SECTION 1. PRODUCT AND COMPANY IDENTIFICATION

Product name : Mirtazapine Solid Formulation

Manufacturer or supplier’s details
Company : MSD
Address : 855 Leandro N. Alem St., 8 Floor,
          Buenos Aires, Argentina C1001AFB
Telephone : 908-740-4000
Emergency telephone : 1-908-423-6000
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
Acute toxicity (Oral) : Category 5
Reproductive toxicity : Category 2
Specific target organ toxicity - repeated exposure (Oral) : Category 2 (Nervous system)
Short-term (acute) aquatic hazard : Category 3
Long-term (chronic) aquatic hazard : Category 3

GHS label elements
Hazard pictograms : 
Signal Word : Warning
Hazard Statements : H303 May be harmful if swallowed.
                  H361fd Suspected of damaging fertility. Suspected of damaging the unborn child.
                  H373 May cause damage to organs (Nervous system) through prolonged or repeated exposure if swallowed.
H412 Harmful to aquatic life with long lasting effects.

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.
P273 Avoid release to the environment.
P280 Wear protective gloves/protective clothing/eye protection/face protection.

Response:
P312 Call a POISON CENTER/doctor if you feel unwell.

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

Components

<table>
<thead>
<tr>
<th>Chemical name</th>
<th>CAS-No.</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(+/-)-1,2,3,4,10,14b-Hexahydro-2-methylpyrazino[2,1-a]pyrido[2,3-c][2]benzazepine</td>
<td>85650-52-8</td>
<td>&gt;= 10 &lt;- 20</td>
</tr>
<tr>
<td>Starch</td>
<td>9005-25-8</td>
<td>&gt;= 10 &lt;- 20</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 be harmful if swallowed.
- Suspected of damaging fertility. Suspected of damaging the unborn child.
- May cause 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

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

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.

Hazardous combustion products:
- Carbon oxides
- Silicon 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 fire-fighters:
- 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 and personal protective equipment recommendations.

Environmental precautions:
- Discharge into the environment must be avoided.
- 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:
- Sweep up or vacuum up spillage and collect in suitable
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: Use only with adequate ventilation.

Advice on safe handling: Do not breathe dust. Do not swallow. Avoid contact with eyes. Avoid prolonged or repeated contact with skin. 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.

Conditions for safe storage: Keep in properly labeled containers. Store locked up. 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

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>(+/-)-1,2,3,4,10,14b-Hexahydro-2-methylpyrazino[2,1-a]pyrido[2,3-c][2]benzazepine</td>
<td>85650-52-8</td>
<td>TWA</td>
<td>25 µg/m³</td>
<td>Internal</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Wipe limit</td>
<td>250 µg/100 cm²</td>
</tr>
<tr>
<td>Starch</td>
<td>9005-25-8</td>
<td>CMP</td>
<td>10 mg/m³</td>
<td>AR OEL</td>
</tr>
</tbody>
</table>

Further information: A4 - Not classifiable as a human carcinogen:
Agents which cause concern that they could be carcinogenic for humans but which cannot be assessed conclusively because of a lack of data. In vitro or animal studies do not provide indications of carcinogenicity which are sufficient to classify the agent into one of the other categories., lung, Dermatitis

| TWA | 10 mg/m³ | ACGIH |

**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**

**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

**Remarks**: Choose gloves to protect hands against chemicals depending on the concentration specific to place of work. Breakthrough time is not determined for the product. Change gloves often! For special applications, we recommend clarifying the resistance to chemicals of the aforementioned protective gloves with the glove manufacturer. Wash hands before breaks and at the end of workday.

**Eye protection**: Wear the following personal protective equipment:

- Safety goggles

**Skin and body protection**: Select appropriate protective clothing based on chemical resistance data and an assessment of the local exposure potential. Skin contact must be avoided by using impervious protective clothing (gloves, aprons, boots, etc).

**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.

### SECTION 9. PHYSICAL AND CHEMICAL PROPERTIES

- **Appearance**: powder
- **Color**: No data available
- **Odor**: No data available
- **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 : No data available
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 : No data available
Relative vapor density : No data available
Relative density : No data available
Density : No data available
Solubility(ies) : No data available
  Water solubility : No data available
Partition coefficient: n-octanol/water : No data available
Autoignition temperature : No data available
Decomposition temperature : No data available
Viscosity : Not explosive
  Viscosity, dynamic : No data available
  Viscosity, kinematic : No data available
Oxidizing properties : The substance or mixture is not classified as oxidizing.
Molecular weight : No data available
Particle size : No data available

SECTION 10. STABILITY AND REACTIVITY
SAFETY DATA SHEET

Mirtazapine Solid Formulation

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
May be harmful if swallowed.

Product:
Acute oral toxicity: Acute toxicity estimate: 3.200 mg/kg
Method: Calculation method

Components:
(+/-)-1,2,3,4,10,14b-Hexahydro-2-methylpyrazino[2,1-a]pyrido[2,3-c][2]benzazepine:
Acute oral toxicity: LD50 (Rat): 320 - 490 mg/kg

Starch:
Acute oral toxicity: LD50 (Mouse): > 5.000 mg/kg

Skin corrosion/irritation
Not classified based on available information.

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

Respiratory or skin sensitization

Skin sensitization
Not classified based on available information.

Respiratory sensitization
Not classified based on available information.

Germ cell mutagenicity
Not classified based on available information.

Components:
(+/-)-1,2,3,4,10,14b-Hexahydro-2-methylpyrazino[2,1-a]pyrido[2,3-c][2]benzazepine:
Genotoxicity in vitro: Test Type: Bacterial reverse mutation assay (AMES)
SAFETY DATA SHEET
Mirtazapine Solid Formulation

Result: negative

Test Type: In vitro mammalian cell gene mutation test
Test system: Chinese hamster lung cells
Result: negative

Test Type: unscheduled DNA synthesis assay
Test system: mammalian cells
Result: negative

Test Type: sister chromatid exchange assay
Test system: mammalian cells
Result: negative

Genotoxicity in vivo:
Test Type: Micronucleus test
Species: Rat
Cell type: Bone marrow
Application Route: Oral
Result: negative

Carcinogenicity:
Not classified based on available information.

Components:
(+/-)1,2,3,4,10,14b-Hexahydro-2-methylpyrazino[2,1-a]pyrido[2,3-c][2]benzazepine:
Species: Mouse
Application Route: Oral
Exposure time: 18 month(s)
LOAEL: 200 mg/kg body weight
Result: equivocal
Target Organs: Liver

Species: Rat
Application Route: Oral
Exposure time: 2 Years
LOAEL: 20 mg/kg body weight
Result: equivocal
Target Organs: Liver, Thyroid

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

Components:
(+/-)1,2,3,4,10,14b-Hexahydro-2-methylpyrazino[2,1-a]pyrido[2,3-c][2]benzazepine:
Effects on fertility: Test Type: Fertility/early embryonic development
Species: Rat
Application Route: Oral
Fertility: LOAEL: 15 mg/kg body weight
Symptoms: Effect on estrous cycle, Increase of early resorptions.
Result: Animal testing did not show any effects on fertility.
Embryotoxic effects and adverse effects on the offspring were...
Effects on fetal development:
Test Type: Development
Species: Rat
Application Route: Oral
Developmental Toxicity: LOAEL: 100 mg/kg body weight
Result: Embryotoxic effects and adverse effects on the offspring were detected. No teratogenic effects.

Test Type: Development
Species: Rabbit
Application Route: Oral
Developmental Toxicity: NOAEL: 40 mg/kg body weight
Result: No adverse effects. 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
Not classified based on available information.

STOT-repeated exposure
May cause damage to organs (Nervous system) through prolonged or repeated exposure if swallowed.

Components:
(+/-)-1,2,3,4,10b-Hexahydro-2-methylpyrazino[2,1-a]pyrido[2,3-c][2]benzazepine:
Routes of exposure: Ingestion
Target Organs: Nervous system
Assessment: May cause damage to organs through prolonged or repeated exposure.

Repeated dose toxicity

Components:
(+/-)-1,2,3,4,10b-Hexahydro-2-methylpyrazino[2,1-a]pyrido[2,3-c][2]benzazepine:
Species: Rat
LOAEL: 120 mg/kg
Application Route: Oral
Exposure time: 13 Weeks
Target Organs: Nervous system

Species: Dog
LOAEL: 15 mg/kg
Application Route: Oral
Exposure time: 52 Weeks
Target Organs: Nervous system
Symptoms: Tremors

Species: Dog
LOAEL: 20 mg/kg
# SAFETY DATA SHEET

## Mirtazapine Solid Formulation

**Version**: 4.2  
**Revision Date**: 09/13/2019  
**SDS Number**: 51079-00014  
**Date of last issue**: 24.04.2019  
**Date of first issue**: 23.01.2015

**Application Route**: Oral  
**Exposure time**: 13 Weeks  
**Target Organs**: Nervous system, Testis  
**Symptoms**: Tremors

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

### Experience with human exposure

**Components**:

\((+/\-)\text{-1,2,3,4,10,14b-Hexahydro-2-methylpyrazino[2,1-a]pyrido[2,3-c][2]benzazepine}\):

**Ingestion**: Symptoms: Drowsiness, constipation, dry mouth, asthenia, Dizziness, Disorientation

### SECTION 12. ECOLOGICAL INFORMATION

#### Ecotoxicity

**Components**:

\((+/\-)\text{-1,2,3,4,10,14b-Hexahydro-2-methylpyrazino[2,1-a]pyrido[2,3-c][2]benzazepine}\):

**Toxicity to fish**:
- LC50 (Pimephales promelas (fathead minnow)): 6,92 mg/l  
  Exposure time: 96 h  
  Method: FDA 4.11

**Toxicity to daphnia and other aquatic invertebrates**:
- EC50 (Daphnia magna (Water flea)): 19,5 mg/l  
  Exposure time: 48 h

**Toxicity to algae/aquatic plants**:
- EC50 (Pseudokirchneriella subcapitata (green algae)): 5,7 mg/l  
  Exposure time: 72 h  
  Method: OECD Test Guideline 201

  NOEC (Pseudokirchneriella subcapitata (green algae)): 3,2 mg/l  
  Exposure time: 72 h  
  Method: OECD Test Guideline 201

**Toxicity to fish (Chronic toxicity)**:
- NOEC (Pimephales promelas (fathead minnow)): 3,6 mg/l  
  Exposure time: 31 d  
  Method: OECD Test Guideline 210

**Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity)**:
- NOEC (Daphnia magna (Water flea)): 0,32 mg/l  
  Exposure time: 21 d  
  Method: OECD Test Guideline 211

**Toxicity to microorganisms**:
- EC50 (Natural microorganism): > 1,000 mg/l  
  Exposure time: 3 h  
  Test Type: Respiration inhibition  
  Method: OECD Test Guideline 209

  NOEC (Natural microorganism): < 100 mg/l  
  Exposure time: 3 h
Persistence and degradability
No data available

Bioaccumulative potential

Components:

(±)-1,2,3,4,10b-Hexahydro-2-methylpyrazino[2,1-a]pyrido[2,3-c][2]benzazepine:

Bioaccumulation: Species: Oncorhynchus mykiss (rainbow trout)
Bioconcentration factor (BCF): 334
Method: OECD Test Guideline 305

Partition coefficient: n-octanol/water: log Pow: 2.78

Mobility in soil

Components:

(±)-1,2,3,4,10b-Hexahydro-2-methylpyrazino[2,1-a]pyrido[2,3-c][2]benzazepine:

Distribution among environmental compartments: log Koc: 4.48

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.
SECTION 15. REGULATORY INFORMATION

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

Argentina. Carcinogenic Substances and Agents Registry: 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

ACGIH: USA. ACGIH Threshold Limit Values (TLV)
AR OEL: Argentina. Occupational Exposure Limits

ACGIH / TWA: 8-hour, time-weighted average
AR OEL / CMP: TLV (Threshold Limit Value)

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.

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