SAFETY DATA SHEET

Nomegestrol / Estradiol Formulation

Version 4.8    Revision Date: 2021/04/09    SDS Number: 17221-00017    Date of last issue: 2020/10/16

1. PRODUCT AND COMPANY IDENTIFICATION

Product name : Nomegestrol / Estradiol Formulation

Manufacturer or supplier’s details
Company : Organon & Co.
Address : JL Raya Pandaan KM. 48
          Pandaan, Jawa Timur - Indonesia
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

GHS Classification
Carcinogenicity : Category 1A
Reproductive toxicity : Category 1A
Specific target organ toxicity - repeated exposure : Category 1 (Liver, Bone, Blood, Endocrine system)
Long-term (chronic) aquatic hazard : Category 1

GHS label elements
Signal word : Danger
Hazard pictograms :

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.
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.
SAFETY DATA SHEET

Nomegestrol / Estradiol Formulation

Version 4.8  Revision Date: 2021/04/09  SDS Number: 17221-00017  Date of last issue: 2020/10/16  Date of first issue: 2014/09/30

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
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>Cellulose</td>
<td>9004-34-6</td>
<td>&gt;= 10 - &lt; 30</td>
</tr>
<tr>
<td>Estradiol</td>
<td>50-28-2</td>
<td>&gt;= 2.5 - &lt; 10</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;= 0.3 - &lt; 2.5</td>
</tr>
<tr>
<td>Talc</td>
<td>14807-96-6</td>
<td>&lt; 10</td>
</tr>
<tr>
<td>Titanium dioxide</td>
<td>13463-67-7</td>
<td>&lt; 1</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.
SAFETY DATA SHEET
Nomegestrol / Estradiol Formulation

Version 4.8  Revision Date: 2021/04/09  SDS Number: 17221-00017  Date of last issue: 2020/10/16  Date of first issue: 2014/09/30

Most important symptoms and effects, both acute and delayed:
- Get medical attention.
- Rinse mouth thoroughly with water.
- 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 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>Cellulose</td>
<td>9004-34-6</td>
<td>NAB</td>
<td>10 mg/m³</td>
<td>ID OEL</td>
</tr>
<tr>
<td></td>
<td></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>
</tbody>
</table>

Further information: Skin
SAFETY DATA SHEET

Nomegestrol / Estradiol Formulation

Version 4.8  
Revision Date: 2021/04/09  
SDS Number: 17221-00017  
Date of last issue: 2020/10/16  
Date of first issue: 2014/09/30

<table>
<thead>
<tr>
<th>Substance</th>
<th>Wipe limit</th>
<th>TWA (Respirable particulate matter)</th>
<th>ACGIH</th>
</tr>
</thead>
<tbody>
<tr>
<td>17-Hydroxy-6-methyl-19-norpregn-4,6-diene-3,20-dione 17-acetate</td>
<td>0.5 µg/100 cm²</td>
<td>0.2 µg/m³</td>
<td>Internal</td>
</tr>
<tr>
<td>Talc</td>
<td>2 µg/100 cm²</td>
<td>2 mg/m³</td>
<td>ID OEL</td>
</tr>
<tr>
<td>Titanium dioxide</td>
<td>10 mg/m³</td>
<td>10 mg/m³</td>
<td>ID OEL</td>
</tr>
</tbody>
</table>

Further information: Not classified as carcinogenic to humans. Not enough data to classify these materials as carcinogenic to humans or animals

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: white

Odour: odourless

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: No data available

Evaporation rate: No data available

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: No data available

Relative vapour density: No data available

Relative density: No data available

Density: 1 g/cm³

Solubility(ies)

Water solubility: No data available

Partition coefficient: n-octanol/water: No data available

Auto-ignition temperature: No data available
Decomposition temperature : No data available

Viscosity
Viscosity, dynamic : No data available
Viscosity, kinematic : No data available

Explosive properties : Not explosive

Oxidizing properties : The substance or mixture is not classified as oxidizing.
Molecular weight : No data available
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
SAFETY DATA SHEET

Nomegestrol / Estradiol Formulation

Version: 4.8  Revision Date: 2021/04/09  SDS Number: 17221-00017  Date of last issue: 2020/10/16  Date of first issue: 2014/09/30

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
LD50 (Mouse): > 2,000 mg/kg
Acute toxicity (other routes of administration): LD50 (Rat): > 2,000 mg/kg
Application Route: Intraperitoneal

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

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

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

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

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)
<table>
<thead>
<tr>
<th>Test Type</th>
<th>Species</th>
<th>Cell type</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chromosome aberration test in vitro</td>
<td>Rat</td>
<td>Bone marrow</td>
<td>negative</td>
</tr>
<tr>
<td>DNA damage and repair, unscheduled DNA synthesis in mammalian cells (in vitro)</td>
<td>Rat</td>
<td>Bone marrow</td>
<td>negative</td>
</tr>
<tr>
<td>In vitro mammalian cell gene mutation test</td>
<td>Mouse</td>
<td>Bone marrow</td>
<td>negative</td>
</tr>
<tr>
<td>In vivo micronucleus test</td>
<td>Rat</td>
<td>Ingestion</td>
<td>negative</td>
</tr>
<tr>
<td>In vivo micronucleus test</td>
<td>Mouse</td>
<td>Ingestion</td>
<td>negative</td>
</tr>
</tbody>
</table>

**Genotoxicity in vivo**

<table>
<thead>
<tr>
<th>Test Type</th>
<th>Species</th>
<th>Application Route</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chromosome aberration test in vitro</td>
<td>Rat</td>
<td>Oral</td>
<td>negative</td>
</tr>
<tr>
<td>DNA damage and repair, unscheduled DNA synthesis in mammalian cells (in vitro)</td>
<td>Rat</td>
<td>Oral</td>
<td>negative</td>
</tr>
<tr>
<td>In vitro mammalian cell gene mutation test</td>
<td>Mouse</td>
<td>Oral</td>
<td>negative</td>
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<tr>
<td>In vivo micronucleus test</td>
<td>Rat</td>
<td>Ingestion</td>
<td>negative</td>
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<td>Mouse</td>
<td>Ingestion</td>
<td>negative</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Test Type</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ames test</td>
<td>negative</td>
</tr>
<tr>
<td>Chromosome aberration test in vitro</td>
<td>negative</td>
</tr>
<tr>
<td>DNA damage and repair, unscheduled DNA synthesis in mammalian cells (in vitro)</td>
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<td>In vitro mammalian cell gene mutation test</td>
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<td>DNA damage and repair, unscheduled DNA synthesis in mammalian cells (in vitro)</td>
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<td>Oral</td>
<td>negative</td>
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<tr>
<td>In vivo micronucleus test</td>
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</table>

**Talc:**

<table>
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<td>DNA damage and repair, unscheduled DNA synthesis in mammalian cells (in vitro)</td>
<td>Rat</td>
<td>Ingestion</td>
<td>negative</td>
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</table>

**Genotoxicity in vivo**

<table>
<thead>
<tr>
<th>Test Type</th>
<th>Species</th>
<th>Application Route</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chromosome aberration test in vitro</td>
<td>Rat</td>
<td>Ingestion</td>
<td>negative</td>
</tr>
</tbody>
</table>

**Genotoxicity in vitro**

<table>
<thead>
<tr>
<th>Test Type</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>DNA damage and repair, unscheduled DNA synthesis in mammalian cells (in vitro)</td>
<td>negative</td>
</tr>
<tr>
<td>Chromosome aberration test in vitro</td>
<td>negative</td>
</tr>
</tbody>
</table>

**Genotoxicity in vivo**
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

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
Result: 10 mg/kg body weight
Result: negative
Species: Mouse
Application Route: oral (feed)
Result: 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
**SAFETY DATA SHEET**

**Nomegestrol / Estradiol Formulation**

---

**Version** 4.8  
**Revision Date:** 2021/04/09  
**SDS Number:** 17221-00017  
**Date of last issue:** 2020/10/16  
**Date of first issue:** 2014/09/30

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**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.

**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
  - Application Route: Oral
  - Result: negative, No teratogenic effects

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

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 days
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:
Species: Mouse
NOAEL: 20 mg/kg
Application Route: Oral
Exposure time: 52 Weeks

Species: Rat
NOAEL: 20 mg/kg
Application Route: Oral
Exposure time: 52 Weeks

Titanium dioxide:
Species: Rat
NOAEL: 24,000 mg/kg
Application Route: Ingestion
Exposure time: 28 Days

Species: Rat
NOAEL: 10 mg/m3
Application Route: Inhalation (dust/mist/fume)
Exposure time: 2 yr
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
<table>
<thead>
<tr>
<th>Substance</th>
<th>Toxicity</th>
<th>Method</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>M-Factor (Chronic aquatic toxicity)</strong></td>
<td>EC50: &gt; 100 mg/l</td>
<td>OECD Test Guideline 209</td>
</tr>
<tr>
<td><strong>Toxicity to microorganisms</strong></td>
<td></td>
<td>NOEC: 100 mg/l</td>
</tr>
<tr>
<td><strong>17-Hydroxy-6-methyl-19-norpregna-4,6-diene-3,20-dione 17-acetate:</strong></td>
<td>EC50: &gt; 3.07 mg/l</td>
<td>OECD Test Guideline 201</td>
</tr>
<tr>
<td><strong>Toxicity to algae/aquatic plants</strong></td>
<td></td>
<td>NOEC: 0.69 mg/l</td>
</tr>
<tr>
<td><strong>Toxicity to fish (Chronic toxicity)</strong></td>
<td>NOEC: 0.0013 mg/l</td>
<td>OECD Test Guideline 201</td>
</tr>
<tr>
<td><strong>Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity)</strong></td>
<td>NOEC: 3.65 mg/l</td>
<td>OECD Test Guideline 211</td>
</tr>
<tr>
<td><strong>M-Factor (Chronic aquatic toxicity)</strong></td>
<td>EC50: &gt; 2.8 mg/l</td>
<td>OECD Test Guideline 209</td>
</tr>
<tr>
<td><strong>Toxicity to microorganisms</strong></td>
<td></td>
<td>NOEC: 2.8 mg/l</td>
</tr>
<tr>
<td><strong>Talc:</strong></td>
<td>LC50: &gt; 100,000 mg/l</td>
<td>OECD Test Guideline 203</td>
</tr>
<tr>
<td><strong>Titanium dioxide:</strong></td>
<td>LC50: &gt; 100 mg/l</td>
<td>OECD Test Guideline 203</td>
</tr>
</tbody>
</table>
Toxicity to daphnia and other aquatic invertebrates: EC50 (Daphnia magna (Water flea)): > 100 mg/l Exposure time: 48 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

Persistence and degradability

Components:

Cellulose:
Biodegradability: Result: Readily biodegradable.

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

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

Mobility in soil

Components:

Estradiol:
Distribution among environmental compartments: log Koc: 3.81

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

Other adverse effects
No data available
SAFETY DATA SHEET

Nomegestrol / Estradiol Formulation

Version 4.8  Revision Date: 2021/04/09  SDS Number: 17221-00017  Date of last issue: 2020/10/16  Date of first issue: 2014/09/30

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
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.

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
15. REGULATORY INFORMATION

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

Minister of Industry Regulation No. 23/M-IND/PER/4/2013 concerning the Revision of Minister of Industry Regulation No. 87/M-IND/PER/9/2009 concerning Globally Harmonized System of Classification and Labelling of Chemicals.

Regulation of the Minister of Health No. 472 of 1996 on the Safeguarding of Substances Hazardous to Health
Hazardous substances that must be registered : Not applicable

Government Regulation No. 74 of 2001 on the Management of Hazardous and Toxic Substances
Hazardous substances approved for use : Not applicable
Prohibited substances : Not applicable
Restricted substances : Not applicable

Regulation of the Minister of Trade No. 44 of 2009 on Procurement, Distribution and Supervision of Hazardous Materials
Type of Hazardous Materials Restricted to Import, Distribution and Supervision : Not applicable

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 : yyyy/mm/dd

Full text of other abbreviations
ACGIH : USA. ACGIH Threshold Limit Values (TLV)
ID OEL : Indonesia. Occupational Exposure Limits
SAFETY DATA SHEET

Nomegestrol / Estradiol Formulation

Version 4.8
Revision Date: 2021/04/09
SDS Number: 17221-00017
Date of last issue: 2020/10/16
Date of first issue: 2014/09/30

ACGIH / TWA : 8-hour, time-weighted average
ID OEL / NAB : Long term exposure limit

AllIC - 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; 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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