less than 1 mg/kg/day. The maximum tolerated dose in this study was considered to be 8 mg/kg/day.

In a 3-month oral study in dogs, 0.3 mg/kg/day (lowest dose tested) produced no effects; doses ≥ 1 mg/kg/day produced effects similar to those observed in the 28-day study; 8 mg/kg/day was considered to be the maximum tolerated dose in this study. The no-observed-adverse-effect level (NOAEL) for the study was considered to be 1 mg/kg/day.

Chronic Toxicity

Oxycodone

No information available.

Carcinogenicity

Oxycodone

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No information available.

Mutagenicity/Genotoxicity

Oxycodone

Bacterial mutagenicity (Ames test): negative.

Mammalian (Human Peripheral Blood Lymphocytes) chromosome aberration: weakly positive.

Mammalian (Human whole blood lymphocytes) chromosome aberration: negative.

In vivo mouse micronucleus: negative.

Mouse lymphoma: positive (in presence of metabolic activation).

Developmental/Reproductive Toxicity

Oxycodone

Oxycodone hydrochloride produced no adverse effects on fertility, reproductive performance, or early embryonic development of rats at dosages as high as 8 mg/kg/day (the highest dosage tested).

Oxycodone did not produce developmental toxicity in rats or rabbits at dosages as high as 8 and 125 mg/kg/day, respectively.

In a pre- and post-natal study in rats, oxycodone hydrochloride produced no toxic effects on maternal reproductive parameters. There was no effect on survival and development of offspring except for decreased body weight of the first generation but not second generation offspring in the highest dosage group (6 mg/kg/day). The no effect dosage for development of offspring was 2 mg/kg/day.

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

Oxycodone has been detected in breast milk.

Safety Pharmacology

No information available.

12. Ecological Information

Ecotoxicological Information

Oxycodone

24 hr LC₅₀: *Daphnia magna*: 300 mg/mL.

Microbial Growth Inhibition EC₁₀: 7 species: > 1,000 mg/mL.

Chemical Fate Information

Oxycodone

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Aerobic biodegradation: sewer sludge: est. $t_{1/2}$: 276 days.

13. Disposal Considerations

Disposal

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

14. Transportation Information

Shipping Information

Non-hazardous.

15. Regulatory/Statutory Information

US Federal: OxyContin[®] 10 mg Tablets are subject to control under the US Federal Controlled Substances Act of 1970 as schedule II (C-II) drugs.

International: None.

EC Labeling: None.

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 by the Nonclinical Drug Safety Evaluation of Purdue Pharma L.P.

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Material Safety Data Sheet

OxyContin® (Oxycodone HCl Controlled Release) Tablets, 15 mg

(NDC 59011-415-10, NDC 59011-415-20)

Version: 16-Sep-10

1. CHEMICAL PRODUCT/COMPANY IDENTIFICATION

Material Identification: OxyContin® 15 mg Tablets.

Chemical Name: Mixture, N/A.

Active Ingredient: Oxycodone hydrochloride.

Synonyms:

Active Ingredient: 4, 5 α -epoxy-14-hydroxy-3-methoxy-17-methylmorphinan-6-one hydrochloride.

Molecular Formula: Mixture.

Molecular

Weight:

Mixture.

Active Ingredient: C₁₈H₂₁NO₄·HCl.

Molecular

Weight:

351.83

CAS Number: N/A (mixture).

Active Ingredient: 124-90-3.

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	%
Oxycodone Hydrochloride	124-90-3	9.6

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3. HAZARDS IDENTIFICATION

Emergency Overview

Gray unscored, film-coated, tablet.

OxyContin[®] 15 mg Tablets do not pose a significant workplace hazard unless tablets are cut, broken or crushed. The following information is provided for those circumstances where uncontrolled exposure to oxycodone may occur due to cutting, breakage or crushing of the OxyContin[®] 15 mg Tablets.

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

Cut, broken or crushed tablets may be harmful by inhalation or skin contact.

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

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

Target organs: central nervous system, gastrointestinal tract, cardiovascular system, respiratory tract.

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.

Warning! Powder may form combustible dust concentrations in air. 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.

Potential Health Effects

OxyContin[®] 15 mg Tablets are a film-coated, tablet product which does not pose a hazard under normal workplace handling conditions.

The active ingredient of OxyContin[®] 15 mg Tablets is oxycodone hydrochloride, an orally active opioid analgesic approximately twice the potency of morphine. OxyContin[®] 15 mg Tablets are designed to provide controlled release of oxycodone in the body. If OxyContin[®] 15 mg Tablets are cut, broken or crushed, workplace exposure to oxycodone may occur. The following information is provided for those circumstances where uncontrolled exposure to oxycodone hydrochloride in OxyContin[®] 15 mg Tablets may occur due to cutting, breakage or crushing of the

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tablet.

Oxycodone

Oxycodone hydrochloride may cause eye irritation and mild skin irritation.

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

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.

Maternal exposure to oxycodone may cause respiratory depression in the neonate. Repeated maternal exposure to oxycodone hydrochloride 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

OxyContin[®] 15 mg Tablets and its components are not 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.

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. Seek medical attention.

INGESTION

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

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Notes to Physicians

OxyContin[®] 15 mg Tablets contain oxycodone hydrochloride. Oxycodone is a pure opioid agonist with an analgesic potency about twice that of morphine. Naloxone is a specific antidote against respiratory depression from opioid overexposure. Opioid antagonists should not be administered in the absence of clinically significant respiratory or circulatory depression secondary to oxycodone overexposure.

In cases of oxycodone overexposure, 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 overexposure 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

OxyContin[®] 15 mg Tablets are not considered flammable. However, concentrated dust from cut, broken or crushed tablets may pose a dust explosion hazard. Eliminate sources of ignition. Bond and ground as necessary. Use non-sparking tools.

For OxyContin[®] 15 mg Tablets

No information available.

For Oxycodone Hydrochloride

Minimum ignition energy: 10-25 mJ

Minimum ignition temperature – dust cloud: 420-440°C

Minimum ignition temperature – dust layer: 225 °C

Maximum explosion pressure (20 L sphere): 9.4 bar

Maximum rate of pressure rise: 779 bar/sec

K_{st}: 212 bar·m/sec

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.

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NFPA

H=1;F=1;R=0

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.

Spill Clean-up

Wear suitable protective clothing and equipment. Sweep up intact tablets or vacuum up cut, broken or crushed tablets and place collected material into a suitable container for reclamation or disposal. Thoroughly wash area with detergent and water. Oxycodone hydrochloride 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 cut, 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

Oxycodone hydrochloride is a Schedule II controlled substance. Keep container 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).

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8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Engineering Controls

Handle material under adequate ventilation (e.g., chemical fume hood).
Keep container tightly closed.

Personal Protective Equipment (PPE)

Wear safety glasses with side shields. Wear full-face protection when judged that the possibility exists for eye and face contact.

Wear an appropriate NIOSH-approved air purifying respirator or positive pressure air-supplied respirator in situations where a respirator is judged appropriate to prevent inhalation.

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

Exposure Guidelines

Exposure Limits

Oxycodone hydrochloride

PEL (OSHA):	None established.
TLV (ACGIH):	None established.
Occupational Exposure Guideline (Purdue Pharma L.P.):	40 µg/m ³ (free base).

Exposure Guideline Comments

Purdue Pharma L.P. has established a workplace exposure limit of 40 µg/m³ for oxycodone (free base) for internal use.

9. PHYSICAL AND CHEMICAL PROPERTIES

Physical Data

Form: Film-coated, controlled-release tablet.
Color: Gray unscored.

Physical Data for Oxycodone hydrochloride

Form:	Solid.
Color:	White.
Vapor Pressure:	No information available.
Melting Point:	270-272°C.
log P _{ow} :	-1.55 (pH 4); 1.18 (pH 9).
Solubility:	10 g in 100g of water.

10. STABILITY AND REACTIVITY

Purdue Pharma L.P.

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. Heating to decomposition may release acrid smoke and fumes.

Polymerization

Material not expected to be subject to polymerization.

11. TOXICOLOGICAL INFORMATION

Relevant Data

OxyContin[®] 15 mg Tablets have not been tested in animals. The following data are for oxycodone hydrochloride reflected as oxycodone free base.

Skin/Eyes

Oxycodone

Oxycodone has not been evaluated in skin and eye irritation studies in animals. It is expected that oxycodone and/or dust from cut, broken or crushed OxyContin[®] 15 mg Tablets may produce mild skin irritation and may cause eye irritation. Oxycodone has not been evaluated in skin sensitization studies in animals; based on structure activity relationships, oxycodone may cause skin sensitization and/or respiratory sensitization.

Acute

<u>Species</u>	<u>Oral LD₅₀</u> <u>(mg/kg)</u>	<u>I.P. LD₅₀</u> <u>(mg/kg)</u>
Mouse	482 (oxycodone)	250 (oxycodone)
Rat	20 (LDL) (oxycodone)	

Subchronic Toxicity

Oxycodone

In a 10-day oral study in rats, 4.5 mg/kg/day (lowest dose tested) produced stereotypic behavior and increased activity only after 5 days of

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treatment. At 45 mg/kg/day, stereotypic behavior, body rigidity, and labored breathing were observed on the first day of dosing. Animals that received ≥ 90 mg/kg/day did not survive past two days of dosing.

In a 28-day oral study in rats, 10 and 25 mg/kg/day produced clinical signs, including rigidity, ocular discharge, chewing on the forelimbs and hyper-reactivity, decreased body weight, and decreased food intake. The no-observed-adverse-effect level (NOAEL) in this study was considered to be 4.0 mg/kg/day.

In a 3-month oral toxicity study in rats, 1.6 mg/kg/day (lowest dose tested) and 4.0 mg/kg/day produced stereotypic behavior and increased and/or decreased activity; these changes were observed after 2-6 weeks of treatment. Prior to that time, no effects were observed. Dosages of 10 and 25 mg/kg/day were associated with stereotypic behavior, increased activity, postural rigidity, and pale color of the extremities. One rat that received 25 mg/kg/day did not survive past 22 days of dosing.

In a 12-day oral study in rabbits, no effects were observed at 4.5 mg/kg/day; ≥ 22 mg/kg/day was associated with decreased activity, reduced fecal output, and convulsions. An animal that received 269 mg/kg/day did not survive six doses.

In a 28-day oral study in dogs, a dosage of 1 mg/kg/day was associated with minimal effects including excessive salivation and slow capillary refill in the oral mucosa; dosages of 4, 8, or 20 mg/kg/day were associated with decreased activity, sedation, ataxia, pale color, and slow capillary refill of the oral mucosa. One dog given 20 mg/kg/day did not survive past 3 days of dosing and one animal given 20 mg/kg/day had convulsions. The no-observed-adverse-effect level (NOAEL) in male dogs was considered to be 1 mg/kg/day; slight effects on food consumption and body weights in females at 1 mg/kg/day might indicate a NOAEL less than 1 mg/kg/day. The maximum tolerated dose in this study was considered to be 8 mg/kg/day.

In a 3-month oral study in dogs, 0.3 mg/kg/day (lowest dose tested) produced no effects; doses ≥ 1 mg/kg/day produced effects similar to those observed in the 28-day study; 8 mg/kg/day was considered to be the maximum tolerated dose in this study. The no-observed-adverse-effect level (NOAEL) for the study was considered to be 1 mg/kg/day.

Chronic Toxicity

Oxycodone

No information available.

Carcinogenicity

Oxycodone

Purdue Pharma L.P.

No information available.

Mutagenicity/Genotoxicity

Oxycodone

Bacterial mutagenicity (Ames test): negative.

Mammalian (Human Peripheral Blood Lymphocytes) chromosome aberration: weakly positive.

Mammalian (Human whole blood lymphocytes) chromosome aberration: negative.

In vivo mouse micronucleus: negative.

Mouse lymphoma: positive (in presence of metabolic activation).

Developmental/Reproductive Toxicity

Oxycodone

Oxycodone hydrochloride produced no adverse effects on fertility, reproductive performance, or early embryonic development of rats at dosages as high as 8 mg/kg/day (the highest dosage tested).

Oxycodone did not produce developmental toxicity in rats or rabbits at dosages as high as 8 and 125 mg/kg/day, respectively.

In a pre- and post-natal study in rats, oxycodone hydrochloride produced no toxic effects on maternal reproductive parameters. There was no effect on survival and development of offspring except for decreased body weight of the first generation but not second generation offspring in the highest dosage group (6 mg/kg/day). The no effect dosage for development of offspring was 2 mg/kg/day.

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

Oxycodone has been detected in breast milk.

Safety Pharmacology

No information available.

12. Ecological Information

Ecotoxicological Information

Oxycodone

24 hr LC₅₀: *Daphnia magna*: 300 mg/mL.

Microbial Growth Inhibition EC₁₀: 7 species: > 1,000 mg/mL.

Chemical Fate Information

Oxycodone

9 of 10; OxyContin[®] 15 mg Tablets MSDS

Purdue Pharma L.P.

Aerobic biodegradation: sewer sludge: est. $t_{1/2}$: 276 days.

13. Disposal Considerations

Disposal

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

14. Transportation Information

Shipping Information

Non-hazardous.

15. Regulatory/Statutory Information

US Federal: OxyContin[®] 15 mg Tablets are subject to control under the US Federal Controlled Substances Act of 1970 as schedule II (C-II) drugs.

International: None.

EC Labeling: None.

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 by the Nonclinical Drug Safety Evaluation of Purdue Pharma L.P.

Purdue Pharma L.P.

Material Safety Data Sheet

OxyContin® (Oxycodone HCl Controlled Release) Tablets, 20 mg

(NDC 59011-420-10, NDC 59011-420-20)

Version: 16-Sep-10

1. CHEMICAL PRODUCT/COMPANY IDENTIFICATION

Material Identification: OxyContin® 20 mg Tablets.

Chemical Name: Mixture, N/A.

Active Ingredient: Oxycodone hydrochloride.

Synonyms:

Active Ingredient: 4, 5 α -epoxy-14-hydroxy-3-methoxy-17-methylmorphinan-6-one hydrochloride.

Molecular Formula: Mixture.

Molecular

Weight:

Mixture.

Active Ingredient: C₁₈H₂₁NO₄·HCl.

Molecular

Weight:

351.83

CAS Number: N/A (mixture).

Active Ingredient: 124-90-3.

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	%
Oxycodone Hydrochloride	124-90-3	12.8

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3. HAZARDS IDENTIFICATION

Emergency Overview

Pink unscored, film-coated, tablet.

OxyContin[®] 20 mg Tablets do not pose a significant workplace hazard unless tablets are cut, broken or crushed. The following information is provided for those circumstances where uncontrolled exposure to oxycodone may occur due to cutting, breakage or crushing of the OxyContin[®] 20 mg Tablets.

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

Cut, broken or crushed tablets may be harmful by inhalation or skin contact.

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

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

Target organs: central nervous system, gastrointestinal tract, cardiovascular system, respiratory tract.

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.

Warning! Powder may form combustible dust concentrations in air. 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.

Potential Health Effects

OxyContin[®] 20 mg Tablets are a film-coated, tablet product which does not pose a hazard under normal workplace handling conditions.

The active ingredient of OxyContin[®] 20 mg Tablets is oxycodone hydrochloride, an orally active opioid analgesic approximately twice the potency of morphine. OxyContin[®] 20 mg Tablets are designed to provide controlled release of oxycodone in the body. If OxyContin[®] 20 mg Tablets are cut, broken or crushed, workplace exposure to oxycodone may occur. The following information is provided for those circumstances where uncontrolled exposure to oxycodone hydrochloride in OxyContin[®] 20 mg Tablets may occur due to cutting, breakage or crushing of the

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tablet.

Oxycodone

Oxycodone hydrochloride may cause eye irritation and mild skin irritation.

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

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.

Maternal exposure to oxycodone may cause respiratory depression in the neonate. Repeated maternal exposure to oxycodone hydrochloride 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

OxyContin[®] 20 mg Tablets and its components are not 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.

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. Seek medical attention.

INGESTION

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

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Notes to Physicians

OxyContin[®] 20 mg Tablets contain oxycodone hydrochloride. Oxycodone is a pure opioid agonist with an analgesic potency about twice that of morphine. Naloxone is a specific antidote against respiratory depression from opioid overexposure. Opioid antagonists should not be administered in the absence of clinically significant respiratory or circulatory depression secondary to oxycodone overexposure.

In cases of oxycodone overexposure, 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 overexposure 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

OxyContin[®] 20 mg Tablets are not considered flammable. However, concentrated dust from cut, broken or crushed tablets may pose a dust explosion hazard. Eliminate sources of ignition. Bond and ground as necessary. Use non-sparking tools.

For OxyContin[®] 20 mg Tablets

No information available.

For Oxycodone Hydrochloride

Minimum ignition energy: 10-25 mJ

Minimum ignition temperature – dust cloud: 420-440°C

Minimum ignition temperature – dust layer: 225 °C

Maximum explosion pressure (20 L sphere): 9.4 bar

Maximum rate of pressure rise: 779 bar/sec

K_{st}: 212 bar·m/sec

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.

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NFPA

H=1;F=1;R=0

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.

Spill Clean-up

Wear suitable protective clothing and equipment. Sweep up intact tablets or vacuum up cut, broken or crushed tablets and place collected material into a suitable container for reclamation or disposal. Thoroughly wash area with detergent and water. Oxycodone hydrochloride 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 cut, 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

Oxycodone hydrochloride is a Schedule II controlled substance. Keep container 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).

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8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Engineering Controls

Handle material under adequate ventilation (e.g., chemical fume hood).
Keep container tightly closed.

Personal Protective Equipment (PPE)

Wear safety glasses with side shields. Wear full-face protection when judged that the possibility exists for eye and face contact.

Wear an appropriate NIOSH-approved air purifying respirator or positive pressure air-supplied respirator in situations where a respirator is judged appropriate to prevent inhalation.

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

Exposure Guidelines

Exposure Limits

Oxycodone hydrochloride

PEL (OSHA):	None established.
TLV (ACGIH):	None established.
Occupational Exposure Guideline (Purdue Pharma L.P.):	40 $\mu\text{g}/\text{m}^3$ (free base).

Exposure Guideline Comments

Purdue Pharma L.P. has established a workplace exposure limit of 40 $\mu\text{g}/\text{m}^3$ for oxycodone (free base) for internal use.

9. PHYSICAL AND CHEMICAL PROPERTIES

Physical Data

Form: Film-coated, controlled-release tablet.
Color: Pink unscored.

Physical Data for Oxycodone hydrochloride

Form:	Solid.
Color:	White.
Vapor Pressure:	No information available.
Melting Point:	270-272°C.
log P_{ow} :	-1.55 (pH 4); 1.18 (pH 9).
Solubility:	10 g in 100g of water.

10. STABILITY AND REACTIVITY

Purdue Pharma L.P.

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. Heating to decomposition may release acrid smoke and fumes.

Polymerization

Material not expected to be subject to polymerization.

11. TOXICOLOGICAL INFORMATION

Relevant Data

OxyContin[®] 20 mg Tablets have not been tested in animals. The following data are for oxycodone hydrochloride reflected as oxycodone free base.

Skin/Eyes

Oxycodone

Oxycodone has not been evaluated in skin and eye irritation studies in animals. It is expected that oxycodone and/or dust from cut, broken or crushed OxyContin[®] 20 mg Tablets may produce mild skin irritation and may cause eye irritation. Oxycodone has not been evaluated in skin sensitization studies in animals; based on structure activity relationships, oxycodone may cause skin sensitization and/or respiratory sensitization.

Acute

<u>Species</u>	<u>Oral LD₅₀</u> <u>(mg/kg)</u>	<u>I.P. LD₅₀</u> <u>(mg/kg)</u>
Mouse	482 (oxycodone)	250 (oxycodone)
Rat	20 (LDL) (oxycodone)	

Subchronic Toxicity

Oxycodone

In a 10-day oral study in rats, 4.5 mg/kg/day (lowest dose tested) produced stereotypic behavior and increased activity only after 5 days of

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treatment. At 45 mg/kg/day, stereotypic behavior, body rigidity, and labored breathing were observed on the first day of dosing. Animals that received ≥ 90 mg/kg/day did not survive past two days of dosing.

In a 28-day oral study in rats, 10 and 25 mg/kg/day produced clinical signs, including rigidity, ocular discharge, chewing on the forelimbs and hyper-reactivity, decreased body weight, and decreased food intake. The no-observed-adverse-effect level (NOAEL) in this study was considered to be 4.0 mg/kg/day.

In a 3-month oral toxicity study in rats, 1.6 mg/kg/day (lowest dose tested) and 4.0 mg/kg/day produced stereotypic behavior and increased and/or decreased activity; these changes were observed after 2-6 weeks of treatment. Prior to that time, no effects were observed. Dosages of 10 and 25 mg/kg/day were associated with stereotypic behavior, increased activity, postural rigidity, and pale color of the extremities. One rat that received 25 mg/kg/day did not survive past 22 days of dosing.

In a 12-day oral study in rabbits, no effects were observed at 4.5 mg/kg/day; ≥ 22 mg/kg/day was associated with decreased activity, reduced fecal output, and convulsions. An animal that received 269 mg/kg/day did not survive six doses.

In a 28-day oral study in dogs, a dosage of 1 mg/kg/day was associated with minimal effects including excessive salivation and slow capillary refill in the oral mucosa; dosages of 4, 8, or 20 mg/kg/day were associated with decreased activity, sedation, ataxia, pale color, and slow capillary refill of the oral mucosa. One dog given 20 mg/kg/day did not survive past 3 days of dosing and one animal given 20 mg/kg/day had convulsions. The no-observed-adverse-effect level (NOAEL) in male dogs was considered to be 1 mg/kg/day; slight effects on food consumption and body weights in females at 1 mg/kg/day might indicate a NOAEL less than 1 mg/kg/day. The maximum tolerated dose in this study was considered to be 8 mg/kg/day.

In a 3-month oral study in dogs, 0.3 mg/kg/day (lowest dose tested) produced no effects; doses ≥ 1 mg/kg/day produced effects similar to those observed in the 28-day study; 8 mg/kg/day was considered to be the maximum tolerated dose in this study. The no-observed-adverse-effect level (NOAEL) for the study was considered to be 1 mg/kg/day.

Chronic Toxicity

Oxycodone

No information available.

Carcinogenicity

Oxycodone

Purdue Pharma L.P.

No information available.

Mutagenicity/Genotoxicity

Oxycodone

Bacterial mutagenicity (Ames test): negative.

Mammalian (Human Peripheral Blood Lymphocytes) chromosome aberration: weakly positive.

Mammalian (Human whole blood lymphocytes) chromosome aberration: negative.

In vivo mouse micronucleus: negative.

Mouse lymphoma: positive (in presence of metabolic activation).

Developmental/Reproductive Toxicity

Oxycodone

Oxycodone hydrochloride produced no adverse effects on fertility, reproductive performance, or early embryonic development of rats at dosages as high as 8 mg/kg/day (the highest dosage tested).

Oxycodone did not produce developmental toxicity in rats or rabbits at dosages as high as 8 and 125 mg/kg/day, respectively.

In a pre- and post-natal study in rats, oxycodone hydrochloride produced no toxic effects on maternal reproductive parameters. There was no effect on survival and development of offspring except for decreased body weight of the first generation but not second generation offspring in the highest dosage group (6 mg/kg/day). The no effect dosage for development of offspring was 2 mg/kg/day.

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

Oxycodone has been detected in breast milk.

Safety Pharmacology

No information available.

12. Ecological Information

Ecotoxicological Information

Oxycodone

24 hr LC₅₀: *Daphnia magna*: 300 mg/mL.

Microbial Growth Inhibition EC₁₀: 7 species: > 1,000 mg/mL.

Chemical Fate Information

Oxycodone

9 of 10; OxyContin[®] 20 mg Tablets MSDS

Purdue Pharma L.P.

Aerobic biodegradation: sewer sludge: est. $t_{1/2}$: 276 days.

13. Disposal Considerations

Disposal

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

14. Transportation Information

Shipping Information

Non-hazardous.

15. Regulatory/Statutory Information

US Federal: OxyContin[®] 20 mg Tablets are subject to control under the US Federal Controlled Substances Act of 1970 as schedule II (C-II) drugs.

International: None.

EC Labeling: None.

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 by the Nonclinical Drug Safety Evaluation of Purdue Pharma L.P.

Purdue Pharma L.P.

Material Safety Data Sheet

OxyContin[®] (Oxycodone HCl Controlled Release) Tablets, 30 mg

(NDC 59011-430-10, NDC 59011-430-20)

Version: 16-Sep-10

1. CHEMICAL PRODUCT/COMPANY IDENTIFICATION

Material Identification: OxyContin[®] 30 mg Tablets.

Chemical Name: Mixture, N/A.

Active Ingredient: Oxycodone hydrochloride.

Synonyms:

Active Ingredient: 4, 5 α -epoxy-14-hydroxy-3-methoxy-17-methylmorphinan-6-one hydrochloride.

Molecular Formula: Mixture.

Molecular

Weight:

Mixture.

Active Ingredient: C₁₈H₂₁NO₄·HCl.

Molecular

Weight:

351.83

CAS Number: N/A (mixture).

Active Ingredient: 124-90-3.

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	%
Oxycodone Hydrochloride	124-90-3	19.2

Purdue Pharma L.P.

3. HAZARDS IDENTIFICATION

Emergency Overview

Brown unscored, film-coated, tablet.

OxyContin[®] 30 mg Tablets do not pose a significant workplace hazard unless tablets are cut, broken or crushed. The following information is provided for those circumstances where uncontrolled exposure to oxycodone may occur due to cutting, breakage or crushing of the OxyContin[®] 30 mg Tablets.

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

Cut, broken or crushed tablets may be harmful by inhalation or skin contact.

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

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

Target organs: central nervous system, gastrointestinal tract, cardiovascular system, respiratory tract.

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.

Warning! Powder may form combustible dust concentrations in air. 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.

Potential Health Effects

OxyContin[®] 30 mg Tablets are a film-coated, tablet product which does not pose a hazard under normal workplace handling conditions.

The active ingredient of OxyContin[®] 30 mg Tablets is oxycodone hydrochloride, an orally active opioid analgesic approximately twice the potency of morphine. OxyContin[®] 30 mg Tablets are designed to provide controlled release of oxycodone in the body. If OxyContin[®] 30 mg Tablets are cut, broken or crushed, workplace exposure to oxycodone may occur. The following information is provided for those circumstances where uncontrolled exposure to oxycodone hydrochloride in OxyContin[®] 30 mg Tablets may occur due to cutting, breakage or crushing of the

Purdue Pharma L.P.

tablet.

Oxycodone

Oxycodone hydrochloride may cause eye irritation and mild skin irritation.

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

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.

Maternal exposure to oxycodone may cause respiratory depression in the neonate. Repeated maternal exposure to oxycodone hydrochloride 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

OxyContin[®] 30 mg Tablets and its components are not 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.

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. Seek medical attention.

INGESTION

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

Purdue Pharma L.P.

Notes to Physicians

OxyContin[®] 30 mg Tablets contain oxycodone hydrochloride. Oxycodone is a pure opioid agonist with an analgesic potency about twice that of morphine. Naloxone is a specific antidote against respiratory depression from opioid overexposure. Opioid antagonists should not be administered in the absence of clinically significant respiratory or circulatory depression secondary to oxycodone overexposure.

In cases of oxycodone overexposure, 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 overexposure 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

OxyContin[®] 30 mg Tablets are not considered flammable. However, concentrated dust from cut, broken or crushed tablets may pose a dust explosion hazard. Eliminate sources of ignition. Bond and ground as necessary. Use non-sparking tools.

For OxyContin[®] 30 mg Tablets

No information available.

For Oxycodone Hydrochloride

Minimum ignition energy: 10-25 mJ

Minimum ignition temperature – dust cloud: 420-440°C

Minimum ignition temperature – dust layer: 225 °C

Maximum explosion pressure (20 L sphere): 9.4 bar

Maximum rate of pressure rise: 779 bar/sec

K_{st}: 212 bar·m/sec

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.

Purdue Pharma L.P.

NFPA

H=1;F=1;R=0

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.

Spill Clean-up

Wear suitable protective clothing and equipment. Sweep up intact tablets or vacuum up cut, broken or crushed tablets and place collected material into a suitable container for reclamation or disposal. Thoroughly wash area with detergent and water. Oxycodone hydrochloride 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 cut, 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

Oxycodone hydrochloride is a Schedule II controlled substance. Keep container 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 (e.g., chemical fume hood).
Keep container tightly closed.

Personal Protective Equipment (PPE)

Wear safety glasses with side shields. Wear full-face protection when judged that the possibility exists for eye and face contact.

Wear an appropriate NIOSH-approved air purifying respirator or positive pressure air-supplied respirator in situations where a respirator is judged appropriate to prevent inhalation.

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

Exposure Guidelines

Exposure Limits

Oxycodone hydrochloride

PEL (OSHA):	None established.
TLV (ACGIH):	None established.
Occupational Exposure Guideline (Purdue Pharma L.P.):	40 µg/m ³ (free base).

Exposure Guideline Comments

Purdue Pharma L.P. has established a workplace exposure limit of 40 µg/m³ for oxycodone (free base) for internal use.

9. PHYSICAL AND CHEMICAL PROPERTIES

Physical Data

Form: Film-coated, controlled-release tablet.

Color: Brown unscored.

Physical Data for Oxycodone hydrochloride

Form:	Solid.
Color:	White.
Vapor Pressure:	No information available.
Melting Point:	270-272°C.
log P _{ow} :	-1.55 (pH 4); 1.18 (pH 9).
Solubility:	10 g in 100g of water.

10. STABILITY AND REACTIVITY

Purdue Pharma L.P.

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. Heating to decomposition may release acrid smoke and fumes.

Polymerization

Material not expected to be subject to polymerization.

11. TOXICOLOGICAL INFORMATION

Relevant Data

OxyContin[®] 30 mg Tablets have not been tested in animals. The following data are for oxycodone hydrochloride reflected as oxycodone free base.

Skin/Eyes

Oxycodone

Oxycodone has not been evaluated in skin and eye irritation studies in animals. It is expected that oxycodone and/or dust from cut, broken or crushed OxyContin[®] 30 mg Tablets may produce mild skin irritation and may cause eye irritation. Oxycodone has not been evaluated in skin sensitization studies in animals; based on structure activity relationships, oxycodone may cause skin sensitization and/or respiratory sensitization.

Acute

<u>Species</u>	<u>Oral LD₅₀</u> <u>(mg/kg)</u>	<u>I.P. LD₅₀</u> <u>(mg/kg)</u>
Mouse	482 (oxycodone)	250 (oxycodone)
Rat	20 (LDL) (oxycodone)	

Subchronic Toxicity

Oxycodone

In a 10-day oral study in rats, 4.5 mg/kg/day (lowest dose tested) produced stereotypic behavior and increased activity only after 5 days of

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treatment. At 45 mg/kg/day, stereotypic behavior, body rigidity, and labored breathing were observed on the first day of dosing. Animals that received ≥ 90 mg/kg/day did not survive past two days of dosing.

In a 28-day oral study in rats, 10 and 25 mg/kg/day produced clinical signs, including rigidity, ocular discharge, chewing on the forelimbs and hyper-reactivity, decreased body weight, and decreased food intake. The no-observed-adverse-effect level (NOAEL) in this study was considered to be 4.0 mg/kg/day.

In a 3-month oral toxicity study in rats, 1.6 mg/kg/day (lowest dose tested) and 4.0 mg/kg/day produced stereotypic behavior and increased and/or decreased activity; these changes were observed after 2-6 weeks of treatment. Prior to that time, no effects were observed. Dosages of 10 and 25 mg/kg/day were associated with stereotypic behavior, increased activity, postural rigidity, and pale color of the extremities. One rat that received 25 mg/kg/day did not survive past 22 days of dosing.

In a 12-day oral study in rabbits, no effects were observed at 4.5 mg/kg/day; ≥ 22 mg/kg/day was associated with decreased activity, reduced fecal output, and convulsions. An animal that received 269 mg/kg/day did not survive six doses.

In a 28-day oral study in dogs, a dosage of 1 mg/kg/day was associated with minimal effects including excessive salivation and slow capillary refill in the oral mucosa; dosages of 4, 8, or 20 mg/kg/day were associated with decreased activity, sedation, ataxia, pale color, and slow capillary refill of the oral mucosa. One dog given 20 mg/kg/day did not survive past 3 days of dosing and one animal given 20 mg/kg/day had convulsions. The no-observed-adverse-effect level (NOAEL) in male dogs was considered to be 1 mg/kg/day; slight effects on food consumption and body weights in females at 1 mg/kg/day might indicate a NOAEL less than 1 mg/kg/day. The maximum tolerated dose in this study was considered to be 8 mg/kg/day.

In a 3-month oral study in dogs, 0.3 mg/kg/day (lowest dose tested) produced no effects; doses ≥ 1 mg/kg/day produced effects similar to those observed in the 28-day study; 8 mg/kg/day was considered to be the maximum tolerated dose in this study. The no-observed-adverse-effect level (NOAEL) for the study was considered to be 1 mg/kg/day.

Chronic Toxicity

Oxycodone

No information available.

Carcinogenicity

Oxycodone

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No information available.

Mutagenicity/Genotoxicity

Oxycodone

Bacterial mutagenicity (Ames test): negative.

Mammalian (Human Peripheral Blood Lymphocytes) chromosome aberration: weakly positive.

Mammalian (Human whole blood lymphocytes) chromosome aberration: negative.

In vivo mouse micronucleus: negative.

Mouse lymphoma: positive (in presence of metabolic activation).

Developmental/Reproductive Toxicity

Oxycodone

Oxycodone hydrochloride produced no adverse effects on fertility, reproductive performance, or early embryonic development of rats at dosages as high as 8 mg/kg/day (the highest dosage tested).

Oxycodone did not produce developmental toxicity in rats or rabbits at dosages as high as 8 and 125 mg/kg/day, respectively.

In a pre- and post-natal study in rats, oxycodone hydrochloride produced no toxic effects on maternal reproductive parameters. There was no effect on survival and development of offspring except for decreased body weight of the first generation but not second generation offspring in the highest dosage group (6 mg/kg/day). The no effect dosage for development of offspring was 2 mg/kg/day.

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

Oxycodone has been detected in breast milk.

Safety Pharmacology

No information available.

12. Ecological Information

Ecotoxicological Information

Oxycodone

24 hr LC₅₀: *Daphnia magna*: 300 mg/mL.

Microbial Growth Inhibition EC₁₀: 7 species: > 1,000 mg/mL.

Chemical Fate Information

Oxycodone

9 of 10; OxyContin[®] 30 mg Tablets MSDS

Purdue Pharma L.P.

Aerobic biodegradation: sewer sludge: est. $t_{1/2}$: 276 days.

13. Disposal Considerations

Disposal

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

14. Transportation Information

Shipping Information

Non-hazardous.

15. Regulatory/Statutory Information

US Federal: OxyContin[®] 30 mg Tablets are subject to control under the US Federal Controlled Substances Act of 1970 as schedule II (C-II) drugs.

International: None.

EC Labeling: None.

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 by the Nonclinical Drug Safety Evaluation of Purdue Pharma L.P.

Purdue Pharma L.P.

Material Safety Data Sheet

OxyContin® (Oxycodone HCl Controlled Release) Tablets, 40 mg

(NDC 59011-440-10, NDC 59011-440-20)

Version: 16-Sep-10

1. CHEMICAL PRODUCT/COMPANY IDENTIFICATION

Material Identification: OxyContin® 40 mg Tablets.

Chemical Name: Mixture, N/A.

Active Ingredient: Oxycodone hydrochloride.

Synonyms:

Active Ingredient: 4, 5 α -epoxy-14-hydroxy-3-methoxy-17-methylmorphinan-6-one hydrochloride.

Molecular Formula: Mixture.

Molecular

Weight:

Mixture.

Active Ingredient: C₁₈H₂₁NO₄·HCl.

Molecular

Weight:

351.83

CAS Number: N/A (mixture).

Active Ingredient: 124-90-3.

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	%
Oxycodone Hydrochloride	124-90-3	25.6

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3. HAZARDS IDENTIFICATION

Emergency Overview

Yellow unscored, film-coated, tablet.

OxyContin[®] 40 mg Tablets do not pose a significant workplace hazard unless tablets are cut, broken or crushed. The following information is provided for those circumstances where uncontrolled exposure to oxycodone may occur due to cutting, breakage or crushing of the OxyContin[®] 40 mg Tablets.

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

Cut, broken or crushed tablets may be harmful by inhalation or skin contact.

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

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

Target organs: central nervous system, gastrointestinal tract, cardiovascular system, respiratory tract.

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.

Warning! Powder may form combustible dust concentrations in air. 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.

Potential Health Effects

OxyContin[®] 40 mg Tablets are a film-coated, tablet product which does not pose a hazard under normal workplace handling conditions.

The active ingredient of OxyContin[®] 40 mg Tablets is oxycodone hydrochloride, an orally active opioid analgesic approximately twice the potency of morphine. OxyContin[®] 40 mg Tablets are designed to provide controlled release of oxycodone in the body. If OxyContin[®] 40 mg Tablets are cut, broken or crushed, workplace exposure to oxycodone may occur. The following information is provided for those circumstances where uncontrolled exposure to oxycodone hydrochloride in OxyContin[®] 40 mg Tablets may occur due to cutting, breakage or crushing of the

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tablet.

Oxycodone

Oxycodone hydrochloride may cause eye irritation and mild skin irritation.

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

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.

Maternal exposure to oxycodone may cause respiratory depression in the neonate. Repeated maternal exposure to oxycodone hydrochloride 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

OxyContin[®] 40 mg Tablets and its components are not 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.

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. Seek medical attention.

INGESTION

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

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Notes to Physicians

OxyContin[®] 40 mg Tablets contain oxycodone hydrochloride. Oxycodone is a pure opioid agonist with an analgesic potency about twice that of morphine. Naloxone is a specific antidote against respiratory depression from opioid overexposure. Opioid antagonists should not be administered in the absence of clinically significant respiratory or circulatory depression secondary to oxycodone overexposure.

In cases of oxycodone overexposure, 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 overexposure 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

OxyContin[®] 40 mg Tablets are not considered flammable. However, concentrated dust from cut, broken or crushed tablets may pose a dust explosion hazard. Eliminate sources of ignition. Bond and ground as necessary. Use non-sparking tools.

For OxyContin[®] 40 mg Tablets

No information available.

For Oxycodone Hydrochloride

Minimum ignition energy: 10-25 mJ

Minimum ignition temperature – dust cloud: 420-440°C

Minimum ignition temperature – dust layer: 225 °C

Maximum explosion pressure (20 L sphere): 9.4 bar

Maximum rate of pressure rise: 779 bar/sec

K_{st}: 212 bar·m/sec

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.

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NFPA

H=1;F=1;R=0

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.

Spill Clean-up

Wear suitable protective clothing and equipment. Sweep up intact tablets or vacuum up cut, broken or crushed tablets and place collected material into a suitable container for reclamation or disposal. Thoroughly wash area with detergent and water. Oxycodone hydrochloride 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 cut, 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

Oxycodone hydrochloride is a Schedule II controlled substance. Keep container 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).

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8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Engineering Controls

Handle material under adequate ventilation (e.g., chemical fume hood).
Keep container tightly closed.

Personal Protective Equipment (PPE)

Wear safety glasses with side shields. Wear full-face protection when judged that the possibility exists for eye and face contact.

Wear an appropriate NIOSH-approved air purifying respirator or positive pressure air-supplied respirator in situations where a respirator is judged appropriate to prevent inhalation.

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

Exposure Guidelines

Exposure Limits

Oxycodone hydrochloride

PEL (OSHA):	None established.
TLV (ACGIH):	None established.
Occupational Exposure Guideline (Purdue Pharma L.P.):	40 µg/m ³ (free base).

Exposure Guideline Comments

Purdue Pharma L.P. has established a workplace exposure limit of 40 µg/m³ for oxycodone (free base) for internal use.

9. PHYSICAL AND CHEMICAL PROPERTIES

Physical Data

Form: Film-coated, controlled-release tablet.
Color: Yellow unscored.

Physical Data for Oxycodone hydrochloride

Form:	Solid.
Color:	White.
Vapor Pressure:	No information available.
Melting Point:	270-272°C.
log P _{ow} :	-1.55 (pH 4); 1.18 (pH 9).
Solubility:	10 g in 100g of water.

10. STABILITY AND REACTIVITY

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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. Heating to decomposition may release acrid smoke and fumes.

Polymerization

Material not expected to be subject to polymerization.

11. TOXICOLOGICAL INFORMATION

Relevant Data

OxyContin[®] 40 mg Tablets have not been tested in animals. The following data are for oxycodone hydrochloride reflected as oxycodone free base.

Skin/Eyes

Oxycodone

Oxycodone has not been evaluated in skin and eye irritation studies in animals. It is expected that oxycodone and/or dust from cut, broken or crushed OxyContin[®] 40 mg Tablets may produce mild skin irritation and may cause eye irritation. Oxycodone has not been evaluated in skin sensitization studies in animals; based on structure activity relationships, oxycodone may cause skin sensitization and/or respiratory sensitization.

Acute

<u>Species</u>	<u>Oral LD₅₀</u> <u>(mg/kg)</u>	<u>I.P. LD₅₀</u> <u>(mg/kg)</u>
Mouse	482 (oxycodone)	250 (oxycodone)
Rat	20 (LDL) (oxycodone)	

Subchronic Toxicity

Oxycodone

In a 10-day oral study in rats, 4.5 mg/kg/day (lowest dose tested) produced stereotypic behavior and increased activity only after 5 days of

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treatment. At 45 mg/kg/day, stereotypic behavior, body rigidity, and labored breathing were observed on the first day of dosing. Animals that received ≥ 90 mg/kg/day did not survive past two days of dosing.

In a 28-day oral study in rats, 10 and 25 mg/kg/day produced clinical signs, including rigidity, ocular discharge, chewing on the forelimbs and hyper-reactivity, decreased body weight, and decreased food intake. The no-observed-adverse-effect level (NOAEL) in this study was considered to be 4.0 mg/kg/day.

In a 3-month oral toxicity study in rats, 1.6 mg/kg/day (lowest dose tested) and 4.0 mg/kg/day produced stereotypic behavior and increased and/or decreased activity; these changes were observed after 2-6 weeks of treatment. Prior to that time, no effects were observed. Dosages of 10 and 25 mg/kg/day were associated with stereotypic behavior, increased activity, postural rigidity, and pale color of the extremities. One rat that received 25 mg/kg/day did not survive past 22 days of dosing.

In a 12-day oral study in rabbits, no effects were observed at 4.5 mg/kg/day; ≥ 22 mg/kg/day was associated with decreased activity, reduced fecal output, and convulsions. An animal that received 269 mg/kg/day did not survive six doses.

In a 28-day oral study in dogs, a dosage of 1 mg/kg/day was associated with minimal effects including excessive salivation and slow capillary refill in the oral mucosa; dosages of 4, 8, or 20 mg/kg/day were associated with decreased activity, sedation, ataxia, pale color, and slow capillary refill of the oral mucosa. One dog given 20 mg/kg/day did not survive past 3 days of dosing and one animal given 20 mg/kg/day had convulsions. The no-observed-adverse-effect level (NOAEL) in male dogs was considered to be 1 mg/kg/day; slight effects on food consumption and body weights in females at 1 mg/kg/day might indicate a NOAEL less than 1 mg/kg/day. The maximum tolerated dose in this study was considered to be 8 mg/kg/day.

In a 3-month oral study in dogs, 0.3 mg/kg/day (lowest dose tested) produced no effects; doses ≥ 1 mg/kg/day produced effects similar to those observed in the 28-day study; 8 mg/kg/day was considered to be the maximum tolerated dose in this study. The no-observed-adverse-effect level (NOAEL) for the study was considered to be 1 mg/kg/day.

Chronic Toxicity

Oxycodone

No information available.

Carcinogenicity

Oxycodone

Purdue Pharma L.P.

No information available.

Mutagenicity/Genotoxicity

Oxycodone

Bacterial mutagenicity (Ames test): negative.

Mammalian (Human Peripheral Blood Lymphocytes) chromosome aberration: weakly positive.

Mammalian (Human whole blood lymphocytes) chromosome aberration: negative.

In vivo mouse micronucleus: negative.

Mouse lymphoma: positive (in presence of metabolic activation).

Developmental/Reproductive Toxicity

Oxycodone

Oxycodone hydrochloride produced no adverse effects on fertility, reproductive performance, or early embryonic development of rats at dosages as high as 8 mg/kg/day (the highest dosage tested).

Oxycodone did not produce developmental toxicity in rats or rabbits at dosages as high as 8 and 125 mg/kg/day, respectively.

In a pre- and post-natal study in rats, oxycodone hydrochloride produced no toxic effects on maternal reproductive parameters. There was no effect on survival and development of offspring except for decreased body weight of the first generation but not second generation offspring in the highest dosage group (6 mg/kg/day). The no effect dosage for development of offspring was 2 mg/kg/day.

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

Oxycodone has been detected in breast milk.

Safety Pharmacology

No information available.

12. Ecological Information

Ecotoxicological Information

Oxycodone

24 hr LC₅₀: *Daphnia magna*: 300 mg/mL.

Microbial Growth Inhibition EC₁₀: 7 species: > 1,000 mg/mL.

Chemical Fate Information

Oxycodone

9 of 10; OxyContin[®] 40 mg Tablets MSDS

Purdue Pharma L.P.

Aerobic biodegradation: sewer sludge: est. $t_{1/2}$: 276 days.

13. Disposal Considerations

Disposal

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

14. Transportation Information

Shipping Information

Non-hazardous.

15. Regulatory/Statutory Information

US Federal: OxyContin[®] 40 mg Tablets are subject to control under the US Federal Controlled Substances Act of 1970 as schedule II (C-II) drugs.

International: None.

EC Labeling: None.

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 by the Nonclinical Drug Safety Evaluation of Purdue Pharma L.P.

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Material Safety Data Sheet

OxyContin[®] (Oxycodone HCl Controlled Release) Tablets, 60 mg

Version: 16-Sep-10

(NDC 59011-460-10, NDC 59011-460-20)

1. CHEMICAL PRODUCT/COMPANY IDENTIFICATION

Material Identification: OxyContin[®] 60 mg Tablets.

Chemical Name: Mixture, N/A.

Active Ingredient: Oxycodone hydrochloride.

Synonyms:

Active Ingredient: 4, 5 α -epoxy-14-hydroxy-3-methoxy-17-methylmorphinan-6-one hydrochloride.

Molecular Formula: Mixture.

Molecular Weight:

Mixture.

Active Ingredient: C₁₈H₂₁NO₄·HCl.

Molecular Weight:

351.83

CAS Number: N/A (mixture).

Active Ingredient: 124-90-3.

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	%
Oxycodone Hydrochloride	124-90-3	25.6

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3. HAZARDS IDENTIFICATION

Emergency Overview

Red unscored, film-coated, tablet.

OxyContin[®] 60 mg Tablets do not pose a significant workplace hazard unless tablets are cut, broken or crushed. The following information is provided for those circumstances where uncontrolled exposure to oxycodone may occur due to cutting, breakage or crushing of the OxyContin[®] 60 mg Tablets.

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

Cut, broken or crushed tablets may be harmful by inhalation or skin contact.

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

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

Target organs: central nervous system, gastrointestinal tract, cardiovascular system, respiratory tract.

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.

Warning! Powder may form combustible dust concentrations in air. 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.

Potential Health Effects

OxyContin[®] 60 mg Tablets are a film-coated, tablet product which does not pose a hazard under normal workplace handling conditions.

The active ingredient of OxyContin[®] 60 mg Tablets is oxycodone hydrochloride, an orally active opioid analgesic approximately twice the potency of morphine. OxyContin[®] 60 mg Tablets are designed to provide controlled release of oxycodone in the body. If OxyContin[®] 60 mg Tablets are cut, broken or crushed, workplace exposure to oxycodone may occur. The following information is provided for those circumstances where uncontrolled exposure to oxycodone hydrochloride in OxyContin[®] 60 mg Tablets may occur due to cutting, breakage or crushing of the

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tablet.

Oxycodone

Oxycodone hydrochloride may cause eye irritation and mild skin irritation.

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

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.

Maternal exposure to oxycodone may cause respiratory depression in the neonate. Repeated maternal exposure to oxycodone hydrochloride 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

OxyContin[®] 60 mg Tablets and its components are not 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.

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. Seek medical attention.

INGESTION

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

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Notes to Physicians

OxyContin[®] 60 mg Tablets contain oxycodone hydrochloride. Oxycodone is a pure opioid agonist with an analgesic potency about twice that of morphine. Naloxone is a specific antidote against respiratory depression from opioid overexposure. Opioid antagonists should not be administered in the absence of clinically significant respiratory or circulatory depression secondary to oxycodone overexposure.

In cases of oxycodone overexposure, 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 overexposure 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

OxyContin[®] 60 mg Tablets are not considered flammable. However, concentrated dust from cut, broken or crushed tablets may pose a dust explosion hazard. Eliminate sources of ignition. Bond and ground as necessary. Use non-sparking tools.

For OxyContin[®] 60 mg Tablets

No information available.

For Oxycodone Hydrochloride

Minimum ignition energy: 10-25 mJ

Minimum ignition temperature – dust cloud: 420-440°C

Minimum ignition temperature – dust layer: 225 °C

Maximum explosion pressure (20 L sphere): 9.4 bar

Maximum rate of pressure rise: 779 bar/sec

K_{st}: 212 bar·m/sec

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.

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NFPA

H=1;F=1;R=0

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.

Spill Clean-up

Wear suitable protective clothing and equipment. Sweep up intact tablets or vacuum up cut, broken or crushed tablets and place collected material into a suitable container for reclamation or disposal. Thoroughly wash area with detergent and water. Oxycodone hydrochloride 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 cut, 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

Oxycodone hydrochloride is a Schedule II controlled substance. Keep container 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).

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8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Engineering Controls

Handle material under adequate ventilation (e.g., chemical fume hood).
Keep container tightly closed.

Personal Protective Equipment (PPE)

Wear safety glasses with side shields. Wear full-face protection when judged that the possibility exists for eye and face contact.

Wear an appropriate NIOSH-approved air purifying respirator or positive pressure air-supplied respirator in situations where a respirator is judged appropriate to prevent inhalation.

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

Exposure Guidelines

Exposure Limits

Oxycodone hydrochloride

PEL (OSHA):	None established.
TLV (ACGIH):	None established.
Occupational Exposure Guideline (Purdue Pharma L.P.):	40 $\mu\text{g}/\text{m}^3$ (free base).

Exposure Guideline Comments

Purdue Pharma L.P. has established a workplace exposure limit of 40 $\mu\text{g}/\text{m}^3$ for oxycodone (free base) for internal use.

9. PHYSICAL AND CHEMICAL PROPERTIES

Physical Data

Form: Film-coated, controlled-release tablet.
Color: Red unscored.

Physical Data for Oxycodone hydrochloride

Form:	Solid.
Color:	White.
Vapor Pressure:	No information available.
Melting Point:	270-272°C.
log P_{ow} :	-1.55 (pH 4); 1.18 (pH 9).
Solubility:	10 g in 100g of water.

10. STABILITY AND REACTIVITY

Purdue Pharma L.P.

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. Heating to decomposition may release acrid smoke and fumes.

Polymerization

Material not expected to be subject to polymerization.

11. TOXICOLOGICAL INFORMATION

Relevant Data

OxyContin[®] 60 mg Tablets have not been tested in animals. The following data are for oxycodone hydrochloride reflected as oxycodone free base.

Skin/Eyes

Oxycodone

Oxycodone has not been evaluated in skin and eye irritation studies in animals. It is expected that oxycodone and/or dust from cut, broken or crushed OxyContin[®] 60 mg Tablets may produce mild skin irritation and may cause eye irritation. Oxycodone has not been evaluated in skin sensitization studies in animals; based on structure activity relationships, oxycodone may cause skin sensitization and/or respiratory sensitization.

Acute

<u>Species</u>	<u>Oral LD₅₀</u> <u>(mg/kg)</u>	<u>I.P. LD₅₀</u> <u>(mg/kg)</u>
Mouse	482 (oxycodone)	250 (oxycodone)
Rat	20 (LDL) (oxycodone)	

Subchronic Toxicity

Oxycodone

In a 10-day oral study in rats, 4.5 mg/kg/day (lowest dose tested) produced stereotypic behavior and increased activity only after 5 days of

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treatment. At 45 mg/kg/day, stereotypic behavior, body rigidity, and labored breathing were observed on the first day of dosing. Animals that received ≥ 90 mg/kg/day did not survive past two days of dosing.

In a 28-day oral study in rats, 10 and 25 mg/kg/day produced clinical signs, including rigidity, ocular discharge, chewing on the forelimbs and hyper-reactivity, decreased body weight, and decreased food intake. The no-observed-adverse-effect level (NOAEL) in this study was considered to be 4.0 mg/kg/day.

In a 3-month oral toxicity study in rats, 1.6 mg/kg/day (lowest dose tested) and 4.0 mg/kg/day produced stereotypic behavior and increased and/or decreased activity; these changes were observed after 2-6 weeks of treatment. Prior to that time, no effects were observed. Dosages of 10 and 25 mg/kg/day were associated with stereotypic behavior, increased activity, postural rigidity, and pale color of the extremities. One rat that received 25 mg/kg/day did not survive past 22 days of dosing.

In a 12-day oral study in rabbits, no effects were observed at 4.5 mg/kg/day; ≥ 22 mg/kg/day was associated with decreased activity, reduced fecal output, and convulsions. An animal that received 269 mg/kg/day did not survive six doses.

In a 28-day oral study in dogs, a dosage of 1 mg/kg/day was associated with minimal effects including excessive salivation and slow capillary refill in the oral mucosa; dosages of 4, 8, or 20 mg/kg/day were associated with decreased activity, sedation, ataxia, pale color, and slow capillary refill of the oral mucosa. One dog given 20 mg/kg/day did not survive past 3 days of dosing and one animal given 20 mg/kg/day had convulsions. The no-observed-adverse-effect level (NOAEL) in male dogs was considered to be 1 mg/kg/day; slight effects on food consumption and body weights in females at 1 mg/kg/day might indicate a NOAEL less than 1 mg/kg/day. The maximum tolerated dose in this study was considered to be 8 mg/kg/day.

In a 3-month oral study in dogs, 0.3 mg/kg/day (lowest dose tested) produced no effects; doses ≥ 1 mg/kg/day produced effects similar to those observed in the 28-day study; 8 mg/kg/day was considered to be the maximum tolerated dose in this study. The no-observed-adverse-effect level (NOAEL) for the study was considered to be 1 mg/kg/day.

Chronic Toxicity

Oxycodone

No information available.

Carcinogenicity

Oxycodone

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No information available.

Mutagenicity/Genotoxicity

Oxycodone

Bacterial mutagenicity (Ames test): negative.

Mammalian (Human Peripheral Blood Lymphocytes) chromosome aberration: weakly positive.

Mammalian (Human whole blood lymphocytes) chromosome aberration: negative.

In vivo mouse micronucleus: negative.

Mouse lymphoma: positive (in presence of metabolic activation).

Developmental/Reproductive Toxicity

Oxycodone

Oxycodone hydrochloride produced no adverse effects on fertility, reproductive performance, or early embryonic development of rats at dosages as high as 8 mg/kg/day (the highest dosage tested).

Oxycodone did not produce developmental toxicity in rats or rabbits at dosages as high as 8 and 125 mg/kg/day, respectively.

In a pre- and post-natal study in rats, oxycodone hydrochloride produced no toxic effects on maternal reproductive parameters. There was no effect on survival and development of offspring except for decreased body weight of the first generation but not second generation offspring in the highest dosage group (6 mg/kg/day). The no effect dosage for development of offspring was 2 mg/kg/day.

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

Oxycodone has been detected in breast milk.

Safety Pharmacology

No information available.

12. Ecological Information

Ecotoxicological Information

Oxycodone

24 hr LC₅₀: Daphnia magna: 300 mg/mL.

Microbial Growth Inhibition EC₁₀: 7 species: > 1,000 mg/mL.

Chemical Fate Information

Oxycodone

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Purdue Pharma L.P.

Aerobic biodegradation: sewer sludge: est. $t_{1/2}$: 276 days.

13. Disposal Considerations

Disposal

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

14. Transportation Information

Shipping Information

Non-hazardous.

15. Regulatory/Statutory Information

US Federal: OxyContin[®] 60 mg Tablets are subject to control under the US Federal Controlled Substances Act of 1970 as schedule II (C-II) drugs.

International: None.

EC Labeling: None.

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 by the Nonclinical Drug Safety Evaluation of Purdue Pharma L.P.

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Material Safety Data Sheet

OxyContin[®] (Oxycodone HCl Controlled Release) Tablets, 80 mg

Version: 16-Sep-10

(NDC 59011-480-10, NDC 59011-480-20)

1. CHEMICAL PRODUCT/COMPANY IDENTIFICATION

Material Identification: OxyContin[®] 80 mg Tablets.

Chemical Name: Mixture, N/A.

Active Ingredient: Oxycodone hydrochloride.

Synonyms:

Active Ingredient: 4, 5 α -epoxy-14-hydroxy-3-methoxy-17-methylmorphinan-6-one hydrochloride.

Molecular Formula: Mixture.

Molecular

Weight:

Mixture.

Active Ingredient: C₁₈H₂₁NO₄·HCl.

Molecular

Weight:

351.83

CAS Number: N/A (mixture).

Active Ingredient: 124-90-3.

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	%
Oxycodone Hydrochloride	124-90-3	30.8

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3. HAZARDS IDENTIFICATION

Emergency Overview

Green unscored, film-coated, tablet.

OxyContin[®] 80 mg Tablets do not pose a significant workplace hazard unless tablets are cut, broken or crushed. The following information is provided for those circumstances where uncontrolled exposure to oxycodone may occur due to cutting, breakage or crushing of the OxyContin[®] 80 mg Tablets.

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

Cut, broken or crushed tablets may be harmful by inhalation or skin contact.

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

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

Target organs: central nervous system, gastrointestinal tract, cardiovascular system, respiratory tract.

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.

Warning! Powder may form combustible dust concentrations in air. 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.

Potential Health Effects

OxyContin[®] 80 mg Tablets are a film-coated, tablet product which does not pose a hazard under normal workplace handling conditions.

The active ingredient of OxyContin[®] 80 mg Tablets is oxycodone hydrochloride, an orally active opioid analgesic approximately twice the potency of morphine. OxyContin[®] 80 mg Tablets are designed to provide controlled release of oxycodone in the body. If OxyContin[®] 80 mg Tablets are cut, broken or crushed, workplace exposure to oxycodone may occur. The following information is provided for those circumstances where uncontrolled exposure to oxycodone hydrochloride in OxyContin[®] 80 mg Tablets may occur due to cutting, breakage or crushing of the

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tablet.

Oxycodone

Oxycodone hydrochloride may cause eye irritation and mild skin irritation.

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

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.

Maternal exposure to oxycodone may cause respiratory depression in the neonate. Repeated maternal exposure to oxycodone hydrochloride 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

OxyContin[®] 80 mg Tablets and its components are not 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.

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. Seek medical attention.

INGESTION

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

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Notes to Physicians

OxyContin[®] 80 mg Tablets contain oxycodone hydrochloride. Oxycodone is a pure opioid agonist with an analgesic potency about twice that of morphine. Naloxone is a specific antidote against respiratory depression from opioid overexposure. Opioid antagonists should not be administered in the absence of clinically significant respiratory or circulatory depression secondary to oxycodone overexposure.

In cases of oxycodone overexposure, 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 overexposure 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

OxyContin[®] 80 mg Tablets are not considered flammable. However, concentrated dust from cut, broken or crushed tablets may pose a dust explosion hazard. Eliminate sources of ignition. Bond and ground as necessary. Use non-sparking tools.

For OxyContin[®] 80 mg Tablets

No information available.

For Oxycodone Hydrochloride

Minimum ignition energy: 10-25 mJ

Minimum ignition temperature – dust cloud: 420-440°C

Minimum ignition temperature – dust layer: 225 °C

Maximum explosion pressure (20 L sphere): 9.4 bar

Maximum rate of pressure rise: 779 bar/sec

K_{st}: 212 bar·m/sec

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.

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NFPA

H=1;F=1;R=0

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.

Spill Clean-up

Wear suitable protective clothing and equipment. Sweep up intact tablets or vacuum up cut, broken or crushed tablets and place collected material into a suitable container for reclamation or disposal. Thoroughly wash area with detergent and water. Oxycodone hydrochloride 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 cut, 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

Oxycodone hydrochloride is a Schedule II controlled substance. Keep container 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).

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8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Engineering Controls

Handle material under adequate ventilation (e.g., chemical fume hood).
Keep container tightly closed.

Personal Protective Equipment (PPE)

Wear safety glasses with side shields. Wear full-face protection when judged that the possibility exists for eye and face contact.

Wear an appropriate NIOSH-approved air purifying respirator or positive pressure air-supplied respirator in situations where a respirator is judged appropriate to prevent inhalation.

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

Exposure Guidelines

Exposure Limits

Oxycodone hydrochloride

PEL (OSHA):	None established.
TLV (ACGIH):	None established.
Occupational Exposure Guideline (Purdue Pharma L.P.):	40 $\mu\text{g}/\text{m}^3$ (free base).

Exposure Guideline Comments

Purdue Pharma L.P. has established a workplace exposure limit of 40 $\mu\text{g}/\text{m}^3$ for oxycodone (free base) for internal use.

9. PHYSICAL AND CHEMICAL PROPERTIES

Physical Data

Form: Film-coated, controlled-release tablet.
Color: Green unscored.

Physical Data for Oxycodone hydrochloride

Form:	Solid.
Color:	White.
Vapor Pressure:	No information available.
Melting Point:	270-272°C.
log P_{ow} :	-1.55 (pH 4); 1.18 (pH 9).
Solubility:	10 g in 100g of water.

10. STABILITY AND REACTIVITY

Purdue Pharma L.P.

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. Heating to decomposition may release acrid smoke and fumes.

Polymerization

Material not expected to be subject to polymerization.

11. TOXICOLOGICAL INFORMATION

Relevant Data

OxyContin[®] 80 mg Tablets have not been tested in animals. The following data are for oxycodone hydrochloride reflected as oxycodone free base.

Skin/Eyes

Oxycodone

Oxycodone has not been evaluated in skin and eye irritation studies in animals. It is expected that oxycodone and/or dust from cut, broken or crushed OxyContin[®] 80 mg Tablets may produce mild skin irritation and may cause eye irritation. Oxycodone has not been evaluated in skin sensitization studies in animals; based on structure activity relationships, oxycodone may cause skin sensitization and/or respiratory sensitization.

Acute

<u>Species</u>	<u>Oral LD₅₀</u> <u>(mg/kg)</u>	<u>I.P. LD₅₀</u> <u>(mg/kg)</u>
Mouse	482 (oxycodone)	250 (oxycodone)
Rat	20 (LDL) (oxycodone)	

Subchronic Toxicity

Oxycodone

In a 10-day oral study in rats, 4.5 mg/kg/day (lowest dose tested) produced stereotypic behavior and increased activity only after 5 days of

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treatment. At 45 mg/kg/day, stereotypic behavior, body rigidity, and labored breathing were observed on the first day of dosing. Animals that received ≥ 90 mg/kg/day did not survive past two days of dosing.

In a 28-day oral study in rats, 10 and 25 mg/kg/day produced clinical signs, including rigidity, ocular discharge, chewing on the forelimbs and hyper-reactivity, decreased body weight, and decreased food intake. The no-observed-adverse-effect level (NOAEL) in this study was considered to be 4.0 mg/kg/day.

In a 3-month oral toxicity study in rats, 1.6 mg/kg/day (lowest dose tested) and 4.0 mg/kg/day produced stereotypic behavior and increased and/or decreased activity; these changes were observed after 2-6 weeks of treatment. Prior to that time, no effects were observed. Dosages of 10 and 25 mg/kg/day were associated with stereotypic behavior, increased activity, postural rigidity, and pale color of the extremities. One rat that received 25 mg/kg/day did not survive past 22 days of dosing.

In a 12-day oral study in rabbits, no effects were observed at 4.5 mg/kg/day; ≥ 22 mg/kg/day was associated with decreased activity, reduced fecal output, and convulsions. An animal that received 269 mg/kg/day did not survive six doses.

In a 28-day oral study in dogs, a dosage of 1 mg/kg/day was associated with minimal effects including excessive salivation and slow capillary refill in the oral mucosa; dosages of 4, 8, or 20 mg/kg/day were associated with decreased activity, sedation, ataxia, pale color, and slow capillary refill of the oral mucosa. One dog given 20 mg/kg/day did not survive past 3 days of dosing and one animal given 20 mg/kg/day had convulsions. The no-observed-adverse-effect level (NOAEL) in male dogs was considered to be 1 mg/kg/day; slight effects on food consumption and body weights in females at 1 mg/kg/day might indicate a NOAEL less than 1 mg/kg/day. The maximum tolerated dose in this study was considered to be 8 mg/kg/day.

In a 3-month oral study in dogs, 0.3 mg/kg/day (lowest dose tested) produced no effects; doses ≥ 1 mg/kg/day produced effects similar to those observed in the 28-day study; 8 mg/kg/day was considered to be the maximum tolerated dose in this study. The no-observed-adverse-effect level (NOAEL) for the study was considered to be 1 mg/kg/day.

Chronic Toxicity

Oxycodone

No information available.

Carcinogenicity

Oxycodone

Purdue Pharma L.P.

No information available.

Mutagenicity/Genotoxicity

Oxycodone

Bacterial mutagenicity (Ames test): negative.

Mammalian (Human Peripheral Blood Lymphocytes) chromosome aberration: weakly positive.

Mammalian (Human whole blood lymphocytes) chromosome aberration: negative.

In vivo mouse micronucleus: negative.

Mouse lymphoma: positive (in presence of metabolic activation).

Developmental/Reproductive Toxicity

Oxycodone

Oxycodone hydrochloride produced no adverse effects on fertility, reproductive performance, or early embryonic development of rats at dosages as high as 8 mg/kg/day (the highest dosage tested).

Oxycodone did not produce developmental toxicity in rats or rabbits at dosages as high as 8 and 125 mg/kg/day, respectively.

In a pre- and post-natal study in rats, oxycodone hydrochloride produced no toxic effects on maternal reproductive parameters. There was no effect on survival and development of offspring except for decreased body weight of the first generation but not second generation offspring in the highest dosage group (6 mg/kg/day). The no effect dosage for development of offspring was 2 mg/kg/day.

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

Oxycodone has been detected in breast milk.

Safety Pharmacology

No information available.

12. Ecological Information

Ecotoxicological Information

Oxycodone

24 hr LC₅₀: *Daphnia magna*: 300 mg/mL.

Microbial Growth Inhibition EC₁₀: 7 species: > 1,000 mg/mL.

Chemical Fate Information

Oxycodone

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Aerobic biodegradation: sewer sludge: est. $t_{1/2}$: 276 days.

13. Disposal Considerations

Disposal

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

14. Transportation Information

Shipping Information

Non-hazardous.

15. Regulatory/Statutory Information

US Federal: OxyContin[®] 80 mg Tablets are subject to control under the US Federal Controlled Substances Act of 1970 as schedule II (C-II) drugs.

International: None.

EC Labeling: None.

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 by the Nonclinical Drug Safety Evaluation of Purdue Pharma L.P.