



# MATERIAL SAFETY DATA SHEET

Revision date: 02-Apr-2009

Version: 1.0

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## 1. IDENTIFICATION OF THE SUBSTANCE/PREPARATION AND THE COMPANY/UNDERTAKING

Pfizer Inc  
Pfizer Pharmaceuticals Group  
235 East 42nd Street  
New York, New York 10017  
1-212-573-2222

Emergency telephone number:  
1-877-777-3180

Contact E-Mail: pfizer-MSDS@pfizer.com

Pfizer Global Manufacturing  
Pfizer Inc  
235 East 42nd Street  
New York, NY 10017

Emergency telephone number:  
ChemSafe (24 hours): +44 (0)208 762 8322

### Material Name: Sildenafil Citrate Powder for Oral Solution

**Trade Name:** Revatio  
**Synonyms:** Sildenafil Citrate Powder for Oral Solution; REVATIO POS  
**Chemical Family:** Mixture  
**Intended Use:** Pharmaceutical product used for Treatment of pulmonary arterial hypertension

## 2. HAZARDS IDENTIFICATION

**Appearance:** Powder

**Statement of Hazard:** Non-hazardous in accordance with international standards for workplace safety.

**Additional Hazard Information:**

**Short Term:** May be harmful if swallowed. May cause eye irritation (based on components)  
**Long Term:** Animal studies indicate that this material may cause adverse effects on the cardiovascular system.

**Known Clinical Effects:** Adverse effects most commonly reported in clinical use include difficult digestion (dyspepsia), nose bleed, headache, flushing, insomnia, abnormal redness of skin (erythema), difficulty breathing, muscle pain, fever, gastrointestinal irritation, tingling/itching (paresthesia), transient changes in light perception and color vision, effects on hearing, and effects on vision.

**EU Indication of danger:** Not classified

**Australian Hazard Classification (NOHSC):** Non-Hazardous Substance. Non-Dangerous Goods.

**Note:** This document has been prepared in accordance with standards for workplace safety, which require the inclusion of all known hazards of the product or its ingredients regardless of the potential risk. The precautionary statements and warnings included may not apply in all cases. Your needs may vary depending upon the potential for exposure in your workplace.

## 3. COMPOSITION/INFORMATION ON INGREDIENTS

**Hazardous**

Ingredient	CAS Number	EU EINECS/ELINCS List	Classification	%
Sildenafil citrate	171599-83-0	Not listed	Xn;R22	3.5
Titanium dioxide	13463-67-7	236-675-5	Not Listed	*

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### 3. COMPOSITION/INFORMATION ON INGREDIENTS

Citric acid	77-92-9	201-069-1	Xi; R36	*
Colloidal silicon dioxide	7631-86-9	231-545-4	Not Listed	*

Ingredient	CAS Number	EU EINECS/ELINCS List	Classification	%
Sucralose	56038-13-2	259-952-2	Not Listed	*
Sorbitol	6706-59-8	Not listed	Not Listed	*
Sodium benzoate	532-32-1	208-534-8	Not Listed	*
Sodium citrate	68-04-2	200-675-3	Not Listed	*
Flavor	NOT ASSIGNED	Not listed	Not Listed	*
Xanthan gum	11138-66-2	234-394-2	Not Listed	*

#### Additional Information:

\* Proprietary

Ingredient(s) indicated as hazardous have been assessed under standards for workplace safety.

For the full text of the R phrases mentioned in this Section, see Section 16

### 4. FIRST AID MEASURES

<b>Eye Contact:</b>	Flush with water while holding eyelids open for at least 15 minutes. Seek medical attention immediately.
<b>Skin Contact:</b>	Remove contaminated clothing. Flush area with large amounts of water. Use soap. Seek medical attention.
<b>Ingestion:</b>	Never give anything by mouth to an unconscious person. Wash out mouth with water. Do not induce vomiting unless directed by medical personnel. Seek medical attention immediately.
<b>Inhalation:</b>	Remove to fresh air and keep patient at rest. Seek medical attention immediately.
<b>Symptoms and Effects of Exposure:</b>	For information on potential signs and symptoms of exposure, See Section 2 - Hazards Identification and/or Section 11 - Toxicological Information.

### 5. FIRE FIGHTING MEASURES

<b>Extinguishing Media:</b>	Use carbon dioxide, dry chemical, or water spray.
<b>Hazardous Combustion Products:</b>	Formation of toxic gases is possible during heating or fire.
<b>Fire Fighting Procedures:</b>	During all fire fighting activities, wear appropriate protective equipment, including self-contained breathing apparatus.
<b>Fire / Explosion Hazards:</b>	Fine particles (such as dust and mists) may fuel fires/explosions.

### 6. ACCIDENTAL RELEASE MEASURES

<b>Health and Safety Precautions:</b>	Personnel involved in clean-up should wear appropriate personal protective equipment (see Section 8). Minimize exposure.
<b>Measures for Cleaning / Collecting:</b>	Contain the source of spill if it is safe to do so. Collect spilled material by a method that controls dust generation. A damp cloth or a filtered vacuum should be used to clean spills of dry solids. Clean spill area thoroughly.

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**Measures for Environmental Protections:** Place waste in an appropriately labeled, sealed container for disposal. Care should be taken to avoid environmental release.

**Additional Consideration for Large Spills:** Non-essential personnel should be evacuated from affected area. Report emergency situations immediately. Clean up operations should only be undertaken by trained personnel.

### 7. HANDLING AND STORAGE

**General Handling:** Minimize dust generation and accumulation. Avoid breathing dust. Avoid contact with eyes, skin and clothing. Refer to Section 12 - Ecological Information, for information on potential effects on the environment. Wash hands and any exposed skin after removal of PPE. Releases to the environment should be avoided. Review and implement appropriate technical and procedural waste water and waste disposal measures to prevent occupational exposure or environmental releases. Potential points of process emissions of this material to the atmosphere should be controlled with dust collectors, HEPA filtration systems or other equivalent controls.

**Storage Conditions:** Store as directed by product packaging.

### 8. EXPOSURE CONTROLS / PERSONAL PROTECTION

Refer to available public information for specific member state Occupational Exposure Limits.

#### Sildenafil citrate

Pfizer OEL TWA-8 Hr: 350µg/m<sup>3</sup>

#### Titanium dioxide

ACGIH Threshold Limit Value (TWA)	10 mg/m <sup>3</sup> TWA
Australia TWA	10 mg/m <sup>3</sup>
Austria OEL - MAKs	Listed
Belgium OEL - TWA	Listed
Bulgaria OEL - TWA	Listed
Denmark OEL - TWA	Listed
Estonia OEL - TWA	Listed
France OEL - TWA	Listed
Greece OEL - TWA	Listed
Ireland OEL - TWAs	Listed
Latvia OEL - TWA	Listed
Lithuania OEL - TWA	Listed
OSHA - Final PELs - TWAs:	15 mg/m <sup>3</sup> total
Poland OEL - TWA	Listed
Portugal OEL - TWA	Listed
Romania OEL - TWA	Listed
Spain OEL - TWA	Listed
Sweden OEL - TWAs	Listed

#### Colloidal silicon dioxide

Australia TWA	2 mg/m <sup>3</sup>
Austria OEL - MAKs	Listed
Czech Republic OEL - TWA	Listed
Estonia OEL - TWA	Listed
Germany - TRGS 900 - TWAs	4 mg/m <sup>3</sup>
Germany (DFG) - MAK	4 mg/m <sup>3</sup> MAK
Ireland OEL - TWAs	Listed

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### 8. EXPOSURE CONTROLS / PERSONAL PROTECTION

Latvia OEL - TWA	Listed
OSHA - Final PELs - Table Z-3 Mineral D:	- (80)/(% SiO <sub>2</sub> ) mg/m <sup>3</sup> TWA TWA-20 mppcf
Slovenia OEL - TWA	Listed

The exposure limit(s) listed for solid components are only relevant if dust may be generated.

<b>Analytical Method:</b>	Analytical method available for Sildenafil. Contact Pfizer Inc for further information.
<b>Engineering Controls:</b>	Engineering controls should be used as the primary means to control exposures. General room ventilation is adequate unless the process generates dust, mist or fumes. Keep airborne contamination levels below the exposure limits listed above in this section.
<b>Environmental Exposure Controls:</b>	Refer to specific Member State legislation for requirements under Community environmental legislation.
<b>Personal Protective Equipment:</b>	Refer to applicable national standards and regulations in the selection and use of personal protective equipment (PPE).
<b>Hands:</b>	Impervious gloves are recommended if skin contact with drug product is possible and for bulk processing operations.
<b>Eyes:</b>	Wear safety glasses or goggles if eye contact is possible.
<b>Skin:</b>	Impervious protective clothing is recommended if skin contact with drug product is possible and for bulk processing operations.
<b>Respiratory protection:</b>	If the applicable Occupational Exposure Limit (OEL) is exceeded, wear an appropriate respirator with a protection factor sufficient to control exposures to below the OEL.

### 9. PHYSICAL AND CHEMICAL PROPERTIES:

<b>Physical State:</b>	Powder	<b>Color:</b>	No data available.
<b>Molecular Formula:</b>	Mixture	<b>Molecular Weight:</b>	Mixture

### 10. STABILITY AND REACTIVITY

<b>Stability:</b>	Stable under normal conditions of use.
<b>Conditions to Avoid:</b>	None known
<b>Incompatible Materials:</b>	As a precautionary measure, keep away from strong oxidizers

### 11. TOXICOLOGICAL INFORMATION

**General Information:** The information included in this section describes the potential hazards of the individual ingredients.

#### Acute Toxicity: (Species, Route, End Point, Dose)

##### **Sildenafil citrate**

Rat Oral LD<sub>min</sub>. 300-500 mg/kg  
Mouse Oral LD<sub>min</sub>. 500-1000 mg/kg  
Rat Dermal LD<sub>50</sub> > 2000 mg/kg

##### **Titanium dioxide**

Rat Oral LD<sub>50</sub> > 7500 mg/kg

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### 11. TOXICOLOGICAL INFORMATION

Rat Subcutaneous LD 50 50 mg/kg

#### Sodium benzoate

Rat Oral LD50 4,070 mg/kg  
Mouse Oral LD50 1600 mg/kg

#### Citric acid

Rat Oral LD50 3000 mg/kg

#### Xanthan gum

Rat Oral LD50 > 5000 mg/kg

#### Acute Toxicity Comments:

A greater than symbol (>) indicates that the toxicity endpoint being tested was not achievable at the highest dose used in the test.

#### Irritation / Sensitization: (Study Type, Species, Severity)

##### Sildenafil citrate

Eye Irritation Rabbit Moderate  
Skin Irritation Rabbit Non-irritating  
Skin Sensitization Guinea Pig Negative

##### Citric acid

Eye Irritation Rabbit Severe  
Skin Irritation Rabbit Mild

#### Repeated Dose Toxicity: (Duration, Species, Route, Dose, End Point, Target Organ)

##### Sildenafil citrate

6 Month(s) Rat Oral 3 mg/kg/day NOAEL Adrenal gland, Liver, Thyroid  
6 Month(s) Dog Oral 15 mg/kg/day NOAEL Cardiovascular system

##### Sodium benzoate

10 Day(s) Rat Oral 27370 mg/kg LOAEL Liver, Blood  
10 Day(s) Mouse Oral 45 g/kg LOAEL Liver Kidney Blood Ureter Bladder

#### Reproduction & Developmental Toxicity: (Study Type, Species, Route, Dose, End Point, Effect(s))

##### Sildenafil citrate

Reproductive & Fertility Rat Oral 60 mg/kg/day NOEL No effects at maximum dose  
Embryo / Fetal Development Rat Oral 50 mg/kg/day NOEL Maternal Toxicity, Not Teratogenic  
Embryo / Fetal Development Rabbit Oral 50 mg/kg/day NOEL Maternal Toxicity, Not Teratogenic

##### Sodium benzoate

Embryo / Fetal Development Rat Oral 44 g/kg LOEL Developmental toxicity

#### Genetic Toxicity: (Study Type, Cell Type/Organism, Result)

##### Sildenafil citrate

*In Vitro* Bacterial Mutagenicity (Ames) *Salmonella* Negative  
*In Vitro* Cytogenetics Human Lymphocytes Negative  
*In Vivo* Micronucleus Chromosome Aberration Mouse Bone Marrow Negative

#### Carcinogenicity: (Duration, Species, Route, Dose, End Point, Effect(s))

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## 11. TOXICOLOGICAL INFORMATION

### Sildenafil citrate

24 Month(s) Mouse Oral 5 mg/kg/day NOAEL Not carcinogenic  
24 Month(s) Rat Oral 60 mg/kg/day NOAEL Not carcinogenic

**Carcinogen Status:** None of the components of this formulation are listed as a carcinogen by IARC, NTP or OSHA.

### Titanium dioxide

**IARC:** Group 3 (Not Classifiable)

### Colloidal silicon dioxide

**IARC:** Group 3

## 12. ECOLOGICAL INFORMATION

**Environmental Overview:** In the environment, the active ingredient in this formulation is expected to remain in water or migrate through the soil to groundwater. Harmful effects to aquatic organisms could occur.

**Mobility, Persistence and Degradability:** The active ingredient in this formulation is water soluble and is expected to remain primarily in water.

**Bioaccumulation and Toxicity:** The active ingredient in this formulation has low potential to bioaccumulate and long-term adverse effects to aquatic organisms are not expected. See aquatic toxicity data, below.

### Aquatic Toxicity: (Species, Method, End Point, Duration, Result)

#### Sildenafil citrate

*Daphnia Magna* TAD EC50 48 Hours 14 mg/L  
*Oncorhynchus mykiss* (Rainbow Trout) OECD LC50 96 Hours > 9.5 mg/L  
*Pseudokirchneriella subcapitata* (Green Alga) OECD EC50 72 Hours 20 mg/L

**Aquatic Toxicity Comments:** A greater than (>) symbol indicates that acute ecotoxicity was not observed at the maximum solubility. Since the substance is insoluble in aqueous solutions above this concentration, an acute ecotoxicity value (i.e. LC/EC50) is not achievable.

### Bacterial Inhibition: (Species, Method, End Point, Duration, Result)

#### Sildenafil citrate

Activated sludge OECD EC50 3 Hours > 1000 mg/L

## 13. DISPOSAL CONSIDERATIONS

**Disposal Procedures:** Dispose of waste in accordance with all applicable laws and regulations. Member State specific and Community specific provisions must be considered. Considering the relevant known environmental and human health hazards of the material, review and implement appropriate technical and procedural waste water and waste disposal measures to prevent occupational exposure and environmental release. It is recommended that waste minimization be practiced. The best available technology should be utilized to prevent environmental releases. This may include destructive techniques for waste and wastewater.

## 14. TRANSPORT INFORMATION

Not regulated for transport under USDOT, EUADR, IATA, or IMDG regulations.

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## 15. REGULATORY INFORMATION

EU Indication of danger: Not classified

### OSHA Label:

Non-hazardous in accordance with international standards for workplace safety.

### Canada - WHMIS: Classifications

#### WHMIS hazard class:

None required

This product has been classified in accordance with the hazard criteria of the CPR and the MSDS contains all of the information required by the CPR.

#### Sucralose

Australia (AICS):	Listed
EU EINECS/ELINCS List	259-952-2

#### Titanium dioxide

Inventory - United States TSCA - Sect. 8(b)	Listed
Australia (AICS):	Listed
EU EINECS/ELINCS List	236-675-5

#### Sodium benzoate

Inventory - United States TSCA - Sect. 8(b)	Listed
Australia (AICS):	Listed
EU EINECS/ELINCS List	208-534-8

#### Sodium citrate

Inventory - United States TSCA - Sect. 8(b)	Listed
Australia (AICS):	Listed
Standard for the Uniform Scheduling for Drugs and Poisons:	Schedule 5 Schedule 6
EU EINECS/ELINCS List	200-675-3

#### Citric acid

Inventory - United States TSCA - Sect. 8(b)	Listed
Australia (AICS):	Listed
EU EINECS/ELINCS List	201-069-1

#### Colloidal silicon dioxide

Inventory - United States TSCA - Sect. 8(b)	Listed
Australia (AICS):	Listed
EU EINECS/ELINCS List	231-545-4

#### Xanthan gum

Inventory - United States TSCA - Sect. 8(b)	Listed
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### 15. REGULATORY INFORMATION

Australia (AICS):	Listed
EU EINECS/ELINCS List	234-394-2

### 16. OTHER INFORMATION

#### Text of R phrases mentioned in Section 3

R22 - Harmful if swallowed.

R36 - Irritating to eyes.

**Data Sources:** Pfizer proprietary drug development information. Safety data sheets for individual ingredients.

**Prepared by:** Toxicology and Hazard Communication  
Pfizer Global Environment, Health, and Safety Operations

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**End of Safety Data Sheet**