

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, 33rd 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:**

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

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 out- : Dust contact with the eyes can lead to mechanical irritation.
lines of the emergency as- : Contact with dust can cause mechanical irritation or drying of
sumed : the skin.
May form explosive dust-air mixture during processing, handling or other means.

3. COMPOSITION/INFORMATION ON INGREDIENTS

Substance / Mixture : Mixture

Components

Chemical name	CAS-No.	Concentration (% w/w)	ENCS No.
Cellulose	9004-34-6	>= 10 - < 20	
Estradiol	50-28-2	>= 2.5 - < 10	
17-Hydroxy-6-methyl-19-norpregna-4,6-diene-3,20-dione 17-acetate	58652-20-3	>= 1 - < 2.5	
Talc	14807-96-6	>= 1 - < 10	1-468
Titanium dioxide	13463-67-7	>= 0.1 - < 1	1-558, 5-5225
Propylene glycol	57-55-6	>= 0.1 - < 1	2-234

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.

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

- 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 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 (NO_x)
- 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 measures : Use personal protective equipment.
Follow safe handling advice (see section 7) and personal pro-

Nomegestrol / Estradiol Formulation

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

- gency procedures : tective 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 : Oxidizing agents
- 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.

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

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

Components	CAS-No.	Value type (Form of exposure)	Control parameters / Permissible concentration	Basis
Cellulose	9004-34-6	TWA	10 mg/m ³	ACGIH
Estradiol	50-28-2	TWA	0.05 µg/m ³ (OEB 5)	Internal
Further information: Skin				
		Wipe limit	0.5 µg/100 cm ²	Internal
17-Hydroxy-6-methyl-19-norpregna-4,6-diene-3,20-dione 17-acetate	58652-20-3	TWA	0.2 µg/m ³	Internal
		Wipe limit	2 µg/100 cm ²	Internal
Talc	14807-96-6	OEL-M (Respirable dust)	0.5 mg/m ³	JP OEL JSOH
Further information: Class 1 Dust				
		OEL-M (Total dust)	2 mg/m ³	JP OEL JSOH
Further information: Class 1 Dust				
		TWA (Respirable particulate matter)	2 mg/m ³	ACGIH
Titanium dioxide	13463-67-7	OEL-M (Respirable dust)	1 mg/m ³ (Titanium)	JP OEL JSOH
Further information: Class 2 Dust				
		OEL-M (Total dust)	4 mg/m ³ (Titanium)	JP OEL JSOH
Further information: Class 2 Dust				
		TWA	10 mg/m ³ (Titanium dioxide)	ACGIH

- 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).

Nomegestrol / Estradiol Formulation

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

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.
Skin contact must be avoided by using impervious protective clothing (gloves, aprons, boots, etc).

9. PHYSICAL AND CHEMICAL PROPERTIES

- Physical state : powder
- Colour : white
- Odour : odourless
- Odour Threshold : No data available
- Melting point/freezing point : No data available
- Boiling point, initial boiling point and boiling range : No data available
- Flammability (solid, gas) : May form explosive dust-air mixture during processing, handling or other means.
- Flammability (liquids) : No data available
- Lower explosion limit and upper explosion limit / flammability limit
Upper explosion limit / Upper flammability limit : No data available
- Lower explosion limit / Lower flammability limit : No data available

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

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.

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

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
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

Propylene glycol:

Acute oral toxicity : LD50 (Rat): > 5,000 mg/kg

Nomegestrol / Estradiol Formulation

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

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

Nomegestrol / Estradiol Formulation

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

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

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:

Nomegestrol / Estradiol Formulation

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

- 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

Nomegestrol / Estradiol Formulation

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

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

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)

Nomegestrol / Estradiol Formulation

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

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

Nomegestrol / Estradiol Formulation

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

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

Nomegestrol / Estradiol Formulation

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

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

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 : $\geq 9,000$ mg/kg
Application Route : Ingestion
Exposure time : 90 Days

Estradiol:

Species : Rat
LOAEL : ≥ 0.17 mg/kg
Application Route : Ingestion
Exposure time : 90 d

Nomegestrol / Estradiol Formulation

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

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

Propylene glycol:

Species : Rat, male
 NOAEL : 1,700 mg/kg
 Application Route : Ingestion
 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

Nomegestrol / Estradiol Formulation

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

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

Nomegestrol / Estradiol Formulation

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

Method: OECD Test Guideline 201

NOEC (Pseudokirchneriella subcapitata (green algae)): 0.69 mg/l

Exposure time: 72 h

Method: OECD Test Guideline 201

Toxicity to fish (Chronic toxicity) : NOEC (Zebrafish): 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
Method: OECD Test Guideline 211
Remarks: No toxicity at the limit of solubility

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

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

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

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

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

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 environ- : log Koc: 3.81

Nomegestrol / Estradiol Formulation

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

mental compartments

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

Distribution among environmental compartments : log K_{oc}: 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

Chemical name	Number
Propane-1,2-diol	106

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)

Chemical name	Number	Concentration (%)
Titanium(IV) oxide	191	≥ 0.1 - < 1

Substances Subject to be Indicated Names

Not applicable

Nomegestrol / Estradiol Formulation

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

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

Nomegestrol / Estradiol Formulation

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

16. OTHER INFORMATION**Further information**

Sources of key data used to compile the Safety Data Sheet : Internal technical data, data from raw material SDSs, OECD eChem Portal search results and European Chemicals Agency, <http://echa.europa.eu/>

Date format : yyyy/mm/dd

Full text of other abbreviations

ACGIH : USA. ACGIH Threshold Limit Values (TLV)
 JP OEL JSOH : Japan. The Japan Society for Occupational Health. Recommendation of Occupational Exposure Limits

ACGIH / TWA : 8-hour, time-weighted average
 JP OEL JSOH / OEL-M : Occupational Exposure Limit-Mean

AIIC - Australian Inventory of Industrial Chemicals; ANTT - National Agency for Transport by Land of Brazil; ASTM - American Society for the Testing of Materials; bw - Body weight; CMR - Carcinogen, Mutagen or Reproductive Toxicant; DIN - Standard of the German Institute for Standardisation; DSL - Domestic Substances List (Canada); ECx - Concentration associated with x% response; ELx - Loading rate associated with x% response; EmS - Emergency Schedule; ENCS - Existing and New Chemical Substances (Japan); ErCx - Concentration associated with x% growth rate response; ERG - Emergency Response Guide; GHS - Globally Harmonized System; GLP - Good Laboratory Practice; IARC - International Agency for Research on Cancer; IATA - International Air Transport Association; IBC - International Code for the Construction and Equipment of Ships carrying Dangerous Chemicals in Bulk; IC50 - Half maximal inhibitory concentration; ICAO - International Civil Aviation Organization; IECSC - Inventory of Existing Chemical Substances in China; IMDG - International Maritime Dangerous Goods; IMO - International Maritime Organization; ISHL - Industrial Safety and Health Law (Japan); ISO - International Organisation for Standardization; KECI - Korea Existing Chemicals Inventory; LC50 - Lethal Concentration to 50 % of a test population; LD50 - Lethal Dose to 50% of a test population (Median Lethal Dose); MARPOL - International Convention for the Prevention of Pollution from Ships; n.o.s. - Not Otherwise Specified; Nch - Chilean Norm; NO(A)EC - No Observed (Adverse) Effect Concentration; NO(A)EL - No Observed (Adverse) Effect Level; NOELR - No Observable Effect Loading Rate; NOM - Official Mexican Norm; NTP - National Toxicology Program; NZIoC - New Zealand Inventory of Chemicals; OECD - Organization for Economic Co-operation and Development; OPPTS - Office of Chemical Safety and Pollution Prevention; PBT - Persistent, Bioaccumulative and Toxic substance; PICCS - Philippines Inventory of Chemicals and Chemical Substances; (Q)SAR - (Quantitative) Structure Activity Relationship; REACH - Regulation (EC) No 1907/2006 of the European Parliament and of the Council concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals; SADT - Self-Accelerating Decomposition Temperature; SDS - Safety Data Sheet; TCSI - Taiwan Chemical Substance Inventory; TDG - Transportation of Dangerous Goods; TSCA - Toxic Substances Control Act (United States); UN - United Nations; UNRTDG - United Nations Recommendations on the Transport of Dangerous Goods; vPvB - Very Persistent and Very Bioaccumulative; WHMIS - Workplace Hazardous Materials Information System

The information provided in this Safety Data Sheet is correct to the best of our knowledge, information and belief at the date of its publication. The information is designed only as a guidance for safe handling, use, processing, storage, transportation, disposal and release and shall not be considered a warranty or quality specification of any type. The information provided relates only to the specific material identified at the top of this SDS and may not be valid when the SDS mate-

SAFETY DATA SHEET



Nomegestrol / Estradiol Formulation



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

rial 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