SECTION 1: Identification of the substance/mixture and of the company/undertaking

1.1 Product identifier
   Trade name : Tibolone Formulation

1.2 Relevant identified uses of the substance or mixture and uses advised against
   Use of the Substance/Mixture : Pharmaceutical

1.3 Details of the supplier of the safety data sheet
   Company : MSD
   Shotton Lane
   NE23 3JU  Cramlington NU - Great Britain
   Telephone : 44 1 670 59 30 00
   Telefax : 908-735-1496
   E-mail address of person responsible for the SDS : EHSDATASTEWARD@msd.com

1.4 Emergency telephone number
   1-908-423-6000

SECTION 2: Hazards identification

2.1 Classification of the substance or mixture
   Classification (REGULATION (EC) No 1272/2008)
   Carcinogenicity, Category 2 : H351: Suspected of causing cancer.
   Reproductive toxicity, Category 1B : H360F: May damage fertility.
   Specific target organ toxicity - repeated exposure, Category 2 : H373: May cause damage to organs through prolonged or repeated exposure.

2.2 Label elements
   Labelling (REGULATION (EC) No 1272/2008)
   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.
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.

Hazardous components which must be listed on the label:
Tibolone

2.3 Other hazards
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**

3.2 Mixtures

<table>
<thead>
<tr>
<th>Components</th>
<th>CAS-No. EC-No. Index-No. Registration number</th>
<th>Classification</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tibolone</td>
<td>5630-53-5 227-069-1</td>
<td>Carc. 2; H351 Repr. 1B; H360Fd STOT RE 1; H372 (Bone, Endocrine system)</td>
<td>&gt; 1 - &lt;= 2,5</td>
</tr>
</tbody>
</table>

For explanation of abbreviations see section 16.

**SECTION 4: First aid measures**

4.1 Description of 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.

**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).

**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.

4.2 Most important symptoms and effects, both acute and delayed

Risks: 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.

4.3 Indication of any immediate medical attention and special treatment needed

Treatment: Treat symptomatically and supportively.

SECTION 5: Firefighting measures

5.1 Extinguishing media

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

Unsuitable extinguishing media: None known.

5.2 Special hazards arising from the substance or mixture

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

5.3 Advice for firefighters

Special protective equipment: In the event of fire, wear self-contained breathing apparatus.
SAFETY DATA SHEET
according to Regulation (EC) No. 1907/2006

Tibolone Formulation

SECTION 6: Accidental release measures

6.1 Personal precautions, protective equipment and emergency procedures

Personal precautions: Use personal protective equipment. Follow safe handling advice (see section 7) and personal protective equipment recommendations (see section 8).

6.2 Environmental precautions

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.

6.3 Methods and material for containment and cleaning up

Methods for 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.

6.4 Reference to other sections
See sections: 7, 8, 11, 12 and 13.

SECTION 7: Handling and storage

7.1 Precautions for safe 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.
- 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.

7.2 Conditions for safe storage, including any incompatibilities

Requirements for storage areas and containers:
- Keep in properly labelled containers. Store locked up. Keep tightly closed. Store in accordance with the particular national regulations.

Advice on common storage:
- Do not store with the following product types:
  - Strong oxidizing agents
  - Organic peroxides
  - Explosives
  - Gases

7.3 Specific end use(s)

Specific use(s):
- No data available

SECTION 8: Exposure controls/personal protection

8.1 Control parameters

Occupational Exposure Limits

<table>
<thead>
<tr>
<th>Components</th>
<th>CAS-No.</th>
<th>Value type (Form of exposure)</th>
<th>Control parameters</th>
<th>Basis</th>
</tr>
</thead>
<tbody>
<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>

8.2 Exposure controls

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**

**Eye protection**

Wear the following personal protective equipment:
- Safety goggles
- Equipment should conform to NS EN 166

**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.

**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).

**Respiratory protection**

If adequate local exhaust ventilation is not available or exposure assessment demonstrates exposures outside the recommended guidelines, use respiratory protection.
- **Equipment should conform to NS EN 143**
- **Filter type**: Particulates type (P)

---

**SECTION 9: Physical and chemical properties**

**9.1 Information on basic 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.
- **Upper explosion limit / Upper**: No data available
Tibolone Formulation

flammmability limit

Lower explosion limit / Lower flammmability 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.

9.2 Other information
Flammability (liquids) : No data available
Particle size : No data available

SECTION 10: Stability and reactivity

10.1 Reactivity
Not classified as a reactivity hazard.

10.2 Chemical stability
Stable under normal conditions.

10.3 Possibility of hazardous reactions
Hazardous reactions : May form explosive dust-air mixture during processing, handling or other means. Can react with strong oxidizing agents.

10.4 Conditions to avoid
Conditions to avoid : Heat, flames and sparks. Avoid dust formation.

10.5 Incompatible materials
Materials to avoid : Oxidizing agents
10.6 Hazardous decomposition products
No hazardous decomposition products are known.

SECTION 11: Toxicological information

11.1 Information on toxicological effects
Information on likely routes of exposure:
- Inhalation
- Skin contact
- Ingestion
- Eye contact

Acute toxicity
Not classified based on available information.

Components:

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
Not classified based on available information.

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.
# Tibolone Formulation

<table>
<thead>
<tr>
<th>Version</th>
<th>Revision Date:</th>
<th>SDS Number:</th>
<th>Date of last issue:</th>
<th>Date of first issue:</th>
</tr>
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<tbody>
<tr>
<td>2.4</td>
<td>16.10.2020</td>
<td>16998-00020</td>
<td>23.03.2020</td>
<td>30.09.2014</td>
</tr>
</tbody>
</table>

## Components:

### Tibolone:

| Target Organs Assessment | Bone, Endocrine system 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, amenorhea, Gastrointestinal discomfort, musculoskeletal pain, liver function change

## SECTION 12: Ecological information

### 12.1 Toxicity

#### Components:

#### Tibolone:

**Ecotoxicology Assessment**

- **Acute aquatic toxicity**: No data available
- **Chronic aquatic toxicity**: No data available
**SAFETY DATA SHEET**
according to Regulation (EC) No. 1907/2006

### Tibolone Formulation

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</tr>
</tbody>
</table>

#### 12.2 Persistence and degradability
No data available

#### 12.3 Bioaccumulative potential

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

#### 12.4 Mobility in soil
No data available

#### 12.5 Results of PBT and vPvB assessment
Not relevant

#### 12.6 Other adverse effects
No data available

### SECTION 13: Disposal considerations

#### 13.1 Waste treatment methods
- **Product:** Dispose of in accordance with local regulations. According to the European Waste Catalogue, Waste Codes are not product specific, but application specific. Waste codes should be assigned by the user, preferably in discussion with the waste disposal authorities.
- **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

#### 14.1 UN number
Not regulated as a dangerous good

#### 14.2 UN proper shipping name
Not regulated as a dangerous good

#### 14.3 Transport hazard class(es)
Not regulated as a dangerous good

#### 14.4 Packing group
Not regulated as a dangerous good

#### 14.5 Environmental hazards
Not regulated as a dangerous good

#### 14.6 Special precautions for user
Not applicable

#### 14.7 Transport in bulk according to Annex II of Marpol and the IBC Code
Remarks: Not applicable for product as supplied.
SECTION 15: Regulatory information

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

REACH - Restrictions on the manufacture, placing on the market and use of certain dangerous substances, preparations and articles (Annex XVII): Not applicable
REACH - Candidate List of Substances of Very High Concern for Authorisation (Article 59): Not applicable
REACH - List of substances subject to authorisation (Annex XIV): Not applicable
Regulation (EC) No 1005/2009 on substances that deplete the ozone layer: Not applicable
Regulation (EU) 2019/1021 on persistent organic pollutants (recast): Not applicable

Other regulations:
Take note of Directive 92/85/EEC regarding maternity protection or stricter national regulations, where applicable.
Young people under the age of 18 are not allowed to use or be exposed to the product professionally. Young people above the age of 15 are, however, except from this rule if the product is a necessary part of their education.

The components of this product are reported in the following inventories:
AICS : not determined
DSL : not determined
IECSC : not determined

15.2 Chemical safety assessment
A Chemical Safety Assessment has not been carried out.

SECTION 16: Other information

Other information : Items where changes have been made to the previous version are highlighted in the body of this document by two vertical lines.

Full text of H-statements
H351 : Suspected of causing cancer.
H360Fd : May damage fertility. Suspected of damaging the unborn child.
H372 : Causes damage to organs through prolonged or repeated exposure.
SAFETY DATA SHEET
according to Regulation (EC) No. 1907/2006

Tibolone Formulation

Version 2.4 Revision Date: 16.10.2020 SDS Number: 16998-00020 Date of last issue: 23.03.2020 Date of first issue: 30.09.2014

Full text of other abbreviations

Carc. : Carcinogenicity
Repr. : Reproductive toxicity
STOT RE : Specific target organ toxicity - repeated exposure

ADN - European Agreement concerning the International Carriage of Dangerous Goods by Inland Waterways; ADR - European Agreement concerning the International Carriage of Dangerous Goods by Road; AIIC - Australian Inventory of Industrial Chemicals; ASTM - American Society for the Testing of Materials; bw - Body weight; CLP - Classification Labelling Packaging Regulation; Regulation (EC) No 1272/2008; CMR - Carcinogen, Mutagen or Reproductive Toxicant; DIN - Standard of the German Institute for Standardisation; DSL - Domestic Substances List (Canada); ECHA - European Chemicals Agency; EC-Number - European Community number; 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; 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; LDD50 - 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; NO(A)EC - No Observed (Adverse) Effect Concentration; NO(A)EL - No Observed (Adverse) Effect Level; NOELR - No Observable Effect Loading Rate; 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; RID - Regulations concerning the International Carriage of Dangerous Goods by Rail; SADT - Self-Accelerating Decomposition Temperature; SDS - Safety Data Sheet; SVHC - Substance of very high concern; TCSI - Taiwan Chemical Substance Inventory; 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

Further information

Classification of the mixture:

<table>
<thead>
<tr>
<th>Carc.</th>
<th>Repr. 1B</th>
<th>STOT RE 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>H351</td>
<td>H360F</td>
<td>H373</td>
</tr>
</tbody>
</table>

Classification procedure:

Calculation method
Calculation method
Calculation method

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.

NO / EN