Tibolone Formulation

1. PRODUCT AND COMPANY IDENTIFICATION

Product name : Tibolone Formulation

Manufacturer or supplier’s details
Company : MSD
Address : 199 Wenhai North Road
          HEDA, Hangzhou - Zhejiang Province - CHINA 310018
Telephone : 908-740-4000
Emergency telephone number : 86-571-87268110
E-mail address : EHSDATASTEWARD@msd.com

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

2. HAZARDS IDENTIFICATION

Emergency Overview
Appearance : powder
Colour : No data available
Odour : No data available
Suspected of causing cancer. May damage fertility. May cause damage to organs through prolonged or repeated exposure.

GHS Classification
Carcinogenicity : Category 2
Reproductive toxicity : Category 1B
Specific target organ toxicity - repeated exposure : Category 2

GHS label elements
Hazard pictograms : 
Signal word : Danger
Hazard statements : H351 Suspected of causing cancer.
                   H360F May damage fertility.
                   H373 May cause damage to organs through prolonged or repeated exposure.
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.
P280 Wear protective gloves/ protective clothing/ eye protection/ 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.

**Physical and chemical hazards**
Not classified based on available information.

**Health hazards**
Suspected of causing cancer. May damage fertility. May cause damage to organs through prolonged or repeated exposure.

**Environmental hazards**
Not classified based on available information.

**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.

### 3. COMPOSITION/INFORMATION ON INGREDIENTS

<table>
<thead>
<tr>
<th>Substance / Mixture</th>
<th>Chemical name</th>
<th>CAS-No.</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mixture</td>
<td>Starch</td>
<td>9005-25-8</td>
<td>&gt; 1 &lt;= 10</td>
</tr>
<tr>
<td></td>
<td>Tibolone</td>
<td>5630-53-5</td>
<td>&gt; 1 &lt;= 2.5</td>
</tr>
</tbody>
</table>

### 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: Suspected of causing cancer. May damage fertility. May cause damage to organs through prolonged or repeated exposure. 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

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 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.

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:
  - If sufficient ventilation is unavailable, use with local exhaust ventilation.
- Advice on safe handling:
  - Do not get on skin or clothing.
  - Do not breathe dust.
  - Do not swallow.
  - Avoid contact with eyes.
  - 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.
  - Take care to prevent spills, waste and minimize release to the environment.

Avoidance of contact:
- Oxidizing agents

Storage
- Conditions for safe storage:
  - Keep in properly labelled containers.
  - Store locked up.
  - Keep tightly closed.
  - 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.
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8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Components 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>Starch</td>
<td>9005-25-8</td>
<td>TWA</td>
<td>10 mg/m³</td>
<td>ACGIH</td>
</tr>
<tr>
<td>Tibolone</td>
<td>5630-53-5</td>
<td>TWA</td>
<td>2 µg/m³</td>
<td>Internal</td>
</tr>
</tbody>
</table>

Engineering measures: 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). If sufficient ventilation is unavailable, use with local exhaust ventilation.

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

Eye/face 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).

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.

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.

9. 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 : 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
Vapour pressure : Not applicable
Relative vapour density : Not applicable
Relative density : No data available
Density : 1 g/cm³
Solubility(ies) Water solubility : No data available
Partition coefficient: n-octanol/water : Not applicable
Auto-ignition temperature : No data available
Decomposition temperature : No data available
Viscosity : Not applicable
Viscosity, kinematic : Not applicable
Explosive properties : Not explosive
Oxidizing properties : The substance or mixture is not classified as oxidizing.
Particle size : No data available

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SAFETY DATA SHEET
according to GB/T 16483 and GB/T 17519

Version 4.4Revision Date: 09/13/2019 SDS Number: 16982-00018 Date of last issue: 2019/04/24

Date of first issue: 2014/09/30
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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

Exposure routes: Inhalation
Skin contact
Ingestion
Eye contact

Acute toxicity
Not classified based on available information.

Components:

Starch:
Acute oral toxicity: LD50 (Mouse): > 5,000 mg/kg

Tibolone:
Acute oral toxicity:
LD50 (Rat): > 2,000 mg/kg
LD50 (Mouse): > 2,000 mg/kg
LD50 (Dog): > 2,000 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 sensitisation

Skin sensitisation
Not classified based on available information.

Respiratory sensitisation
Not classified based on available information.

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

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

Test Type: Chromosome aberration test in vitro Test system: Chinese hamster ovary cells Result: negative

Test Type: Chromosome aberration test in vitro Test system: Chinese hamster fibroblasts Result: negative

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

Carcinogenicity
Suspected of causing cancer.

Components:

Tibolone:
Species: Rat Application Route: Oral Exposure time: 2 Years Result: positive Target Organs: Liver, Urinary bladder, Pituitary gland, Testes, Mammary gland, Uterus (including cervix)

Species: Mouse Application Route: Oral Exposure time: 18 Months Result: positive Target Organs: Liver, Respiratory system, Urinary bladder

Carcinogenicity - Assessment: Limited evidence of carcinogenicity in animal studies

Reproductive toxicity
May damage fertility.

Components:

Tibolone:
Effects on fertility: Test Type: Fertility Species: Rat, female Symptoms: Effects on fertility

Effects on foetal development: Test Type: Embryo-foetal development Species: Rabbit Application Route: Oral
Embryo-foetal toxicity: LOAEL: 0.07 mg/kg body weight
Symptoms: Preimplantation loss, Reduced number of viable fetuses, Malformations were observed.

Reproductive toxicity - Assessment:
Clear 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 through prolonged or repeated exposure.

Components:

Tibolone:

Target Organs: Bone, Endocrine system
Assessment: Causes damage to organs through prolonged or repeated exposure.

Repeated dose toxicity
Components:

Tibolone:

Species: Rat
NOAEL: 0.05 mg/kg
LOAEL: 0.5 mg/kg
Application Route: Oral
Exposure time: 52 Weeks
Target Organs: Endocrine system, Reproductive organs, Mammary gland, Adrenal gland, Bone

Species: Dog
NOAEL: 0.05 mg/kg
LOAEL: 0.5 mg/kg
Application Route: Oral
Exposure time: 1 yr
Target Organs: Endocrine system, Reproductive organs, Adrenal gland, Kidney

Aspiration toxicity
Not classified based on available information.

Experience with human exposure
Components:

Tibolone:

Ingestion: Symptoms: Dizziness, Headache, Blurred vision, Skin disorders, pruritis, breast tenderness, vaginitis, Abdominal pain, fluid accumulation, amenorrhea, Gastrointestinal discomfort, musculoskeletal pain, liver function change
12. ECOLOGICAL INFORMATION

Ecotoxicity

Components:

Tibolone:

Ecotoxicology Assessment
Acute aquatic toxicity: No data available
Chronic aquatic toxicity: No data available

Persistence and degradability
No data available

Bioaccumulative potential

Components:

Tibolone:
Partition coefficient: n-octanol/water: log Pow: 3.9

Mobility in soil
No data available

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
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GB 6944/12268
Not regulated as a dangerous good

Special precautions for user
Not applicable

15. REGULATORY INFORMATION

National regulatory information
Law on the Prevention and Control of Occupational Diseases

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
Sources of key data used to compile the Safety Data Sheet:

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 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
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<tr>
<th>Version</th>
<th>Revision Date</th>
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<td>4.4</td>
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</tr>
</tbody>
</table>

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

Disclaimer

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.

CN / EN