HALOBETASOL PROPIONATE

MATERIAL SAFETY DATA SHEET

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

Revision no. 4 - Revision date: April 5, 2012

SECTION 1.
IDENTIFICATION OF THE SUBSTANCE AND OF THE COMPANY

1.1. Substance identifier

Substance name:	**HALOBETASOL PROPIONATE**
Other names (if available): Name in Annex VI-CLP: Name reported in the inventory of harmonized classification and labelling:	21-chloro-6(a),9-difluoro-11(b),17-dihydroxy-16(b)-methylpregna-1,4-diene-3,20-dione-17-propionate unlisted not available
CAS number	66852-54-8
REACH registration number	Exempt of registration

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

Relevant use(s)	Anti infiammatory - 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.r.l**
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:
Aragona Anna Alessandra
e-mail: aragona@sterling.it

1.4. Emergency telephone 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:**

Hazard class	Class code and hazard category	Hazard statement	Hazard warning
Reproductive toxicity	**Repr. Cat. 2**	**H361d**	**Suspected of damaging the unborn child.**

- **Classification in accordance with Directive 67/548/CEE :**

Classification	Risk phrases	
Repr. Cat 3, R63	**R63**	**Possible risk of harm to the unborn child.**

Main adverse effects

Physico-chemical effects No adverse effects known.

Health effects This material is a potent topical steroid. The incidence of adverse effects from therapeutic use of corticosteroids increases with dose and duration of exposure; effects are rare with administration of less than three weeks.
Glucocorticoid effects may include bone fractures, back pain, joint pain or stiffness, weakness, high blood sugar, high blood pressure, increased appetite, infection, delayed wound healing, thinning skin, bruising, purple lines on skin, increased hair growth, acne, redistribution of body fat, menstrual irregularities, impotence, headache, increased sweating, eye pain, change in vision, and mental or behavioral changes. The mineralocorticoid actions of this material may cause disruption of fluid and electrolyte imbalance, causing swelling, increased blood pressure, confusion, lightheadedness, nausea, vomiting, numbness, and tremors.
Possible allergic reaction to material if inhaled, ingested or in contact with skin.

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**

Warning	
Signal Word	**Warning**
Hazard indication (H))[1]	**H361d - Suspected of damaging the unborn child.**
Safety statements (P)[1]	
- *Prevention*	**P201, P202, P281**
- *Reaction*	**P308+313**
- *Storage*	**P405**
- *Disposal*	**P501**

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

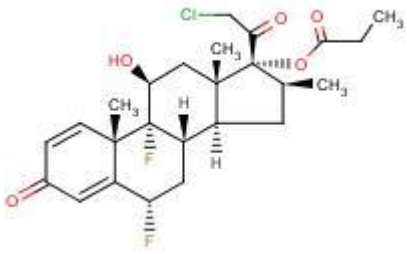
2.3 Other hazards (which do not results in the classification)

The substance satisfies the PBT criteria	YES	NO
- PBT		X
- vPvB		X

- Health hazards: May be harmful if ingested, inhaled or in contact with skin. May be irritant or sensitizer.
- Environmental hazards: not known
- Physico-chemical hazards: none
- Specific effects: unknown

SECTION 3
COMPOSITION/INFORMATION ON INGREDIENTS

Description: Active Pharmaceutical Principle; synthetic corticosteroid for topical dermatological use.

Name of the component	Halobetasol propionate
Concentration	Pure substance
Structural formula	
Chemical formula	$C_{25}H_{31}ClF_2O_5$
Molecular weight	485.0 g/mol
Substance with Community OEL	No
CAS name	Pregna-1,4-diene-3,20-dione, 21-chloro-6,9-difluoro-11-hydroxy-16-methyl-17-(1-oxopropoxy)-, (6.alpha.,11.beta.,16.beta.)-
CAS number	66852-54-8
IUPAC name	[(6S,9R,16S,17R)-17-(2-chloroacetyl)-6,9-difluoro-11-hydroxy-10,13, 16-trimethyl-3-oxo-6,7,8,11,12,14,15, 16-octahydrocyclopenta[a]phenanthren-17-yl] propanoate
EC number	not assigned
Index number	not assigned
Impurity/ies (if classified)	-
Additive/ies (if classified)	-

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)

- Acute effects	Possible eye, skin, gastrointestinal, and/or respiratory tract irritation.
- Delayed effects:	Possible hypersensitization, adrenal suppression, immune system depression, and hypercorticism or Cushing's syndrome. Withdrawal effects after chronic exposure is discontinued include fever, muscle pain, joint pain, and malaise.

4.3 Indication of any immediate medical attention and special treatment needed

Medical monitoring:	In case of prolonged exposure
- Antidotes, if known	unknow
- Contraindications	unknow
- Immediate treatment at workplace	not known

SECTION 5
FIREFIGHTING MEASURES

5.1 Extinguishing media

- Suitable estinguishing media	Water spray or chemical foam, dry foam, CO_2.
- Unsuitable estinguishing media	not known

5.2 Special hazards arising from the substance

- Hazardous combustion products	May generate toxic fumes of COx, F^- and Cl^-.
- Other special hazards	not known

5.3 Advice fo 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

- Containment procedures:	Coverage of the discharges
- Cleaning up procedures:	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

- Recommandation for handling:	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
- Recommandation for personal hygiene:	Do not absolutely 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

	Store at controlled room temperature
	Store in the original package
- *Ventilation requirements*	Use in a well ventilated place at room temperature
- *Containers*	Keep containers tightly closed and correctly labelled
- *Specific design of storage rooms*	Not requested on the base of the classification
- *Quantity limits for storage*	Not requested on the base of the classification
- *Packaging compatibilities*	See also section 10.5

7.3. Specific end use(s)

- Recommendation for specific final use(s): Active Pharmaceutical Principle

	YES	NO
- Exposure scenario attached		X
- Chemical Safety Assessment (CSA) attached		X
- Industry or sector specific guidance available and attached		X

SECTION 8
EXPOSURE CONTROLS/PERSONAL PROTECTION

8.1. Control parameters

- National/European Occupational Exposure Limits	unknow
- Other National/European Occupational Exposure Limits	unknow
- 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.
- DNEL values (components)	unknow
- PNEC values (components)	unknow

8.2. Exposure controls

	YES	NO
- Exposure scenario attached		X
- Chemical Safety Assessment (CSA) attached		X

8.2.1. Appropriate engineering controls

The adoption of the most appropriate technical controls is also based on the local Risk Assessment done by the employer in its workplace conditions (use of the substance) when a unique and standardized exposure scenario described in a dossier registered REACH is not available.

8.2.2. Individual protection measures, such as Personal Protective Equipment (PPE)

a) Eye and Face protection	Safety goggles as for EN 166; facial shield
b) Skin protection	
- *hands protection*	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.
- *other, body protection*	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.
c) 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
d) Thermal hazards	Not foreseen in the standard use. Assess possible Personal Protection Equipment on the basis of specific uses of the substance.

8.2.3 Environmental exposure controls

	YES	NO
- Exposure scenario attached		X
- Chemical Safety Assessment (CSA) attached		X

SECTION 9
PHYSICAL AND CHEMICAL PROPERTIES

9.1. Information on basic physical and chemical properties

Appearance:	white to ivory white solid (Crystalline powder)
Odor:	odourless
Odour threshold:	-
pH:	Data not available in the literature search carried out
Melting point/freezing point:	220-221 °C
Boiling point:	521.2 °C (predicted) (1)

Flash point:	298.9 °C (predicted) (1)
Auto-ignition temperature:	Data not available in the literature search carried out
Surface tension:	47.4 dyne/cm (predicted) (1)
Vapour pressure:	2.12x 10^{-15} mmHg at 25°C (predicted) (1)
Density:	1,31 g/cm³ (predicted) (1)
Water solubility:	Insoluble;
Organic solvent solubility:	Data not available in the literature search carried out
Partition coefficient Octonol/water (Log Kow):	3.73 (predicted by ACS/Lab); 2.85 (predicted by EPISuite) (1)
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

Henrys Law Constant (25 deg C) : 4.61E-014 atm-m³/mole (predicted) (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.

	NO	YES	Used stabiliser
- Stabilisers:	X	-	
- Change in physical appearance	X	-	

10.3. Possibility of hazardous reactions

	NO	YES
- Possibility of an exothermic reaction:	X	-
- Possibility of a reaction releasing excessive pressure	X	-
- Possible degradation with instable product formation	X	-

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 re leasing fumes and toxic gases of COx, F^- and Cl^-.

SECTION 11
INFORMATION ON TOXICOLOGICAL EFFECTS

- **Exposure routes:**	YES	NO
- Inhalation:	X	
- Ingestion:	X	
- Skin contact:	X	
- Eye contact:	X	

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

- Inhalation:	Suspected of damaging the unborn child. May be harmful or sensitizing by inhalation
- Ingestion:	May be harmful if swallowed
- Skin contact:	May be irritant or sensitizing.
- Eye contact:	May be irritant

-Toxico-kinetics information (ADME=Adsorption,Distribution,Metabolism,Excretion): (2)

The extent of percutaneous absorption of topical corticosteroids is determined by many factors including the vehicle and the integrity of the epidermal barrier. Topical corticosteroids can be absorbed from normal intact skin. Inflammation and/or other disease processes in the skin may increase percutaneous absorption.

Human and animal studies indicate that less than 6% of the applied dose of halobetasol propionate enters the circulation within 96 hours following topical administration of the cream. Studies performed with halobetasol propionate cream indicate that it is in the super-high range of potency as compared with other topical corticosteroids.

- Acute toxicity effects:

- Oral:	DL50 Orale - ratto > 15 ml/kg (3)
- Dermal:	Data not available in the literature search carried out
- Inhalation:	Data not available in the literature search carried out
- Other effects:	-
RTECS Number:	TU3723500

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

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

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

- **Repeated dose toxicity** (experimental.): Data not available in the literature search carried out

- CMR effects:

- **Germinal cell mutagenicity** (2):

Ames test: negative
Sister chromatid exchange test in somatic cells of the Chinese hamster: negative
Chromosome aberration: negative
Mammalian spot test to determine point mutations: negative
Mouse lymphoma gene mutation assay in vitro: positive
Chinese hamster Micronucleus test: positive

- **Carcinogenicity** [2]:
Long-term animal studies have not been performed to evaluate the carcinogenic potential of halobetasol propionate.

- **Reproductive toxicity** [2]:
Corticosteroids have been shown to be teratogenic in laboratory animals when administered systemically at relatively low dosage levels. Some corticosteroids have been shown to be teratogenic after dermal application in laboratory animals.
Halobetasol propionate has been shown to be teratogenic in SPF rats and chinchilla-type rabbits when given systemically during gestation at doses of 0.04 to 0.1 mg/kg in rats and 0.01 mg/kg in rabbits (approx.13, 33 and 3 times respectively the human topical dose).
Halobetasol propionate was embryotoxic in rabbits but not in rats. Cleft palate was observed in both rats and rabbits. Omphalocele was seen in rats, but not in rabbits. There are no adequate and well-controlled studies of the teratogenic potential of halobetasol propionate in pregnant women. Halobetasol Propionate Cream should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus; Pregnancy Category C.

- **Impairment of fertility** [2]:
Studies in the rat following oral administration at dose levels up to 50 µg/kg/day indicated no impairment of fertility or general reproductive performance.

- 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: [2] [4]
Systemically administered corticosteroids appear in human milk and could suppress growth, interfere with endogenous corticosteroid production, or cause other untoward effects. Halobetasol has not been studied during breastfeeding. Since only extensive application of the most potent corticosteroids may cause systemic effects in the mother, it is unlikely that short-term application of topical corticosteroids would pose a risk to the breastfed infant by passage into breastmilk.

SECTION 12
ECOLOGICAL INFORMATION

12.1. Toxicity

Data not available in the literature search carried out

12.2. Persistence and degradability

Data not available in the literature search carried out

12.3. Bioaccumulative potential

BCF = 400.27 (predicted) [1]
Log Pow = 3.73 (predicted by ACS/Lab); 2.85 (predicted by EPISuite) [1]

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 value of logPow and BCF a medium bioaccumulation potential is expected.

12.6. Other adverse effects

Not known

SECTION 13
DISPOSAL CONSIDERATION

13.1. Waste treatment methods

	Incineration	Recycling	Landfilling
- Mixture wastes:	X		
- Contaminated packaging:		X	

Should never be disposed through wastewater.
Refers to Community/National/Local requirements concerning the waste disposal.

SECTION 14
TRANSPORT INFORMATION

The substance is not classified for transport.

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

YES	NO

- Exposure scenario attached		X
- Chemical Safety Assessment (CSA) attached		X

SECTION 16
OTHER INFORMATION

Revisions:

- **Revision n. 03 dated** January 2011 (regarding all sections in according to Regulation no. 453/2010).

Bibliographic sources:

(1) Chemspider data base, search for CAS 66852-54-8
(2) Daily Med, Current Medication Information, HALOBETASOL PROPIONATE (halobetasol propionate) cream
(3) Medicamentos de Actualidad. Vol. 27, Pg. 304, 1991.
(4) Halobetasol - National Library of Medicine LactMed Database

Acronyms

- ACGIH: American Conference of Governmental Industrial Hygienists
- ADR: Agreement concerning the carriage of dangerous goods by Road
- BCF: Bioaccumulative factor
- BEI : Biological Esposure 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 re production substances
- EINECS: European Inventory of existing Commercial Substances
- EPA: US Environmental Protection Agency
- GHS: Globally Harmonised System
- IARC: International Agency for Research on Cancer
- IATA: International Air Transport Association Code
- IMDG: International Maritime Dangerous Goods Code
- 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
- PPE : Personal protective Equipment
- PBT: Persistent, Bioaccumulative and Toxic substances
- RID: Regulation concerning the International carriage of Dangerous goods by rail
- TLV/TWA: Threshold Limit Value/Threshold Weighted Average
- vPvB: very Persistent, very Bioaccumulative

Information related to the regulation CE/1272/2008

List of hazards statements

H361d: **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 havebeen 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 local/regional/ national/international regulation.**

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

R phrases

R63: **Possible risk of harm to the unborn child.**

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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