



SAFETY DATA SHEET

1. Identification

Product identifier Adcirca®

Other means of identification

Item Code ZD4467, TA4469, TA4468, ND1053, ND1054, ND1105, ND1106, TA4462, TA4463, TA4464, TA4465, VF0371, VF0372, VF0373, VF0378, ZD4125, TA4467, CT4465

LY Number LY450190

Recommended use Pharmaceutical

Recommended restrictions None known.

Manufacturer/Importer/Supplier/Distributor information

Manufacturer

Company name Eli Lilly and Company

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United States

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2. Hazard(s) identification

Physical hazards Not classified.

Health hazards Not classified.

OSHA defined hazards Not classified.

Label elements

Hazard symbol None.

Signal word None.

Hazard statement The mixture does not meet the criteria for classification.

Precautionary statement

Prevention Not available.

Response Not available.

Storage Not available.

Disposal Not available.

Hazard(s) not otherwise classified (HNOC) None known.

Supplemental information None.

3. Composition/information on ingredients

Mixtures

Chemical name	Common name and synonyms	CAS number	%
Tadalafil	Pyrazinopyridoindole-dione (6R,12aR)-6-(1,3-benzodioxol-5-yl)-2-methyl-2,3,6,7,12,12a-hexahydro-2-methyl-, hexahydropyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione 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)-	171596-29-5	1 - 7

Composition comments Remaining components of this product are non-hazardous and/or are present at concentrations below reportable levels.

4. First-aid measures

Inhalation	Remove to fresh air. If breathing stops, provide artificial respiration. Get medical attention immediately.
Skin contact	Wash off immediately with plenty of water. Continue to rinse for at least 15 minutes. Immediately take off all contaminated clothing. 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. Get medical attention.
Ingestion	Immediately give large quantities of water to drink. Never give anything by mouth to a victim who is unconscious or is having convulsions. Call a physician immediately.
Most important symptoms/effects, acute and delayed	Headache. Flushing.
Indication of immediate medical attention and special treatment needed	PRE-EXISTING MEDICAL CONDITIONS WHICH MAY BE AGGRAVATED BY EXPOSURE: Individuals on nitrate or alpha blocker therapy.
General information	The recommendations in this section are intended for manufacturing or other situations where exposure to contents may occur.

5. Fire-fighting measures

Suitable extinguishing media	Carbon dioxide, dry chemical or water.
Unsuitable extinguishing media	None known.
Specific hazards arising from the chemical	The recommendations in this section are intended for manufacturing or other situations where exposure to contents may occur. Hazardous decomposition products formed under fire conditions. If small particles are generated during further processing, handling, or by other means, may form combustible dust concentrations in air.
Special protective equipment and precautions for firefighters	Wear self-contained breathing apparatus and protective clothing.

6. Accidental release measures

Personal precautions, protective equipment and emergency procedures	Wear suitable protective clothing, gloves and eye/face protection. See Section 8 of the SDS for Personal Protective Equipment.
Methods and materials for containment and cleaning up	The recommendations in this section are intended for manufacturing or other situations where exposure to contents may occur. Do not sweep. Collect spill using a vacuum cleaner with a HEPA filter. 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.
Environmental precautions	Avoid discharge into drains, water courses or onto the ground.

7. Handling and storage

Precautions for safe handling	Avoid contact with eyes, skin, and clothing. Wash hands thoroughly after handling. See Section 8 of the SDS for Personal Protective Equipment.
Conditions for safe storage, including any incompatibilities	Storage temperature: between 15 C and 30 C.

8. Exposure controls/personal protection

Occupational exposure limits

Lilly (LEG)

Components

Tadalafil (CAS
171596-29-5)

Type

TWA (12hrs)

TWA (8hrs)

Value

13 ug/m3

20 ug/m3

Biological limit values

No biological exposure limits noted for the ingredient(s).

Appropriate engineering controls	The recommendations in this section are intended for manufacturing or other situations where exposure to contents may occur.
	Open handling is not recommended. Use appropriate control measures such as fume hood, ventilated enclosure, isolator (i.e. glove bag/glove box) and/or closed transfers to maintain airborne levels below occupational exposure level (OEL).
Individual protection measures, such as personal protective equipment	
Eye/face protection	Safety glasses with side shields recommended. If splash potential or dusty operations, wear goggles/faceshield.
Skin protection	
Hand protection	Chemical resistant gloves.
Other	Chemical-resistant gloves and impermeable body covering to minimize skin contact.
Respiratory protection	If the applicable occupational exposure level (OEL) is anticipated to be exceeded, wear an approved respirator with sufficient protection factor to control exposure below the OEL.
Thermal hazards	Not available.
General hygiene considerations	Engineering controls should be used as the primary means to control workplace exposures. Follow good workplace hygiene practices such as washing hands after handling this material.

9. Physical and chemical properties

Appearance

Physical state	Solid.
Form	Tablet.
Color	Yellow, Orange or White.
Odor	Odorless
Odor threshold	Not available.
pH	Not available.
Melting point/freezing point	Not available.
Initial boiling point and boiling range	Not available.
Flash point	Not applicable.
Evaporation rate	Not available.
Flammability (solid, gas)	No test data available.
Upper/lower flammability or explosive limits	
Flammability limit - lower (%)	Not available.
Flammability limit - upper (%)	Not available.
Explosive limit - lower (%)	Not available.
Explosive limit - upper (%)	Not available.
Vapor pressure	Not applicable.
Vapor density	Not applicable.
Relative density	Not available.
Solubility(ies)	
Solubility (water)	Not available.
Partition coefficient (n-octanol/water)	Not available.
Auto-ignition temperature	Not available.
Decomposition temperature	Not available.
Viscosity	Not available.
Other information	
Explosive properties	Not explosive.
Oxidizing properties	The substance or mixture is not classified as oxidizing.

10. Stability and reactivity

Reactivity	Not water reactive.
Chemical stability	Material is stable under normal conditions.
Possibility of hazardous reactions	Hazardous polymerization does not occur.
Conditions to avoid	None known.
Incompatible materials	Strong oxidizing substances.
Hazardous decomposition products	Hazardous decomposition products formed under fire conditions.

11. Toxicological information

Information on toxicological effects

Acute toxicity

Components	Species	Test Results
Tadalafil (CAS 171596-29-5)		
Acute		
Dermal		
LD	Rabbit	> 1000 mg/kg No mortality. No toxicity.
Oral		
LD	Rat	> 2000 mg/kg No mortality. No toxicity.
Other		
LD	Rat	> 62.5 mg/kg (Intravenous) No mortality. Convulsions.

Skin corrosion/irritation Rabbit: Slight irritation.
Based on available data, the classification criteria are not met.

Serious eye damage/eye irritation Rabbit: Slightly irritating.
Based on available data, the classification criteria are not met.

Respiratory or skin sensitization

Respiratory sensitization Due to lack of data the classification is not possible.

Skin sensitization Due to lack of data the classification is not possible.

Germ cell mutagenicity Result in genetic toxicity assays (in vitro and in vivo): Negative
Based on available data, the classification criteria are not met.

Carcinogenicity Not listed by ACGIH, IARC, NIOSH, NTP OR OSHA.
Based on available data, the classification criteria are not met.

IARC Monographs. Overall Evaluation of Carcinogenicity

Not listed.

OSHA Specifically Regulated Substances (29 CFR 1910.1001-1052)

Not regulated.

US. National Toxicology Program (NTP) Report on Carcinogens

Not listed.

Reproductive toxicity 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.
Based on available data, the classification criteria are not met.

Specific target organ toxicity - single exposure Due to lack of data the classification is not possible.

Specific target organ toxicity - repeated exposure 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. Based on available data, the classification criteria are not met.

Aspiration hazard Not applicable.

Further information Based on animal studies with Tadalafil, chronic overexposure by ingestion may cause testicular tissue changes and decreased sperm production. However, two six-month human clinical studies reported no changes in sperm parameters. The most common adverse effects related to drug treatment were headache, lower back pain, and vasodilation (flushing), which can result in transient decreases in blood pressure.

12. Ecological information

Ecotoxicity Harmful to aquatic life with long lasting effects.

Components		Species	Test Results
Tadalafil (CAS 171596-29-5)			
<i>Acute</i>			
	EC50		> 1000 mg/l, 3 hr (Respiration inhibition of activated sludge)
Other	EC50	Pseudokirchnerella subcapitata	> 1200 µg/l, 72 hr (yield)
<i>Chronic</i>			
	NOEC		1000 mg/l, 3 hr (Respiration inhibition of activated sludge) (highest concentration tested)
		Chironomus riparius (sediment dwelling midge)	250 mg/kg, 28 d (sediment exposure)
Other	NOEC	Pseudokirchnerella subcapitata	> 1200 µg/l, 72 hr (average specific growth rate) (highest concentration tested) 300 µg/l, 72 hr (yield)
Aquatic			
<i>Acute</i>			
Crustacea	EC50	Daphnia magna	> 2000 mg/l, 48 hr
	NOEC	Daphnia magna	1200 µg/l, 21 d (Full Life-Cycle Toxicity)
Fish	LC50	Rainbow trout,donaldson trout (Oncorhynchus mykiss)	> 2100 µg/l, 96 hr
<i>Chronic</i>			
Crustacea	LOEC	Daphnia magna	1200 µg/l, 21 d (Full Life-Cycle Toxicity)
	NOEC	Daphnia magna	2000 µg/l, 48 hr (highest concentration tested) 480 µg/l, 21 d (Full Life-Cycle Toxicity)
Fish	NOEC	Fathead minnow (Pimephales promelas)	1200 µg/l (embryo and 28 days post hatch) (highest concentration tested)
		Rainbow trout,donaldson trout (Oncorhynchus mykiss)	2100 µg/l, 96 hr (highest concentration tested)

LILLY AQUATIC EXPOSURE GUIDELINES:

Tadalafil

Drinking water LAEG (at the point where surface water is taken for drinking water): 2.5 µg/l
 Acute LAEG (at the edge of the acute mixing zone): 1000 µg/l
 Chronic LAEG (at the edge of the chronic mixing zone): 200 µg/l

Persistence and degradability Additional ecological information
Tadalafil
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
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 No data available on bioaccumulation.

Partition coefficient n-octanol / water (log Kow)

Tadalafil 2.32

Mobility in soil No data available.

Adsorption

Soil/sediment sorption - log Koc

Tadalafil 1.95

Other adverse effects Not available.

13. Disposal considerations

Disposal instructions Dispose in accordance with all applicable regulations.

14. Transport information

DOT

Not regulated as dangerous goods.

IATA

Not regulated as dangerous goods.

IMDG

Not regulated as dangerous goods.

Transport in bulk according to Annex II of MARPOL 73/78 and the IBC Code Not available.

15. Regulatory information

US federal regulations This product is not known to be a "Hazardous Chemical" as defined by the OSHA Hazard Communication Standard, 29 CFR 1910.1200.
One or more components are not listed on TSCA.

Toxic Substances Control Act (TSCA)

TSCA Section 12(b) Export Notification (40 CFR 707, Subpt. D)

Not regulated.

CERCLA Hazardous Substance List (40 CFR 302.4)

Not listed.

SARA 304 Emergency release notification

Not regulated.

OSHA Specifically Regulated Substances (29 CFR 1910.1001-1052)

Not regulated.

Superfund Amendments and Reauthorization Act of 1986 (SARA)

SARA 313 (TRI reporting)

Not regulated.

Other federal regulations

Clean Air Act (CAA) Section 112 Hazardous Air Pollutants (HAPs) List

Not regulated.

Clean Air Act (CAA) Section 112(r) Accidental Release Prevention (40 CFR 68.130)

Not regulated.

US state regulations

California Safe Drinking Water and Toxic Enforcement Act of 1986 (Proposition 65): This material is not known to contain any chemicals currently listed as carcinogens or reproductive toxins.

International Inventories

Country(s) or region	Inventory name	On inventory (yes/no)*
Canada	Domestic Substances List (DSL)	No
Canada	Non-Domestic Substances List (NDSL)	No
United States & Puerto Rico	Toxic Substances Control Act (TSCA) Inventory	No

*A "Yes" indicates that all components of this product comply with the inventory requirements administered by the governing country(s)

A "No" indicates that one or more components of the product are not listed or exempt from listing on the inventory administered by the governing country(s).

16. Other information, including date of preparation or last revision

Issue date 11-17-2014

Revision date 02-24-2019

Version # 08

List of abbreviations LEG: Lilly Exposure Guideline.
TWA: Time Weighted Average

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