



ZHEJIANG HUAHAI PHARMACEUTICAL Co., Ltd.
Xunqiao, Linhai, Zhejiang 317024, China

Material Safety Data Sheet

Compliant with Regulation (EC) No. 1907/2006 (Reach) and No. 1272/2008 (CLP)

Tadalafil

Revision Date: January 19, 2016

Supersedes: November 1, 2011

SECTION 1 – IDENTIFICATION OF THE SUBSTANCE / MIXTURE OF THE COMPANY / UNDERTAKING

Product identifier

Trade Name: Tadalafil
Common Name: Tadalafil
IUPAC Name: (6R,12aR)-6-(1,3-benzodioxol-5-yl)-2-methyl-2,3,6,7,12,12a-hexahydropyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione
Chemical Name: Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)-
Chemical Family: Indole
Formula: C₂₂H₁₉N₃O₄

Relevant identified uses of the substance and uses advised against:

Use of the Substance: Pharmaceutical

Company /undertaking identification:

Registered company name: Zhejiang Huahai Pharmaceutical Co Ltd.
Address: Xunqiao, Linhai, Zhejiang 317024, China
Telephone: 0086 576 8501 6200
Fax: 0086 576 8501 6474
E-mail: regulatory_affairs@huahaipharm.com
Web site: <http://www.huahaipharm.com>

SECTION 2 - HAZARD INFORMATION

Classification of the substance or mixture

Classification according to Regulation (EC) No 1272/2008[CLP]:



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Acute toxicity, Oral (Category 4)

Classification according to European Directives 67/548/EEC as amended

Harmful if swallowed.

EEC Label symbol and Classification



Signal word: Warning

Hazard Statement: H302

Precautionary statements:

P260: Do not breathe dust/fume/gas/mist/vapours/spray.

P280: Wear protective gloves/protective clothing/eye protection/face protection.

P270, P264: Do not eat, drink or smoke when using this product, and wash thoroughly after handling.

Other hazards

None

SECTION 3 - COMPOSITION/INFORMATION ON INGREDIENTS

Chemical Name	CAS-No.	EC and / or Registration number	Classification REGULATION (EC) No 1272/2008	Classification 67/548/EEC	Concentration [%]
Tadalafil	171596-29-5	NA	Acute toxicity, Oral (Category 4)	Harmful if swallowed.	100

SECTION 4 - FIRST AID MEASURES

Description of first aid measures

Inhalation: Remove to fresh air. If breathing is irregular or stopped, administer artificial respiration. Call a physician immediately.

Skin contact: Wash off immediately with plenty of water for at least 15 minutes. Take off all contaminated clothing immediately. Get medical attention if irritation develops and persists.

Eye contact: In case of eye contact, remove contact lens and rinse immediately with plenty of water, also under the eyelids, for at least 15 minutes. Obtain medical attention.

Ingestion: If conscious, give the victim plenty of water to drink. Never give anything by mouth to



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an unconscious person. Call a physician immediately.

Most important symptoms and effects, both acute and delayed

Symptoms: None known.

Hazards: May cause mild eye/skin irritation.

Indication of immediate medical attention and special treatment needed

Treatment: None known

SECTION 5 - FIREFIGHTING MEASURES

Extinguisher Media

Suitable extinguishing media: Water Carbon dioxide (CO₂) Dry chemical

Special hazards arising from the substance or mixture

Dust may form explosive mixture in air. Hazardous decomposition products formed under fire conditions.

Advice for firefighters

Wear self-contained breathing apparatus and protective clothing to prevent contact with skin and eyes.

SECTION 6 - ACCIDENTAL RELEASE MEASURES

Personal precautions, protective equipment and emergency procedures

Wear protective equipment, including eye protection, to avoid exposure (see Section 8 for specific handling precautions).

Environmental precautions

Try to prevent the material from entering drains or water courses. Refer to Sections 11 and 12 for health and environmental hazard information.

Methods and materials for containment and cleaning up

Do not sweep. Preferred method for spill cleanup is by using a HEPA equipped vacuum. Be aware of potential for dust explosion when using electrical equipment. If vacuum is not available, lightly mist/wet material and remove by mopping or wet wiping.

Reference to other sections

Refer to Sections 8, 11, 12 and 13 for more information.

SECTION 7 - HANDLING AND STORAGE



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Precautions for safe handling

Avoid contact with skin, eyes and clothing. Wash hands thoroughly after handling. For personal protection see section 8.

Conditions for safe storage, including any incompatibilities

Requirements for storage areas and containers: Keep container tightly closed in a dry and well-ventilated place.

Specific end uses

Not applicable.

SECTION 8 - EXPOSURE CONTROL / PERSONAL PROTECTION

Control parameters

Components	Exposure Limit Values
Tadalafil	LEG: 12 hour TWA 13 µg/m ³ LEG: 8 hour TWA 20 µg/m ³

Exposure controls

Engineering measures

Open handling is not recommended. Use appropriate control measures such as fume hood, ventilated enclosure, isolator (eg. glovebag, glovebox), or closed material transfer systems.

Personal protective equipment

Respiratory Protection: Respirator selection must be based on known or anticipated exposure levels, the hazards of the product and the safe working limits of the respirator. Use respirators and components tested and approved under appropriate government standards such as NIOSH (US) or CEN (EU).

Eye protection: Safety glasses with side-shields conforming to EN166

Skin and body protection: Chemical-resistant gloves and impermeable body covering to minimize skin contact. Protective gloves complying with EN 374.

SECTION 9 - PHYSICAL AND CHEMICAL PROPERTIES

Information on basic physical and chemical properties

Form: Solid

Physical state: Solid

Colour: practically white



Odour:	odourless
pH:	No data available
Melting point:	Approximate 300°C
Boiling point:	No data available
Flash point:	not applicable
Autoignition temperature:	No data available
Oxidizing properties:	The substance or mixture is not classified as oxidizing.
Lower explosion limit:	No data available
Upper explosion limit:	No data available
Vapour pressure:	No data available
Vapour pressure:	No data available
Density:	No data available
Specific Gravity:	No data available
Water solubility:	1,63 mg/l(pH 4), 1,29 mg/l(pH 7), 1,47 mg/l(pH 9)
log Pow:	2,32
Viscosity, dynamic:	No data available
Explosive properties:	Not explosive
Relative vapour density:	No data available
Evaporation rate:	No data available
Odor Threshold:	No data available

Other information

No information available.

SECTION 10 - STABILITY AND REACTIVITY

Reactivity

Reaction with water: Not water reactive.

Chemical stability

This material should not be packaged or stored above the following temperature: 180 °C.

This temperature is based on a laboratory test (DSC) and assumes near atmospheric pressures and quantities of less than 500kg (1100 lb) or 208 L (55 gal). For additional information refer to the CHL database on LillyNet or contact the Lilly Chemical Hazards Laboratory.

Possibility of hazardous reactions

Hazardous polymerisation does not occur.

Conditions to avoid



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None known.

Incompatible materials

Strong oxidizing agents.

Hazardous decomposition products

Hazardous decomposition products formed under fire conditions.

SECTION 11 - TOXICOLOGICAL PROPERTIES

Information on toxicological effects

Acute oral toxicity

Tadalafil: LD (rat) > 2 000 mg/kg
No mortality. No toxicity.

Acute inhalation toxicity

Tadalafil: This information is not available.

Acute dermal toxicity

Tadalafil: LD (rabbit) > 1 000 mg/kg
No mortality.

Acute toxicity (other routes of administration)

Tadalafil: Intravenous - LD (rat) > 62,5 mg/kg
No mortality. Convulsions.

Skin corrosion/irritation

Tadalafil: rabbit, slight irritation

Serious eye damage/eye irritation

Tadalafil: rabbit, slight irritation

Respiratory or skin sensitization

Tadalafil: This information is not available.

STOT - single exposure

No effects identified in animal studies.

STOT - repeated exposure

Tadalafil: Repeated oral doses of tadalafil for more than six months resulted in decreased testicular weight in dogs. The decreased testes weights (reported at doses of 25 mg/kg/day and above in the 12-month study) correlated with degeneration and atrophy of the seminiferous epithelium. Decreased sperm in the epididymes was also reported



with aspermia in the most severely affected dogs. No effects on semen parameters reported in humans after six-months of daily dosing (10 or 20 mg/day). When administered orally for 5 or 28 days at 5 mg/kg/day, blood pressure was reduced in rats. No significant findings were reported in rats or mice administered up to 800 mg/kg by oral gavage for up to 3 months.

Carcinogenicity

Tadalafil: Animal testing did not show any carcinogenic effects.

Reproductive toxicity

Tadalafil: There was no impairment of fertility in male and female rats. In beagle dogs given tadalafil daily for 6 to 12 months at doses of 25 mg/kg/day and above, there were alterations to the seminiferous tubular epithelium that resulted in a decrease in spermatogenesis in some dogs. These findings were not observed in rats or mice. Furthermore, in men taking tadalafil 10 or 20 mg/daily for 6 months, there were no clinically relevant effects on sperm concentration, count, motility, or morphology. Additionally, there were no significant effects of serum levels of testosterone, luteinizing hormone, or follicle stimulating hormone. There was no evidence of teratogenicity, embryotoxicity or fetotoxicity in rats or mice that received up to 1000 mg/kg/day. In a rat pre- and postnatal development study, the observed no effect dose was 30 mg/kg/day.

Germ cell mutagenicity

Tadalafil: Result in genetic toxicity assays (in vitro and in vivo): Negative.

Aspiration hazard

Tadalafil: No aspiration toxicity classification

SECTION 12 - ECOLOGICAL INFORMATION

Toxicity

Tadalafil: NOEC / 96 h / *Oncorhynchus mykiss* (rainbow trout): 2 100 µg/l (highest concentration tested)
LC50 / 96 h / *Oncorhynchus mykiss* (rainbow trout): > 2 100 µg/l
NOEC (embryo + 28 days post hatch) / *Pimephales promelas* (fathead minnow): 1 200 µg/l (highest concentration tested)
NOEC / 28 d / *C. riparius*: 250 mg/kg
EC50 / 72 h / *Pseudokirchneriella subcapitata* (green algae): > 1 200 µg/l (yield)
EC50 / 72 h / *Pseudokirchneriella subcapitata* (green algae): > 1 200 µg/l (average specific growth rate)
NOEC / 72 h / *Pseudokirchneriella subcapitata* (green algae): 300 µg/l (yield)
NOEC / 72 h / *Pseudokirchneriella subcapitata* (green algae): 1 200 µg/l (average specific growth rate) (highest concentration tested)
EC50 / 3 h / Respiration inhibition of activated sludge: > 1 000 mg/l
NOEC / 3 h / Respiration inhibition of activated sludge: 1 000 mg/l (highest concentration tested)
EC50 / 48 h / *Daphnia magna* (Water flea): > 2 000 µg/l



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NOEC / 48 h / Daphnia magna (Water flea): 2 000µg/l (highest concentration tested)

NOEC / 21 d / Daphnia magna (Water flea): 480µg/l (Full Life-Cycle Toxicity)

LOEC / 21 d / Daphnia magna (Water flea): 1 200µg/l (Full Life-Cycle Toxicity)

Aquatic Exposure Guideline

Tadalafil: Drinking Water: 2,5 µg/l

Chronic Exposure of Aquatic Organisms: 200µg/l

Acute Exposure of Aquatic Organisms: 1 000µg/l

Persistence and degradability

Biodegradability

Tadalafil: Log Koc: 1.95

Adsorption to sewage sludge after 4 hours, Kd: 183 to 644 (determined at a range of sludge concentrations from 313 to 2500 mg/L)

Biodegradation in Sludge:

DT50: 9 days

Degradation in Aquatic Sediments (108 day aerobic incubation):

DT50 from overlying water: 3.8 to 4.6 days

DT50 from water/sediment systems: 70 to 117 days

24-Hour municipal sewage sludge Kd (g total suspended solids/L): 180

24-Hour biodegradation in municipal sewage sludge (g total suspended solids/L): none

Bioaccumulative potential

Tadalafil: Log Kow: < 4.

Mobility in soil

No data available

Results of PBT and vPvB assessment

A Chemical Safety Assessment is not required for this substance.

Other adverse effects

None known

SECTION 13 - DISPOSAL CONSIDERATIONS

Waste treatment methods

In accordance with local and nation regulations.

SECTION 14 -TRANSPORT INFORMATION



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Special precautions for users

Not dangerous goods in the meaning of ADR, IMO/IMDG, ICAO/IATA

SECTION 15 - REGULATORY INFORMATION

This SDS complies with the requirement of Regulation (EC) No. 1907/2006

Symbol(s) None

Risk Phrase(s): None

Safety Phrase(s): S22: Do not breathe dust.
S36/37: Wear suitable protective clothing and gloves.

Labeling elements according to Regulation (EC) No. 1272/2008

Pictogram(s):



Signal Word: Warning

Hazard Statement(s) H302:Harmful if swallowed

Precautionary Statement(s): P260: Do not breathe dust/fume/gas/mist/vapours/spray.
P280: Wear protective gloves/protective clothing/eye protection/face protection.
P270, P264: Do not eat, drink or smoke when using this product, and wash thoroughly after handling.

Other Hazards: None.

SECTION 16 - OTHER INFORMATION

The contents and format of this SDS are in accordance with REGULATION (EC) No 1907/2006 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL, as amended.

Notice to reader:

The information and recommendations in this safety data sheet are, to the best of our knowledge, accurate as of the date of issue. Nothing herein shall be deemed to create any warranty, express or implied. It is the responsibility of the user to determine the applicability of this information and the suitability of the material or product for any particular purpose.