SAFETY DATA SHEET

Buprenorphine Solid Formulation

SECTION 1. PRODUCT AND COMPANY IDENTIFICATION

Product name: Buprenorphine Solid Formulation

Manufacturer or supplier's details

Company: MSD
Address: 26 Talavera Road, Talavera Corp Centre, Macquarie Park New South Wales, 2113 Australia
Telephone: (61)-02-8988-8000
Emergency telephone number: (61)-02-8988-8000
E-mail address: EHSDATASTEWARD@msd.com
Telefax: 908-735-1496

Recommended use of the chemical and restrictions on use

Recommended use: Pharmaceutical

SECTION 2. HAZARDS IDENTIFICATION

GHS Classification

Reproductive toxicity: Category 1A

GHS label elements

Hazard pictograms: 

Signal word: Danger
Hazard statements: H360D May damage the unborn child.
Precautionary statements: 

Prevention:
P201 Obtain special instructions before use.
P202 Do not handle until all safety precautions have been read and understood.
P281 Use personal protective equipment as required.

Response:
P308 + P313 IF exposed or concerned: Get medical advice/attention.

Storage:
P405 Store locked up.

Disposal:
P501 Dispose of contents/container to an approved waste...
disposal plant.

Other hazards which do not result in classification
Dust contact with the eyes can lead to mechanical irritation.
Contact with dust can cause mechanical irritation or drying of the skin.
May form explosive dust-air mixture during processing, handling or other means.

SECTION 3. COMPOSITION/INFORMATION ON INGREDIENTS

<table>
<thead>
<tr>
<th>Substance / Mixture</th>
<th>Components</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Chemical name</td>
</tr>
<tr>
<td></td>
<td>Starch</td>
</tr>
<tr>
<td></td>
<td>Buprenorphine Hydrochloride</td>
</tr>
<tr>
<td></td>
<td>Citric acid</td>
</tr>
</tbody>
</table>

SECTION 4. FIRST AID MEASURES

General advice
In the case of accident or if you feel unwell, seek medical advice immediately. When symptoms persist or in all cases of doubt seek medical advice.

If inhaled
If inhaled, remove to fresh air. Get medical attention.

In case of skin contact
In case of contact, immediately flush skin with soap and plenty of water. Remove contaminated clothing and shoes. Get medical attention. Wash clothing before reuse. Thoroughly clean shoes before reuse.

In case of eye contact
If in eyes, rinse well with water. Get medical attention if irritation develops and persists.

If swallowed
If swallowed, DO NOT induce vomiting. Get medical attention. Rinse mouth thoroughly with water.

Most important symptoms and effects, both acute and delayed
May damage the unborn child. Contact with dust can cause mechanical irritation or drying of the skin. Dust contact with the eyes can lead to mechanical irritation.

Protection of first-aiders
First Aid responders should pay attention to self-protection, and use the recommended personal protective equipment when the potential for exposure exists (see section 8).

Notes to physician
Treat symptomatically and supportively.

SECTION 5. FIREFIGHTING MEASURES

Suitable extinguishing media
Water spray
Alcohol-resistant foam
Carbon dioxide (CO2)
Dry chemical

Unsuitable extinguishing media
None known.
Specific hazards during firefighting:
- Exposure to combustion products may be a hazard to health.
- Carbon oxides
- Nitrogen oxides (NOx)

Hazardous combustion products:
- Carbon oxides
- Nitrogen oxides (NOx)

Specific extinguishing methods:
- Use extinguishing measures that are appropriate to local circumstances and the surrounding environment.
- Use water spray to cool unopened containers.
- Remove undamaged containers from fire area if it is safe to do so.
- Evacuate area.

Special protective equipment for firefighters:
- In the event of fire, wear self-contained breathing apparatus.
- Use personal protective equipment.

SECTION 6. ACCIDENTAL RELEASE MEASURES

Personal precautions, protective equipment and emergency procedures:
- Use personal protective equipment.
- Follow safe handling advice (see section 7) and personal protective equipment recommendations (see section 8).

Environmental precautions:
- Avoid release to the environment.
- Prevent further leakage or spillage if safe to do so.
- Retain and dispose of contaminated wash water.
- Local authorities should be advised if significant spillages cannot be contained.

Methods and materials for containment and cleaning up:
- Sweep up or vacuum up spillage and collect in suitable container for disposal.
- Avoid dispersal of dust in the air (i.e., clearing dust surfaces with compressed air).
- Dust deposits should not be allowed to accumulate on surfaces, as these may form an explosive mixture if they are released into the atmosphere in sufficient concentration.
- Local or national regulations may apply to releases and disposal of this material, as well as those materials and items employed in the cleanup of releases. You will need to determine which regulations are applicable.
- Sections 13 and 15 of this SDS provide information regarding certain local or national requirements.

SECTION 7. HANDLING AND STORAGE

Technical measures:
- Static electricity may accumulate and ignite suspended dust causing an explosion.
- Provide adequate precautions, such as electrical grounding and bonding, or inert atmospheres.

Local/Total ventilation:
- If sufficient ventilation is unavailable, use with local exhaust ventilation.

Advice on safe handling:
- Do not get on skin or clothing.
- Do not breathe dust.
- Do not swallow.
- Avoid contact with eyes.
- Handle in accordance with good industrial hygiene and safety practice, based on the results of the workplace exposure as-
Hygiene measures: If exposure to chemical is likely during typical use, provide eye flushing systems and safety showers close to the working place.
When using do not eat, drink or smoke.
Wash contaminated clothing before re-use.
The effective operation of a facility should include review of engineering controls, proper personal protective equipment, appropriate degowning and decontamination procedures, industrial hygiene monitoring, medical surveillance and the use of administrative controls.

Conditions for safe storage: Keep in properly labelled containers.
Store locked up.
Keep tightly closed.
Store in accordance with the particular national regulations.

Materials to avoid: Do not store with the following product types:
Strong oxidizing agents

SECTION 8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Components with workplace control parameters

<table>
<thead>
<tr>
<th>Components</th>
<th>CAS-No.</th>
<th>Value type (Form of exposure)</th>
<th>Control parameters / Permissible concentration</th>
<th>Basis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Starch</td>
<td>9005-25-8</td>
<td>TWA</td>
<td>10 mg/m³</td>
<td>AU OEL</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Further information: This value is for inhalable dust containing no asbestos and &lt; 1% crystalline silica</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA</td>
<td>10 mg/m³</td>
<td>ACGIH</td>
</tr>
<tr>
<td>Buprenorphine Hydrochloride</td>
<td>53152-21-9</td>
<td>TWA</td>
<td>0.2 µg/m³ (OEB 5)</td>
<td>Internal</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Wipe limit 2 µg/100 cm²</td>
<td>Internal</td>
</tr>
</tbody>
</table>

Engineering measures: Use closed processing systems or containment technologies to control at source (e.g., glove boxes/isolators) and to prevent leakage of compounds into the workplace.
All engineering controls should be implemented by facility design and operated in accordance with GMP principles to protect products, workers, and the environment.
No open handling permitted.
Totally enclosed processes and materials transport systems are required.
Operations require the use of appropriate containment technology designed to prevent leakage of compounds into the workplace.
SAFETY DATA SHEET

Buprenorphine Solid Formulation

Personal protective equipment

Respiratory protection: If adequate local exhaust ventilation is not available or exposure assessment demonstrates exposures outside the recommended guidelines, use respiratory protection.

Filter type: Particulates type

Hand protection: Chemical-resistant gloves

Eye protection: Wear safety glasses with side shields or goggles. If the work environment or activity involves dusty conditions, mists or aerosols, wear the appropriate goggles. Wear a faceshield or other full face protection if there is a potential for direct contact to the face with dusts, mists, or aerosols.

Skin and body protection: Work uniform or laboratory coat. Additional body garments should be used based upon the task being performed (e.g., sleevelets, apron, gauntlets, disposable suits) to avoid exposed skin surfaces. Use appropriate degowning techniques to remove potentially contaminated clothing.

SECTION 9. PHYSICAL AND CHEMICAL PROPERTIES

Appearance: solid

Colour: white

Odour: No data available

Odour Threshold: No data available

pH: No data available

Melting point/freezing point: No data available

Initial boiling point and boiling range: No data available

Flash point: Not applicable

Evaporation rate: Not applicable

Flammability (solid, gas): May form explosive dust-air mixture during processing, handling or other means.

Flammability (liquids): No data available

Upper explosion limit / Upper flammability limit: No data available

Lower explosion limit / Lower flammability limit: No data available
Vapour pressure: Not applicable
Relative vapour density: Not applicable
Relative density: No data available
Density: No data available
Solubility(ies)
  Water solubility: No data available
Partition coefficient: n-octanol/water: Not applicable
Auto-ignition temperature: No data available
Decomposition temperature: No data available
Viscosity
  Viscosity, kinematic: Not applicable
Explosive properties: Not explosive
Oxidizing properties: The substance or mixture is not classified as oxidizing.
Particle size: No data available

SECTION 10. STABILITY AND REACTIVITY

Reactivity: Not classified as a reactivity hazard.
Chemical stability: Stable under normal conditions.
Possibility of hazardous reactions:
  May form explosive dust-air mixture during processing, handling or other means.
  Can react with strong oxidizing agents.
Conditions to avoid: Heat, flames and sparks.
  Avoid dust formation.
Incompatible materials: Oxidizing agents
Hazardous decomposition products: No hazardous decomposition products are known.

SECTION 11. TOXICOLOGICAL INFORMATION

Exposure routes:
  Inhalation
  Skin contact
  Ingestion
  Eye contact

Acute toxicity:
Not classified based on available information.

Product:
Acute oral toxicity: Acute toxicity estimate: > 2,000 mg/kg
  Method: Calculation method
Components:

Starch:
Acute oral toxicity: LD50 (Rat): > 5,000 mg/kg
Acute dermal toxicity: LD50 (Rabbit): > 2,000 mg/kg

Buprenorphine Hydrochloride:
Acute oral toxicity: LD50 (Mouse): 261 mg/kg
LD50 (Rat): 600 mg/kg
Acute inhalation toxicity: Remarks: No data available
Acute dermal toxicity: Remarks: No data available
Acute toxicity (other routes of administration):
LD50 (Rat): 31 mg/kg
Application Route: Intravenous
LD50 (Mouse): 24 mg/kg
Application Route: Intravenous

Citric acid:
Acute oral toxicity: LD50 (Mouse): 5,400 mg/kg
Acute dermal toxicity: LD50 (Rat): > 2,000 mg/kg
Method: OECD Test Guideline 404
Assessment: The substance or mixture has no acute dermal toxicity

Skin corrosion/irritation
Not classified based on available information.

Components:

Buprenorphine Hydrochloride:
Remarks: No data available

Citric acid:
Species: Rabbit
Method: OECD Test Guideline 404
Result: No skin irritation

Serious eye damage/eye irritation
Not classified based on available information.

Components:

Starch:
Species: Rabbit
Result: No eye irritation
Buprenorphine Hydrochloride:
Remarks : No data available

Citric acid:
Species : Rabbit
Result : Irritation to eyes, reversing within 21 days
Method : OECD Test Guideline 405

Respiratory or skin sensitisation
Skin sensitisation
Not classified based on available information.
Respiratory sensitisation
Not classified based on available information.

Components:
Starch:
Test Type : Maximisation Test
Exposure routes : Skin contact
Species : Guinea pig
Result : negative

Buprenorphine Hydrochloride:
Remarks : No data available

Chronic toxicity
Germ cell mutagenicity
Not classified based on available information.

Components:
Starch:
Genotoxicity in vitro : Test Type: Bacterial reverse mutation assay (AMES)
Result: negative

Buprenorphine Hydrochloride:
Genotoxicity in vitro : Test Type: Bacterial reverse mutation assay (AMES)
Result: equivocal

Test Type: Chromosomal aberration
Result: negative

Test Type: DNA damage and repair, unscheduled DNA synthesis in mammalian cells (in vitro)
Result: positive

Germ cell mutagenicity - Assessment : Weight of evidence does not support classification as a germ cell mutagen.
Citric acid:
Genotoxicity in vitro:
- Test Type: Bacterial reverse mutation assay (AMES)
  Result: negative
- Test Type: in vitro micronucleus test
  Result: positive
- Test Type: Bacterial reverse mutation assay (AMES)
  Result: negative

Genotoxicity in vivo:
- Test Type: Mutagenicity (in vivo mammalian bone-marrow cytogenetic test, chromosomal analysis)
  Species: Rat
  Application Route: Ingestion
  Result: negative

Carcinogenicity
Not classified based on available information.

Components:
Buprenorphine Hydrochloride:
Species: Rat
Application Route: Oral
Exposure time: 27 Months
LOAEL: 56 mg/kg body weight
Result: positive
Target Organs: Testes
Remarks: The significance of these findings for humans is not certain.

Species: Mouse
Application Route: Oral
Exposure time: 86 weeks
NOAEL: 100 mg/kg body weight
Result: negative
Carcinogenicity - Assessment: Weight of evidence does not support classification as a carcinogen

Reproductive toxicity
May damage the unborn child.

Components:
Buprenorphine Hydrochloride:
Effects on fertility:
- Test Type: Fertility
  Species: Rat
  Application Route: Oral
  Fertility: NOAEL: 80 mg/kg body weight
  Result: No effects on fertility

Test Type: Fertility
Species: Rat
Application Route: Subcutaneous
### Fertility
- **NOAEL:** 5 mg/kg body weight
- **Result:** No effects on fertility

**Test Type:** Fertility  
**Species:** Rabbit  
**Application Route:** Oral  
**Fertility:** LOAEL: 1 mg/kg body weight  
**Result:** Preimplantation loss

**Test Type:** Fertility  
**Species:** Rabbit  
**Application Route:** Intravenous  
**Fertility:** LOAEL: 0.2 mg/kg body weight  
**Result:** Postimplantation loss

### Effects on foetal development

<table>
<thead>
<tr>
<th>Effects on foetal development</th>
<th>Test Type: Development</th>
<th>Species: Rat</th>
<th>Application Route: Subcutaneous</th>
<th>Developmental Toxicity: LOAEL: 5 mg/kg body weight</th>
<th>Result: Embryo-foetal toxicity, No teratogenic effects, Skeletal malformations</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Effects on foetal development</th>
<th>Test Type: Development</th>
<th>Species: Rat</th>
<th>Application Route: Oral</th>
<th>Developmental Toxicity: NOAEL: 160 mg/kg body weight</th>
<th>Result: No effects on foetal development</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Effects on foetal development</th>
<th>Test Type: Development</th>
<th>Species: Rat</th>
<th>Application Route: Subcutaneous</th>
<th>Developmental Toxicity: LOAEL: 0.1 mg/kg body weight</th>
<th>Result: Effects on newborn</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Effects on foetal development</th>
<th>Test Type: Development</th>
<th>Species: Rabbit</th>
<th>Application Route: Intramuscular</th>
<th>Developmental Toxicity: LOAEL: 5 mg/kg body weight</th>
<th>Result: Embryo-foetal toxicity, Skeletal malformations</th>
</tr>
</thead>
</table>

### Reproductive toxicity - Assessment
- May damage the unborn child. Suspected of damaging fertility.

### Citric acid

**Effects on foetal development**  
- **Test Type:** One-generation reproduction toxicity study  
- **Species:** Rat  
- **Application Route:** Ingestion  
- **Result:** negative
STOT - single exposure
Not classified based on available information.

Components:
Buprenorphine Hydrochloride:
Assessment : May cause drowsiness or dizziness.

STOT - repeated exposure
Not classified based on available information.

Repeated dose toxicity

Components:

Starch:
Species : Rat
NOAEL : >= 2,000 mg/kg
Application Route : Skin contact
Exposure time : 28 Days
Method : OECD Test Guideline 410

Citric acid:
Species : Rat
NOAEL : 4,000 mg/kg
LOAEL : 8,000 mg/kg
Application Route : Ingestion
Exposure time : 10 Days

Aspiration toxicity
Not classified based on available information.

Experience with human exposure

Components:

Buprenorphine Hydrochloride:
Inhalation : Target Organs: Central nervous system
Symptoms: Drowsiness, sedation, Headache, Nausea, Vomiting, Dizziness, Vertigo, Sweating, constipation, insomnia, Pain, respiratory depression, constriction of pupils, decrease in heart rate, Lowered blood pressure
Remarks: May cause neonatal withdrawal

SECTION 12. ECOLOGICAL INFORMATION

Ecotoxicity

Components:

Buprenorphine Hydrochloride:
Toxicity to algae/aquatic plants : EC50 (Pseudokirchneriella subcapitata (green algae)): 6.25 mg/l
**Exposure time:** 72 h  
Method: OECD Test Guideline 201

NOEC (Pseudokirchneriella subcapitata (green algae)): 0.319 mg/l  
Exposure time: 72 h  
Method: OECD Test Guideline 201

**Toxicity to fish (Chronic toxicity):**  
NOEC (Pimephales promelas (fathead minnow)): 0.137 mg/l  
Exposure time: 28 d  
Method: OECD Test Guideline 210

**Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity):**  
NOEC (Daphnia magna (Water flea)): 0.883 mg/l  
Exposure time: 21 d  
Method: OECD Test Guideline 211

LOEC (Daphnia magna (Water flea)): 1.95 mg/l  
Exposure time: 21 d  
Method: OECD Test Guideline 211

**Toxicity to microorganisms:**  
EC50: 588 mg/l  
Exposure time: 3 h  
Test Type: Respiration inhibition  
Method: OECD Test Guideline 209

NOEC: 135 mg/l  
Exposure time: 3 h  
Test Type: Respiration inhibition  
Method: OECD Test Guideline 209

**Citric acid:**  
**Toxicity to fish:**  
LC50 (Pimephales promelas (fathead minnow)): > 100 mg/l  
Exposure time: 96 h

**Toxicity to daphnia and other aquatic invertebrates:**  
EC50 (Daphnia magna (Water flea)): 1,535 mg/l  
Exposure time: 24 h

**Persistence and degradability**

**Components:**

**Buprenorphine Hydrochloride:**  
Biodegradability: Result: Not readily biodegradable.

**Citric acid:**  
Biodegradability: Result: Readily biodegradable.  
Biodegradation: 97%  
Exposure time: 28 d  
Method: OECD Test Guideline 301B
Bioaccumulative potential

Components:

Buprenorphine Hydrochloride:
Bioaccumulation: Species: Oncorhynchus mykiss (rainbow trout)
Bioconcentration factor (BCF): 0.4
Method: OECD Test Guideline 305

Partition coefficient: n-octanol/water: log Pow: 3.11

Citric acid:
Partition coefficient: n-octanol/water: log Pow: -1.72

Mobility in soil

Components:

Buprenorphine Hydrochloride:
Distribution among environmental compartments: log Koc: 4.11

Other adverse effects
No data available

SECTION 13. DISPOSAL CONSIDERATIONS

Disposal methods
Waste from residues: Dispose of in accordance with local regulations.
Contaminated packaging: Empty containers should be taken to an approved waste handling site for recycling or disposal.
If not otherwise specified: Dispose of as unused product.

SECTION 14. TRANSPORT INFORMATION

International Regulations

UNRTDG
Not regulated as a dangerous good

IATA-DGR
Not regulated as a dangerous good

IMDG-Code
Not regulated as a dangerous good

Transport in bulk according to Annex II of MARPOL 73/78 and the IBC Code
Not applicable for product as supplied.

National Regulations

ADG
Not regulated as a dangerous good
SAFETY DATA SHEET

Buprenorphine Solid Formulation

Version: 2.6  Revision Date: 10.10.2020  SDS Number: 918674-00009  Date of last issue: 23.03.2020  Date of first issue: 03.10.2016

SECTION 15. REGULATORY INFORMATION

Safety, health and environmental regulations/legislation specific for the substance or mixture

Prohibition/Licensing Requirements:
There is no applicable prohibition, authorisation and restricted use requirements, including for carcinogens referred to in Schedule 10 of the model WHS Act and Regulations.

The components of this product are reported in the following inventories:

- AICS: not determined
- DSL: not determined
- IECSC: not determined

SECTION 16. OTHER INFORMATION

Further information

Revision Date: 10.10.2020
Sources of key data used to compile the Safety Data Sheet:

Date format: dd.mm.yyyy

Full text of other abbreviations

- ACGIH: USA. ACGIH Threshold Limit Values (TLV)
- ACGIH / TWA: 8-hour, time-weighted average
- AU OEL / TWA: Exposure standard - time weighted average

AIIC - Australian Inventory of Industrial Chemicals; ANTT - National Agency for Transport by Land of Brazil; ASTM - American Society for the Testing of Materials; bw - Body weight; CMR - Carcinogen, Mutagen or Reproductive Toxicant; DIN - Standard of the German Institute for Standardisation; DSL - Domestic Substances List (Canada); ECx - Concentration associated with x% response; ELx - Loading rate associated with x% response; EmS - Emergency Schedule; ENCS - Existing and New Chemical Substances (Japan); ErCx - Concentration associated with x% growth rate response; ERG - Emergency Response Guide; GHS - Globally Harmonized System; GLP - Good Laboratory Practice; IARC - International Agency for Research on Cancer; IATA - International Air Transport Association; IBC - International Code for the Construction and Equipment of Ships carrying Dangerous Chemicals in Bulk; IC50 - Half maximal inhibitory concentration; ICAO - International Civil Aviation Organization; IECSC - Inventory of Existing Chemical Substances in China; IMDG - International Maritime Dangerous Goods; IMO - International Maritime Organization; ISHL - Industrial Safety and Health Law (Japan); ISO - International Organisation for Standardization; KECl - Korea Existing Chemicals Inventory; LC50 - Lethal Con-
The information provided in this Safety Data Sheet is correct to the best of our knowledge, information and belief at the date of its publication. The information is designed only as a guidance for safe handling, use, processing, storage, transportation, disposal and release and shall not be considered a warranty or quality specification of any type. The information provided relates only to the specific material identified at the top of this SDS and may not be valid when the SDS material is used in combination with any other materials or in any process, unless specified in the text. Material users should review the information and recommendations in the specific context of their intended manner of handling, use, processing and storage, including an assessment of the appropriateness of the SDS material in the user’s end product, if applicable.

AU / EN