

DEFLAZACORT

MATERIAL SAFETY DATA SHEET

In accordance with Regulation (CE) 1907/2006, (CE) 1272/2008 and (EU) 453/2010 (Annex I)

Revision no. 6 - Revision date: January 09, 2013

SECTION 1. IDENTIFICATION OF THE SUBSTANCE AND OF THE COMPANY

1.1. Substance identifier

Substance name:	DEFLAZACORT
Other names (if available):	(11 β ,16 β)-21-(acetyloxy)-11-hydroxy-2'-methyl-5'H-pregna-1,4-dione-[17,16d]-oxazole-3,20-dione
Name in Annex VI-CLP:	unlisted
Name reported in the inventory of harmonized classification and labelling:	not available
CAS number	14484-47-0
REACH registration number	Exempt of registration

1.2. Relevant identified uses of the substance and uses advised against

Relevant use(s)	Anti - inflammatory API (Active Pharmaceutical Ingredient)
Uses advised against	none

1.3. Details of the supplier of the safety data sheet

Manufacturer/Distributor:

Company name: **STERLING S.p.A**
Address: **Via della Carboneria, 30 Solomeo**
06073 Corciano (PG) – Italy
Phone number : 075/5294001
Fax number: 075/5294000

Competent person responsible for the safety data sheet: Canali Claudia
e-mail: ccanali@sterling.it

1.4. Emergency telephone number

Phone number: 02 66101029 (Centro Antiveleni Niguarda Ca' Granda – Milano)

SECTION 2 HAZARDS IDENTIFICATION

2.1 Classification of the substance

Classification of the substance in accordance with Regulation (CE) n. 1272/2008:

<i>Hazard class</i>	<i>Class code and hazard category</i>	<i>Hazard statement</i>	<i>Hazard warning</i>
Reproductive toxicity	Repr. 2	H361d	Suspected of damaging the unborn child
Reproductive toxicity	Lact.	H362	May cause harm to breast-fed children
Specific Target Organ Toxicity after repeated exposure	STOT RE 2	H373	May cause damage to organs through prolonged or repeated exposure.

Classification in accordance with Directive 67/548/CEE:

<i>Classification</i>	<i>Risk phrases</i>
Repr. Cat. 3; R63	Possible risk of harm to the unborn child
R64	May cause harm to breast-fed babies
Xn; R48/20/22	Harmful: danger of serious damage to health by prolonged exposure through inhalation and if swallowed

Main adverse effects

Physico-chemical effects

Health effects

No adverse effects known.

Possible teratogenic, possible risk of irreversible effects; danger of serious damage to health by prolonged exposure through inhalation and if swallowed; danger to unborn children, can be harmful to infants who are breastfed, can have effects on the endocrine system.


Environmental effects

No adverse effects known

See also sections from 9 to 12

2.2 Label elements

Labelling in accordance with regulation n. 1272/2008/EC:

Pictograms	
Signal Word	Warning
Hazard indication (H) ^[1]	H361d: Suspected of damaging the unborn child H362: May cause harm to breast-fed children H373: May cause damage to organs through prolonged or repeated exposure
Safety statements (P) ^[1]	P201, P308 + P313, P260, P263, P281, P501

^[1] For the explanation of H and P statements: see Section 16

2.3 Other hazards (which do not results in the classification)

The substance satisfies the PBT criteria

- PBT

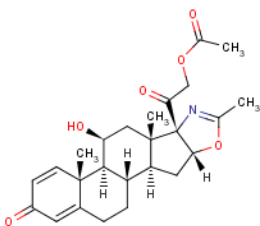
- vPvB

YES	NO
	X
	X

- Health hazards	May be harmful if ingested, inhaled or in contact with skin. May be irritant or sensitizer.
- Environmental hazards	The incidence of adverse effects increases with dose and duration of exposure.
- Physico-chemical hazards	Not known.
	Not known.
	The substance is an organic powder, explosive mixtures with air may be formed under certain conditions (e.g. temperature, pressure, particle size, moisture, concentration comburent).
	The grounding system of the instrumentation in contact with the substance is recommended to perform to avoid the accumulation of electrostatic charger. The substance emits toxic fumes in case of fire.
- Specific effects	Unknown.

SECTION 3 COMPOSITION/INFORMATION ON INGREDIENTS

Description: Active Pharmaceutical Principle; anti-inflammatory corticosteroid

Name of the component	Deflazacort
Concentration	Pure substance
Structural formula	
Chemical formula	C ₂₅ H ₃₁ NO ₆
Molecular weight	441.52 g/mol
Substance with Community OEL	No
CAS name	5'H-Pregna-1,4-dieno[17,16-d]oxazole-3,20-dione, 21-(acetyloxy)-11-hydroxy-2'-methyl-, (11.β.,16.β.)-
CAS number	14484-47-0
IUPAC name	(11β,16β)-21-(acetyloxy)-11-hydroxy-2'-methyl-5'H-pregna-1,4-dieno[17,16-d]oxazole-3,20-dione
EC number	238-483-7
Index number	not assigned

SECTION 4 FIRST AID MEASURES

4.1 Description of the first aid measures

- Eye contact	Wash immediately with large amounts of water or normal saline. Keep eyelid open during the washing. Get medical advice if adverse symptoms will appear.
- Skin contact	Remove contaminated clothes (eventually shoes). Wash affected area with soap or mild detergent and large amount of water until no evidence of substance remains. Get medical advice if adverse symptoms will appear.
- Ingestion	If swallowed wash mouth with large amounts of water provided person is conscious. If victim is conscious and alert, give milk or water. Get medical advice if adverse symptoms will appear.

- | | |
|--------------|---|
| - Inhalation | Remove the person from the exposed area to fresh air immediately. If breathing has stopped perform artificial respiration, keep person warm and at rest. Get medical advice if the exposure was significant in terms of quantity or time. |
|--------------|---|

4.2 Most important symptoms and effects (acute and delayed)

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|--------------------|---|
| - Acute effects | Symptoms may include euphoria, insomnia, humor changes, depression or psychosis, cutaneous alterations, dizziness, cefalea. |
| - Delayed effects: | Possible allergic reaction to material if inhaled, ingested or in contact with skin. |

4.3 Indication of any immediate medical attention and special treatment needed

- | | |
|------------------------------------|---|
| - Medical monitoring: | Required based on the classification of the substance |
| - Antidotes, if known | unknow |
| - Contraindications | unknow |
| - Immediate treatment at workplace | not known |

SECTION 5 FIREFIGHTING MEASURES

5.1 Extinguishing media

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|----------------------------------|---|
| - Suitable extinguishing media | Water spray or chemical foam, dry foam, CO ₂ . |
| - Unsuitable extinguishing media | not known |

5.2 Special hazards arising from the substance

- | | |
|---------------------------------|---|
| - Hazardous combustion products | May generate toxic fumes of CO _x . |
| - Other special hazards | not known |

5.3 Advice to firefighters

- | | |
|---|---|
| - Technical actions for protection | Keep containers cool with water. |
| - Special protective equipment for firefighters | Wear boots, overalls, gloves, eye and face protection and breathing apparatus. Equipment must be conformed with EN criteria and used in highest condition of protection on the basis of the information reported in the previous sub-sections |

SECTION 6 ACCIDENTAL RELEASE MEASURES

6.1 Personal precautions, protective equipment and emergency procedures

- For non-emergency personnel

Wear appropriate protective equipment (see Section 8) to prevent contamination of the skin, eyes and personal clothing. In case of fire and/or and explosions avoid breathing fumes and vapors. Use a self-contained breathing apparatus (SCBA) and appropriate protective clothing. The fumes can be eliminated by spraying with water.
See also section 8

- For emergency responders

See section 8.

6.2 Environmental precautions

In case of accidental release in the environment avoid that the substance can reach drains, surface water and ground water. Contact local authorities in case of environmental release.

6.3 Methods and material for containment and clearing up

- | | |
|----------------------------------|---|
| - <i>Containment procedures:</i> | Coverage of the discharges |
| - <i>Cleaning up procedures:</i> | Recover the substance for suction or other mechanical means and wash the area with plenty of water and detergents. Store the material into a company that specializes pending disposal. Containers must be cleaned up and disposed of as waste remediation above. |

6.4 Reference to other sections

See also section 8 and 13.

SECTION 7 HANDLING AND STORAGE

7.1. Precautions for safe handling

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|---|--|
| <i>Recommendation for handling:</i> | Avoid prolonged exposure through inhalation and swallowed.
Handle away from sparkles and flames - sources of ignition
Handle in a well ventilated place
Avoid contact with incompatible materials
Wear suitable Personal Protection Equipment (see section 8)
Keep the substance away from drains, surface or ground waters |
| <i>Recommendation for personal hygiene:</i> | Do not eat, drink and smoke in the working areas
Wash hands after handling the substance
Remove contaminated clothing and protective equipment before entering eating areas |

7.2. Condition for safe storage including any incompatibilities

The substance is not classified for any physical and chemical properties and no risk management is foreseen.

Other advice

- | | |
|---|--|
| | The API does not require any special storage conditions
Store in the original package |
| - <i>Ventilation requirements</i> | Use in a well ventilated place at room temperature |
| - <i>Containers</i> | Keep containers tightly closed and correctly labeled |
| - <i>Specific design of storage rooms</i> | Not requested on the base of the classification |
| - <i>Quantity limits for storage</i> | Not requested on the base of the classification |
| - <i>Packaging compatibilities</i> | See also section 10.5 |

7.3. Specific end use(s)

Recommendations for specific end use as active pharmaceutical principle: avoid prolonged exposure through inhalation and swallowed.

SECTION 8 EXPOSURE CONTROLS/PERSONAL PROTECTION

8.1. Control parameters

- National/ European Occupational Exposure Limits	Not defined.
- Other National/ European Occupational Exposure Limits	Not defined.
- Recommended monitoring procedures	The measurement of substances in the workplace must be carried out with standardized methods (eg EN 689:1997: Workplace atmospheres - Guide for assessment of exposure by inhalation to chemical agents for comparison with limit values and measurement strategy; UNI EN 482:2006: atmospheres in the workplace - General requirements for the provision of procedures for the measurement of chemical agents) or, failing that, with appropriate methods.

8.2. Exposure controls

Appropriate risk management measures, that must be adopted at the workplace, have to be selected and applied, following the risks assessment carried out by the employer, in connection with his working activity (in accordance with Directive 98/24/EEC). If the results of this evaluation show that the general and collective prevention measures are not sufficient to reduce the risk, and if you can not prevent exposure to the mixture by other means, adequate personal protective equipments must be adopted, complying with the relevant technical EN standards.

Eye/ Face protection:	Safety goggles as for EN 166; facial shield
Skin protection:	
- <i>hands protection</i>	Wear protective gloves. Gloves resistant to chemical agents as for the EN 374, parts 1, 2 e 3 and the European Directive 89/89/CEE. The glove material has to be made of rubber or polyethylene impermeable and resistant to the substance. Make the choice of the glove material on consideration of the penetration times, rates of diffusion and degradation. The selection of suitable gloves not only depends on the material, but also on further marks of quality and varies from manufacturer to manufacturer.
- <i>other, body protection</i>	Select the suitable protective equipment based on the activity of use and possible exposure. Wear gauntlets, boots, bodysuit and other devices in accordance with EN 13982.
Respiratory protection:	Dust mask with approved dust filter. Use only devices approved by the Competent Authorities such as NIOSH (USA) and CEN (EU) In the case of brief exposure or minimal exposure use respiratory filter; in case of intensive and sustained exposition wear self-contained breathing. Where risk assessment shows air-purifying respirators are appropriate use a dust mask type P3 (EN 143) respirator
Environmental exposure controls:	Prevent the product from reaching surface water or groundwater.

SECTION 9 PHYSICAL AND CHEMICAL PROPERTIES

9.1. Information on basic physical and chemical properties

Appearance:	White or slightly yellow solid (crystalline powder)
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Odor:	Odourless
Odour threshold:	-
pH:	Data not available in the literature search carried out
Melting point:	256 °C ⁽¹⁾
Boiling point:	595.4 °C (predicted) ⁽²⁾
Flash point:	3136.9 °C (predicted) ⁽²⁾
Auto-ignition temperature:	Data not available in the literature search carried out
Surface tension:	53 dyne/cm (predicted) ⁽²⁾
Vapour pressure:	1.16x 10 ⁻¹⁶ mmHg at 25°C (predicted) ⁽²⁾
Density:	1.41 g/cm ³ (predicted) ⁽²⁾
Water solubility:	128.7 mg/L at 25°C (predicted) ⁽²⁾
Organic solvent solubility:	Easily soluble in acetic acid and dichloromethane. Slightly soluble in methanol and acetone
Partition coefficient Octanol/ water (Log Kow):	1.310 (predicted) ⁽¹⁾⁽²⁾
Explosive properties:	Data not available in the literature search carried out
Oxidising properties:	Data not available in the literature search carried out

9.2. Other information

Atmospheric OH Rate Constant 9.17 x 10⁻¹¹cm³/molecule-sec ⁽¹⁾

SECTION 10 STABILITY AND REACTIVITY

10.1. Reactivity

Stable in normal conditions of storage.

10.2. Chemical stability

The substance is stable at the normal condition of temperature and pressure and if stored in closed containers in well ventilated and cool place.

10.3. Possibility of hazardous reactions

No hazardous reactions occur under normal conditions of storage and use.

The substance is an organic powder, explosive mixtures with air may be formed under certain conditions (e.g. temperature, pressure, particle size, moisture, concentration comburent). The grounding system of the instrumentation in contact with the substance is recommended to perform to avoid the accumulation of electrostatic charger. The substance emits toxic fumes in case of fire.

10.4. Condition to avoid

Keep protected from light, humidity and high temperatures.

10.5. Incompatible materials

Strong oxidizing agents.

10.6. hazardous decomposition products

If heated at high temperatures, decomposes releasing fumes and toxic gases of COx.

SECTION 11 INFORMATION ON TOXICOLOGICAL EFFECTS

- Effects (acute, delayed, chronic) following the exposure (short and/or prolonged):

- *Inhalation:* Danger of serious damage caused by prolonged exposure
- *Ingestion:* Danger of serious damage caused by prolonged exposure
- *Skin contact:* Danger of serious damage caused by prolonged exposure

-Toxico-kinetics information (ADME = Adsorption, Distribution, Metabolism, Excretion):

Data not available in the literature search carried out

- Acute toxicity effects:

- *Oral:* LD₅₀ mouse = 5200 mg/kg ⁽¹⁾
- *Dermal:* Data not available in the literature search carried out
- *Inhalation:* Data not available in the literature search carried out
- *Other effects:* Data not available in the literature search carried out

- Corrosion/Irritation effects: Data not available in the literature search carried out

- Severe ocular lesion : Data not available in the literature search carried out

- Sensitization: Data not available in the literature search carried out

- Repeated dose toxicity: Data not available in the literature search carried out

CMR effects:

- **Germinal cell mutagenicity:** Data not available in the literature search carried out
- **Carcinogenicity :** TD_{L0} oral rat = 182 mg/kg (Duration 2Y – C) ⁽³⁾
- **Reproductive toxicity:** The administration of corticosteroids to pregnant animals showed reproductive toxicity. In reproduction studies, corticosteroids induced malformations (cleft palate and skeletal malformations) and intrauterine growth retardation. However, the effects were observed only at exposures considered sufficiently in excess the maximum human exposure, indicating little relevance to human use. ⁽⁴⁾
The Gur C. et al. supports that GCS do not represent a major teratogenic risk in humans. ⁽⁵⁾
Corticosteroids are excreted in breast milk in amounts presumed not high, but the long-term administration and/or high doses of corticosteroids may cause a reduction in height growth, body weight gain, intracranial hypertension (swelling of the fontanelle, headaches, bilateral papilledema), reduced plasma concentrations of cortisol, lack of response to adrenocorticotrophic hormone stimulation test (ACTH). ⁽⁴⁾

- Specific Target Organ Toxicity (STOT) - single exposure: Data not available in the literature search carried out

- Specific Target Organ Toxicity (STOT) - repeated exposure : Data not available in the literature search carried out

- Aspiration hazards: Data not available in the literature search carried out

- Epidemiological information: Data not available in the literature search carried out

SECTION 12 ECOLOGICAL INFORMATION

12.1. Toxicity

EC₅₀ Daphnia magna: > 3300 mg/l/24h

EC₅₀ Daphnia magna: > 2750 mg/l/48h

12.2. Persistence and degradability

Not easily degradable.

12.3. Bioaccumulative potential

BCF = 20.13 (predicted) ⁽²⁾

Log Pow = 1.31 (predicted)^{(1)/(2)}

12.4. Mobility in soil

Data not available in the literature search carried out.

12.5. Results of PBT e vPvB assessment

Assessment is not available - in relation to the available values a bioaccumulation potential is not expected.

12.6. Other adverse effects

Not known.

SECTION 13 DISPOSAL CONSIDERATION

13.1. Waste treatment methods

- Mixture wastes:
- Contaminated packaging:

Incineration	Recycling	Landfilling
X		
	X	

Should never be disposed through wastewater.

Refers to Community/National/Local requirements concerning the waste disposal.

SECTION 14 TRANSPORT INFORMATION

Not classified for transport in accordance with ADR/RID, IMDG, IATA regulations.

SECTION 15 REGULATORY INFORMATION

15.1 Safety, Health and Environmental regulation/legislation specific for the mixture or its ingredients

Council Directive 89/391/EEC of 12 June 1989 on the introduction of measures to encourage improvements in the safety and health of workers at work and following amendment and National reinforcements..

Council Directive 89/686/EEC of 21 December 1989 on the approximation of the laws of the Member States relating to the personal protective equipment

Council Directive 98/24/EC of 7 April 1998 on the protection of the health and safety of workers from the risks related to chemical agents at work (fourteenth individual Directive within the meaning of Article 16(1) of Directive 89/391/EEC) Official Journal L 131 , 05/05/1998 P. 0011 – 0023

Regulation (EC) no 689/2008 of the European parliament and of the council of 17 June 2008 concerning the export and import of dangerous chemicals.

15.2. Chemical Safety Assessment

Not performed.

SECTION 16 OTHER INFORMATION

Revision:

- **Revision n. 06** dated January, 2013 (regarding from section 2 to section 16).

Bibliographic sources:

- (1) ChemIDplus lite data base, search for CAS 14484-47-0
- (2) Chemspider data base, search for CAS 14484-47-0
- (3) TOPADD Toxicologic Pathology (c/o Dr. F.A. de la Iglesia, Warner-Lambert Co., Pharmaceutical Research Div., POB 1047, Ann Arbor, MI 48106) V.6(3/4)-1978
- (4) Purdy IB, Wiley DJ; Perinatal corticosteroids: A review of research. Part I: Antenatal administration; Neonatal Netw. 2004 Mar-Apr;23(2):15-30.
- (5) Gur C, Diav-Citrin O, Shechtman S, Arnon J, Ornoy A, Pregnancy outcome after first trimester exposure to corticosteroids: a prospective controlled study. Reproductive Toxicology (Elmsford, N.Y.) (2004) 18(1):93-101

Acronyms

- BEI : Biological Exposure Indices (Indici di esposizione biologica)
- CAS: Chemical Abstract Service (division of the American Chemical Society)
- CLP: Classification, Labelling and Packaging
- CMR: Carcinogens, Mutagens, Toxic for reproduction substances
- EINECS: European Inventory of existing Commercial Substances
- IUPAC: International Union of Pure and Applied Chemistry
- PPE : Personal protective Equipment
- PBT: Persistent, Bioaccumulative and Toxic substances
- vPvB: very Persistent, very Bioaccumulative

Information related to the regulation CE/1272/2008

List of hazards statements :

H361d	Suspected of damaging the unborn child
H362	May cause harm to breast-fed children
H373	May cause damage to organs through prolonged or repeated exposure.

List of Precautionary statements

P201	Obtain special instructions before use.
P308 + P313	IF exposed or concerned: Get medical advice/attention.
P260	Do not breathe dust/fume/gas/mist/vapours/spray.
P263	Avoid contact during pregnancy/while nursing.
P281	Use personal protective equipment as required.
P501	Dispose of contents/container to Community/National/Local requirements

Information related to the Directive 67/ 548/ CEE, Directive 1999/45/CE and Regulation (CE) n. 1907/2006

R phrase:

R63	Possible risk of harm to the unborn child
R64	May cause harm to breast-fed babies
R48/20/22	Harmful: danger of serious damage to health by prolonged exposure through inhalation and if swallowed

Information on workers training

Follow criteria of Directive 98/24/CE, its amendments and National reinforcements

Restriction of use : None

Substance under authorisation : no

DISCLAIMER

This document aims to provide guidance for appropriate handling and precaution of this product by qualified personnel or operating under the supervision of personnel trained in handling chemicals. The product should not be used for purposes other than those mentioned in section 1, unless they are given adequate written information received on how to handle the material. The provider of this document can not provide any warnings about the dangers of ' use or interaction with other chemicals or materials. And 'the user's safe use of the product, the product suitability for the purpose for which it is applied and proper disposal. The information below should not be considered a declaration or guarantee, 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 Annex I of Regulation No 453/2010/EU.

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