1. PRODUCT AND COMPANY IDENTIFICATION

Chemical product name : Buprenorphine Liquid Formulation

Supplier's company name, address and phone number

Company name of supplier : MSD
Address : Kumagaya, Saitama Prefecture, Xicheng 810 MSD Co., Ltd.
Menuma factory

Telephone : 048-588-8411
E-mail address : EHSDATASTEWARD@msd.com
Emergency telephone number : 1-908-423-6000

Recommended use of the chemical and restrictions on use
Recommended use : Pharmaceutical

2. HAZARDS IDENTIFICATION

GHS classification of chemical product
Not a hazardous substance or mixture according to the Globally Harmonised System (GHS).

GHS label elements
Not a hazardous substance or mixture according to the Globally Harmonised System (GHS).

Other hazards which do not result in classification
None known.

3. COMPOSITION/INFORMATION ON INGREDIENTS

Substance / Mixture : Mixture

Components

<table>
<thead>
<tr>
<th>Chemical name</th>
<th>CAS-No.</th>
<th>Concentration (% w/w)</th>
<th>ENCS No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buprenorphine Hydrochloride</td>
<td>53152-21-9</td>
<td>&gt;= 0.025 - &lt; 0.1</td>
<td></td>
</tr>
</tbody>
</table>

4. FIRST AID MEASURES

If inhaled : If inhaled, remove to fresh air.
Get medical attention if symptoms occur.

In case of skin contact : Wash with water and soap as a precaution.
Get medical attention if symptoms occur.

In case of eye contact : Flush eyes with water as a precaution.
Get medical attention if irritation develops and persists.

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

Most important symptoms : None known.
and effects, both acute and delayed
Protection of first-aiders : No special precautions are necessary for first aid responders.
Notes to physician : Treat symptomatically and supportively.

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.

Hazardous combustion products : Carbon oxides

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 : Wear self-contained breathing apparatus for firefighting if necessary.
 Use personal protective equipment.

6. ACCIDENTAL RELEASE MEASURES

Personal precautions, protective equipment and emergency procedures : Follow safe handling advice and personal protective equipment recommendations.

Environmental precautions : Discharge into the environment must be avoided.
 Prevent further leakage or spillage if safe to do so.
 Prevent spreading over a wide area (e.g. by containment or oil barriers).
 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 : Soak up with inert absorbent material.
 For large spills, provide dyeing or other appropriate containment to keep material from spreading. If dyed material can be pumped, store recovered material in appropriate container.
 Clean up remaining materials from spill with suitable absorbent.
 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.
7. HANDLING AND STORAGE

Handling
Technical measures: See Engineering measures under EXPOSURE CONTROLS/PERSONAL PROTECTION section.
Local/Total ventilation: Use only with adequate ventilation.
Advice on safe handling: Handle in accordance with good industrial hygiene and safety practice, based on the results of the workplace exposure assessment. Take care to prevent spills, waste and minimize release to the environment.
Avoidance of contact: Oxidizing agents
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.

Storage
Conditions for safe storage: Keep in properly labelled containers. Store in accordance with the particular national regulations.
Materials to avoid: Do not store with the following product types: Strong oxidizing agents
Packaging material: Unsuitable material: None known.

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Threshold limit value and permissible exposure limits for each component in the work environment

<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>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>Wipe limit</td>
<td>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.

**Personal protective equipment**

Respiratory protection: No personal respiratory protective equipment normally required.

Hand protection

Material: Chemical-resistant gloves

Remarks: Consider double gloving.

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 face shield 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.

### 9. PHYSICAL AND CHEMICAL PROPERTIES

- **Physical state**: liquid
- **Colour**: No data available
- **Odour**: No data available
- **Odour Threshold**: No data available
- **Melting point/freezing point**: No data available
- **Boiling point, initial boiling point and boiling range**: No data available
- **Flammability (solid, gas)**: Not applicable
- **Flammability (liquids)**: No data available
- **Lower explosion limit and upper explosion limit / flammability limit**
  - **Upper explosion limit / Upper flammability limit**: No data available
  - **Lower explosion limit / Lower flammability limit**: No data available
- **Flash point**: No data available
- **Decomposition temperature**: No data available
- **pH**: No data available
Evaporation rate: No data available

Auto-ignition temperature: No data available

Viscosity
  Viscosity, kinematic: No data available

Solubility(ies)
  Water solubility: No data available

Partition coefficient: n-octanol/water: Not applicable

Vapour pressure: No data available

Density and / or relative density
  Relative density: No data available
  Density: No data available
  Relative vapour density: No data available

Explosive properties: Not explosive

Oxidizing properties: The substance or mixture is not classified as oxidizing.

Particle characteristics
  Particle size: Not applicable

10. STABILITY AND REACTIVITY

Reactivity: Not classified as a reactivity hazard.
Chemical stability: Stable under normal conditions.
Possibility of hazardous reac-
tions: Can react with strong oxidizing agents.
Conditions to avoid: None known.
Incompatible materials: Oxidizing agents
Hazardous decomposition products: No hazardous decomposition products are known.

11. TOXICOLOGICAL INFORMATION

Information on likely routes of exposure:
  Inhalation
  Skin contact
  Ingestion
  Eye contact

Acute toxicity
Not classified based on available information.

Components:
  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

Skin corrosion/irritation
Not classified based on available information.

Components:
Buprenorphine Hydrochloride:
Remarks: No data available

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

Components:
Buprenorphine Hydrochloride:
Remarks: No data available

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

Components:
Buprenorphine Hydrochloride:
Remarks: No data available

Germ cell mutagenicity
Not classified based on available information.

Components:
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.

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
Not classified based on available information.

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
Effects on foetal development:

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

- Test Type: Development
- Species: Rat
- Application Route: Subcutaneous
- Developmental Toxicity: LOAEL: 5 mg/kg body weight
- Result: Embryo-foetal toxicity, No teratogenic effects, Skeletal malformations

- Test Type: Development
- Species: Rat
- Application Route: Oral
- Developmental Toxicity: NOAEL: 160 mg/kg body weight
- Result: No effects on foetal development

- Test Type: Development
- Species: Rat
- Application Route: Subcutaneous
- Developmental Toxicity: LOAEL: 0.1 mg/kg body weight
- Result: Effects on newborn

- Test Type: Development
- Species: Rabbit
- Application Route: Intramuscular
- Developmental Toxicity: LOAEL: 5 mg/kg body weight
- Result: Embryo-foetal toxicity, Skeletal malformations

- Test Type: Development
- Species: Rabbit
- Application Route: Oral
- Developmental Toxicity: LOAEL: 1 mg/kg body weight
- Result: Embryo-foetal toxicity, Skeletal malformations

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

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.

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

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
Persistence and degradability

Components:

Buprenorphine Hydrochloride:
Biodegradability: Result: Not readily biodegradable.

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

Mobility in soil

Components:

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

Hazardous to the ozone layer
Not applicable

Other adverse effects
No data available

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.

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.
SAFETY DATA SHEET

Buprenorphine Liquid Formulation

Version 2.0  Revision Date: 2020/03/23  SDS Number: 744996-00009  Date of last issue: 2019/09/13  Date of first issue: 2016/06/08

15. REGULATORY INFORMATION

Related Regulations

Fire Service Law
Not applicable to dangerous materials / designated flammables.

Chemical Substance Control Law
Not applicable for Specified Chemical Substance, Monitoring Chemical Substance and Priority Assessment Chemical Substance.

Industrial Safety and Health Law

Harmful Substances Prohibited from Manufacture
Not applicable

Harmful Substances Required Permission for Manufacture
Not applicable

Substances Prevented From Impairment of Health
Not applicable

Circular concerning Information on Chemicals having Mutagenicity - Annex 2: Information on Existing Chemicals having Mutagenicity
Not applicable

Circular concerning Information on Chemicals having Mutagenicity - Annex 1: Information on Notified Substances having Mutagenicity
Not applicable

Substances Subject to be Notified Names
Not applicable

Substances Subject to be Indicated Names
Not applicable

Ordinance on Prevention of Hazards Due to Specified Chemical Substances
Not applicable

Ordinance on Prevention of Lead Poisoning
Not applicable

Ordinance on Prevention of Tetraalkyl Lead Poisoning
Not applicable

Ordinance on Prevention of Organic Solvent Poisoning
Not applicable

Enforcement Order of the Industrial Safety and Health Law - Attached table 1 (Dangerous Substances)
Not applicable

Poisonous and Deleterious Substances Control Law
Not applicable
SAFETY DATA SHEET

Buprenorphine Liquid Formulation

Version 2.0  Revision Date: 2020/03/23  SDS Number: 744996-00009  Date of last issue: 2019/09/13  Date of first issue: 2016/06/08

Act on Confirmation, etc. of Release Amounts of Specific Chemical Substances in the Environment and Promotion of Improvements to the Management Thereof
Not applicable

High Pressure Gas Safety Act
Not applicable

Explosive Control Law
Not applicable

Vessel Safety Law
Not regulated as a dangerous good

Aviation Law
Not regulated as a dangerous good

Marine Pollution and Sea Disaster Prevention etc Law
Bulk transportation  :  Not classified as noxious liquid substance
Pack transportation  :  Not classified as marine pollutant

Narcotics and Psychotropics Control Act
Narcotic or Psychotropic Raw Material (Export / Import Permission)
Not applicable
Specific Narcotic or Psychotropic Raw Material (Export / Import permission)
Not applicable

Waste Disposal and Public Cleansing Law
Industrial waste

The components of this product are reported in the following inventories:
AICS  :  not determined
DSL  :  not determined
IECSC  :  not determined

16. OTHER INFORMATION

Further information

Items where changes have been made to the previous version are highlighted in the body of this document by two vertical lines.

Date format  :  yyyy/mm/dd

Full text of other abbreviations

AICS - Australian Inventory of Chemical Substances; 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; KECI - Korea Existing Chemicals Inventory; LC50 - Lethal Concentration to 50% of a test population; LD50 - Lethal Dose to 50% of a test population (Median Lethal Dose); MARPOL - International Convention for the Prevention of Pollution from Ships; n.o.s. - Not Otherwise Specified; Nch - Chilean Norm; NO(A)EC - No Observed (Adverse) Effect Concentration; NO(A)EL - No Observed (Adverse) Effect Level; NOELR - No Observable Effect Loading Rate; NOM - Official Mexican Norm; NTP - National Toxicology Program; NZIoC - New Zealand Inventory of Chemicals; OECD - Organization for Economic Co-operation and Development; OPPTS - Office of Chemical Safety and Pollution Prevention; PBT - Persistent, Bioaccumulative and Toxic substance; PICCS - Philippines Inventory of Chemicals and Chemical Substances; (Q)SAR - (Quantitative) Structure Activity Relationship; REACH - Regulation (EC) No 1907/2006 of the European Parliament and of the Council concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals; SADT - Self-Accelerating Decomposition Temperature; SDS - Safety Data Sheet; TCSI - Taiwan Chemical Substance Inventory; TDG - Transportation of Dangerous Goods; TSCA - Toxic Substances Control Act (United States); UN - United Nations; UNRTDG - United Nations Recommendations on the Transport of Dangerous Goods; vPvB - Very Persistent and Very Bioaccumulative; WHMIS - Workplace Hazardous Materials Information System

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.

JP / EN