1. PRODUCT AND COMPANY IDENTIFICATION

Product name: Tibolone Formulation

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

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

2. HAZARDS IDENTIFICATION

Manufacture, Storage and Import of Hazardous Chemicals Rules 1989

Classification
Not classified as hazardous according to criteria laid down in Part I of Schedule-1.

GHS Classification
Carcinogenicity: Category 2
Reproductive toxicity: Category 1B
Specific target organ toxicity - repeated exposure: Category 2 (Bone, Endocrine system)

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 (Bone, Endocrine system) through prolonged or repeated exposure.

Precautionary statements:
Prevention:
P203 Obtain, read and follow all safety instructions before use.
P260 Do not breathe dust.
P280 Wear protective gloves/ protective clothing/ eye protec-

tion/ face protection.

Response:
P318 IF exposed or concerned, get medical advice.

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.

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>Starch</td>
<td>9005-25-8</td>
<td>&gt; 1 - &lt;= 10</td>
</tr>
<tr>
<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 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.

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 (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.
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.

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

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>
<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 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.

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
   Viscosity, kinematic: Not applicable
Explosive properties: Not explosive
Oxidizing properties: The substance or mixture is not classified as oxidizing.
Particle size: No data available

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.

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 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
### 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:

<table>
<thead>
<tr>
<th>Species</th>
<th>Application Route</th>
<th>Exposure time</th>
<th>Result</th>
<th>Target Organs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rat</td>
<td>Oral</td>
<td>2 Years</td>
<td>positive</td>
<td>Liver, Urinary bladder, Pituitary gland, Testes, Mammary gland, Uterus (including cervix)</td>
</tr>
<tr>
<td>Mouse</td>
<td>Oral</td>
<td>18 Months</td>
<td>positive</td>
<td>Liver, Respiratory system, Urinary bladder</td>
</tr>
</tbody>
</table>

**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 (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 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, amenorhea, 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 IMO instruments
Not applicable for product as supplied.

15. REGULATORY INFORMATION

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

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
Date format: dd.mm.yyyy

Full text of other abbreviations
- ACGIH: USA. ACGIH Threshold Limit Values (TLV)
- ACGIH / TWA: 8-hour, time-weighted average

AICL - 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.

IN / EN