

Material Safety Data Sheet



SILDENAFIL CITRATE

No: 075/5

Edition date: 14.07.2010

Update: 01.12.2010

MSDS compliant with Regulation (EC) no 1907/2006 REACH, no 453/2010 and no 1272/2008 CLP

SECTION 1. Identification of the substance/mixture and of the company/undertaking

1.1. Product identifier

Trade name: **SILDENAFIL CITRATE**
CL inventory no:
EC no: ---
CAS no: 171599-83-0
IUPAC name: 5-[2-ethoxy-5-(4-methylpiperazin-1-ylsulphonyl)-phenyl]-1-methyl-3-n-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-on citrate
Registration no: ---

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

Sildenafil citrate is an active pharmaceutical ingredient used to treat erectile dysfunction.

1.3. Details of the supplier of the safety data sheet

Manufacturer: Pharmaceutical Works POLPHARMA S.A., BU Fine Chemicals
Address: 19 Pelplińska Str., 83-200 Starogard Gdański, POLAND
Phone: +48 58-563-20-02(04)
Fax: +48 58-563-20-08
E-mail address of the person responsible for the MSDS: karty.charakterystyk@polpharma.com

1.4. Emergency telephone number: +48 58-563-14-77 (available 24 h) or 112

SECTION 2. Hazard identification

2.1. Classification of the substance or mixture

The substance is not listed in the list of harmonised classification and labelling of hazardous substances (Regulation CLP no 1272/2008; Annex IV tab. 3.2.)

Basing on the available data the substance is classified as hazardous.

2.1.1. Classification according to the Directive 67/548/EEC with amendments

Adverse human effects

Xi Irritant substance
R: 36/37/38 Irritating to eyes, respiratory system and skin.

Environmental effects

Substance is not classified as dangerous to aquatic organisms.

2.1.2. Classification according to the Regulation (EU) No 1272/2008

Adverse human effects

Skin Irrit. 2 Skin irritation (category 2)
Eye Irrit. 2 Eye irritation (category 2)
Specific target organ toxicity - single exposure (category 3).

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Environmental effects

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2.2. Label elements

Hazard pictogram and signal word



Warning

Hazard statements

H315 Causes skin irritation.
H319 Causes serious eye irritation.
H335 May cause respiratory irritation.

Precautionary statements

P281 Use personal protective equipment as required
P305 + P351 + P338 IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.

Identification of the substance and the producer are the same as in the Section 1.

2.3. Other hazards

Under fire conditions toxic vapours can be emitted.

PBT and vPvB assessment according to the Annex XIII of REACH regulation was not conducted.

SECTION 3. Composition/information on ingredients

3.1. Substances

Substance name <i>IUPAC name</i>	Index no	WE no	CAS no	Molecular formula	Molecular weight [g/mol]	Content %
Sildenafil citrate <i>5-[2-ethoxy-5-(4-methylpiperazin-1-ylsulphonyl)-phenyl]-1-methyl-3-n-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-on citrate</i>	---	---	171599-83-0	$C_{22}H_{30}N_6O_4S \cdot C_6H_8O_7$	666.70	100

3.2. Mixtures

N/A

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SECTION 4. First aid measures

4.1. Description of first aid measures

Move victim to fresh air. If unconscious, place in a safe position, do not give anything by mouth, and call a physician.

In case of doubts or if symptoms persist, consult a physician, showing him this data sheet, container or label.

4.1.1. Exposure routes

After inhalation

Remove to fresh air, if not breathing give artificial respiration, if breathing is difficult, give oxygen. Call a physician.

After contact with skin

Remove contaminated clothing and shoes. Immediately wash skin with soap and large amounts of water. Call a physician.

After contact with eyes

Flush the eyes immediately with plenty of water for at least 15 minutes by separating eyelids with fingers. Call a physician.

After ingestion

Wash out mouth with water provided that person is conscious. Call a physician.

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

Symptoms include: headache, nausea, vomiting, feeling of fullness in nose, feeling of heat in the face, temporary vision disorders. Serious side effects occurs seldom. Increases the blood pressure. Can cause vision disorders and vertigo.

4.3. Indication of the immediate medical attention and special treatment needed.

Special treatment - observe the victim in the case of delayed symptoms. If breathing difficult give oxygen. Secure safety shower with the eye-wash station in the work place.

SECTION 5. Fire-fighting measures

5.1. Extinguishing media

Suitable extinguishing media: dispersed water, carbon dioxide, dry powders, foam

Unsuitable extinguishing media: no

5.2. Special hazards arising from the substance or mixture

May produce toxic fumes of carbon dioxide, carbon monoxide, nitrogen oxide if burning.

5.3. Advice for fire-fighters

The fire-fighters should use breathing apparatus with independent air circulation and with anti-chemical equipment. The clothes of the fire-fighting action participants should be heat-resistant.

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SECTION 6. Accidental release measures

6.1. Personal precautions, protective equipment and emergency procedures

Avoid contact with skin, eyes, breathing dust. Use personal protection described in section 8. Ensure a suitable ventilation system. Protect from contact with ignition sources.

6.2. Environmental precautions

Avoid pollution of soil, water and wastes.

6.3. Methods and materials for containment and cleaning up

Collect waste material on dry, place in containers and hold for waste disposal. Clean up affected area. Do not allow the release of substance to sewage system.

6.4. Reference to other sections.

Instructions and safety precautions which should be kept – refer to sections 7 and 8.
For disposal of solid materials or residues refer to section 13.

SECTION 7. Handling and storage

General rules of occupational safety and hygiene should be followed.

7.1. Precautions for safe handling

Avoid breathing dust. Do not allow for a contact with eyes, skin, clothing. Avoid prolonged or repeated exposure. Ensure a suitable ventilation system. Protect from contact with ignition sources.

Personal protection – refer to Section 8.

Wash hands carefully after the contact with the substance. Do not eat or drink or smoke in the work place. Separate the working clothes from the normal clothes.

7.2. Conditions for safe storage, including any incompatibilities

Store in tight, original, light-resistant containers

Protect from high temperature and strong oxidizing agents.

Secure measures to avoid contact with humidity or water.

In the storage area do not eat nor drink, do not smoke, do not use open fire or sparkling equipment.

7.3. Specific end use

Active pharmaceutical substance used in pharmaceutical industry

SECTION 8. Exposure controls / personal protection

8.1. Control parameters

Monitoring procedures

Procedures of monitoring of the hazardous substances concentrations in the air and procedures of the air purity control in the working environment – if are available and justified in the working place, should be applied according to the proper standards for the exposed working places with accurate measurements methodologies.

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8.2. Exposure controls

General rules of occupational safety and hygiene should be followed. All necessary technical means of precaution should be applied in order not to allow the product to spread in the environment. Shower with eye-wash stations should be ensured. Wash hands carefully after the contact with the substance. Do not eat or drink or smoke in the work place. Separate the working clothes from the normal clothes.

Personal protection means

Personal protection measures have to be in compliance with requirements from the Directive 89/686/WE (with later corrigendum). Employer is obliged to ensure proper protection means adequate to the activities conducted by the employees and which meet the quality requirements, are maintained and cleaned.

Hands protection: safety gloves

Gloves material should be impermeable and resistant to the product. The selection of the material should be done basing on the data: breakthrough time, penetration rate and degradation. Moreover the selection of the proper gloves should take into account also the quality characteristics and the producer. The information about the breakthrough time should be received from the producer and followed by the users.

Skin protection: protective suit and boots

Eye protection: safety goggles or face shield

Respiratory protection: mask with ProFlow respiration and filtering cartridge

Environmental exposure controls

Do not allow to release of the product to the ground waters, sewage, sewerage system or soil.

SECTION 9. Physical and chemical properties

9.1. Information on basic physical and chemical properties

Physical state:	crystalline powder
Colour:	white to almost white
Odour:	not tested
Odour threshold:	not tested
pH:	not tested
Melting / freezing point:	185 ÷ 195°C
Initial boiling point and boiling range:	672,4 (at pressure 760 mmHg)
Flash point:	380 ± 3,6°C
Evaporation rate:	not tested
Flammability:	not tested

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Flammability / explosive limits:

Lower: $80 \pm 6,3 \text{ g/m}^3$

Upper: not tested

Vapour pressure: not tested

Vapour density: not tested

Relative density (in temp. 20°C): not tested

Solubility(ies): very slightly soluble in water

freely soluble in ~2% sodium hydroxide solution, soluble in 0,1 mol/l hydrochloric acid solution, practically insoluble in chloroform, slightly soluble in methanol, very slightly soluble in 96% ethanol.

Partition coefficient: n-octanol/water: 0,93 (according to OSIRIS)

Auto-ignition temperature: not tested

Decomposition temperature: not tested

Viscosity: not tested

Explosive properties: dusts of the product can create explosive mixtures with air

Oxidising properties: not tested

Note: above data is typical and should not be taken as specification.

9.2. Other information

Maximum explosion pressure: $8,0 \pm 0,4 \text{ bar}$

Maximum speed of escalation of the pressure: $751 \pm 75 \text{ bar/s}$

Minimum dust/air mixture ignition energy: $< 2,9 \text{ mJ}$

Explosive index: $204 \pm 21 \text{ m-bar/s}$

Dust explosion class: St2

SECTION 10. Stability and reactivity

10.1. Reactivity

In standard conditions of use no hazardous reactions occur.

10.2. Chemical stability

Product is stabile provided that it is used and stored appropriately.

10.3. Possibility of hazardous reactions

No data available

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10.4. Conditions to avoid

Avoid ignition sources, high temperatures and lights.

10.5. Incompatible materials

Protect from strong oxidizing agents.

10.6. Hazardous decomposition products

May produce toxic fumes if burning.

SECTION 11. Toxicological information

11.1. Information on toxicological effects

11.1.1. Hazard classes

Acute toxicity

Not available

Skin corrosion / Irritation

Irritating to skin.

Serious eye damage / Irritation

Irritating to eyes.

Respiratory or skin sensitisation

Not available

Germ cell mutagenicity

Not available

Carcinogenicity

Not available

Reproductive toxicity

Not available

STOT – single exposure

May cause respiratory irritation.

STOT – repeated exposure

Not available

Aspiration hazard

Not available

11.1.2. Routes of exposure

After ingestion: may be harmful

After inhalation: may be harmful, irritation of mucous membranes and upper respiratory system

After eye contact: irritation,

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After skin contact: may be harmful if absorbed through the skin, irritation

11.1.3. Signs and symptoms of adverse exposure

Symptoms include: headache, nausea, vomiting, feeling of fullness in nose, feeling of heat in the face, temporary vision disorders. Serious side effects occurs seldom. Increases the blood pressure. Can cause vision disorders and vertigo.

Overdosage may cause abnormal prolonged erection, which in the extreme case may last for 6 hours. Drug abuse by healthy men cause erectile dysfunction without sildenafil, painful swelling of the penis, which may cause inflammatory condition and destruction of corpus cavernosum.

Side effect of consumption of sildenafil citrate are „blue vision” (the most frequent symptom), out-of-control movement of the eye and temporary blindness, which occurs very seldom (once on 1.5 million cases).

Person with arrhythmia, hypertension and predisposition to infarct, especially with medications causes release of nitric oxide by sympathetic nervous system, may occurs a heart attack and death.

11.1.4. Other information

Pharmacological activity: erectile dysfunction

TD (terapeutic dose) - 25 mg

LDD (max daily dose) - 100 mg

RTECS: TL4284390

SECTION 12. Ecological information

12.1. Toxicity

According to our best knowledge, ecotoxicological properties are not tested fully.

Do not allow the release of substance to water, sewage or soil.

12.2. Persistence and degradability

Not available

12.3. Bioaccumulative potential

Partition: The substance has low potential for bioaccumulation - $\log P(o/w)$: 0.93. ($\log P(o/w) < 4$)

12.4. Mobility in soil

Not available

12.5. Results of PBT and vPvB assessment

Not conducted

12.6. Other adverse effects

Not available

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SECTION 13. Disposal considerations

13.1. Waste treatment methods

Incineration - wastes formed at manufacturer/user site should mixed with a combustible solvent and burnt in a chemical incinerator equipped with an afterburner and scrubber according to current site manufacturing/using regulations.

Do not dispose the product to sewage pipes or water circulation.

Packaging after product follow current instructions of substance turnover site.

Observe all federal, state and local environmental regulations.

SECTION 14. Transport information

Substance is not dangerous in transport.

14.1. UN Number (ONZ)

N/A

14.2. UN proper shipping name

N/A

14.3. Transport hazard class

N/A

14.4. Packaging group

N/A

14.5. Environmental hazards

Substance is not classified as dangerous to aquatic organisms

14.6. Special precautions for users

Do not allow the release of substance to water, sewage or soil

14.7. Transport in bulk according to Annex II of MARPOL73/78 and the IBC Code

Not predicted

SECTION 15. Regulatory information

15.1. Regulations

REACH – Regulation concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals and establishing a European Chemicals Agency (Regulation (EC) no. 1907/2006 of December 18, 2006, OJ L136, 29.5.2007),

Commission Regulation (EU) No 453/2010 of 20 May 2010 amending Regulation (EC) No 1907/2006 of the European Parliament and of the Council on the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) OJ L133/53, 31.05.2010,

CLP – Regulation on classification, labelling and packaging of substances and mixtures, amending and repealing Directives 67/548/EEC, and amending Regulation (EC) No 1907/2006 (Regulation (EC) no. 1272/2008 of 16 December 2008, OJ L353/1, 31.12.2008),

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Council Directive 67/548/EEC of June 27, 1967 on the approximation of laws, regulations and administrative provisions relating to the classification, packaging and labelling of dangerous substances (OJ L 196, 16.08.1967),

The European Agreements concerning the International Carriage of Dangerous Goods by Road (ADR) and rail (RID).

15.2. Chemical Safety Assessment

According to Regulation (EU) num 1907/2006 REACH; art. 2 point 5a) chemical safety assessment for the active pharmaceutical ingredients is not required.

SECTION 16. Other information

Trainings

Before starting to work with the product, user should be trained and informed about the safe chemicals management rules, particularly pass the work station training.

Further information

Information included in this material safety data sheet applies for the Sildenafil citrate only and cannot be broaden on the other similar products.

This Material Safety Data Sheet has been prepared according to the best of our knowledge, gained current information and it characterizes the product from the safety point of view.

Calculation of the partition coefficient $P(o/w)$ was done using program OSIRIS Property Explorer which predicts the properties of substance basing on the chemical structure.

We shall not be held liable for any damage resulting from handling or from contact with the above described product.

Change control

General update in order to make it in compliance with the legal requirements.