SAFETY DATA SHEET

1. IDENTIFICATION OF THE SUBSTANCE/PREPARATION

Product Name
Butrans® (buprenorphine) Transdermal System CIII 5, 7.5, 10, 15, 20 mcg/hour

Synonyms
BTDS

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

Recommended Use
Opioid analgesic

Uses advised against
Do not use without a prescription.

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

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

2. HAZARDS IDENTIFICATION

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

Emergency Overview

| Appearance | Dermal patch | Physical state | Solid | Odor | No information available. |

Hazards Not Otherwise Classified (HNOC)
Not Applicable.

Other Information
No information available.

3. COMPOSITION/INFORMATION ON INGREDIENTS

Chemical Family
Opioid analgesic.

<table>
<thead>
<tr>
<th>Chemical Name</th>
<th>CAS No</th>
<th>Weight %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buprenorphine</td>
<td>52485-79-7</td>
<td>1-5</td>
</tr>
<tr>
<td>Levulinic acid</td>
<td>123-76-2</td>
<td>1-5</td>
</tr>
<tr>
<td>Povidone (cros pividone)</td>
<td>9003-39-8</td>
<td>1-5</td>
</tr>
<tr>
<td>Polyacrylate</td>
<td>9003-04-7</td>
<td>80-90</td>
</tr>
</tbody>
</table>
4. FIRST AID MEASURES

First aid measures

Eye contact
In case of eye contact, immediately flush eyes with fresh water for at least 15 minutes while holding the eyelids open. Remove contact lenses if worn. Get medical attention if irritation persists.

Skin contact
In case of contact, remove contaminated clothing. Immediately flush skin with copious amounts of water for at least 15 minutes. Obtain medical attention if skin reaction occurs.

Inhalation
In case of inhalation, remove to fresh air. If not breathing, provide artificial respiration. If breathing is difficult, administer oxygen. Seek medical attention immediately.

Ingestion
In case of accidental ingestion, wash out mouth with copious amounts of water. Seek medical attention immediately. Do not induce vomiting unless directed by medical personnel. Never give anything by mouth to an unconscious person.

Self-protection of the first aider
Do not use mouth-to-mouth method if victim ingested or inhaled the substance; give artificial respiration with the aid of a pocket mask equipped with a one-way valve or other proper respiratory medical device.

Most important symptoms and effects, both acute and delayed

Symptoms
May cause drowsiness, dizziness, or respiratory depression.

Indication of any immediate medical attention and special treatment needed

Note to physicians
This material is an opioid or derivative. Reduced sensation of pain, CNS effects, and opioid-related effects may occur, including respiratory depression. Naloxone has been known to counter the effects of opioids.

5. FIRE-FIGHTING MEASURES

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

Unsuitable Extinguishing Media
No information available.

Specific hazards arising from the chemical
No information available.

Explosion Data
Sensitivity to Mechanical Impact
No information available.

Sensitivity to Static Discharge
No information available.

Protective equipment and precautions for firefighters
As in any fire, wear self-contained breathing apparatus pressure-demand, MSHA/NIOSH (approved or equivalent), and full protective gear.
6. ACCIDENTAL RELEASE MEASURES

Personal precautions, protective equipment and emergency procedures

Personal precautions
Use personal protective equipment as required.

Other Information
Do not smoke, eat or drink in areas where this material is handled or stored.

Environmental precautions

Methods and material for containment and cleaning up

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

Methods for cleaning up
Collect the spilled Butrans® Transdermal System pouches for reuse or disposal as appropriate. Buprenorphine is a Schedule III controlled substance. All cleanup 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 in accordance with federal, state, and local regulations.

7. HANDLING AND STORAGE

Precautions for safe handling

Advice on safe handling
Avoid contact with skin and eyes. Use personal protective equipment as required.

Conditions for safe storage, including any incompatibilities

Storage conditions
Buprenorphine is a Schedule III controlled substance and requires DEA-compliant storage. Keep container tightly closed. Protect from light.

Incompatible materials
None known based on available information.

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Exposure Guidelines

<table>
<thead>
<tr>
<th>Chemical Name</th>
<th>Performance-Based Exposure Band (PBEB)</th>
<th>Company OEG (ug/m³)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buprenorphine</td>
<td>4 (1-10 ug/m³)</td>
<td>None</td>
</tr>
</tbody>
</table>

Engineering Controls
None under normal use conditions.

Individual Protection Measures (Personal Protective Equipment)

Eye/face protection
No special protective measures are necessary.

Skin and body protection
No special protective measures are necessary.

Respiratory protection
No protective equipment is needed under normal use conditions. If exposure limits are exceeded or irritation is experienced, ventilation and evacuation may be required.

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

9. PHYSICAL AND CHEMICAL PROPERTIES

Physical and Chemical Properties
### Physical state
- **Solid**

### Appearance
- Dermal patch

### Odor
- No information available.

### Color
- Beige

### Odor threshold
- No information available.

### Property
<table>
<thead>
<tr>
<th>Value</th>
<th>Remarks • Method</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>pH</strong></td>
<td>No information available.</td>
</tr>
<tr>
<td>Melting point / melting range</td>
<td>No information available.</td>
</tr>
<tr>
<td>Boiling point / boiling range</td>
<td>No information available.</td>
</tr>
<tr>
<td>Flash point</td>
<td>No information available.</td>
</tr>
<tr>
<td>Evaporation rate</td>
<td>No information available.</td>
</tr>
<tr>
<td>Flammability (solid, gas)</td>
<td>No information available.</td>
</tr>
<tr>
<td>Flammability limits in air</td>
<td>No information available.</td>
</tr>
<tr>
<td>- Upper flammability limits</td>
<td>No information available.</td>
</tr>
<tr>
<td>- Lower flammability limits</td>
<td>No information available.</td>
</tr>
<tr>
<td>Vapor pressure</td>
<td>No information available.</td>
</tr>
<tr>
<td>Vapor density</td>
<td>No information available.</td>
</tr>
<tr>
<td>Specific gravity</td>
<td>No information available.</td>
</tr>
<tr>
<td>Water solubility</td>
<td>No information available.</td>
</tr>
<tr>
<td>Solubility in other solvents</td>
<td>No information available.</td>
</tr>
<tr>
<td>Partition coefficient</td>
<td>No information available.</td>
</tr>
<tr>
<td>(n-octanol/water)</td>
<td>No information available.</td>
</tr>
<tr>
<td>Autoignition temperature</td>
<td>No information available.</td>
</tr>
<tr>
<td>Decomposition temperature</td>
<td>No information available.</td>
</tr>
<tr>
<td>Kinematic viscosity</td>
<td>No information available.</td>
</tr>
<tr>
<td>Dynamic viscosity</td>
<td>No information available.</td>
</tr>
<tr>
<td>Explosive properties</td>
<td>No information available.</td>
</tr>
<tr>
<td>Oxidizing properties</td>
<td>No information available.</td>
</tr>
</tbody>
</table>

### Other Information
- Softening point: No information available.
- Molecular weight: No information available.
- VOC content; (%): No information available.
- Density: No information available.
- Bulk density: No information available.

### 10. STABILITY AND REACTIVITY

#### Chemical stability
- Stable under recommended storage conditions.

#### Possibility of hazardous reactions
- No information available.

#### Hazardous polymerization
- Hazardous polymerization does not occur.

#### Conditions to avoid
- Temperatures above 30 °C / 85 °F.

#### Incompatible materials
- None known based on available information.

#### Hazardous decomposition products
- None known based on available information.

### 11. TOXICOLOGICAL INFORMATION

#### Information on likely routes of exposure

<table>
<thead>
<tr>
<th>Route</th>
<th>Remarks • Method</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Product Information</strong></td>
<td>No data available.</td>
</tr>
<tr>
<td>Inhalation</td>
<td>No data available.</td>
</tr>
<tr>
<td>Eye contact</td>
<td>No data available.</td>
</tr>
<tr>
<td>Skin contact</td>
<td>No data available.</td>
</tr>
</tbody>
</table>
Ingestion

No data available.

<table>
<thead>
<tr>
<th>Chemical Name</th>
<th>Oral LD50</th>
<th>Dermal LD50</th>
<th>Inhalation LC50</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buprenorphine</td>
<td>&gt;1000 mg/kg (Rat)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Levulinic acid</td>
<td>1850 mg/kg (Rat)</td>
<td>5 g/kg (Rabbit)</td>
<td>-</td>
</tr>
<tr>
<td>Povidone (crospovidone)</td>
<td>100 g/kg (Rat)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Polyaacrylate</td>
<td>40 g/kg (Rat)</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Information on toxicological effects

Symptoms
May cause drowsiness, dizziness, or respiratory depression.

Sensitization
No information available.

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

Germ cell mutagenicity
Buprenorphine results were negative in tests using Chinese hamster bone marrow and spermatogonia cells, and in a mouse lymphoma L5178Y assay. Results were equivocal in the Ames bacterial reverse mutation test (negative in studies conducted in two laboratories, but positive in frame shift mutation assay at high plate concentrations (5 mg/plate) in a third study).

Carcinogenicity
Buprenorphine administered in rat diet at doses of 0.6, 5.5, and 56 mg/kg/day for 27 months resulted in statistically significant dose-related increases in testicular interstitial (Leydig's) cell tumors, according to the trend test adjusted for survival. Pair-wise comparison of the high dose against control, however, failed to show statistical significance. In an 86 week mouse study, buprenorphine was administered in the diet at doses of 8, 50, and 100 mg/kg/day and was not carcinogenic. Not listed by IARC, NTP, or US OSHA.

Chemical Name | ACGIH | IARC | NTP | OSHA
---|---|---|---|---
Povidone (crospovidone) 9003-39-8 | | Group 3 | | |

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

Reproductive toxicity
Buprenorphine reproductive studies in rats demonstrated no evidence of impaired fertility at daily oral doses up to 80 mg/kg, or up to 5 mg/kg I.M. or S.C. Buprenorphine was not teratogenic in rats or rabbits after I.M. or S.C. doses up to 5 mg/kg/day, IV doses up to 0.8 mg/kg/day, or oral doses in rats (up to 160 mg/kg/day), and rabbits (up to 25 mg/kg/day). Significant increases in skeletal abnormalities (e.g. extra thoracic vertebra or ribs) were noted in rats after S.C. administration of 1 mg/kg/day and up, and in rabbits after I.M. administration of 5 mg/kg/day. However, these increases were not statistically significant. Increases in skeletal abnormalities after oral administration were not observed in rats, and increases in rabbits (1-25 mg/kg/day), were not statistically significant. An apparent lack of milk production during general reproduction studies with buprenorphine in rats caused decreased viability and lactation indices.

Developmental Toxicity
No information available.

Teratogenicity
No information available.

STOT-single exposure
No information available.

STOT-repeated exposure
No information available.

Chronic Toxicity
No information available.

Subchronic toxicity
No information available.

Aspiration hazard
Not Applicable.

The following values are calculated based on chapter 3.1 of the GHS document:
Oral LD50 663 mg/kg
12. ECOLOGICAL INFORMATION

<table>
<thead>
<tr>
<th>Chemical Name</th>
<th>Algae/aquatic plants</th>
<th>Fish</th>
<th>Toxicity to microorganisms</th>
<th>Crustacea</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buprenorphine</td>
<td>NOEC 3.6 mg/L Growth Rate</td>
<td>NOEC 0.13 mg/L (FHM) for 28 days</td>
<td>NOEC 0.26 mg/L (Daphnia) for 21 days</td>
<td></td>
</tr>
</tbody>
</table>

Persistence and degradability: No information available.

Bioaccumulation: Material does not bioaccumulate.

<table>
<thead>
<tr>
<th>Chemical Name</th>
<th>Partition coefficient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buprenorphine</td>
<td>3.4</td>
</tr>
</tbody>
</table>

Other adverse effects: No information available.

13. DISPOSAL CONSIDERATIONS

Waste treatment methods

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

Contaminated Packaging: Do not reuse container.

14. TRANSPORT INFORMATION

DOT: Not regulated.

IATA: Not regulated.

15. REGULATORY INFORMATION

International Inventories

<table>
<thead>
<tr>
<th>Inventory</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>TSCA</td>
<td>Not determined.</td>
</tr>
<tr>
<td>DSL</td>
<td>Not determined.</td>
</tr>
</tbody>
</table>

Legend:

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

US Federal Regulations

SARA 313

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

SARA 311/312 Hazard Categories

<table>
<thead>
<tr>
<th>Category</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute Health Hazard</td>
<td>No</td>
</tr>
<tr>
<td>Chronic Health Hazard</td>
<td>No</td>
</tr>
</tbody>
</table>
**Butrans® (buprenorphine) Transdermal System CIII 5, 7.5, 10, 15, 20 mcg/hour**

**Revision Date** 25-Sep-2015

<table>
<thead>
<tr>
<th>Fire Hazard</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sudden Release of Pressure Hazard</td>
<td>No</td>
</tr>
<tr>
<td>Reactive Hazard</td>
<td>No</td>
</tr>
</tbody>
</table>

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

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

**US State Regulations**

**California Proposition 65**
This product does not contain any Proposition 65 chemicals.

**US State Right-to-Know Regulations**
**US EPA Label Information**
**EPA Pesticide Registration Number** Not Applicable.

### 16. OTHER INFORMATION

<table>
<thead>
<tr>
<th>NFPA</th>
<th>Health Hazards</th>
<th>0</th>
<th>Flammability</th>
<th>0</th>
<th>Instability</th>
<th>0</th>
<th>Physical and Chemical Properties</th>
</tr>
</thead>
<tbody>
<tr>
<td>HMIS</td>
<td>Health Hazards</td>
<td>0</td>
<td>Flammability</td>
<td>0</td>
<td>Physical Hazards</td>
<td>0</td>
<td>Personal protection</td>
</tr>
</tbody>
</table>

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

**Prepared By**
This SDS was prepared by the Occupational and Environmental Assessment Section of Purdue Pharma L.P.

**Issue Date** 17-Jul-2010

**Revision Date** 25-Sep-2015

**Revision Note** No information available.

**Disclaimer**
The information contained in this 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 Safety Data Sheet relate only to the specific material designated herein and do not relate to use in combination with any other material. The data in this Safety Data Sheet are subject to revision as additional knowledge and experience are gained.

End of Safety Data Sheet