SAFETY DATA SHEET
Buprenorphine Liquid Formulation

SECTION 1: Identification of the substance/mixture and of the company/undertaking

1.1 Product identifier
   Trade name: Buprenorphine Liquid Formulation

1.2 Relevant identified uses of the substance or mixture and uses advised against
   Use of the Substance/Mixture: Pharmaceutical

1.3 Details of the supplier of the safety data sheet
   Company: MSD
   117 16th Road
   07033 Halfway house, Midrand, South Africa
   Telephone: +27 11 655 3000
   Telefax: 908-735-1496
   E-mail address of person responsible for the SDS: EHSDATASTEWARD@msd.com

1.4 Emergency telephone number
   1-908-423-6000

SECTION 2: Hazards identification

2.1 Classification of the substance or mixture
   Classification (REGULATION (EC) No 1272/2008)
   Not a hazardous substance or mixture.

2.2 Label elements
   Labelling (REGULATION (EC) No 1272/2008)
   Not a hazardous substance or mixture.

2.3 Other hazards
   None known.

SECTION 3: Composition/information on ingredients

3.2 Mixtures
   Components
<table>
<thead>
<tr>
<th>Chemical name</th>
<th>CAS-No. EC-No. Index-No. Registration number</th>
<th>Classification</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buprenorphine Hydrochloride</td>
<td>53152-21-9</td>
<td>Acute Tox.3; H301</td>
<td>&gt;= 0.025 - &lt;</td>
</tr>
</tbody>
</table>
SECTION 4: First aid measures

4.1 Description of first aid measures

Protection of first-aiders: No special precautions are necessary for first aid responders.

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.

4.2 Most important symptoms and effects, both acute and delayed

None known.

4.3 Indication of any immediate medical attention and special treatment needed

Treatment: Treat symptomatically and supportively.

SECTION 5: Firefighting measures

5.1 Extinguishing media

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

Unsuitable extinguishing media: None known.

5.2 Special hazards arising from the substance or mixture

Specific hazards during firefighting: Exposure to combustion products may be a hazard to health.

Hazardous combustion products: Carbon oxides

5.3 Advice for firefighters

Special protective equipment: Wear self-contained breathing apparatus for firefighting if nec-
for firefighters

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.

SECTION 6: Accidental release measures

6.1 Personal precautions, protective equipment and emergency procedures

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

6.2 Environmental precautions

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.

6.3 Methods and material for containment and cleaning up

Methods for cleaning up:
Soak up with inert absorbent material.
For large spills, provide dyking or other appropriate containment to keep material from spreading. If dyked 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.

6.4 Reference to other sections

See sections: 7, 8, 11, 12 and 13.

SECTION 7: Handling and storage

7.1 Precautions for safe 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.
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.

7.2 Conditions for safe storage, including any incompatibilities
Requirements for storage areas and containers: Keep in properly labelled containers. Store in accordance with the particular national regulations.
Advice on common storage: Do not store with the following product types: Strong oxidizing agents

7.3 Specific end use(s)
Specific use(s): No data available

SECTION 8: Exposure controls/personal protection

8.1 Control parameters

<table>
<thead>
<tr>
<th>Components</th>
<th>CAS-No.</th>
<th>Value type (Form of exposure)</th>
<th>Control parameters</th>
<th>Basis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buprenorphine Hydrochloride</td>
<td>53152-21-9</td>
<td>TWA</td>
<td>0.2 µg/m^3 (OEB 5)</td>
<td>Internal</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Wipe limit</td>
<td>2 µg/100 cm^2</td>
<td>Internal</td>
</tr>
</tbody>
</table>

8.2 Exposure controls

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
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.
Material: Chemical-resistant gloves

Remarks: Consider double gloving.

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.

Respiratory protection: No personal respiratory protective equipment normally required.

SECTION 9: Physical and chemical properties

9.1 Information on basic physical and chemical properties

Appearance: liquid

Colour: No data available

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: No data available

Evaporation rate: No data available

Flammability (solid, gas): Not applicable

Upper explosion limit / Upper flammability limit: No data available

Lower explosion limit / Lower flammability limit: No data available

Vapour pressure: No data available

Relative vapour density: No data available

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 : No data available

Explosive properties : Not explosive

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

9.2 Other information
Flammability (liquids) : No data available

Particle size : Not applicable

SECTION 10: Stability and reactivity

10.1 Reactivity
Not classified as a reactivity hazard.

10.2 Chemical stability
Stable under normal conditions.

10.3 Possibility of hazardous reactions
Hazardous reactions : Can react with strong oxidizing agents.

10.4 Conditions to avoid
Conditions to avoid : None known.

10.5 Incompatible materials
Materials to avoid : Oxidizing agents

10.6 Hazardous decomposition products
No hazardous decomposition products are known.

SECTION 11: Toxicological information

11.1 Information on toxicological effects
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
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</table>

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

Test Type: Fertility
Species: Rabbit
Application Route: Intravenous
Fertility: LOAEL: 0,2 mg/kg body weight
Result: Postimplantation loss.

Effects on foetal development:
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

SECTION 12: Ecological information

12.1 Toxicity

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 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

Toxicity to fish (Chronic toxicity):
NOEC: 0,137 mg/l
Exposure time: 28 d
Species: Pimephales promelas (fathead minnow)
Method: OECD Test Guideline 210

Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity):
NOEC: 0,883 mg/l
Exposure time: 21 d
Species: Daphnia magna (Water flea)
Method: OECD Test Guideline 211

LOEC: 1,95 mg/l
Exposure time: 21 d
Species: Daphnia magna (Water flea)
Method: OECD Test Guideline 211
12.2 Persistence and degradability

Components:

Buprenorphine Hydrochloride:
Biodegradability: Result: Not readily biodegradable.

12.3 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

12.4 Mobility in soil

Components:

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

12.5 Results of PBT and vPvB assessment
Not relevant

12.6 Other adverse effects
No data available

SECTION 13: Disposal considerations

13.1 Waste treatment methods
Product:
Dispose of in accordance with local regulations.
According to the European Waste Catalogue, Waste Codes are not product specific, but application specific.
Waste codes should be assigned by the user, preferably in discussion with the waste disposal authorities.

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

14.1 UN number
Not regulated as a dangerous good

14.2 UN proper shipping name
Not regulated as a dangerous good

14.3 Transport hazard class(es)
Not regulated as a dangerous good
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</tr>
</thead>
</table>

14.4 Packing group
Not regulated as a dangerous good

14.5 Environmental hazards
Not regulated as a dangerous good

14.6 Special precautions for user
Not applicable

14.7 Transport in bulk according to Annex II of Marpol and the IBC Code
Remarks: Not applicable for product as supplied.

SECTION 15: Regulatory information

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

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

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

15.2 Chemical safety assessment
A Chemical Safety Assessment has not been carried out.

SECTION 16: Other information

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

Full text of H-statements

- **H301**: Toxic if swallowed.
- **H336**: May cause drowsiness or dizziness.
- **H360DI**: May damage the unborn child. Suspected of damaging fertility.
- **H411**: Toxic to aquatic life with long lasting effects.

Full text of other abbreviations

- **Acute Tox.**: Acute toxicity
- **Aquatic Chronic**: Long-term (chronic) aquatic hazard
- **Repr.**: Reproductive toxicity
- **STOT SE**: Specific target organ toxicity - single exposure

ADN - European Agreement concerning the International Carriage of Dangerous Goods by Inland Waterways; ADR - European Agreement concerning the International Carriage of Dangerous Goods by Road; AICS - Australian Inventory of Chemical Substances; ASTM - American Society for the Testing of Materials; bw - Body weight; CLP - Classification Labelling Packaging Regulation; Regulation (EC) No 1272/2008; CMR - Carcinogen, Mutagen or Reproductive Toxicant; DIN - Standard of the German Institute for Standardisation; DSL - Domestic Substances List (Canada); ECHA - European Chemicals Agency; EC-Number - European Community number; ECx - Concentration associated with x% response; ELx - Loading rate associated with x% response;
Further information


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.

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