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

1.1 Product identifier

   Trade name: Alvimopan 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
   1685 Halfway house, Midrand, South Africa

   Telephone: +27 11 655 3000

   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.

   Additional Labelling
   EUH210 Safety data sheet available on request.

2.3 Other hazards

   This substance/mixture contains no components considered to be either persistent, bioaccumulative and toxic (PBT), or very persistent and very bioaccumulative (vPvB) at levels of 0.1% or higher.
   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

3.2 Mixtures

<table>
<thead>
<tr>
<th>Components</th>
<th>Chemical name</th>
<th>CAS-No.</th>
<th>Classification</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Alvimopan</td>
<td>170098-38-1</td>
<td>Acute Tox. 4; H302</td>
<td>&gt;= 1 - &lt; 10</td>
</tr>
</tbody>
</table>

For explanation of abbreviations see section 16.

SECTION 4: First aid measures

4.1 Description of 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.

**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. Get medical attention if symptoms occur.

**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 if symptoms occur. Rinse mouth thoroughly with water.

4.2 Most important symptoms and effects, both acute and delayed

**Risks**: Contact with dust can cause mechanical irritation or drying of the skin. Dust contact with the eyes can lead to mechanical irritation.

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
5.2 Special hazards arising from the substance or mixture
Specific hazards during firefighting:
- 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.
- Exposure to combustion products may be a hazard to health.

Hazardous combustion products:
- Carbon oxides

5.3 Advice for firefighters
- Wear self-contained breathing apparatus for firefighting if necessary. Use personal protective equipment.
- 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
- Follow safe handling advice (see section 7) and personal protective equipment recommendations (see section 8).

6.2 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.

6.3 Methods and material 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 deter-
mine 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:
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:
Use only with adequate ventilation.

Advice on safe handling:
Do not breathe dust.
Handle in accordance with good industrial hygiene and safety practice, based on the results of the workplace exposure assessment
Minimize dust generation and accumulation.
Keep container closed when not in use.
Keep away from heat and sources of ignition.
Take precautionary measures against static discharges.
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.

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>Alvimopan</td>
<td>170098-38-1</td>
<td>TWA</td>
<td>10 µg/m³</td>
<td>Internal</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Wipe limit</td>
<td>100 µg/100 cm²</td>
<td>Internal</td>
</tr>
</tbody>
</table>
8.2 Exposure controls

**Engineering measures**
- Ensure adequate ventilation, especially in confined areas.
- Minimize workplace exposure concentrations.
- Apply measures to prevent dust explosions.
- Ensure that dust-handling systems (such as exhaust ducts, dust collectors, vessels, and processing equipment) are designed in a manner to prevent the escape of dust into the work area (i.e., there is no leakage from the equipment).

**Personal protective equipment**
- **Eye protection**: Wear the following personal protective equipment:
  - Safety goggles
- **Hand protection**: Chemical-resistant gloves
- **Skin and body protection**: Skin should be washed after contact.
- **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 (P)

**SECTION 9: Physical and chemical properties**

9.1 Information on basic physical and chemical properties

- **Appearance**: powder
- **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**: Not applicable
- **Evaporation rate**: No data available
- **Flammability (solid, gas)**: May form explosive dust-air mixture during processing, handling or other means.
- **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

Density : No data available

Solubility(ies)
Water solubility : No data available
Partition coefficient: n-octanol/water : No data available

Auto-ignition temperature : No data available

Decomposition temperature : No data available

Viscosity
Viscosity, dynamic : No data available
Viscosity, kinematic : No data available

Explosive properties : Not explosive

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

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 : May form explosive dust-air mixture during processing, handling or other means. Can react with strong oxidizing agents.

10.4 Conditions to avoid
Conditions to avoid : Heat, flames and sparks. Avoid dust formation.

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.

Product:
Acute oral toxicity: Acute toxicity estimate: > 2.000 mg/kg
Method: Calculation method

Components:

Alvimopan:
Acute oral toxicity: LD50 (Rat): > 500 mg/kg
LD50 (Mouse): > 4.000 mg/kg
Acute dermal toxicity: LD50 (Mouse): > 2.000 mg/kg
Acute toxicity (other routes of administration): LD50 (Rat): > 20 mg/kg
Application Route: Intravenous
Remarks: No significant adverse effects were reported

Skin corrosion/irritation
Not classified based on available information.

Components:

Alvimopan:
Species: Rabbit
Result: Mild skin irritation

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

Components:

Alvimopan:
Species: Rabbit
Result: Mild eye irritation

Respiratory or skin sensitisation

Skin sensitisation
Not classified based on available information.

Respiratory sensitisation
Not classified based on available information.
Components:
Alvimopan:
Test Type: Maximisation Test
Exposure routes: Dermal
Result: negative

Germ cell mutagenicity
Not classified based on available information.

Components:
Alvimopan:
Genotoxicity in vitro:
Test Type: Bacterial reverse mutation assay (AMES)
Result: negative
Test Type: Chromosome aberration test in vitro
Result: negative
Test Type: In vitro mammalian cell gene mutation test
Test system: mouse lymphoma cells
Result: negative

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

Carcinogenicity
Not classified based on available information.

Components:
Alvimopan:
Species: Rat
Application Route: Oral
Exposure time: 2 Years
NOAEL: 500 mg/kg body weight
Result: negative

Species: Mouse
Application Route: Oral
Exposure time: 2 Years
LOAEL: 4,000 mg/kg body weight
Result: positive
Target Organs: Bone, Skin
Remarks: Benign and malignant tumor(s)
Adverse effects were observed in females only. There is no evidence that these findings are relevant to humans.

Reproductive toxicity
Not classified based on available information.
Components:

Alvimopan:

Effects on fertility:
- Test Type: Fertility/early embryonic development
  - Species: Rat
  - Application Route: Intravenous injection
  - Fertility: NOAEL: 5 mg/kg body weight
  - Result: No effects on fertility

- Test Type: Fertility/early embryonic development
  - Species: Rat
  - Application Route: Oral
  - Fertility: NOAEL: 200 mg/kg body weight
  - Result: No effects on fertility

- Test Type: Fertility/early embryonic development
  - Species: Rabbit
  - Application Route: Intravenous
  - Fertility: NOAEL: 15 mg/kg body weight
  - Result: No effects on fertility

Effects on foetal development:
- Test Type: Embryo-foetal development
  - Species: Rat
  - Application Route: Oral
  - Developmental Toxicity: NOAEL: 100 mg/kg body weight

- Test Type: Embryo-foetal development
  - Species: Rat
  - Application Route: Oral
  - Developmental Toxicity: LOAEL: 200 mg/kg body weight
  - Result: Embryo-foetal toxicity

- Test Type: Embryo-foetal development
  - Species: Rat
  - Application Route: Intravenous injection
  - Developmental Toxicity: NOAEL: 10 mg/kg body weight
  - Result: No significant adverse effects were reported

- Test Type: Embryo-foetal development
  - Species: Rabbit
  - Application Route: Intravenous injection
  - Developmental Toxicity: NOAEL: 15 mg/kg body weight
  - Result: No significant adverse effects were reported

STOT - single exposure
Not classified based on available information.

STOT - repeated exposure
Not classified based on available information.

Repeated dose toxicity

Components:

Alvimopan:
SAFETY DATA SHEET
Alvimopan Formulation

Species : Mouse
NOAEL : 1000 mg/kg
Application Route : Oral
Exposure time : 13 Weeks
Remarks : No significant adverse effects were reported

Species : Dog
NOAEL : 1000 mg/kg
Application Route : Oral
Exposure time : 39 Weeks
Remarks : No significant adverse effects were reported

Species : Rat
NOAEL : 500 mg/kg
Application Route : Oral
Exposure time : 1 yr
Remarks : No significant adverse effects were reported

Species : Dog
NOAEL : 2 mg/kg
Application Route : Intravenous
Exposure time : 1 Months
Remarks : No significant adverse effects were reported

Aspiration toxicity
Not classified based on available information.

Experience with human exposure

Components:

Alvimopan:

Ingestion : Symptoms: stomach discomfort, Gastrointestinal disturbance, Nausea, Vomiting, Abdominal pain

SECTION 12: Ecological information

12.1 Toxicity

Components:

Alvimopan:

Toxicity to fish : LC50 (Pimephales promelas (fathead minnow)): > 17 mg/l
Exposure time: 96 h
Method: OECD Test Guideline 203
Remarks: No toxicity at the limit of solubility

Toxicity to daphnia and other aquatic invertebrates : EC50 (Daphnia magna (Water flea)): > 17 mg/l
Exposure time: 48 h
Method: OECD Test Guideline 202
Remarks: No toxicity at the limit of solubility

Toxicity to algae/aquatic plants : EC50 (Scenedesmus subspicatus): > 17 mg/l
Exposure time: 72 h
Method: OECD Test Guideline 201
12.2 Persistence and degradability

Components:

Alvimopan:

Biodegradability: Result: Not readily biodegradable.
Biodegradation: 4%
Exposure time: 28 d

12.3 Bioaccumulative potential

Components:

Alvimopan:

Partition coefficient: n-octanol/water: log Pow: 0.52

12.4 Mobility in soil

No data available

12.5 Results of PBT and vPvB assessment

Product:
Assessment: This substance/mixture contains no components considered to be either persistent, bioaccumulative and toxic (PBT), or very persistent and very bioaccumulative (vPvB) at levels of 0.1% or higher.

12.6 Other adverse effects

Product:
Endocrine disrupting potential: The substance/mixture does not contain components considered to have endocrine disrupting properties according to REACH Article 57(f) or Commission Delegated regulation (EU) 2017/2100 or Commission Regulation (EU) 2018/605 at levels of 0.1% or higher.
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

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
SAFETY DATA SHEET
Alvimopan Formulation

Version: 1.12  Revision Date: 09.04.2021  SDS Number: 643704-00013  Date of last issue: 10.10.2020
Date of first issue: 02.05.2016

are highlighted in the body of this document by two vertical lines.

Full text of H-Statements
H302 : Harmful if swallowed.

Full text of other abbreviations
Acute Tox. : Acute toxicity
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; AIIC - Australian Inventory of Industrial Chemicals; 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; Emergency Schedule; ENCS - Existing and New Chemical Substances (Japan); ErCx - Concentration associated with x% growth rate response; 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 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; NO(A)EC - No Observed (Adverse) Effect Concentration; NO(A)EL - No Observed (Adverse) Effect Level; NOELR - No Observable Effect Loading Rate; NZIoC - New Zealand Inventory of Chemicals; OECD - Organization of 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; RID - Regulations concerning the International Carriage of Dangerous Goods by Rail; SADT - Self-Accelerating Decomposition Temperature; SDS - Safety Data Sheet; SVHC - Substance of very high concern; TCSI - Taiwan Chemical Substance Inventory; 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

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.

ZA / EN