SAFETY DATA SHEET

Nomegestrol / Estradiol Formulation

Version 7.3  Revision Date: 09/13/2019  SDS Number: 17229-00014  Date of last issue: 03.05.2019

SECTION 1. PRODUCT AND COMPANY IDENTIFICATION

Product name: Nomegestrol / Estradiol Formulation

Manufacturer or supplier's details

Company name of supplier: MSD
Address: Avenida 16 de Septiembre No. 301
Xaltocan - Xochimilco Mexico  16090
Telephone: 52 55 57284444
Telefax: 908-735-1496
Emergency telephone: 1-908-423-6000
E-mail address: EHSDATASTEWARD@msd.com

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

SECTION 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)

GHS label elements

Hazard pictograms: [Image]

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.

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.
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.

Disposal:
P501 Dispose of contents/ container to an approved waste disposal plant.

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

<table>
<thead>
<tr>
<th>Substance / Mixture</th>
<th>Components</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Chemical name</td>
</tr>
<tr>
<td>Mixture</td>
<td>Cellulose</td>
</tr>
<tr>
<td></td>
<td>Estradiol</td>
</tr>
<tr>
<td></td>
<td>17-Hydroxy-6-methyl-19-norpregna-4,6-diene-3,20-dione 17-acetate</td>
</tr>
<tr>
<td></td>
<td>Talc</td>
</tr>
<tr>
<td></td>
<td>Titanium dioxide</td>
</tr>
</tbody>
</table>

SECTION 4. FIRST AID MEASURES

General advice: In the case of accident or if you feel unwell, seek medical advice immediately. When symptoms persist or in all cases of doubt seek medical advice.

If inhaled: If inhaled, remove to fresh air.
Get medical attention.

In case of skin contact: In case of contact, immediately flush skin with soap and plenty of water.
Remove contaminated clothing and shoes.
Get medical attention.
Wash clothing before reuse.
Thoroughly clean shoes before reuse.

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,
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and use the recommended personal protective equipment when the potential for exposure exists (see section 8).

Notes to physician:  Treat symptomatically and supportively.

SECTION 5. FIRE-FIGHTING MEASURES

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

Unsuitable extinguishing media:  None known.

Specific hazards during fire fighting:  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 fire-fighters:  In the event of fire, wear self-contained breathing apparatus.
Use personal protective equipment.

SECTION 6. ACCIDENTAL RELEASE MEASURES

Personal precautions, protective equipment and emergency procedures:  Use personal protective equipment.
Follow safe handling advice and personal protective equipment recommendations.

Environmental precautions:  Discharge into the environment must be avoided.
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.
SECTION 7. HANDLING AND STORAGE

Technical measures: Static electricity may accumulate and ignite suspended dust causing an explosion. Provide adequate precautions, such as electrical grounding and bonding, or inert atmospheres.

Local/Total ventilation: If sufficient ventilation is unavailable, use with local exhaust ventilation.

Advice on safe handling:
- Do not get on skin or clothing.
- Do not breathe dust.
- Do not swallow.
- Avoid contact with eyes.
- 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.
- Take care to prevent spills, waste and minimize release to the environment.

Hygiene measures:
- If exposure to chemical is likely during typical use, provide eye flushing systems and safety showers close to the working place.
- When using do not eat, drink or smoke.
- Wash contaminated clothing before re-use.

Conditions for safe storage:
- Keep in properly labeled containers.
- Store locked up.
- Keep tightly closed.
- Store in accordance with the particular national regulations.

Materials to avoid:
- Do not store with the following product types:
  - Strong oxidizing agents
  - Organic peroxides
  - Explosives
  - Gases

SECTION 8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Ingredients with workplace control parameters

<table>
<thead>
<tr>
<th>Components</th>
<th>CAS-No.</th>
<th>Value type (Form of exposure)</th>
<th>Control parameters / Permissible concentration</th>
<th>Basis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cellulose</td>
<td>9004-34-6</td>
<td>VLE-PPT</td>
<td>10 mg/m³</td>
<td>NOM-010-STPS-2014</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>
<tr>
<td>Further information: Skin</td>
<td></td>
<td>Wipe limit</td>
<td>0.5 µg/100 cm²</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>
</tbody>
</table>
### SECTION 9. PHYSICAL AND CHEMICAL PROPERTIES

<table>
<thead>
<tr>
<th>Property</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appearance</td>
<td>powder</td>
</tr>
<tr>
<td>Color</td>
<td>white</td>
</tr>
<tr>
<td>Odor</td>
<td>odorless</td>
</tr>
<tr>
<td>Odor Threshold</td>
<td>No data available</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

#### 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.).
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<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>No data available</td>
</tr>
<tr>
<td>Melting point/freezing point</td>
<td>No data available</td>
</tr>
<tr>
<td>Initial boiling point and boiling range</td>
<td>No data available</td>
</tr>
<tr>
<td>Flash point</td>
<td>No data available</td>
</tr>
<tr>
<td>Evaporation rate</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>
<tr>
<td>Vapor pressure</td>
<td>No data available</td>
</tr>
<tr>
<td>Relative vapor density</td>
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</tr>
<tr>
<td>Relative density</td>
<td>No data available</td>
</tr>
<tr>
<td>Density</td>
<td>1 g/cm³</td>
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<tr>
<td>Solubility(ies)</td>
<td></td>
</tr>
<tr>
<td>Water solubility</td>
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<td>Partition coefficient: n-octanol/water</td>
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<td>Autoignition temperature</td>
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<tr>
<td>Decomposition temperature</td>
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<tr>
<td>Viscosity</td>
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<td>Viscosity, dynamic</td>
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</tr>
<tr>
<td>Viscosity, kinematic</td>
<td>No data available</td>
</tr>
<tr>
<td>Explosive properties</td>
<td>Not explosive</td>
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<tr>
<td>Oxidizing properties</td>
<td>The substance or mixture is not classified as oxidizing.</td>
</tr>
<tr>
<td>Molecular weight</td>
<td>No data available</td>
</tr>
<tr>
<td>Particle size</td>
<td>No data available</td>
</tr>
</tbody>
</table>

**SECTION 10. STABILITY AND REACTIVITY**
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SECTION 11. TOXICOLOGICAL INFORMATION

Information on likely routes of exposure
Inhalation
Skin contact
Ingestion
Eye contact

Acute toxicity
Not classified based on available information.

Product:
Acute oral toxicity : Acute toxicity estimate: > 5,000 mg/kg
Method: Calculation method

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

Skin sensitization
Not classified based on available information.

Respiratory sensitization
Not classified based on available information.
Components:

Estradiol:
- Routes of exposure: Skin contact
- Species: Guinea pig
- Assessment: Does not cause skin sensitization.
- Result: negative

Talc:
- Routes of exposure: Skin contact
- Species: Humans
- Result: negative

Titanium dioxide:
- Test Type: Local lymph node assay (LLNA)
- Routes of exposure: 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
  - Test Type: In vitro mammalian cell gene mutation test
  - Result: negative
- Genotoxicity in vivo: Test Type: Mammalian erythrocyte micronucleus test (in vivo cytogenetic assay)
  - Species: Mouse
  - Application Route: Ingestion
  - 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
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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
  Application Route: Ingestion
  Result: negative

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
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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: negative

Species: Mouse
Application Route: oral (feed)
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.

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 fetal 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 fetal development: Test Type: Embryo-fetal 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
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<table>
<thead>
<tr>
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<th>SDS Number</th>
<th>Date of last issue</th>
<th>Date of first issue</th>
</tr>
</thead>
<tbody>
<tr>
<td>7.3</td>
<td>09/13/2019</td>
<td>17229-00014</td>
<td>03.05.2019</td>
<td>30.09.2014</td>
</tr>
</tbody>
</table>

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-fetal 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 fetal development:
Test Type: Development
Species: Rat
Application Route: Oral
Result: negative

Test Type: Embryo-fetal 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 fetal development:
Test Type: Embryo-fetal 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 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:**
- 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 y

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, Diarrhea, water retention, liver function change, changes in libido, breast tenderness, menstrual irreg-
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

### SECTION 12. ECOLOGICAL INFORMATION

**Ecotoxicity**

**Components:**

**Cellulose:**

<table>
<thead>
<tr>
<th>Toxicity to fish</th>
<th>LC50 (Oryzias latipes (Japanese medaka)): &gt; 100 mg/l</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exposure time</td>
<td>48 h</td>
</tr>
<tr>
<td>Remarks</td>
<td>Based on data from similar materials</td>
</tr>
</tbody>
</table>

**Estradiol:**

<table>
<thead>
<tr>
<th>Toxicity to fish</th>
<th>LC50 (Oryzias latipes (Japanese medaka)): 3.9 mg/l</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exposure time</td>
<td>96 h</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Toxicity to daphnia and other aquatic invertebrates</th>
<th>EC50 (Daphnia magna (Water flea)): 2.7 mg/l</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exposure time</td>
<td>48 h</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Toxicity to algae/aquatic plants</th>
<th>NOEC (Pseudokirchneriella subcapitata (green algae)): 1.7 mg/l</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exposure time</td>
<td>72 h</td>
</tr>
<tr>
<td>Method</td>
<td>OECD Test Guideline 201</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Toxicity to fish (Chronic toxicity)</th>
<th>NOEC (Oryzias latipes (Japanese medaka)): 0.000003 mg/l</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exposure time</td>
<td>160 d</td>
</tr>
<tr>
<td>Method</td>
<td>OECD Test Guideline 210</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity)</th>
<th>NOEC (Daphnia magna (Water flea)): 0.2 mg/l</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exposure time</td>
<td>21 d</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Toxicity to microorganisms</th>
<th>EC50: &gt; 100 mg/l</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exposure time</td>
<td>3 h</td>
</tr>
<tr>
<td>Test Type</td>
<td>Respiration inhibition</td>
</tr>
<tr>
<td>Method</td>
<td>OECD Test Guideline 209</td>
</tr>
</tbody>
</table>

| 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:

<table>
<thead>
<tr>
<th>Toxicity to algae/aquatic</th>
<th>EC50 (Pseudokirchneriella subcapitata (green algae)): &gt; 3.07</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exposure time</td>
<td></td>
</tr>
</tbody>
</table>
### Exposure to Plants

**Exposure time:** 72 h  
**Method:** OECD Test Guideline 201  
**NOEC (Pseudokirchneriella subcapitata (green algae)):** 0.69 mg/l  
**Exposure time:** 72 h  
**Method:** OECD Test Guideline 201

### Exposure to Fish (Chronic toxicity)

**NOEC (Zebrafish):** 0.0013 mg/l  
**Exposure time:** 27 d

### Exposure to Daphnia and Other Aquatic Invertebrates (Chronic toxicity)

**NOEC (Daphnia magna (Water flea)):** 3.65 mg/l  
**Exposure time:** 21 d  
**Method:** OECD Test Guideline 211  
**Remarks:** No toxicity at the limit of solubility.

### Exposure to Microorganisms

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

### Other Components

**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  
**Method:** OECD Test Guideline 203

**Toxicity to daphnia and other aquatic invertebrates:**  
**EC50 (Daphnia magna (Water flea)):** > 100 mg/l  
**Exposure time:** 48 h  
**Method:** OECD Test Guideline 209

**Toxicity to algae/aquatic plants:**  
**EC50 (Skeletonema costatum (marine diatom)):** > 10,000 mg/l  
**Exposure time:** 72 h  
**Method:** OECD Test Guideline 209

**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

SECTION 13. DISPOSAL CONSIDERATIONS

Disposal methods
Waste from residues: Dispose of in accordance with local regulations.
Contaminated packaging: Empty containers should be taken to an approved waste handling site for recycling or disposal.
If not otherwise specified: Dispose of as unused product.

SECTION 14. TRANSPORT INFORMATION

International Regulations

UNRTDG
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)
SAFETY DATA SHEET

Nomegestrol / Estradiol Formulation

Version: 7.3
Revision Date: 09/13/2019
SDS Number: 17229-00014
Date of last issue: 03.05.2019
Date of first issue: 30.09.2014

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-norpregn-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-norpregn-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.

Domestic regulation

NOM-002-SCT
UN number: UN 3077
Proper shipping name: ENVIRONMENTALLY HAZARDOUS SUBSTANCE, SOLID, N.O.S.
(Estradiol, 17-Hydroxy-6-methyl-19-norpregn-4,6-diene-3,20-dione 17-acetate)

Class: 9
Packing group: III
Labels: 9

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.

SECTION 15. REGULATORY INFORMATION

Safety, health and environmental regulations/legislation specific for the substance or mixture
Federal Law for the control of chemical precursors, essential chemical products and machinery for: Not applicable
producing capsules, tablets and pills.

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

SECTION 16. OTHER INFORMATION

Full text of other abbreviations
ACGIH : USA. ACGIH Threshold Limit Values (TLV)
NOM-010-STPS-2014 : Mexico. Norm NOM-010-STPS-2014 on Chemicals Polluting the Work Environment - Identification, Assessment and Control - Appendix 1 Occupational Exposure Limits
ACGIH / TWA : 8-hour, time-weighted average
NOM-010-STPS-2014 / VLE-PPT : Time weighted average limit value
NOM-010-STPS-2014 / VLE-CT : Short term exposure limit value

AICS - Australian Inventory of Chemical Substances; 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 Standardisation; KECI - Korea Existing Chemicals Inventory; LC50 - Lethal Concentration to 50 % of a test population; LD50 - Lethal Dose to 50% of a test population (Median Lethal Dose); MARPOL - International Convention for the Prevention of Pollution from Ships; n.o.s. - Not Otherwise Specified; Nch - Chilean Norm; NO(A)EC - No Observed (Adverse) Effect Concentration; NO(A)EL - No Observed (Adverse) Effect Level; NOELR - No Observable Effect Loading Rate; NOM - Official Mexican Norm; NTP - National Toxicology Program; NZIoC - New Zealand Inventory of Chemicals; OECD - Organization for Economic Co-operation and Development; OPPTS - Office of Chemical Safety and Pollution Prevention; PBT - Persistent, Bioaccumulative and Toxic substance; PICCS - Philippines Inventory of Chemicals and Chemical Substances; (Q)SAR - (Quantitative) Structure Activity Relationship; REACH - Regulation (EC) No 1907/2006 of the European Parliament and of the Council concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals; SADT - Self-Accelerating Decomposition Temperature; SDS - Safety Data Sheet; TCSI - Taiwan Chemical Substance Inventory; TDG - Transportation of Dangerous Goods; TSCA - Toxic Substances Control Act (United States); UN - United Nations; UNRTDG - United Nations Recommendations on the Transport of Dangerous Goods; vPvB - Very Persistent and Very Bioaccumulative; WHMIS - Workplace Hazardous Materials Information System
SAFETY DATA SHEET

Nomegestrol / Estradiol Formulation

Version 7.3  Revision Date: 09/13/2019  SDS Number: 17229-00014  Date of last issue: 03.05.2019  Date of first issue: 30.09.2014


Revision Date: 09/13/2019

The information is considered as correct, but not exhaustive, and will be used only as a guide, which is based in the current knowledge of the substance or mixture, and is applicable to proper safety precautions for the product.

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