1. PRODUCT AND COMPANY IDENTIFICATION

Chemical product name : Mirtazapine Solid 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
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 : 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 protec-
tion/ face protection.

Response:
P308 + P313 IF exposed or concerned: Get medical advice/
attention.

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
Important symptoms and out-
lines of the emergency as-
sumed

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, han-
dling or other means.

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>Starch</td>
<td>9005-25-8</td>
<td>&gt;= 10 - &lt; 20</td>
<td>8-98</td>
</tr>
</tbody>
</table>
| (±)-1,2,3,4,10,14b-Hexahydro-2-
methylpyrazino[2,1-a]pyrido[2,3-
c][2]benzazepine | 85650-52-8  | >= 10 - < 20           |          |

4. FIRST AID MEASURES

General advice : In the case of accident or if you feel unwell, seek medical ad-
vice 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.
SAFETY DATA SHEET

Mirtazapine Solid Formulation

Version 5.0 Revision Date: 2020/03/23 SDS Number: 50162-00015 Date of last issue: 2019/09/13 Date of first issue: 2015/01/23

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: 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.

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: 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 firefighters: In the event of fire, wear self-contained breathing apparatus. Use personal protective equipment.

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 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
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.

7. HANDLING AND STORAGE

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. 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.

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.

Storage

Conditions for safe storage: Keep in properly labelled 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.

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</th>
<th>Control parameter</th>
<th>Basis</th>
</tr>
</thead>
</table>

4 / 15
Mirtazapine Solid Formulation

(Form of exposure) | ters / Permissible concentration |
------------------|---------------------------------|
(+/−)-1,2,3,4,10,14b-Hexahydro-2-methylpyrazino[2,1-a]pyrido[2,3-c][2]benzazepine 85650-52-8 TWA 25 µg/m³ Internal
Starch 9005-25-8 TWA Wipe limit 250 µg/100 cm² Internal

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 and quantity of the hazardous substance and 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).

9. PHYSICAL AND CHEMICAL PROPERTIES

Physical state: powder
Colour: No data available
Odour: No data available
Odour Threshold: No data available
Melting point/freezing point: No data available
Boiling point, initial boiling: No data available
<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flammability (solid, gas)</td>
<td>May form explosive dust-air mixture during processing, handling or other means.</td>
</tr>
<tr>
<td>Flammability (liquids)</td>
<td>No data available</td>
</tr>
<tr>
<td>Lower explosion limit and upper explosion limit / flammability limit</td>
<td>No data available</td>
</tr>
<tr>
<td>Upper explosion limit / Upper flammability limit</td>
<td>No data available</td>
</tr>
<tr>
<td>Lower explosion limit / Lower flammability limit</td>
<td>No data available</td>
</tr>
<tr>
<td>Flash point</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Decomposition temperature</td>
<td>No data available</td>
</tr>
<tr>
<td>pH</td>
<td>No data available</td>
</tr>
<tr>
<td>Evaporation rate</td>
<td>No data available</td>
</tr>
<tr>
<td>Auto-ignition temperature</td>
<td>No data available</td>
</tr>
<tr>
<td>Viscosity</td>
<td>No data available</td>
</tr>
<tr>
<td>Viscosity, dynamic</td>
<td>No data available</td>
</tr>
<tr>
<td>Viscosity, kinematic</td>
<td>No data available</td>
</tr>
<tr>
<td>Solubility(ies)</td>
<td>No data available</td>
</tr>
<tr>
<td>Water solubility</td>
<td>No data available</td>
</tr>
<tr>
<td>Partition coefficient: n-octanol/water</td>
<td>No data available</td>
</tr>
<tr>
<td>Vapour pressure</td>
<td>No data available</td>
</tr>
<tr>
<td>Density and / or relative density</td>
<td>No data available</td>
</tr>
<tr>
<td>Relative density</td>
<td>No data available</td>
</tr>
<tr>
<td>Density</td>
<td>No data available</td>
</tr>
<tr>
<td>Relative vapour density</td>
<td>No data available</td>
</tr>
<tr>
<td>Explosive properties</td>
<td>Not explosive</td>
</tr>
<tr>
<td>Oxidizing properties</td>
<td>The substance or mixture is not classified as oxidizing.</td>
</tr>
<tr>
<td>Molecular weight</td>
<td>No data available</td>
</tr>
<tr>
<td>Particle characteristics</td>
<td>No data available</td>
</tr>
<tr>
<td>Particle size</td>
<td>No data available</td>
</tr>
</tbody>
</table>
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.

11. TOXICOLOGICAL INFORMATION

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:

Starch:
- Acute oral toxicity: LD50 (Rat): > 5,000 mg/kg
- Acute dermal toxicity: LD50 (Rabbit): > 2,000 mg/kg

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

Skin corrosion/irritation:
Not classified based on available information.

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

Components:

Starch:
- Species: Rabbit
- Result: No eye irritation
Respiratory or skin sensitisation

Skin sensitisation
Not classified based on available information.

Respiratory sensitisation
Not classified based on available information.

Components:

Starch:
Test Type: Maximisation Test
Exposure routes: Skin contact
Species: Guinea pig
Result: negative

Germ cell mutagenicity
Not classified based on available information.

Components:

Starch:
Genotoxicity in vitro: Test Type: Bacterial reverse mutation assay (AMES) Result: negative

(+/−)-1,2,3,4,10b-Hexahydro-2-methylpyrazino[2,1-a]pyrido[2,3-c][2]benzazepine:
Genotoxicity in vitro: Test Type: Bacterial reverse mutation assay (AMES) 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:

(+/−)-1,2,3,4,10b-Hexahydro-2-methylpyrazino[2,1-a]pyrido[2,3-c][2]benzazepine:
Species: Mouse
Mirtazapine Solid Formulation

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 detected.

Effects on foetal 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:

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

Exposure routes: Ingestion
Target Organs: Nervous system
Assessment: May cause damage to organs through prolonged or repeated exposure.

Repeated dose toxicity

Components:

Starch:

Species: Rat
NOAEL: >= 2,000 mg/kg
Application Route: Skin contact
Exposure time: 28 Days
Method: OECD Test Guideline 410

(+/-)-1,2,3,4,10,14b-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
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:

(+/-)-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
12. ECOLOGICAL INFORMATION

Ecotoxicity

Components:

(+/-)-1,2,3,4,10b-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
  Test Type: Respiration inhibition
  Method: OECD Test Guideline 209

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
SAFETY DATA SHEET

Mirtazapine Solid Formulation

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

Mobility in soil

Components:

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

Distribution among environmental compartments: log Koc: 4.48

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.

National Regulations
Refer to section 15 for specific national regulation.

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
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
ACGIH: USA. ACGIH Threshold Limit Values (TLV)
ACGIH / TWA: 8-hour, time-weighted average

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
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