SECTION 1. PRODUCT AND COMPANY IDENTIFICATION

Product name : Asenapine Formulation

Manufacturer or supplier's details
Company : Organon & Co.
Address : 30 Hudson Street, 33rd floor
          Jersey City, New Jersey, U.S.A 07302
Telephone : 551-430-6000
Emergency telephone : 215-631-6999
E-mail address : EHSSTEWARD@organon.com

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

SECTION 2. HAZARDS IDENTIFICATION

GHS Classification
Acute toxicity (Oral) : Category 3
Acute toxicity (Inhalation) : Category 4
Reproductive toxicity : Category 2
Specific target organ toxicity - single exposure (Oral) : Category 1 (Central nervous system, Cardio-vascular system)
Specific target organ toxicity - repeated exposure (Oral) : Category 1 (Central nervous system)
Short-term (acute) aquatic hazard : Category 1
Long-term (chronic) aquatic hazard : Category 1

GHS label elements
Hazard pictograms :

Signal Word : Danger
Hazard Statements : H301 Toxic if swallowed. H332 Harmful if inhaled.
Precautionary Statements:

**Prevention:**
P201 Obtain special instructions before use.
P202 Do not handle until all safety precautions have been read and understood.
P260 Do not breathe dust.
P264 Wash skin thoroughly after handling.
P270 Do not eat, drink or smoke when using this product.
P271 Use only outdoors or in a well-ventilated area.
P273 Avoid release to the environment.
P280 Wear protective gloves/protective clothing/eye protection/face protection.

**Response:**
P301 + P310 + P330 IF SWALLOWED: Immediately call a POISON CENTER/doctor. Rinse mouth.
P304 + P340 + P312 IF INHALED: Remove person to fresh air and keep comfortable for breathing. Call a POISON CENTER/doctor if you feel unwell.
P308 + P311 IF exposed or concerned: Call a POISON CENTER/doctor.
P391 Collect spillage.

**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

**Substance / Mixture:** Mixture

<table>
<thead>
<tr>
<th>Chemical name</th>
<th>CAS-No.</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
</table>

### SECTION 4. FIRST AID MEASURES
SAFETY DATA SHEET
Asenapine Formulation

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. If not breathing, give artificial respiration. If breathing is difficult, give oxygen. 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. Call a physician or poison control center immediately. Rinse mouth thoroughly with water. Never give anything by mouth to an unconscious person.

Most important symptoms and effects, both acute and delayed: Toxic if swallowed. Harmful if inhaled. Suspected of damaging fertility. Suspected of damaging the unborn child. Causes damage to organs if swallowed. Causes damage to organs through prolonged or repeated exposure if swallowed. 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. FIRE-FIGHTING MEASURES


Unsuitable extinguishing media: None known.

Specific hazards during fire fighting: 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.


Specific extinguishing methods: Use extinguishing measures that are appropriate to local circumstances and the surrounding environment. Use water spray to cool unopened containers.
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 breathe dust. Do not swallow. Avoid contact with eyes. Avoid prolonged or repeated contact with skin. Wash skin thoroughly after handling. Handle in accordance with good industrial hygiene and safety practice, based on the results of the workplace exposure assessment. Keep container tightly closed. 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. Do not eat, drink or smoke when using this product.
Take care to prevent spills, waste and minimize release to the environment.

**Conditions for safe storage :**
- Keep in properly labeled containers.
- Store locked up.
- Keep tightly closed.
- Keep in a cool, well-ventilated place.
- Store in accordance with the particular national regulations.

**Materials to avoid :**
- Do not store with the following product types:
  - Strong oxidizing agents
  - Organic peroxides
  - Explosives
  - Gases

### SECTION 8. EXPOSURE CONTROLS/PERSO[NAL PROTECTION

#### Ingredients 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>trans-5-Chloro-2,3,3a,12b-tetrahydro-2-methyl-1H-dibenz[2,3;6,7]oxepino[4,5-c]pyrrole maleate</td>
<td>85650-56-2</td>
<td>TWA</td>
<td>1 µg/m³ (OEB 4)</td>
<td>Internal</td>
</tr>
</tbody>
</table>

Further information: Skin

- Wipe limit 10 µg/100 cm² Internal

#### Engineering measures : Containment technologies suitable for controlling compounds are required to control at source and to prevent migration of the compound to uncontrolled areas (e.g., vacuum conveying from a closed system, packout head with inflatable seal from stationary container, ventilated enclosure, etc.).
- All engineering controls should be implemented by facility design and operated in accordance with GMP principles to protect products, workers, and the environment.
- Essentially no open handling permitted.
- Use closed processing systems or containment technologies.

#### 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**
- Material: Chemical-resistant gloves

**Eye protection**
- Remarks: Consider double gloving.
- 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.

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.

SECTION 9. PHYSICAL AND CHEMICAL PROPERTIES

Appearance: powder
Color: white to off-white
Odor: odorless
Odor 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
Vapor pressure: Not applicable
Relative vapor density: Not applicable
Relative density: No data available
SAFETY DATA SHEET
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Density: No data available

Solubility(ies)
  Water solubility: No data available

Partition coefficient: n-octanol/water: Not applicable

Autoignition 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

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

Acute toxicity
  Toxic if swallowed.
  Harmful if inhaled.

Product:
  Acute oral toxicity: Acute toxicity estimate: 238,4 mg/kg
    Method: Calculation method

  Acute inhalation toxicity: Acute toxicity estimate: 1,08 mg/l
    Exposure time: 4 h
    Test atmosphere: dust/mist
    Method: Calculation method
Components:

trans-5-Chloro-2,3,3a,12b-tetrahydro-2-methyl-1H-dibenz[2,3:6,7]oxepino[4,5-c]pyrrole maleate:

Acute oral toxicity: LD50 (Rat): 110 - 178 mg/kg
LD50 (Dog): > 200 mg/kg
Remarks: No mortality observed at this dose.

Acute inhalation toxicity: LC50 (Rat): 0.5 - 2 mg/l
Exposure time: 1 h
Test atmosphere: dust/mist

Acute toxicity (other routes of administration): LD50 (Rat): > 200 mg/kg
Application Route: Intravenous
Target Organs: Central nervous system
Remarks: No mortality observed at this dose.

Skin corrosion/irritation
Not classified based on available information.

Components:

trans-5-Chloro-2,3,3a,12b-tetrahydro-2-methyl-1H-dibenz[2,3:6,7]oxepino[4,5-c]pyrrole maleate:
Remarks: No data available

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

Components:

trans-5-Chloro-2,3,3a,12b-tetrahydro-2-methyl-1H-dibenz[2,3:6,7]oxepino[4,5-c]pyrrole maleate:
Remarks: No data available

Respiratory or skin sensitization

Skin sensitization
Not classified based on available information.

Respiratory sensitization
Not classified based on available information.

Components:

trans-5-Chloro-2,3,3a,12b-tetrahydro-2-methyl-1H-dibenz[2,3:6,7]oxepino[4,5-c]pyrrole maleate:
Species: Guinea pig
Result: Not a skin sensitizer.

Germ cell mutagenicity
Not classified based on available information.
Components:

trans-5-Chloro-2,3,3a,12b-tetrahydro-2-methyl-1H-dibenz[2,3:6,7]oxepino[4,5-c]pyrrole malate:

Genotoxicity in vitro:
- Test Type: Bacterial reverse mutation assay (AMES)
  Result: negative
- Test Type: Mouse Lymphoma
  Result: negative
- Test Type: sister chromatid exchange assay
  Result: negative
- Test Type: Chromosomal aberration
  Test system: Human lymphocytes
  Result: negative

Genotoxicity in vivo:
- Test Type: Micronucleus test
  Species: Rat
  Application Route: Oral
  Result: negative

Carcinogenicity
Not classified based on available information.

Components:

trans-5-Chloro-2,3,3a,12b-tetrahydro-2-methyl-1H-dibenz[2,3:6,7]oxepino[4,5-c]pyrrole malate:

Species: Mouse
Application Route: Subcutaneous
Exposure time: 89 - 98 weeks
Result: negative

Species: Rat
Application Route: Subcutaneous
Exposure time: 100 - 106 weeks
Result: negative

Reproductive toxicity
Suspected of damaging fertility. Suspected of damaging the unborn child.

Components:

trans-5-Chloro-2,3,3a,12b-tetrahydro-2-methyl-1H-dibenz[2,3:6,7]oxepino[4,5-c]pyrrole malate:

Effects on fertility:
- Test Type: One-generation reproduction toxicity study
  Species: Rat
  Application Route: Oral
  Fertility: LOAEL: 1,0 mg/kg body weight
  Symptoms: Reduced maternal body weight gain., Reduced offspring weight gain., Effects on fertility., Effects on F1 offspring.
  Result: Embryotoxic effects and adverse effects on the
Effects on fetal development:
- Test Type: Embryo-fetal development
- Species: Rabbit
- Application Route: Oral
- Developmental Toxicity: LOAEL: 30 mg/kg body weight
- Result: Embryotoxic effects and adverse effects on the offspring were detected only at high maternally toxic doses, No teratogenic effects.
- Test Type: Embryo-fetal development
- Species: Rabbit
- Application Route: Intravenous injection
- Developmental Toxicity: NOAEL: 0.626 mg/kg body weight
- Result: No teratogenic effects.

Reproductive toxicity - Assessment:
- Some evidence of adverse effects on sexual function and fertility, based on animal experiments., Some evidence of adverse effects on development, based on animal experiments.

STOT-single exposure
Causes damage to organs (Central nervous system, Cardio-vascular system) if swallowed.

Components:
trans-5-Chloro-2,3,3a,12b-tetrahydro-2-methyl-1H-dibenz[2,3:6,7]oxepino[4,5-c]pyrrole maleate:
- Routes of exposure: Oral
- Target Organs: Central nervous system, Cardio-vascular system
- Assessment: Causes damage to organs.

STOT-repeated exposure
Causes damage to organs (Central nervous system) through prolonged or repeated exposure if swallowed.

Components:
trans-5-Chloro-2,3,3a,12b-tetrahydro-2-methyl-1H-dibenz[2,3:6,7]oxepino[4,5-c]pyrrole maleate:
- Routes of exposure: Ingestion
- Target Organs: Central nervous system
- Assessment: Causes damage to organs through prolonged or repeated exposure.

Repeated dose toxicity

Components:
trans-5-Chloro-2,3,3a,12b-tetrahydro-2-methyl-1H-dibenz[2,3:6,7]oxepino[4,5-c]pyrrole maleate:
- Species: Rat
- LOAEL: 0.6 mg/kg
- Application Route: Oral
Exposure time : 52 Weeks  
Target Organs : Central nervous system  
Symptoms : constriction of pupils  
Species : Rat  
LOAEL : 0,1 mg/kg  
Application Route : Intravenous  
Exposure time : 14 Weeks  
Symptoms : constriction of pupils, Lachrymation  
Species : Rat  
LOAEL : 0,5 mg/kg  
Application Route : Subcutaneous  
Exposure time : 13 Weeks  
Target Organs : Central nervous system  
Species : Dog  
LOAEL : > 1,25 mg/kg  
Application Route : Oral  
Exposure time : 13 - 52 Weeks  
Target Organs : Central nervous system  
Symptoms : constriction of pupils, Tremors, Irritability

**Aspiration toxicity**
Not classified based on available information.

**Components:**

trans-5-Chloro-2,3,3a,12b-tetrahydro-2-methyl-1H-dibenz[2,3:6,7]oxepino[4,5-c]pyrrole maleate:
Not applicable

**Experience with human exposure**

**Components:**

trans-5-Chloro-2,3,3a,12b-tetrahydro-2-methyl-1H-dibenz[2,3:6,7]oxepino[4,5-c]pyrrole maleate:

Ingestion : Symptoms: restlessness, Drowsiness, Dizziness, decrease in heart rate, hypotension

**SECTION 12. ECOLOGICAL INFORMATION**

**Ecotoxicity**

**Components:**

trans-5-Chloro-2,3,3a,12b-tetrahydro-2-methyl-1H-dibenz[2,3:6,7]oxepino[4,5-c]pyrrole maleate:

Toxicity to fish : LC50 (Cyprinus carpio (Carp)): 0,53 mg/l  
Exposure time: 96 h  
Method: OECD Test Guideline 203

Toxicity to algae/aquatic : EC50 (Pseudokirchneriella subcapitata (green algae)): 0,27
plants  
mg/l  
Exposure time: 72 h  
Method: OECD Test Guideline 201

NOEC (Pseudokirchneriella subcapitata (green algae)): 0,084 mg/l  
Exposure time: 72 h  
Method: OECD Test Guideline 201

M-Factor (Acute aquatic toxicity): 1
Toxicity to fish (Chronic toxicity): NOEC (Pimephales promelas (fathead minnow)): 0,04 mg/l  
Exposure time: 21 d

Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity): NOEC (Daphnia magna (Water flea)): 0,00086 mg/l  
Exposure time: 21 d  
Method: OECD Test Guideline 211

M-Factor (Chronic aquatic toxicity): 100
Toxicity to microorganisms: EC50: 37 mg/l  
Exposure time: 3 h  
Test Type: Respiration inhibition  
Method: OECD Test Guideline 209

NOEC: 10 mg/l  
Exposure time: 3 h  
Test Type: Respiration inhibition  
Method: OECD Test Guideline 209

Persistence and degradability
No data available

Bioaccumulative potential

Components:
trans-5-Chloro-2,3,3a,12b-tetrahydro-2-methyl-1H-dibenz[2,3:6,7]oxepino[4,5-c]pyrrole maleate:
Bioaccumulation: Species: Cyprinus carpio (Carp)  
Bioconcentration factor (BCF): 2.424

Partition coefficient: n-octanol/water: log Pow: 4,9

Mobility in soil
No data available

Other adverse effects
No data available

SECTION 13. DISPOSAL CONSIDERATIONS

Disposal methods
Waste from residues: Dispose of in accordance with local regulations.
SECTION 14. TRANSPORT INFORMATION

International Regulations

UNRTDG
UN number : UN 2811
Proper shipping name : TOXIC SOLID, ORGANIC, N.O.S.
(trans-5-Chloro-2,3,3a,12b-tetrahydro-2-methyl-1H-dibenzo[2,3:6,7]oxepino[4,5-c]pyrrole maleate)
Class : 6.1
Packing group : III
Labels : 6.1

IATA-DGR
UN/ID No. : UN 2811
Proper shipping name : Toxic solid, organic, n.o.s.
(trans-5-Chloro-2,3,3a,12b-tetrahydro-2-methyl-1H-dibenzo[2,3:6,7]oxepino[4,5-c]pyrrole maleate)
Class : 6.1
Packing group : III
Labels : Toxic
Packing instruction (cargo aircraft) : 677
Packing instruction (passenger aircraft) : 670

IMDG-Code
UN number : UN 2811
Proper shipping name : TOXIC SOLID, ORGANIC, N.O.S.
(trans-5-Chloro-2,3,3a,12b-tetrahydro-2-methyl-1H-dibenzo[2,3:6,7]oxepino[4,5-c]pyrrole maleate)
Class : 6.1
Packing group : III
Labels : 6.1
EmS Code : F-A, S-A
Marine pollutant : yes

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

Special precautions for user
The transport classification(s) provided herein are for informational purposes only, and solely based upon the properties of the unpackaged material as it is described within this Safety Data Sheet. Transportation classifications may vary by mode of transportation, package sizes, and variations in regional or country regulations.

SECTION 15. REGULATORY INFORMATION

Safety, health and environmental regulations/legislation specific for the substance or mixture
Argentina. Carcinogenic Substances and Agents : Not applicable
Control of precursors and essential chemicals for the preparation of drugs. : Not applicable

**International Regulations**

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

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

**SECTION 16. OTHER INFORMATION**

**Further information**


**Full text of other abbreviations**

AIIIC - 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; 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.

AR / Z8