SECTION 1. PRODUCT AND COMPANY IDENTIFICATION

Product name : Tibolone Formulation

Manufacturer or supplier’s details
Company : Organon & Co.
Address : Rua Treze de Maio, 1161
          Campinas, São Paulo, Brazil  B-2220
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 in accordance with ABNT NBR 14725 Standard
Carcinogenicity : Category 2
Reproductive toxicity : Category 1B
Specific target organ toxicity - repeated exposure : Category 2 (Bone, Endocrine system)

GHS label elements in accordance with ABNT NBR 14725 Standard
Hazard pictograms
Signal Word : Danger
Hazard Statements
H351 Suspected of causing cancer.
H360F May damage fertility.
H373 May cause damage to organs (Bone, Endocrine system) through prolonged or repeated exposure.

Precautionary Statements
Prevention:
P201 Obtain special instructions before use.
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/
SAFETY DATA SHEET

Tibolone Formulation

Version 4.1  Revision Date: 16.10.2020  SDS Number: 16975-00020  Date of last issue: 23.03.2020  Date of first issue: 30.09.2014

attention.

Storage:
P405 Store locked up.

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>Classification</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Starch</td>
<td>9005-25-8</td>
<td>Carcinogenicity, Category 2, Reproductive toxicity, Category 1B, Specific target organ toxicity - repeated exposure (Bone, Endocrine system), Category 1</td>
<td>&gt; 1 - &lt;= 10</td>
</tr>
<tr>
<td>Tibolone</td>
<td>5630-53-5</td>
<td></td>
<td>&gt; 1 - &lt;= 2.5</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.

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.

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 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 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 (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 spills 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 get on skin or clothing. Do not breathe dust. Do not swallow. Avoid contact with eyes. 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.

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.

Conditions for safe storage: Keep in properly labeled 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 Organic peroxides Explosives Gases

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>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>
<tr>
<td></td>
<td></td>
<td>Wipe limit</td>
<td>20 µg/100 cm²</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

**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).

**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**: Not applicable

**Flammability (solid, gas)**: May form explosive dust-air mixture during processing, handling or other means.
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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
Density : 1 g/cm³
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

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Ingestion
Eye contact

Acute toxicity
Not classified based on available information.

Components:
Starch:
Acute oral toxicity : LD50 (Rat): > 5.000 mg/kg
Acute dermal toxicity : LD50 (Rabbit): > 2.000 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.

Components:
Starch:
Species : Rabbit
Result : No eye irritation

Respiratory or skin sensitization

Skin sensitization
Not classified based on available information.

Respiratory sensitization
Not classified based on available information.

Components:
Starch:
Test Type : Maximization Test
Routes of exposure : 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

**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 fetal development : Test Type: Embryo-fetal development
Species: Rabbit
Application Route: Oral
Embryo-fetal 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 (Bone, Endocrine system) 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:

Starch:
Species : Rat
NOAEL : >= 2.000 mg/kg
Application Route : Skin contact
Exposure time : 28 Days
Method : OECD Test Guideline 410

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 y
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, amenorhea, Gastrointestinal discomfort, musculoskeletal pain, liver function change

**SECTION 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

**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.

Domestic regulation

ANTT
Not regulated as a dangerous good

SECTION 15. REGULATORY INFORMATION

Safety, health and environmental regulations/legislation specific for the substance or mixture
National List of Carcinogenic Agents for Humans - (LINACH) : Not applicable

Brazil. List of chemicals controlled by the Federal Police : 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)
ACGIH / TWA : 8-hour, time-weighted average

AIIC - 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.

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