

Tadalafil

sc-208412

Material Safety Data Sheet



The Power is Question

Hazard Alert Code Key:

EXTREME

HIGH

MODERATE

LOW

Section 1 - CHEMICAL PRODUCT AND COMPANY IDENTIFICATION

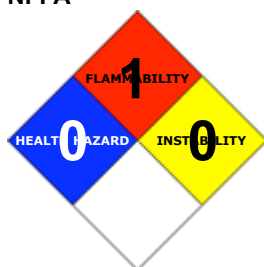
PRODUCT NAME

Tadalafil

STATEMENT OF HAZARDOUS NATURE

CONSIDERED A HAZARDOUS SUBSTANCE ACCORDING TO OSHA 29 CFR 1910.1200.

NFPA



SUPPLIER

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EMERGENCY:

ChemWatch
Within the US & Canada: 877-715-9305
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SYNONYMS

C22-H19-N3-O4, "(6R, 12aR)-6-(1, 3-benzodioxol-5-yl)-2, 3, 6, 7, 12, 12a-hexahydro-2-", "methyl-pyrazino[1', 2':1, 6]pyrido[3, 4-b]indole-1, 4-dione", "(6R-trans)-6-(1, 3-benzodioxol-5-yl)-2, 3, 6, 7, 12, 12a-hexahydro-2-", "methylpyrazino[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)-", Cialis, CIA, "vasodilator/ erectile dysfunction treatment", "phosphodiesterase inhibitor", (PDEI-V), "PDE-5 inhibitor"

Section 2 - HAZARDS IDENTIFICATION

CHEMWATCH HAZARD RATINGS

		Min	Max
Flammability:	1		
Toxicity:	2		
Body Contact:	2		
Reactivity:	1		
Chronic:	0		
			Min/Nil=0 Low=1 Moderate=2 High=3 Extreme=4

CANADIAN WHMIS SYMBOLS

None

EMERGENCY OVERVIEW RISK

POTENTIAL HEALTH EFFECTS

ACUTE HEALTH EFFECTS

SWALLOWED

■ Accidental ingestion of the material may be damaging to the health of the individual.

■ The material may produce biochemical inhibition of the enzyme, phosphodiesterase. Several families of drug (including xanthines, papaverine, bipyridines, imidazolines, imidazolones, dihydropyridazinones, dihydroquinilones, pyrrolidinones) produce this effect. Synthetic inhibitors of these types, (PDEIs), may produce a wide range of adverse effects in a clinical setting. These include tachycardia (elevated pulse rate), decreased blood pressure (hypotension), central nervous system effects, altered colour perception (a blue-green haze persists), an increased sensitivity to light (photophobia), dizziness, light-headedness, fainting, nausea, vomiting and diarrhoea, dyspepsia (upset stomach), facial flushing, nasal congestion, urinary tract infection, skin rash, muscle aches in the pelvic area and, rarely, heart attack or even stroke. Other reported effects include hepatotoxicity, especially in long-term treatment, dose-dependent thrombocytopenia, cardiac arrhythmia, headache, fever, chest pain and hypersensitivity reactions.

■ Penile erection during sexual stimulation is caused by increased penile blood flow resulting from the relaxation of penile arteries and corpus cavernosal smooth muscle. This response is mediated by the release of nitric oxide (NO) from nerve terminals and endothelial cells, which stimulates the synthesis of cGMP in smooth muscle cells. Cyclic GMP causes smooth muscle relaxation and increased blood flow into the corpus cavernosum. The inhibition of phosphodiesterase type 5 (PDE5) enhances erectile function by increasing the amount of cGMP. Certain drugs such as sildenafil, tadalafil, vardenafil inhibit PDE5 and are used in the treatment of erectile dysfunction. Because sexual stimulation is required to initiate the local release of nitric oxide, the inhibition of PDE5 by these drugs has no effect in the absence of sexual stimulation.

The most common side effects when using these drugs are headache, indigestion, back pain, muscle aches, flushing, and stuffy or runny nose. These side effects reflect the ability of PDE5 inhibition to vasodilate (cause blood vessels to widen) and usually go away after a few hours. Back pain and muscle aches can occur 12 to 24 hours after taking the drugs, and the symptom usually disappears after 48 hours.

Other symptoms include tinnitus, vertigo and dizziness.

Since PDE5 inhibitors may cause transiently low blood pressure (hypotension), organic nitrates should not be taken for at least 48 hours after taking the last dose. Using organic nitrites (such as the sex drug amyl nitrite) within this timeframe may increase the risk of life-threatening hypotension.

Since people who have taken PDE5 inhibitors within the past 48 hours cannot take organic nitrates to relieve angina (such as glyceryl trinitrate spray), these patients should seek immediate medical attention if they experience anginal chest pain.[5] In the event of a medical emergency, paramedics and medical personnel should be notified of any recent doses of the drug.

PDE5 inhibitors are associated with vision impairment related to NAION (non-arteritic anterior ischemic optic neuropathy) in certain patients taking these drugs in the post-marketing (outside of clinical trials) setting. Most, but not all, of these patients had underlying anatomic or vascular risk factors for development of NAION unrelated to PDE5 use, including: low cup to disc ratio ("crowded disc"), age over 50, diabetes, hypertension, coronary artery disease, hyperlipidemia and smoking. Given the small number of NAION events with PDE5 use (less than 1 in 1 million), the large number of users of PDE5 inhibitors (millions) and the fact that this event occurs in a similar population to those who do not take these medicines, the FDA concluded that they were not able to draw a cause and effect relationship, given these patients underlying vascular risk factors or anatomical defects.

The FDA also announced that the labeling for all PDE5 inhibitors requires a more prominent warning of the potential risk of sudden hearing loss as the result of postmarketing reports of deafness associated with use of PDE5 inhibitors. In most cases hearing loss involved one ear and about a third of the time it is temporary.

In patients with pulmonary arterial hypertension, it is believed that there is an imbalance of the PDE5/NO system in the pulmonary vasculature that favors selective vasoconstriction of the pulmonary artery. The use of PDE5 inhibitors in this disease assumes that PDE5 inhibition will result in pulmonary artery vasodilation, thus lowering pulmonary artery pressure and pulmonary vascular resistance. These physiologic changes may then reduce the workload of the right ventricle of the heart. Right heart failure is the main consequence of pulmonary arterial hypertension.

PDE5 inhibitors are primarily metabolised by the cytochrome P450 enzyme CYP3A4. The potential exists for adverse drug interactions with other drugs which inhibit or induce CYP3A4, including HIV protease inhibitors, ketoconazole, itraconazole, and other anti-hypertensive drugs such as Nitro-spray (due to its capacity to diminish blood pressure).

■ When given by mouth or by injection, in therapeutic doses, vasodilators may produce transient flushing of the face, a sensation of heat, a pounding in the head, peripheral oedema, headache, hypotension, palpitations, dizziness and fatigue. Most reactions are dose dependent and transient. High doses may cause flushing and dryness of the skin, skin lesions, abdominal cramps, diarrhoea, nausea, vomiting, malaise, anorexia, activation of peptic ulcer, jaundice and impairment of liver function, decrease in glucose tolerance, mild diabetes and hyperuricaemia. Most of these effects subside with withdrawal of the drug.

EYE

■ Although the material is not thought to be an irritant, direct contact with the eye may cause transient discomfort characterized by tearing or conjunctival redness (as with windburn). Slight abrasive damage may also result.

</p>

SKIN

■ The material is not thought to be a skin irritant (as classified using animal models). Abrasive damage however, may result from prolonged exposures.

</p>

■ Skin contact with the material may damage the health of the individual; systemic effects may result following absorption.

■ Entry into the blood-stream, through, for example, cuts, abrasions or lesions, may produce systemic injury with harmful effects. Examine the skin prior to the use of the material and ensure that any external damage is suitably protected.

INHALED

■ The material is not thought to produce either adverse health effects or irritation of the respiratory tract following inhalation (as classified using animal models). Nevertheless, adverse effects have been produced following exposure of animals by at least one other route and good hygiene practice requires that exposure be kept to a minimum and that suitable control measures be used in an occupational setting.

CHRONIC HEALTH EFFECTS

■ Long-term exposure to the product is not thought to produce chronic effects adverse to the health (as classified using animal models); nevertheless exposure by all routes should be minimized as a matter of course.

Long term exposure to high dust concentrations may cause changes in lung function i.e. pneumoconiosis; caused by particles less than 0.5 micron penetrating and remaining in the lung.

Section 3 - COMPOSITION / INFORMATION ON INGREDIENTS

NAME	CAS RN	%
tadalafil	171596-29-5	>98

Section 4 - FIRST AID MEASURES

SWALLOWED

· If swallowed do NOT induce vomiting. · If vomiting occurs, lean patient forward or place on left side (head-down position, if possible) to maintain open airway and prevent aspiration.

EYE

■ If this product comes in contact with the eyes: · Wash out immediately with fresh running water. · Ensure complete irrigation of the eye by keeping eyelids apart and away from eye and moving the eyelids by occasionally lifting the upper and lower lids.

SKIN

■ If skin contact occurs: · Immediately remove all contaminated clothing, including footwear · Flush skin and hair with running water (and soap if available).

INHALED

· If fumes or combustion products are inhaled remove from contaminated area. · Other measures are usually unnecessary.

NOTES TO PHYSICIAN

■ Treat symptomatically.

Section 5 - FIRE FIGHTING MEASURES

Vapour Pressure (mmHG):	Negligible
Upper Explosive Limit (%):	Not available.
Specific Gravity (water=1):	Not available
Lower Explosive Limit (%):	Not available

EXTINGUISHING MEDIA

· Foam.
· Dry chemical powder.

FIRE FIGHTING

· Alert Emergency Responders and tell them location and nature of hazard.
· Wear breathing apparatus plus protective gloves.

GENERAL FIRE HAZARDS/HAZARDOUS COMBUSTIBLE PRODUCTS

· Combustible solid which burns but propagates flame with difficulty.
· Avoid generating dust, particularly clouds of dust in a confined or unventilated space as dusts may form an explosive mixture with air, and any source of ignition, i.e. flame or spark, will cause fire or explosion. Dust clouds generated by the fine grinding of the solid are a particular hazard; accumulations of fine dust may burn rapidly and fiercely if ignited.
Combustion products include: carbon monoxide (CO), carbon dioxide (CO₂), nitrogen oxides (NO_x), sulfur oxides (SO_x), other pyrolysis products typical of burning organic material.
May emit poisonous fumes.

FIRE INCOMPATIBILITY

■ Avoid contamination with oxidizing agents i.e. nitrates, oxidizing acids, chlorine bleaches, pool chlorine etc. as ignition may result.

PERSONAL PROTECTION

Glasses:
Chemical goggles.
Gloves:
Respirator:
Particulate

Section 6 - ACCIDENTAL RELEASE MEASURES

MINOR SPILLS

· Clean up waste regularly and abnormal spills immediately.
· Avoid breathing dust and contact with skin and eyes.
· Wear protective clothing, gloves, safety glasses and dust respirator.
· Use dry clean up procedures and avoid generating dust.
· Vacuum up or sweep up. NOTE: Vacuum cleaner must be fitted with an exhaust micro filter (HEPA type) (consider explosion-proof

machines designed to be grounded during storage and use).

- Dampen with water to prevent dusting before sweeping.
- Place in suitable containers for disposal.

MAJOR SPILLS

- Moderate hazard.
- CAUTION: Advise personnel in area.
- Alert Emergency Responders and tell them location and nature of hazard.

Section 7 - HANDLING AND STORAGE

PROCEDURE FOR HANDLING

- Avoid all personal contact, including inhalation.
 - Wear protective clothing when risk of exposure occurs.
- Empty containers may contain residual dust which has the potential to accumulate following settling. Such dusts may explode in the presence of an appropriate ignition source.
- Do NOT cut, drill, grind or weld such containers.
 - In addition ensure such activity is not performed near full, partially empty or empty containers without appropriate workplace safety authorisation or permit.

RECOMMENDED STORAGE METHODS

- Glass container.
- Polyethylene or polypropylene container.
- Check all containers are clearly labelled and free from leaks.

STORAGE REQUIREMENTS

- Store in original containers.
- Keep containers securely sealed.

Section 8 - EXPOSURE CONTROLS / PERSONAL PROTECTION

EXPOSURE CONTROLS

The following materials had no OELs on our records

- tadalafil: CAS:171596-29-5 CAS:337376-15-5

PERSONAL PROTECTION



RESPIRATOR

Particulate

Consult your EHS staff for recommendations

EYE

- When handling very small quantities of the material eye protection may not be required.

For laboratory, larger scale or bulk handling or where regular exposure in an occupational setting occurs:

- Chemical goggles
- Face shield. Full face shield may be required for supplementary but never for primary protection of eyes
- Contact lenses may pose a special hazard; soft contact lenses may absorb and concentrate irritants. A written policy document, describing the wearing of lens or restrictions on use, should be created for each workplace or task. This should include a review of lens absorption and adsorption for the class of chemicals in use and an account of injury experience. Medical and first-aid personnel should be trained in their removal and suitable equipment should be readily available. In the event of chemical exposure, begin eye irrigation immediately and remove contact lens as soon as practicable. Lens should be removed at the first signs of eye redness or irritation - lens should be removed in a clean environment only after workers have washed hands thoroughly. [CDC NIOSH Current Intelligence Bulletin 59].

HANDS/FEET

- Suitability and durability of glove type is dependent on usage. Important factors in the selection of gloves include: such as:

- frequency and duration of contact,
- chemical resistance of glove material,
- glove thickness and
- dexterity

Select gloves tested to a relevant standard (e.g. Europe EN 374, US F739).

- When prolonged or frequently repeated contact may occur, a glove with a protection class of 5 or higher (breakthrough time greater than 240 minutes according to EN 374) is recommended.
- When only brief contact is expected, a glove with a protection class of 3 or higher (breakthrough time greater than 60 minutes according to EN 374) is recommended.
- Contaminated gloves should be replaced.

Gloves must only be worn on clean hands. After using gloves, hands should be washed and dried thoroughly. Application of a non-perfumed moisturiser is recommended.

- Rubber gloves (nitrile or low-protein, powder-free latex). Employees allergic to latex gloves should use nitrile gloves in preference.
- Double gloving should be considered.
- PVC gloves.
- Protective shoe covers.
- Head covering.

Experience indicates that the following polymers are suitable as glove materials for protection against undissolved, dry solids, where abrasive particles are not present.

- polychloroprene
- nitrile rubber
- butyl rubber
- fluorocarbon
- polyvinyl chloride

Gloves should be examined for wear and/ or degradation constantly.

OTHER

- For quantities up to 500 grams a laboratory coat may be suitable.
- For quantities up to 1 kilogram a disposable laboratory coat or coverall of low permeability is recommended. Coveralls should be buttoned at collar and cuffs.
- For quantities over 1 kilogram and manufacturing operations, wear disposable coverall of low permeability and disposable shoe covers.
- For manufacturing operations, air-supplied full body suits may be required for the provision of advanced respiratory protection.
- Eye wash unit.
- Ensure there is ready access to an emergency shower.
- For Emergencies: Vinyl suit.

ENGINEERING CONTROLS

- Enclosed local exhaust ventilation is required at points of dust, fume or vapor generation.

HEPA terminated local exhaust ventilation should be considered at point of generation of dust, fumes or vapors.

Section 9 - PHYSICAL AND CHEMICAL PROPERTIES

PHYSICAL PROPERTIES

Solid.

Does not mix with water.

State	Divided solid	Molecular Weight	389.4
Melting Range (°F)	Not available	Viscosity	Not Applicable
Boiling Range (°F)	1254.2 (calc)	Solubility in water (g/L)	Partly miscible
Flash Point (°F)	687.2 (calc)	pH (1% solution)	Not applicable
Decomposition Temp (°F)	Not available	pH (as supplied)	Not applicable
Autoignition Temp (°F)	Not available	Vapour Pressure (mmHG)	Negligible
Upper Explosive Limit (%)	Not available.	Specific Gravity (water=1)	Not available
Lower Explosive Limit (%)	Not available	Relative Vapor Density (air=1)	>1
Volatile Component (%vol)	Negligible	Evaporation Rate	Not applicable

APPEARANCE

White to off-white crystalline powder; does not mix well with water .

Section 10 - CHEMICAL STABILITY

CONDITIONS CONTRIBUTING TO INSTABILITY

- Presence of incompatible materials.
- Product is considered stable.

STORAGE INCOMPATIBILITY

- Avoid reaction with oxidizing agents.

For incompatible materials - refer to Section 7 - Handling and Storage.

Section 11 - TOXICOLOGICAL INFORMATION

TADALAFIL

TOXICITY AND IRRITATION

TADALAFIL:

- No significant acute toxicological data identified in literature search.

Section 12 - ECOLOGICAL INFORMATION

No data

Section 13 - DISPOSAL CONSIDERATIONS

Disposal Instructions

All waste must be handled in accordance with local, state and federal regulations.

† Legislation addressing waste disposal requirements may differ by country, state and/ or territory. Each user must refer to laws operating in their area. In some areas, certain wastes must be tracked.

A Hierarchy of Controls seems to be common - the user should investigate:

- Reduction
- Reuse
- Recycling
- Disposal (if all else fails)

This material may be recycled if unused, or if it has not been contaminated so as to make it unsuitable for its intended use. Shelf life considerations should also be applied in making decisions of this type. Note that properties of a material may change in use, and recycling or reuse may not always be appropriate.

DO NOT allow wash water from cleaning equipment to enter drains. Collect all wash water for treatment before disposal.

- Recycle wherever possible.
- Consult manufacturer for recycling options or consult Waste Management Authority for disposal if no suitable treatment or disposal facility can be identified.

Section 14 - TRANSPORTATION INFORMATION

NOT REGULATED FOR TRANSPORT OF DANGEROUS GOODS: DOT, IATA, IMDG

Section 15 - REGULATORY INFORMATION

No data for tadalafil (CAS: , 171596-29-5, 337376-15-5)

Section 16 - OTHER INFORMATION

LIMITED EVIDENCE

- Skin contact and/or ingestion may produce health damage*.

* (limited evidence).

Ingredients with multiple CAS Nos

Ingredient Name CAS tadalafil 171596-29-5, 337376-15-5

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- Classification of the preparation and its individual components has drawn on official and authoritative sources as well as independent review by the Chemwatch Classification committee using available literature references.

A list of reference resources used to assist the committee may be found at:

www.chemwatch.net/references.

- The (M)SDS is a Hazard Communication tool and should be used to assist in the Risk Assessment. Many factors determine whether the reported Hazards are Risks in the workplace or other settings. Risks may be determined by reference to Exposures Scenarios. Scale of use, frequency of use and current or available engineering controls must be considered.

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