SAFETY DATA SHEET

Nomegestrol / Estradiol Formulation

Version 6.2  Revision Date: 2021/04/09  SDS Number: 17227-00017  Date of last issue: 2020/10/16  Date of first issue: 2014/09/30

1. PRODUCT AND COMPANY IDENTIFICATION

Chemical product name: Nomegestrol / Estradiol Formulation

**Supplier’s company name, address and phone number**

Company name of supplier: Organon & Co.

Address: 30 Hudson Street, 33nd floor
       Jersey City, New Jersey, U.S.A 07302

Telephone: 551-430-6000

E-mail address: EHSSTEWARD@organon.com

Emergency telephone number: 215-631-6999

**Recommended use of the chemical and restrictions on use**

Recommended use: Pharmaceutical

2. HAZARDS IDENTIFICATION

**GHS classification of chemical product**

Carcinogenicity: Category 1A

Reproductive toxicity: Category 1A

Specific target organ toxicity - repeated exposure: Category 1 (Liver, Bone, Blood, Endocrine system)

Short-term (acute) aquatic hazard: Category 3

Long-term (chronic) aquatic hazard: Category 1

**GHS label elements**

Hazard pictograms:

Signal word: Danger

Hazard statements:

H350 May cause cancer.

H360FD May damage fertility. May damage the unborn child.

H372 Causes damage to organs (Liver, Bone, Blood, Endocrine system) through prolonged or repeated exposure.

H402 Harmful to aquatic life.

H410 Very toxic 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.
P264 Wash skin thoroughly after handling.
P270 Do not eat, drink or smoke when using this product.
P273 Avoid release to the environment.
P280 Wear protective gloves/ protective clothing/ eye protection/ face protection.

Response:
P308 + P313 IF exposed or concerned: Get medical advice/ attention.
P391 Collect spillage.

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 outlines of the emergency assumed:
- 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>Mixture</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Components</th>
<th>Chemical name</th>
<th>CAS-No.</th>
<th>Concentration (% w/w)</th>
<th>ENCS No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cellulose</td>
<td>9004-34-6</td>
<td>&gt;= 10 - &lt; 20</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Estradiol</td>
<td>50-28-2</td>
<td>&gt;= 2.5 - &lt; 10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>17-Hydroxy-6-methyl-19-norpregna-4,6-diene-3,20-dione 17-acetate</td>
<td>58652-20-3</td>
<td>&gt;= 1 - &lt; 2.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Talc</td>
<td>14807-96-6</td>
<td>&gt;= 1 - &lt; 10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Titanium dioxide</td>
<td>13463-67-7</td>
<td>&gt;= 0.1 - &lt; 1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Propylene glycol</td>
<td>57-55-6</td>
<td>&gt;= 0.1 - &lt; 1</td>
<td></td>
<td></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: May cause cancer. May damage fertility. May damage the unborn child. Causes 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
Nitrogen oxides (NOx)

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 pro-
agency procedures: 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

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.

Avoidance of contact:

Hygiene measures:
Oxidizing agents
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.
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**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.

**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 (Form of exposure)</th>
<th>Control parameters / Permissible concentration</th>
<th>Basis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cellulose</td>
<td>9004-34-6</td>
<td>TWA</td>
<td>10 mg/m³</td>
<td>ACGIH</td>
</tr>
<tr>
<td>Estradiol</td>
<td>50-28-2</td>
<td>TWA</td>
<td>0.05 µg/m³ (OEB 5)</td>
<td>Internal</td>
</tr>
<tr>
<td>17-Hydroxy-6-methyl-19-norpregna-4,6-diene-3,20-dione 17-acetate</td>
<td>58652-20-3</td>
<td>TWA</td>
<td>0.2 µg/m³</td>
<td>Internal</td>
</tr>
<tr>
<td>Talc</td>
<td>14807-96-6</td>
<td>OEL-M (Respirable dust)</td>
<td>0.5 mg/m³</td>
<td>JP OEL JSOH</td>
</tr>
<tr>
<td>Titanium dioxide</td>
<td>13463-67-7</td>
<td>OEL-M (Respirable dust)</td>
<td>1 mg/m³ (Titanium)</td>
<td>JP OEL JSOH</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA (Respirable particulate matter)</td>
<td>2 mg/m³</td>
<td>ACGIH</td>
</tr>
<tr>
<td></td>
<td></td>
<td>OEL-M (Total dust)</td>
<td>4 mg/m³ (Titanium)</td>
<td>JP OEL JSOH</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA</td>
<td>10 mg/m³ (Titanium dioxide)</td>
<td>ACGIH</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**: 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

<table>
<thead>
<tr>
<th>Property</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical state</td>
<td>powder</td>
</tr>
<tr>
<td>Colour</td>
<td>white</td>
</tr>
<tr>
<td>Odour</td>
<td>odourless</td>
</tr>
<tr>
<td>Odour Threshold</td>
<td>No data available</td>
</tr>
<tr>
<td>Melting point/freezing point</td>
<td>No data available</td>
</tr>
<tr>
<td>Boiling point, initial boiling point and boiling range</td>
<td>No data available</td>
</tr>
<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>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>
</tbody>
</table>
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<table>
<thead>
<tr>
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<tbody>
<tr>
<td>6.2</td>
<td>2021/04/09</td>
<td>17227-00017</td>
<td>2020/10/16</td>
<td>2014/09/30</td>
</tr>
</tbody>
</table>

- Flash point: No data available
- Decomposition temperature: No data available
- pH: No data available
- Evaporation rate: No data available
- Auto-ignition temperature: No data available
- Viscosity
  - Viscosity, dynamic: No data available
  - Viscosity, kinematic: No data available
- Solubility(ies)
  - Water solubility: No data available
- Partition coefficient: n-octanol/water: No data available
- Vapour pressure: No data available
- Density and/or relative density
  - Relative density: No data available
- Density: 1 g/cm³
- Relative vapour density: No data available
- Explosive properties: Not explosive
- Oxidizing properties: The substance or mixture is not classified as oxidizing.
- Molecular weight: No data available
- Particle characteristics
  - 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:**

**Cellulose:**
- Acute oral toxicity: LD50 (Rat): > 5,000 mg/kg
- Acute inhalation toxicity: LC50 (Rat): > 5.8 mg/l
  - Exposure time: 4 h
  - Test atmosphere: dust/mist
- Acute dermal toxicity: LD50 (Rabbit): > 2,000 mg/kg

**Estradiol:**
- Acute oral toxicity: LD50 (Rat): > 2,000 mg/kg
- Acute toxicity (other routes of administration): LD50 (Rat): > 300 mg/kg
  - Application Route: Subcutaneous

**17-Hydroxy-6-methyl-19-norpregna-4,6-diene-3,20-dione 17-acetate:**
- Acute oral toxicity: LD50 (Rat): > 2,000 mg/kg

**Talc:**
- Acute oral toxicity: LD50 (Rat): > 5,000 mg/kg
  - Remarks: Based on data from similar materials

**Titanium dioxide:**
- Acute oral toxicity: LD50 (Rat): > 5,000 mg/kg
- Acute inhalation toxicity: LC50 (Rat): > 6.82 mg/l
  - Exposure time: 4 h
  - Test atmosphere: dust/mist
  - Assessment: The substance or mixture has no acute inhalation toxicity

**Propylene glycol:**
- Acute oral toxicity: LD50 (Rat): > 5,000 mg/kg
**Acute inhalation toxicity**
- LC₅₀ (Rabbit): > 159 mg/l
- Exposure time: 4 h
- Test atmosphere: dust/mist

**Acute dermal toxicity**
- LD₅₀ (Rabbit): > 2,000 mg/kg
- Assessment: The substance or mixture has no acute dermal toxicity

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

### Components:

**Talc:**
- Species: Rabbit
- Result: No skin irritation

**Titanium dioxide:**
- Species: Rabbit
- Result: No skin irritation

**Propylene glycol:**
- Species: Rabbit
- Method: OECD Test Guideline 404
- Result: No skin irritation

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

### Components:

**Estradiol:**
- Result: No eye irritation

**Talc:**
- Species: Rabbit
- Result: No eye irritation

**Titanium dioxide:**
- Species: Rabbit
- Result: No eye irritation

**Propylene glycol:**
- Species: Rabbit
- Result: No eye irritation
- Method: OECD Test Guideline 405
Respiratory or skin sensitisation

Skin sensitisation
Not classified based on available information.

Respiratory sensitisation
Not classified based on available information.

Components:

Estradiol:
Exposure routes : Skin contact
Species : Guinea pig
Assessment : Does not cause skin sensitisation.
Result : negative

Talc:
Exposure routes : Skin contact
Species : Humans
Result : negative

Titanium dioxide:
Test Type : Local lymph node assay (LLNA)
Exposure routes : Skin contact
Species : Mouse
Result : negative

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

Germ cell mutagenicity
Not classified based on available information.

Components:

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

Genotoxicity in vivo : Test Type: In vitro mammalian cell gene mutation test
Result: negative

Estradiol:
Genotoxicity in vitro:
- Test Type: DNA damage and repair, unscheduled DNA synthesis in mammalian cells (in vitro)
  Test system: mammalian cells
  Result: positive
- Test Type: Chromosome aberration test in vitro
  Test system: mammalian cells
  Result: positive
- Test Type: Chromosomal aberration
  Test system: mammalian cells
  Result: positive

Genotoxicity in vivo:
- Test Type: Chromosomal aberration
  Species: Rat
  Cell type: Bone marrow
  Result: negative
- Test Type: Chromosomal aberration
  Species: Mouse
  Cell type: Bone marrow
  Result: negative

17-Hydroxy-6-methyl-19-norpregna-4,6-diene-3,20-dione 17-acetate:
Genotoxicity in vitro:
- Test Type: Ames test
  Result: negative
- Test Type: Chromosome aberration test in vitro
  Result: negative
- Test Type: DNA damage and repair, unscheduled DNA synthesis in mammalian cells (in vitro)
  Result: negative
- Test Type: In vitro mammalian cell gene mutation test
  Result: negative

Genotoxicity in vivo:
- Test Type: In vivo micronucleus test
  Species: Rat
  Application Route: Oral
  Result: negative
- Test Type: In vivo micronucleus test
  Species: Mouse
  Application Route: Oral
  Result: negative

Talc:
Genotoxicity in vitro:
- Test Type: DNA damage and repair, unscheduled DNA synthesis in mammalian cells (in vitro)
  Result: negative

Genotoxicity in vivo:
- Test Type: Chromosome aberration test in vitro
  Species: Rat
Titanium dioxide:
Genotoxicity in vitro: Test Type: Bacterial reverse mutation assay (AMES)
Result: negative
Genotoxicity in vivo: Test Type: In vivo micronucleus test
Species: Mouse
Result: negative

Propylene glycol:
Genotoxicity in vitro: Test Type: Bacterial reverse mutation assay (AMES)
Result: negative
Genotoxicity in vivo: Test Type: Mammalian erythrocyte micronucleus test (in vivo cytogenetic assay)
Species: Mouse
Application Route: Intraperitoneal injection
Result: negative

Carcinogenicity
May cause cancer.

Components:

Cellulose:
Species: Rat
Application Route: Ingestion
Exposure time: 72 weeks
Result: negative

Estradiol:
Species: Mouse
Application Route: Ingestion
Exposure time: 24 Months
LOAEL: 100 µg/kg
Result: positive
Target Organs: female reproductive organs

Species: Rat
Application Route: Subcutaneous
Exposure time: 13 weeks
LOAEL: 20 mg/kg body weight
Result: positive
Target Organs: Endocrine system

Carcinogenicity - Assessment
Positive evidence from human epidemiological studies

17-Hydroxy-6-methyl-19-norpregna-4,6-diene-3,20-dione 17-acetate:
Species: Rat
Application Route: oral (feed)
Activity duration : 52 Weeks
                    : 10 mg/kg body weight
Result               : negative
Species              : Mouse
Application Route    : oral (feed)
                    : 20 mg/kg body weight
Result               : positive
Target Organs        : Mammary gland, Pituitary gland
Carcinogenicity - Assessment : Weight of evidence does not support classification as a carcinogen

Talc:
Species              : Mouse
Application Route    : inhalation (dust/mist/fume)
Exposure time        : 2 Years
Result               : negative

Titanium dioxide:
Species              : Rat
Application Route    : inhalation (dust/mist/fume)
Exposure time        : 2 Years
Method               : OECD Test Guideline 453
Result               : positive
Remarks               : The mechanism or mode of action may not be relevant in humans.
Carcinogenicity - Assessment : Limited evidence of carcinogenicity in inhalation studies with animals.

Propylene glycol:
Species              : Rat
Application Route    : Ingestion
Exposure time        : 2 Years
Result               : negative

Reproductive toxicity
May damage fertility. May damage the unborn child.

Components:
Cellulose:
Effects on fertility : Test Type: One-generation reproduction toxicity study
                      : Species: Rat
                      : Application Route: Ingestion
                      : Result: negative
Effects on foetal development : Test Type: Fertility/early embryonic development
                                 : Species: Rat
                                 : Application Route: Ingestion
                                 : Result: negative
**Estradiol:**

**Effects on fertility**
- Test Type: One-generation reproduction toxicity study
  - Species: Rat
  - Application Route: Ingestion
  - Fertility: LOAEL: 0.5 mg/kg body weight
  - Result: Effects on fertility

- Test Type: One-generation reproduction toxicity study
  - Species: Rat
  - Duration of Single Treatment: 90 d
  - Fertility: LOAEL: 0.69 mg/kg body weight
  - Result: Effects on fertility

- Test Type: Two-generation study
  - Species: Mouse
  - Application Route: Oral
  - Fertility: LOAEL: 0.1 mg/kg body weight
  - Result: Effects on fertility

**Effects on foetal development**
- Test Type: Embryo-foetal development
  - Species: Mouse, female
  - Application Route: Subcutaneous
  - Teratogenicity: LOAEL: 4 mg/kg body weight
  - Symptoms: Malformations were observed
  - Result: positive, Teratogenic effects

- Test Type: One-generation reproduction toxicity study
  - Species: Rat
  - Application Route: Subcutaneous
  - Teratogenicity: LOAEL: 2.5 µg/kg body weight
  - Symptoms: Reduced body weight
  - Result: positive, Embryotoxic effects and adverse effects on the offspring were detected.

- Test Type: Embryo-foetal development
  - Species: Rat
  - Application Route: Subcutaneous
  - Developmental Toxicity: LOAEL: 0.2 mg/kg body weight
  - Symptoms: Early Resorptions / resorption rate, Reduced number of viable fetuses, Reduced body weight
  - Result: Embryotoxic effects and adverse effects on the offspring were detected only at high maternally toxic doses

**Reproductive toxicity - Assessment**
- May damage fertility. May damage the unborn child.

**17-Hydroxy-6-methyl-19-norpregna-4,6-diene-3,20-dione 17-acetate:**

**Effects on foetal development**
- Test Type: Development
  - Species: Rat
  - Application Route: Oral
  - Result: negative

- Test Type: Embryo-foetal development
  - Species: Rabbit
Reproductive toxicity - Assessment:
Positive evidence of adverse effects on sexual function and fertility from human epidemiological studies.

Talc:
Effects on foetal development:
Test Type: Embryo-foetal development
Species: Rat
Application Route: Ingestion
Result: negative

Propylene glycol:
Effects on fertility:
Test Type: Three-generation reproduction toxicity study
Species: Mouse
Application Route: Ingestion
Result: negative

Effects on foetal development:
Test Type: Embryo-foetal development
Species: Mouse
Application Route: Ingestion
Result: negative

STOT - single exposure
Not classified based on available information.

STOT - repeated exposure
Causes damage to organs (Liver, Bone, Blood, Endocrine system) through prolonged or repeated exposure.

Components:

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

Repeated dose toxicity

Components:

Cellulose:
Species: Rat
NOAEL: >= 9,000 mg/kg
Application Route: Ingestion
Exposure time: 90 Days

Estradiol:
Species: Rat
LOAEL: >= 0.17 mg/kg
Application Route: Ingestion
Exposure time: 90 d
**Target Organs**: Mammary gland, Ovary, Uterus (including cervix), Liver, Bone, Endocrine system, Blood, Testis

### 17-Hydroxy-6-methyl-19-norpregna-4,6-diene-3,20-dione 17-acetate:

<table>
<thead>
<tr>
<th>Species</th>
<th>Mouse</th>
</tr>
</thead>
<tbody>
<tr>
<td>NOAEL</td>
<td>20 mg/kg</td>
</tr>
<tr>
<td>Application Route</td>
<td>Oral</td>
</tr>
<tr>
<td>Exposure time</td>
<td>52 Weeks</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Species</th>
<th>Rat</th>
</tr>
</thead>
<tbody>
<tr>
<td>NOAEL</td>
<td>20 mg/kg</td>
</tr>
<tr>
<td>Application Route</td>
<td>Oral</td>
</tr>
<tr>
<td>Exposure time</td>
<td>52 Weeks</td>
</tr>
</tbody>
</table>

### Titanium dioxide:

<table>
<thead>
<tr>
<th>Species</th>
<th>Rat</th>
</tr>
</thead>
<tbody>
<tr>
<td>NOAEL</td>
<td>24,000 mg/kg</td>
</tr>
<tr>
<td>Application Route</td>
<td>Ingestion</td>
</tr>
<tr>
<td>Exposure time</td>
<td>28 Days</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Species</th>
<th>Rat</th>
</tr>
</thead>
<tbody>
<tr>
<td>NOAEL</td>
<td>10 mg/m3</td>
</tr>
<tr>
<td>Application Route</td>
<td>Inhalation (dust/mist/fume)</td>
</tr>
<tr>
<td>Exposure time</td>
<td>2 yr</td>
</tr>
</tbody>
</table>

### Propylene glycol:

<table>
<thead>
<tr>
<th>Species</th>
<th>Rat, male</th>
</tr>
</thead>
<tbody>
<tr>
<td>NOAEL</td>
<td>1,700 mg/kg</td>
</tr>
<tr>
<td>Application Route</td>
<td>Ingestion</td>
</tr>
<tr>
<td>Exposure time</td>
<td>2 yr</td>
</tr>
</tbody>
</table>

**Aspiration toxicity**

Not classified based on available information.

**Experience with human exposure**

**Components:**

### Estradiol:

**Inhalation**

- Symptoms: tingling, Nose bleeding

**Skin contact**

- Symptoms: Skin irritation, Redness, pruritis

**Ingestion**

- Symptoms: Headache, Gastrointestinal disturbance, Dizziness, Vomiting, Diarrhoea, water retention, liver function change, changes in libido, breast tenderness, menstrual irregularities

### 17-Hydroxy-6-methyl-19-norpregna-4,6-diene-3,20-dione 17-acetate:

**Ingestion**

- Symptoms: acne, amenorhea, Headache, Dizziness, Nausea, breast tenderness, changes in libido, insomnia, musculoskeletal pain, mood swings, muscle pain, muscle twitching
12. ECOLOGICAL INFORMATION

Ecotoxicity

Components:

Cellulose:
Toxicity to fish: LC50 (Oryzias latipes (Japanese medaka)): > 100 mg/l
 Exposure time: 48 h
 Remarks: Based on data from similar materials

Estradiol:
Toxicity to fish: LC50 (Oryzias latipes (Japanese medaka)): 3.9 mg/l
 Exposure time: 96 h

Toxicity to daphnia and other aquatic invertebrates:
EC50 (Daphnia magna (Water flea)): 2.7 mg/l
 Exposure time: 48 h

Toxicity to algae/aquatic plants:
NOEC (Pseudokirchneriella subcapitata (green algae)): 1.7 mg/l
 Exposure time: 72 h
 Method: OECD Test Guideline 201

EC50 (Pseudokirchneriella subcapitata (green algae)): > 1.7 mg/l
 Exposure time: 72 h
 Method: OECD Test Guideline 201

Toxicity to fish (Chronic toxicity):
NOEC (Oryzias latipes (Japanese medaka)): 0.000003 mg/l
 Exposure time: 160 d
 Method: OECD Test Guideline 210

Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity):
NOEC (Daphnia magna (Water flea)): 0.2 mg/l
 Exposure time: 21 d

M-Factor (Chronic aquatic toxicity):
1,000

Toxicity to microorganisms:
EC50: > 100 mg/l
 Exposure time: 3 h
 Test Type: Respiration inhibition
 Method: OECD Test Guideline 209

NOEC: 100 mg/l
 Exposure time: 3 h
 Test Type: Respiration inhibition
 Method: OECD Test Guideline 209

17-Hydroxy-6-methyl-19-norpregna-4,6-diene-3,20-dione 17-acetate:
Toxicity to algae/aquatic plants:
EC50 (Pseudokirchneriella subcapitata (green algae)): > 3.07 mg/l
 Exposure time: 72 h
### Name: Nomegestrol / Estradiol Formulation

**Method:** OECD Test Guideline 201

NOEC (Pseudokirchneriella subcapitata (green algae)): 0.69 mg/l  
Exposure time: 72 h

**Toxicity to fish (Chronic toxicity):** NOEC (Zebrfish): 0.0013 mg/l  
Exposure time: 27 d

**Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity):** NOEC (Daphnia magna (Water flea)): 3.65 mg/l  
Exposure time: 21 d

**M-Factor (Chronic aquatic toxicity):** 10

**Toxicity to microorganisms:** EC50 (Natural microorganism): > 2.8 mg/l  
Exposure time: 3 h  
Test Type: Respiration inhibition  
Method: OECD Test Guideline 209

**Remarks:** No toxicity at the limit of solubility

**M-Factor:** 10

**Toxicity to microorganisms:** EC50 (Natural microorganism): 2.8 mg/l  
Exposure time: 3 h  
Test Type: Respiration inhibition  
Method: OECD Test Guideline 209

**Remarks:** No toxicity at the limit of solubility

### Talc:

**Toxicity to fish:** LC50 (Brachydanio rerio (zebrafish)): > 100,000 mg/l  
Exposure time: 24 h

### Titanium dioxide:

**Toxicity to fish:** LC50 (Oncorhynchus mykiss (rainbow trout)): > 100 mg/l  
Exposure time: 96 h

**Toxicity to algae/aquatic plants:** EC50 (Skeletonema costatum (marine diatom)): > 10,000 mg/l  
Exposure time: 72 h

**Toxicity to microorganisms:** EC50: > 1,000 mg/l  
Exposure time: 3 h

**Method:** OECD Test Guideline 209

### Propylene glycol:

**Toxicity to fish:** LC50 (Oncorhynchus mykiss (rainbow trout)): 40,613 mg/l  
Exposure time: 96 h

**Toxicity to daphnia and other aquatic invertebrates:** EC50 (Ceriodaphnia dubia (water flea)): 18,340 mg/l  
Exposure time: 48 h
Toxicity to algae/aquatic plants: ErC50 (Skeletonema costatum (marine diatom)): 19,300 mg/l Exposure time: 72 h Method: OECD Test Guideline 201

Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity): NOEC (Ceriodaphnia dubia (water flea)): 13,020 mg/l Exposure time: 7 d

Toxicity to microorganisms: NOEC (Pseudomonas putida): > 20,000 mg/l Exposure time: 18 h

Persistence and degradability

Components:

Cellulose:
Biodegradability Result: Readily biodegradable.

Estradiol:
Biodegradability Result: rapidly degradable
Biodegradation: 84 %
Exposure time: 24 hrs

Propylene glycol:
Biodegradability Result: Readily biodegradable.
Biodegradation: 98.3 %
Exposure time: 28 d
Method: OECD Test Guideline 301F

Bioaccumulative potential

Components:

Estradiol:
Partition coefficient: n-octanol/water log Pow: 4.01

17-Hydroxy-6-methyl-19-norpregna-4,6-diene-3,20-dione 17-acetate:
Bioaccumulation Species: Zebrafish
Bioconcentration factor (BCF): 44

Partition coefficient: n-octanol/water log Pow: 3.7

Propylene glycol:
Partition coefficient: n-octanol/water log Pow: -1.07

Mobility in soil

Components:

Estradiol:
Distribution among environment log Koc: 3.81
mental compartments

17-Hydroxy-6-methyl-19-norpregna-4,6-diene-3,20-dione 17-acetate:
Distribution among environmental compartments : log Koc: 3.35
Method: OECD Test Guideline 106

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
UN number : UN 3077
Proper shipping name : ENVIRONMENTALLY HAZARDOUS SUBSTANCE, SOLID, N.O.S.
(Estradiol, 17-Hydroxy-6-methyl-19-norpregna-4,6-diene-3,20-dione 17-acetate)

Class : 9
Packing group : III
Labels : 9

IATA-DGR
UN/ID No. : UN 3077
Proper shipping name : Environmentally hazardous substance, solid, n.o.s.
(Estradiol, 17-Hydroxy-6-methyl-19-norpregna-4,6-diene-3,20-dione 17-acetate)

Class : 9
Packing group : III
Labels : Miscellaneous
Packing instruction (cargo aircraft) : 956
Packing instruction (passenger aircraft) : 956
Environmentally hazardous : yes

IMDG-Code
UN number : UN 3077
Proper shipping name : ENVIRONMENTALLY HAZARDOUS SUBSTANCE, SOLID, N.O.S.
(Estradiol, 17-Hydroxy-6-methyl-19-norpregna-4,6-diene-3,20-dione 17-acetate)

Class : 9
SAFETY DATA SHEET

Nomegestrol / Estradiol Formulation

Version 6.2 Revision Date: 2021/04/09 SDS Number: 17227-00017 Date of last issue: 2020/10/16

Date of first issue: 2014/09/30

Packing group: III
Labels: 9
EmS Code: F-A, S-F
Marine pollutant: yes

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.

Special precautions for user
The transport classification(s) provided herein are for informational purposes only, and solely based upon the properties of the unpackaged material as it is described within this Safety Data Sheet. Transportation classifications may vary by mode of transportation, package sizes, and variations in regional or country regulations.

15. REGULATORY INFORMATION

Related Regulations

Fire Service Law
Not applicable to dangerous materials / designated flammables.

Chemical Substance Control Law
Priority Assessment Chemical Substance

<table>
<thead>
<tr>
<th>Chemical name</th>
<th>Chemical name</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Propane-1,2-diol</td>
<td>Propane-1,2-diol</td>
<td>106</td>
</tr>
</tbody>
</table>

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

Article 57-2 (Enforcement Order Table 9)

<table>
<thead>
<tr>
<th>Chemical name</th>
<th>Number</th>
<th>Concentration (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Titanium(IV) oxide</td>
<td>191</td>
<td>&gt;=0.1 - &lt;1</td>
</tr>
</tbody>
</table>

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
Miscellaneous dangerous substances and articles (Article 2 and 3 of rules on shipping and storage of dangerous goods and its Attached Table 1)

Aviation Law
Miscellaneous dangerous substances and articles (Article 194 of The Enforcement Rules of Aviation Law and its Attached Table 1)

Marine Pollution and Sea Disaster Prevention etc Law
Bulk transportation : Not classified as noxious liquid substance
Pack transportation : 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
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
- JP OEL JSOH / OEL-M: Occupational Exposure Limit-Mean

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 mate-
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