



MATERIAL SAFETY DATA SHEET

Cayman Pharma s.r.o.
277 11 NERATOVICE
CZECH REPUBLIC

ALPROSTADIL

Prepared: 1. 5. 2004
Revision No.: 4
Revised: 30. 11. 2010
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1. Identification of the substance/mixture and of the company/undertaking

1.1. Product identifier:

Product Name: **ALPROSTADIL**

Chemical name: (11 α ,13E,15S)-11,15-dihydroxy-9-oxoprost-13-en-1-oic acid

Synonyms: Prostaglandin E₁; PGE₁; Prost-13-en-1-oic acid, 11,15-dihydroxy-9-oxo-, (11 α ,13E,15S)

CAS No.: 745-65-3

ES No.: 212-017-2

1.2. Relevant identified uses of the substance or mixture and uses advised against:

Active pharmaceutical ingredient for production of drug products.

For professional use only. Caution: avoid exposure – obtain special instructions before use.

1.3. Details of the supplier of the safety data sheet:

Manufacturer name: Cayman Pharma s.r.o.

Address: ul. Práce 657, 277 11 Neratovice, Czech Republic

Company ID No.: 26499258

Telephone: +420 315 665 360

Fax: +420 315 665 384

E-mail: caymanpharma@caymanpharma.cz

www.caymanpharma.com

1.4. Emergency telephone number:

Toxikologické informační středisko (Information Centre of Toxicology)

Na Bojišti 1, 128 08 Praha 2, Czech Republic

24-hour telephone service: +420 224 919 293, +420 224 915 402, Fax: +420 224 914 570

2. Hazards identification

2.1. Classification of the substance or mixture:

Classification according to Regulation EC 1272/2008: Repr. 1B - Reproductive toxicity Category 1B, H360F - May damage fertility, Acute Tox. 3 - Acute toxicity Category 3, H301 - Toxic if swallowed.

Classification according to European Directive 67/548/EEC: toxic for reproduction of Category 2, Xn - harmful, R60-22 - May impair fertility. Harmful if swallowed.

Major hazards to human health and to the environment:

Hormonal substance, irritating to all mucous membranes, harmful if swallowed, may impair fertility. No negative impact on environment, easy biological decomposition.

2.2. Label elements:



Danger

H360F May damage fertility.

H301 Toxic if swallowed.

P201 Obtain special instructions before use.

P270 Do not eat, drink or smoke when using this product.

P281 Use personal protective equipment as required.



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P301 + P310 IF SWALLOWED: Immediately call a POISON CENTER or doctor/physician.

2.3. Other hazards: using the product differently than approved

3. Composition/information on ingredients

Substances:

ALPROSTADIL

Chemical name: (11 α ,13E,15S)-11,15-dihydroxy-9-oxoprost-13-en-1-oic acid

Synonyms: Prostaglandin E₁; PGE₁; Prost-13-en-1-oic acid, 11,15-dihydroxy-9-oxo-, (11 α ,13E,15S)

Formula: C₂₀H₃₄O₅

CAS No.: 745-65-3

ES No.: 212-017-2

MOLECULAR WEIGHT: 354.50

Assay: min. 95 %

Classification according to Regulation EC 1272/2008: Repr. 1B - Reproductive toxicity Category 1B, H360F - May damage fertility, Acute Tox. 3 - Acute toxicity Category 3, H301 - Toxic if swallowed

Classification according to European Directive 67/548/EEC: toxic for reproduction of Category 2, Xn - harmful, R60-22 - May impair fertility. Harmful if swallowed.

4. First aid measures

4.1. Description of first aid measures:

First of all, it is necessary to ensure safety both the exposed and aiding person!

Conditions endangering life:

- | | |
|------------------------|---|
| No breathing | - immediately resuscitate |
| Cardiac arrest | - immediately start indirect massage of heart |
| Unconsciousness | - stabilize position of the injured on his/her side |

Inhalation:

- stop the exposure immediately, transfer the injured to the fresh air (watch for contaminated clothing)
- keep the injured person warm
- ensure medical attention

Skin contact:

- remove contaminated clothing
- wash the exposed skin with large amount of tepid water (if available)
- if the skin is not injured, you may use soap
- ensure medical attention

Eye contact:

- start washing eyes immediately with running water, open eyelids (use force if necessary), or remove contact lenses
- keep washing for at least 10 minutes
- ensure medical attention

Ingestion:

- induce vomiting
- make the injured drink 0.5 litre of tepid water and induce vomiting again
- apply medicinal coal, if available
- ensure medical attention



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4.2. Most important symptoms and effects, both acute and delayed:

INHALATION - intensive irritation to upper respiratory tract. It may cause asthma.

SKIN CONTACT - causes blushing with potential for allergic reactions.

EYE CONTACT - may cause conjunctivitis.

INGESTION - nausea, diarrhoea, vomiting, stomach pain, difficult breathing, convulsions

4.3. Indication of any immediate medical attention and special treatment needed:

For more information, especially in serious events of health hazards, the attending physician may consult Information Centre of Toxicology.

24-hour telephone service: +420 224 919 293, +420 224 915 402, fax: +420 224 914 570

5. Firefighting measures

5.1. Extinguishing media:

Suitable extinguishing media: CO₂, water, foam.

Fire fighting: Remove material from fire area if it can be done without risk. Use extinguishing agents appropriate for specific fire. Stay downwind and keep out of low areas.

Unsuitable extinguishing media: not stated

5.2. Special hazards arising from the substance or mixture:

Avoid inhalation of combustion products. Carbon oxides may be formed by thermal decomposition in the center of fire decomposition.

5.3. Advice for firefighters:

Use isolating breathing apparatus to protect respiratory tract.

6. Accidental release measures

6.1. Personal precautions, protective equipment and emergency procedures:

Keep unauthorized people out of the hazard area. It is forbidden to smoke, eat and drink during work with the product. Wash yourself with soap and warm water after finishing the work.

6.2. Environmental precautions:

Clean the contaminated area as soon as possible.

6.3. Methods and material for containment and cleaning up:

Collect any spilled material in a suitable container for further processing or disposal. Wash contaminated place with water and detergent. The substance shall be liquidated in agreement with local regulations concerning disposals handling. While handling, minimize dusting.

6.4. Reference to other sections:

Use personal protective equipment (see section 8).

7. Handling and storage

7.1. Precautions for safe handling:

Work in a chemical fume hood. Avoid contact with eyes and skin. Wear protective gloves. Use anti-dust respirator to avoid inhaling of dust. It is forbidden to eat, drink and smoke during work.

Women are not allowed to work with the substance.

7.2. Conditions for safe storage, including any incompatibilities:

Store in a dark, dry place at a temperature of 2 to 8 °C.

7.3. Specific end use: The product is transported in original packing while following appropriate shipping rules (see section 14). The product is intended for production of drug products.



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8. Exposure controls/personal protection

8.1. Control parameters:

Exposure limits are not determined.

8.2. Exposure controls:

While working with the material, the concentrations of dust in the air must be kept as low as possible using properly designed technical equipment (ventilation, local exhaust etc.).

Respiratory tract protection

Suitable anti-dust respirator or other protective equipment against dust for respiratory tract protection is needed during handling the crystalline form of the material.

Hand protection

Use appropriate protective gloves.

Eye protection

Where needed, wear safety goggles or protective helmets.

Skin protection

Wear appropriate type of protective clothing to prevent long-term contact with the substance.

Environment exposure reduction: not applicable

9. Physical and chemical properties

9.1. Information on basic physical and chemical properties:

Appearance: fine, crystalline powder / white or almost white

Odor: odorless

pH: no data available

Melting point: 113 - 116 °C

Boiling point: no data available

Flash point: incombustible

Evaporation rate: no data available

Flammability: incombustible

Upper/lower flammability or explosive limits: no data available

Vapour pressure: no data available

Vapour density: no data available

Relative density: no data available

Solubility: soluble in ethanol, slightly soluble in chlorinated hydrocarbons, aromatic hydrocarbons, and ethyl acetate

Water solubility: partly soluble

Partition coefficient: n-octanol/water: no data available

Auto-ignition temperature: no data available

Decomposition temperature: no data available

Viscosity: no data available

Explosive properties: non-explosive

Oxidising properties: none

9.2. Other information: no data available

10. Stability and reactivity

10.1. Reactivity: no data available

10.2. Chemical stability: stable under recommended storage conditions (see section 7).

10.3. Possibility of hazardous reactions: no data available



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10.4. Conditions to avoid: dusting, moisture, light, temperature exceeding 8 °C

10.5. Incompatible materials: strong oxidizing agents

10.6. Hazardous decomposition products: thermal decomposition may cause formation of carbon oxides

11. Toxicological information

Information on toxicological effects:

Acute toxicity: LD₅₀ oral - rat = 228 mg/kg; LD₅₀ oral - mouse = 186 mg/kg

Skin corrosion/irritation: Upon contact with the skin it causes blushing. Potential risk of allergic reactions.

Serious eye damage/irritation: Direct contact may cause irritation and conjunctivitis.

Respiratory or skin sensitisation: May cause irritation to respiratory tract and skin.

Germ cell mutagenicity: no data available

Carcinogenicity: Not classified as a human carcinogen.

Reproductive toxicity: rat - Intraperitoneal

Maternal Effects: Postpartum.

Developmental Toxicity - rat - Subcutaneous

Specific developmental abnormalities: Central nervous system. Specific developmental abnormalities: eye, ear. Specific developmental abnormalities: Homeostasis

Developmental toxicity - mouse - Subcutaneous

Effects on embryo or fetus: Fetal death.

Specific target organ toxicity - single exposure: Ingestion may cause nausea, vomiting, stomach pain, diarrhoea, difficult breathing, and convulsions.

Specific target organ toxicity - repeated exposure: Repeated exposure causes hypersensitivity and has a negative impact on bone strength.

Aspiration hazard: no data available

Women are not allowed to work with the substance, it can cause hormonal disturbances. It can intensify vaginal contraction and induce abortion in pregnant women.

12. Ecological information

12.1. Toxicity: no data available

12.2. Persistence and degradability: The product is easily biologically degradable.

12.3. Bioaccumulative potential: no data available

12.4. Mobility in soil: no data available

12.5. Results of PBT and vPvB assessment: no data available

12.6. Other adverse effects: no data available

13. Disposal considerations

Waste treatment methods:

Product: Dissolve the substance residues in an inflammable solvent (e.g. ethanol) and then incinerate in an approved incinerator of chemical waste. Disposal shall be made by a competent firm. Respect all local laws and regulations concerning wastes and environment.

Contaminated packaging: Wash contaminated package with ethanol and subsequently with water. Disposal should be made according to the all local regulations and law valid in the relevant country.

Regulations of waste disposal in the Czech Republic: Act on wastes No. 185/2001 Coll., Catalogue of wastes (Regulation No. 381/2001 Coll.), as amended.



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14. Transport information

Special preventive measures: API/ active pharmaceutical ingredient for manufacture of drug products. Packed in controlled environment (clean rooms of Class 100,000). Tested on microbial contamination. DO NOT OPEN IMMEDIATE PACKAGING! The product may be opened only in controlled environment and sampled by sterile tools in order to prevent microbial contamination.

Transport conditions:

Transport conditions: temperature lower than +25 °C, dry place

Transport duration: within 10 days

Transport classification:

Road transport (ADR/RID):

UN 2811, Class 6.1 TOXIC SOLID, ORGANIC, N.O.S. (Alprostadil), Packing group: III

Air transport (IATA):

UN 2811, Class 6.1 TOXIC SOLID, ORGANIC, N.O.S. (Alprostadil), Packing group: III

15. Regulatory information

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

Czech Law No. 378/2007 Coll.

Regulation No. 229/2008 Coll.

Czech Law No. 356/2003 Coll.

Regulation No. 232/2004 Coll.

Czech Law No. 258/2000 Coll.

Government Directive No. 361/2007 Coll.

Regulation EC No. 1907/2006

Regulation EC No. 1272/2008

15.2. Chemical safety assessment: it has not been carried out

16. Other information

Changes implemented in Revision 4:

- The substance is classified in accordance with Regulation EC No. 1272/2008
- Change of the form of Material Safety Data Sheet in accordance with the Commission Regulation (EU) No. 453/2010

Declaration:

The Material Safety Data Sheet was prepared in accordance with the Regulation (EC) No 1907/2006 of the European Parliament and of the Council. The Material Safety Data Sheet contains data needed for securing safety and health protection as well as environment protection. Aforesaid data are in accordance with current knowledge and experience, and current regulations. However, there is no warranty of any kind, expressed or implied, applicable to its use and the user shall consider all risks and liabilities in connection therewith.