

LEVONORGESTREL

MATERIAL SAFETY DATA SHEET

According to Regulation (EC) No. 1907/2006, (EC) No. 1272/2008 and (UE) No. 453/2010 (Annex I)

Revision date: January 2011 – Revision No. 00

SECTION 1.

IDENTIFICATION OF THE SUBSTANCE AND OF THE COMPANY

1.1. Product identifier

Product name:	LEVONORGESTREL
Synonyms (if available):	18,19-Dinorpregn-4-en-20-yn-3-one, 13-ethyl-17-hydroxy- (17.alpha.)- (-)-13-ethyl-17-hydroxy-18,19-Dinorpregn-4-en-20-yn-3-one 13-Ethyl-17-alpha-ethynyl-17- hydroxy-4-gonen-3-one
CLP Annex VI Name:	Not applicable
C&L Inventory Name:	No data available
CAS Number:	797-63-7
EC Number:	212-349-8
REACH Registration Number:	Not applicable
Molecular Weight:	312.45
Molecular Formula:	C ₂₁ H ₂₈ O ₂

1.2. Relevant identified uses of the substance

Common uses:	API (Active Pharmaceutical Ingredient)
Uses advised:	none

1.3. Details of the supplier of the safety data sheet

Manufacturer/Distributor:

Company name: **STERLING S.r.l**

Address: **Via della Carboneria, 30
06073 Solomeo di Corciano (PG) – Italy**

Telephone: 075/5294001

Fax: 075/5294000

Person Responsible for the compilation of Safety Data Sheet:

Aragona Anna Alessandra

E-mail address: aragona@sterling.it

1.4. Emergency telephone number

Italy: +39 02 66101029 (Poison Information Centre Niguarda Ca' Granda – Milano)

Foreign countries: Contact the closest Poisons Information Centre.

SECTION 2 HAZARDS IDENTIFICATION

2.1 Classification of the substance

Classification according to Regulation (EC) N. 1272/2008 (CLP/GHS):

Hazard Class	Hazard Class and Category Code(s)	Hazard statement Code(s)	Hazard statement
Carcerogenicity	Carc. Cat. 2	H351	Suspected of causing cancer.
Reproductive toxicity	Repr. Cat. 2	H361fd	Suspected of damaging fertility. Suspected of damaging the unborn child.

Classification of the substance according to Directive 67/548/EEC:

Classification	Risk phrases	
Carc. Cat. 3, R40	R40	Limited evidence of a carcinogenic effect.
Repr. Cat. 3, R62, R63	R62	Possible risk of impaired fertility.
	R63	Possible risk of harm to the unborn child.

Main adverse effects

Physico-chemical hazards

Human health hazard

Not reported evidence concerning this effect.

Suspected of damaging fertility and the unborn child. Suspected of causing cancer.

The most common adverse effects include nausea, abdominal pain, fatigue, headaches and menstrual disorders. Possible allergic reaction to material if inhaled, ingested or in contact with skin.


Environmental hazard

See also sections from 9 to 12.

Not reported evidence concerning this effect.

2.2 Label elements

Labelling according to Regulation (EC) N. 1272/2008 (CLP/GHS)

Pictogram/s	 GHS08	
Signal Word	Warning	
Hazard Statement (H) ^[1]	H351	H361fd
Precautionary Statement (P) ^[1]	P201, P202, P281 P308+313 P405 P501	
- Prevention		
- Response		
- Storage		
- Disposal		

^[1] Full text of R and H-phrases: see section 16

2.3 Other hazards

The substance meets the criteria for:

- PBT
- vPvB

YES	NO
	X
	X

- Human health hazard

Could be harmful if swallowed, inhaled or in contact with skin. Possible irritation or sensitization to the eyes, skin and gastrointestinal and / or respiratory tract.

- Environmental hazard

May cause damage to aquatic life with long lasting effects.

- Physico-chemical hazards:

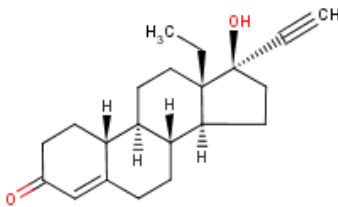
Not reported evidence concerning this effect.

- Specific effects

Not reported evidence concerning this effect.

SEZIONE 3 COMPOSIZIONE/INFORMAZIONE SUGLI INGREDIENTI

Description: Active Pharmaceutical Ingredient – synthetic progestin

<i>Product name:</i>	Levonorgestrel
<i>Concentration:</i>	> 97%
<i>Structural formula:</i>	
<i>Chemical formula:</i>	C ₂₁ H ₂₈ O ₂
<i>Molecular weight:</i>	312.45 g/mol
<i>Substance subjected to threshold limit value (TLV):</i>	No
<i>CAS Name:</i>	18,19-Dinorgest-4-en-20-yn-3-one, 13-ethyl-17-hydroxy- (17.alpha.)-
<i>CAS Number:</i>	797-63-7
<i>IUPAC Name:</i>	(8R,9S,10R,13S,14S,17R)-13-ethyl-17-ethynyl-17-hydroxy-1,2,6,7,8,9,10,11,12,14,15,16-dodecahydrocyclopenta[a]phenanthren-3-one
<i>EC Number:</i>	212-349-8
<i>Index Number:</i>	No data available
<i>Impurities (if classified)</i>	-
<i>Additives (if classified)</i>	-

SECTION 4 FIRST AID MEASURES

4.1 Description of first aid measures

- | | |
|-----------------------|--|
| - <i>Eye contact</i> | Irrigate eyes with copious amounts of water or saline solution for at least 10-15 min, holding eyelids apart to ensure thorough rinsing. Seek medical attention in case of adverse symptoms. |
| - <i>Skin contact</i> | In case of skin contact with powders or solutions immediately rinse affected area with copious amount of water and then wash with soap or mild detergent, and water. Remove contaminated clothing and shoes. Seek medical attention in case of adverse symptoms. |
| - <i>Ingestion</i> | In case of ingestion, if conscious, rinse mouth with water. If the casualty is unconscious, place in the recovery position. Seek medical attention in case of adverse symptoms. |
| - <i>Inhalation</i> | Remove casualty to fresh air as quickly as possible. Keep warm and at rest. If breathing is difficult, give oxygen if possible, or assisted ventilation. Consult the physician if the exposure was significant in terms of quantity or time. |

4.2 Most important symptoms and effects, both acute and delayed

- | | |
|---------------------------|--|
| - <i>Acute effects:</i> | Possible irritation to eyes, skin, and gastrointestinal and / or respiratory tract. |
| - <i>Delayed effects:</i> | May cause sensitization, menstrual irregularities, jaundice, hepatitis, porphyry, depression and cancer. |

4.3 Indication of any immediate medical attention and special treatment needed

- | | |
|--|-------------------------------|
| - <i>Medical monitoring:</i> | In case of prolonged exposure |
| - <i>Antidotes, if known:</i> | Not known |
| - <i>Counter-indication:</i> | Not known |
| - <i>Immediate specific treatment:</i> | Not known |

SECTION 5 FIRE-FIGHTING MEASURES

5.1 Extinguishing media

- | | |
|---|---|
| - <i>Suitable extinguishing media</i> | Carbon Dioxide (CO ₂), foam, dry chemical powder, and water jet, unless otherwise stated. |
| - <i>Unsuitable extinguishing media</i> | None |

5.2 Special hazards arising from the substance

- | | |
|-----------------------------|---|
| - <i>Specific hazard(s)</i> | The product is combustible and, like the dust in general, can make an explosive mixture with air. When heated or in the event of a fire, vapors may be harmful to health: carbon oxides (CO _x). |
| - <i>Others</i> | Not known. |

5.3 Advice for firefighters

- *Special fire fighting procedures*

Ensure the availability of equipment for cooling containers to prevent the danger of overheating in the event of a fire nearby.

- *Protective Equipment*

Wear full fire resistant self-contained breathing apparatus and protective clothing to prevent contact with skin and eyes. Use the protective equipment in the best conditions of care, based on information reported in the previous subsections.

SECTION 6 ACCIDENTAL RELEASE MEASURES

6.1 Personal precautions, protective equipment and emergency procedures

- **Not involved personnel**

Keep non-involved personnel away from the area of spillage. Wear appropriate personal protective equipment and protective clothing (see Section 8). Avoid the generation and spreading of dust. Ventilate area. Eliminate sources of ignition. Avoid contact with skin, eyes and inhalation of dust.

In case of fire and / or explosion do not breathe fumes or vapors. Use self-contained breathing apparatus (SCBA) and appropriate protective clothing. The vapors can be removed by spraying with water.

- **For involved personnel**

see Section 8.

6.2 Environmental precautions

I In case of accidental release or spill prevent product from entering sewers, rivers or other bodies of water. If required, notify relevant authorities according to all applicable regulations.

6.3 Methods and material for containment and cleaning up

- *Spill Containment:*

Coverage of the discharges.

- *Cleaning up spills:*

Collect free product with suitable mechanical means. Ventilate area and wash spill site after material pickup is complete. Transfer the gathered product and the washings to suitable tanks or containers and store/dispose according to relevant regulations.

6.4 Reference to other sections

See also sections 8 (protective equipment) and 13 (disposal).

SECTION 7 HANDLING AND STORAGE

7.1 Precautions for safe handling

- *Recommendations for handling:*

Use of personal protective equipment must be consistent with good occupational hygiene practices (see section 8).

Use in ventilated place.

Use away from all heat sources, open flame, sources of ignition, sparks, and

- Good occupational hygiene practices:
- incompatible materials.
 - Keep the substance out of sewers.
 - Do not eat, drink or smoke when using this product.
 - Wash hands thoroughly with soap and water before meals and after work shift.
 - Remove contaminated clothing and protective equipment before entering eating areas.

7.2 Conditions for safe storage

The substance is not classified for any physical and chemical properties thus no method to manage the risk is planned.

Other:

- Ventilation: Use in ventilated place at room temperature.
- Container: Keep container tightly closed and properly labelled.
- Specific planning of local: Not required based on the classification.
- Quantitative limits of storage: Not required based on the classification.
- Compatibility of packaging: See section 10.5

7.3 Specific end use

- Recommendations for specific end-use: Active Pharmaceutical Ingredient

	YES	NO
- Exposure scenario attached		X
- Chemical Safety Assessment attached		X
- Other safety assessments available (industry, specific sector)		X

SECTION 8 EXPOSURE CONTROLS/PERSONAL PROTECTION

8.1. Control Parameter

- Exposure limit values (ACGIH 2010):
 - TLV TWA: No data available
 - TLV STEL: No data available
- Monitoring procedure: The measurement of substances in the workplace must be carried out using standardized methods (i.e. EN 689:1997: Workplace atmospheres - Guidance for the assessment of exposure by inhalation to chemical agents for comparison with limit values and measurements strategy; EN 482:2006: Workplace atmospheres - General requirements for the performance of procedures for the measurement of chemical agents) or, failing that, with other appropriate methods.
- DNEL: No data available
- PNEC: No data available

8.2 Exposure Controls

	YES	NO
- Exposure scenario attached		X
- Chemical Safety Assessment attached		X

8.2.1 Appropriate engineering controls

The choice of appropriate engineering controls shall be carried out based on risk assessments carried out by the employer in its employment practices (use of the substance) in the absence of a unique exhibition and standardized scenario described in the REACH registration dossier.

8.2.2 Personal protection measures, such as personal protective equipment

- a) Eye / Face Protection Wear safety goggles (EN 166).
Provide eyewash fountains at the workplace.
- b) Skin and body Protection
 - *Hands protection* Use protective rubber or synthetic gloves (EN 374 parts 1, 2 and 3).
The glove material has to be impermeable and resistant to the product / the substance / the preparation.
Make the choice of the glove material by considering the penetration times, rates of diffusion and degradation.
The choice of the suitable gloves does not only depend on the material, but also on further marks of quality and varies from manufacturer to manufacturer.
- *Body protection* Choose the Body protection according to the activity and exposure. Wear apron, boots and suited, according to EN 13982.
- c) Respiratory Protection Avoid inhalation of dust, respiratory protection: dust mask with proper filter type.
Use respirators and components tested and approved under appropriate government standards such as NIOSH (US) or CEN (EU).
In the case of brief exposure or low pollution use breathing filter. In case of intensive and protracted exposure wear self-contained breathing apparatus (SCBA).
- d) Heat Dangers Not specified in the standard practice of use of the substance. Assess any personal protective equipment according to particular conditions of usage.

8.2.3 Environmental Exposure Controls

	YES	NO
- Exposure scenario attached		X
- Chemical Safety Assessment attached		X

Use according to good manufacturing practices avoiding litter.

Take all the technical precautions necessary to prevent the spread of the product into the surrounding.



SECTION 9 PHYSICAL AND CHEMICAL PROPERTIES

9.1 Information on basic physical and chemical properties

Appearance:	White to whitish crystalline powder
Odor:	Odorless
Odor threshold:	-
pH	No data available
Melting point/freezing point:	240 °C ⁽¹⁾
Initial boiling point and boiling range:	459.1 °C @ 760 mmHg (estimated) ⁽²⁾
Flash point:	195.4 °C (estimated) ⁽²⁾
Auto-ignition temperature:	No data available
Surface tension:	48.3 dyne/cm (estimated) ⁽²⁾
Vapor pressure:	3.93 x 10 ⁻¹⁰ mmHg @ 25 °C (estimated) ⁽¹⁾
Relative density:	1,13 g/cm ³ (estimated) ⁽²⁾
Water solubility:	insoluble; 2.05 mg/l a 25 °C (estimated) ⁽¹⁾
Solubility in organic solvents:	Soluble in dioxane and acetone; slightly soluble in ethanol
Partition coefficient: n-octanol/water:	3.92 Log Kow (estimated) ⁽²⁾
Explosive properties:	No data available
Oxidising properties:	No data available

9.2 Other information

Specific optical rotation:	-30°~ -35° (chloroform)
Henry constant (Henry's law)	7.70 x 10 ⁻¹⁰ atm·m ³ /mole

SECTION 10 STABILITY AND REACTIVITY

10.1 Reactivity

Stable under normal storage conditions.

10.2 Chemical stability

The substance is stable under normal conditions of temperature and pressure and when stored in closed containers in a cool and ventilated place.

- Need for stabilizers:

- Dangers of change in physical state:

NO	YES	Stabilizer used
X	-	
X	-	

10.3 Possibility of hazardous reactions

- Possibility of a hazardous exothermic reaction:
- Possibility of a decomposition reaction with increasing pressure:
- Possibility of degradation to unstable products:

NO	YES
X	-
X	-
X	-

10.4 Conditions to avoid

Protect from light, moisture and high temperatures.

10.5 Incompatible materials

Store separately from strong oxidizing agents.

10.6 Hazardous decomposition products

Heating at high temperatures decomposes releasing toxic fumes and gases (COx).

SECTION 11 TOXICOLOGICAL INFORMATION

- Exposure routes:

- Inhalation:
- Ingestion:
- Skin contact:
- Eye contact:

YES	NO
X	
X	
X	
X	

- Effects (immediate, delayed, chronic) following exposure (short and / or long-term):

- Inhalation: Possible risk of impaired fertility or harm to the fetus. Suspected of causing cancer. Could be harmful if inhaled or sensitizing.
- Ingestion: Could be harmful if swallowed
- Skin contact: It may be irritating or sensitizing.
- Eye contact: May be irritating

- Toxicokinetics (Absorption, Distribution, Metabolism, Excretion): ⁽³⁾

Absorption: Rapidly and completely absorbed after oral administration (bioavailability 100%).

Distribution: Levonorgestrel in serum is primarily bound to proteins, particularly albumin and globulin.

Metabolism: Following a single oral dose, levonorgestrel not appears to be extensively metabolized by the liver. The primary metabolites are 3 α , 5 β - and 3 α , 5 α -tetrahydrolevonorgestrel.

Excretion: Following a single oral dose, the half-life is 24.4 \pm 5.3 h. Levonorgestrel and its metabolites are primarily excreted in the urine.

- Acute toxicity:

- Oral: LD₅₀ rat >4000 mg/kg ⁽⁴⁾
- Dermal: Not reported evidence concerning this effect
- Inhalation: Not reported evidence concerning this effect

- Other: -
RTECS Number **JF8225000**

- **Corrosion/Irritation:** Not reported evidence concerning this effect

- **Serious eye damage / irritation:** Not reported evidence concerning this effect

- **Sensitization:** Not reported evidence concerning this effect

- **Toxicity by prolonged exposure (experim.):** Not reported evidence concerning this effect

- **CMR effects:**

- **Germ cell mutagenicity:** Ames test negative ⁽⁵⁾

- **Carcinogenicity:** Levonorgestrel is a synthetic progestin. Progestins are classified by IARC in Group 2B - possibly carcinogenic to humans. There is no evidence of carcinogenicity in humans, but there is sufficient evidence in experimental animals.

- **Reproductive toxicity:** Genetic abnormalities and birth defects can occur in fetuses exposed to progestins. Progestins cause a decrease in quality, or change in cervical mucus, and these changes may interfere with fertility.

Studies on rats with oral administration of 2 µg / day showed a decrease in the number of plants.

At a dose of 1.2 mg / kg / day administered during the differentiation of the sexual organs of the fetus was noted masculinisation of female fetuses.

- **Specific target organ toxicity (STOT)-Single exposure:**

Not reported evidence concerning this effect

- **Specific target organ toxicity (STOT)-Repeated exposure:**

Not reported evidence concerning this effect

- **Aspiration hazard:** Not applicable

- **Other information:** Studies have shown that levonorgestrel does not cause adverse effects to the composition of human milk, growth and development of breastfed infants.

SECTION 12 ECOLOGICAL INFORMATION

12.1 Toxicity

LC₅₀-96 h - fish: > 100 mg/L

CE₅₀-48 h - Daphnia magna: > 1.3 mg/L

12.2 Persistence and degradability

Not reported evidence concerning this effect

12.3 Bioaccumulative potential

BCF = 557.22 (estimated) ⁽²⁾
Log Pow = 3.92 (estimated) ⁽²⁾

12.4 Mobility in soil

Not reported evidence concerning this effect

12.5 Results of PBT and vPvB assessment

Rating not available - in relation to the ecotoxicological values available do not expect a potential for bioaccumulation.

12.6 Other adverse effects

No data available.

SECTION 13 DISPOSAL CONSIDERATIONS

13.1 Waste treatment methods

- Waste of substance:
- Contaminated Packaging/containers:

Incineration	Recycling	Landfill disposal
X		
	X	

Prevent environmental discharge.
Dispose of waste or used sacks/containers according to local regulations.

SECTION 14 TRANSPORT INFORMATION

The substance is not considered dangerous within the meaning of the regulations governing the transport of dangerous goods by road (ADR), rail (RID), sea (IMDG Code) and by air (IATA/ICAO).

SECTION 15 REGULATORY INFORMATION

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

Authorizations according to REACH Regulation: the substance is not subjected
Restrictions according to REACH Regulation: the substance is not subjected

Other UE:

The substance is not dangerous under the Seveso Regulation (Dir. 96/82/CE and f.a.)

15.2 Chemical Safety Assessment

- Exposure scenario attached
- Chemical Safety Assessment attached

YES	NO
	X
	X

SECTION 16 OTHER INFORMATION

Revision:

- **Created on** January 2011 (according to Annex I of Regulation UE453/2010 which amended Annex II of EC Regulation 1907/2006 (REACH))
- **Revision n. 00**

Fonti Bibliografiche:

- (1) ChemIDplus Lite data base, ricerca per CAS 797-63-7
- (2) Chempider data base, ricerca per CAS 797-63-7
- (3) DailyMed Current Medication Information, NEXT CHOICE (levonorgestrel) tablet
- (4) Scheda di sicurezza EDQM L0551000, LEVONORGESTREL CRS
- (5) [LANG,R AND REIMANN,R; STUDIES FOR A GENOTOXIC POTENTIAL OF SOME ENDOGENOUS AND EXOGENOUS SEX STEROIDS. I. COMMUNICATION: EXAMINATION FOR THE INDUCTION OF GENE MUTATIONS USING THE AMES SALMONELLA / MICROSOME TEST AND THE HGPRT TEST IN V79 CELLS; ENVIRON. MOL. MUTAGEN. 21(3):272-304, 1993]

Legend to abbreviations and acronyms:

- ACGIH: American Conference of Governmental Industrial Hygienists
- ADR: Accord Dangerousness Route
- BCF: Bioconcentration factor
- BEI : Biological Exposure Indices
- CAS: Chemical Abstract Service (division of the American Chemical Society)
- CHETAH : Computer programme for chemical thermodynamics and energy release evaluation
- CLP: Classification, Labelling and Packaging
- CMR: Carcinogenic, mutagenic and reprotoxic
- EINECS: European Inventory of Existing Commercial Chemical Substances
- EPA: US Environmental Protection Agency
- GHS: Global Harmonized System
- IARC: International Agency for Research on Cancer
- IATA: International Air Transport Association
- IMDG: International Maritime Dangerous Goods

- IUPAC: International Union of Pure and Applied Chemistry
- LOEL: Lowest Observed Effect Level
- NOAEL: No Observed Adverse Effect Level
- NTP: National Toxicology Program
- OEL: Occupational Exposure Limit
- OSHA: Occupational Safety and Health Administration
- PBT: Persistent, Bioaccumulative and Toxic substance
- RID: Regulations Concerning the International Carriage of Dangerous Goods by Rail
- TLV/TWA: Threshold Limit Values
- vPvB: Very Persistent and Very Bioaccumulative

Information relating to health, safety, and environmental protection in accordance with Regulation (EC) No 1272/2008

List of hazards statements:

H351 Suspected of causing cancer.
H361fd Suspected of damaging fertility. Suspected of damaging the unborn child.

List of P statements:

Prevention

P201 Obtain special instructions before use.
P202 Do not handle until all safety precautions have been read and understood.
P281 Use personal protective equipment as required.

Reaction

P308+P313 IF exposed or concerned: Get medical advice/attention.

Storage

P405 Store locked up.

Disposal

P501 Dispose of contents/container in accordance with applicable local, regional, national, and/or international regulation.

Information related to Directive 67 / 548 / EEC, Directive 1999/45/EC and Regulation (EC) No 1907/2006

R Phrases

R40 Limited evidence of a carcinogenic effect.
R62 Possible risk of impaired fertility.
R63 Possible risk of harm to the unborn child.

Guidelines for the formation

Workers potentially exposed to this substance must be trained adequately on the basis of the contents of this MSDS (Dir. 98/24/CE).

Authorizations according to REACH Regulation: No

Restrictions according to REACH Regulation: No

WARNING TO USERS

This document is intended to provide guidance and appropriate precautionary handling of this substance by qualified personnel or operating under the supervision of experienced personnel in the handling of chemicals. The substance should not be used for purposes other than those mentioned in section 1, except when they have received adequate written information on safe handling of the material.

The head of this document cannot provide warnings of the dangers arising from the use or interaction with other chemicals or materials. The user is responsible for the safe use of the substance, the adequacy of the substance which is applied to the use and proper disposal. The following information is not intended to be a representation or warranty, either expressed or implied, of merchantability, fitness for a particular purpose, quality, or any other. The information contained in this SDS are in accordance with the provisions of Annex I to Council Regulation No 453/2010/EU.

MSDS Code XXXX

Created on January 2011

The contained information is based upon our current understanding. It is applicable only to the indicated product and does not constitute any guarantee of the properties of the product. The user is responsible to ensure his or her own fitness and completeness of such information in relation to the specific use. The contained information is intended for the use of the product exclusively by appropriately qualified personnel. STERLING S.r.l. shall not be held liable for any damages caused from handling or from contact with the substance.

STERLING S.r.l.