SAFETY DATA SHEET

Revision date: 08-Mar-2018
Version: 3.2
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1. IDENTIFICATION OF THE SUBSTANCE/MIXTURE AND THE COMPANY/UNDERTAKING

Product Identifier

Material Name: Sildenafil citrate tablets
Trade Name: Revatio, VERVENTI
Synonyms: Sildenafil citrate tablets
Chemical Family: Mixture

Relevant Identified Uses of the Substance or Mixture and Uses Advised Against

Intended Use: Pharmaceutical product used for Treatment of pulmonary arterial hypertension

2. HAZARDS IDENTIFICATION

Classification of the Substance or Mixture

GHS - Classification
Serious Eye Damage/Eye Irritation: Category 2B

Label Elements

Signal Word: Warning
Hazard Statements: H320 - Causes eye irritation

Precautionary Statements:
P264 - Wash hands thoroughly after handling
P305 + P351 + P338 - IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing
P337 + P313 - If eye irritation persists: Get medical advice/attention

Other Hazards

An Occupational Exposure Value has been established for one or more of the ingredients (see Section 8).

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

<table>
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<tr>
<th>Ingredient</th>
<th>CAS Number</th>
<th>EU EINECS/ELINCS List</th>
<th>GHS Classification</th>
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<td>Aquatic Acute 3 (H402)</td>
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<td>Aquatic Chronic 3 (H412)</td>
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<td>Magnesium stearate</td>
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<td>209-150-3</td>
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</table>

Additional Information:

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

In accordance with 29 CFR 1910.1200, the exact percentage composition of this mixture has been withheld as a trade secret.

For the full text of the CLP/GHS abbreviations mentioned in this Section, see Section 16

4. FIRST AID MEASURES

Description of First Aid Measures

Eye Contact: Flush with water while holding eyelids open for at least 15 minutes. Seek medical attention immediately.

Skin Contact: Remove contaminated clothing. Flush area with large amounts of water. Use soap. Seek medical attention.

Ingestion: 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.

Inhalation: Remove to fresh air and keep patient at rest. Seek medical attention immediately.

Most Important Symptoms and Effects, Both Acute and Delayed

Symptoms and Effects of Exposure: For information on potential signs and symptoms of exposure, See Section 2 - Hazards Identification and/or Section 11 - Toxicological Information.

Medical Conditions Aggravated by Exposure: None known

Indication of the Immediate Medical Attention and Special Treatment Needed

Notes to Physician: None
5. FIRE FIGHTING MEASURES

Extinguishing Media: Extinguish fires with CO2, extinguishing powder, foam, or water.

Special Hazards Arising from the Substance or Mixture

Hazardous Combustion Products: Formation of toxic gases is possible during heating or fire.

Fire / Explosion Hazards: Fine particles (such as dust and mists) may fuel fires/explosions.

Advice for Fire-Fighters

During all firefighting activities, wear appropriate protective equipment, including self-contained breathing apparatus.

Additional Information: Not applicable

6. ACCIDENTAL RELEASE MEASURES

Personal Precautions, Protective Equipment and Emergency Procedures

Personnel involved in clean-up should wear appropriate personal protective equipment (see Section 8). Minimize exposure.

Environmental Precautions

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

Methods and Material for Containment and Cleaning Up

Collecting: 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.

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

7. HANDLING AND STORAGE

Precautions for Safe Handling

Minimize dust generation and accumulation. If tablets or capsules are crushed and/or broken, avoid breathing dust and avoid contact with eyes, skin, and clothing. When handling, use appropriate personal protective equipment (see Section 8). Wash thoroughly after handling. Refer to Section 12 - Ecological Information, for information on potential effects on the environment. 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.

Conditions for Safe Storage, Including any Incompatibilities

Storage Conditions: Store as directed by product packaging.

Specific end use(s): Pharmaceutical drug product

8. EXPOSURE CONTROLS / PERSONAL PROTECTION

Control Parameters

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

Sildenafil citrate

Pfizer OEL TWA-8 Hr: 350µg/m³

Titanium dioxide

ACGIH Threshold Limit Value (TWA) 10 mg/m³

Australia TWA 10 mg/m³
8. EXPOSURE CONTROLS / PERSONAL PROTECTION

Engineering Controls: 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.
8. EXPOSURE CONTROLS / PERSONAL PROTECTION

Personal Protective Equipment:

Refer to applicable national standards and regulations in the selection and use of personal protective equipment (PPE). Contact your safety and health professional or safety equipment supplier for assistance in selecting the correct protective clothing/equipment based on an assessment of the workplace conditions, other chemicals used or present in the workplace and specific operational processes.

Hands:
Impervious gloves (e.g. Nitrile, etc.) are recommended if skin contact with drug product is possible and for bulk processing operations. (Protective gloves must meet the standards in accordance with EN374, ASTM F1001 or international equivalent.)

Eyes:
Wear safety glasses or goggles if eye contact is possible. (Eye protection must meet the standards in accordance with EN166, ANSI Z87.1 or international equivalent.)

Skin:
Impervious protective clothing is recommended if skin contact with drug product is possible and for bulk processing operations. (Protective clothing must meet the standards in accordance with EN13982, ANSI 103 or international equivalent.)

Respiratory protection:
Under normal conditions of use, 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 (e.g. particulate respirator with a half mask, P3 filter). (Respirators must meet the standards in accordance with EN140, EN143, ASTM F2704-10 or international equivalent.)

9. PHYSICAL AND CHEMICAL PROPERTIES

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<th>Physical State:</th>
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<tr>
<td>Molecular Formula:</td>
<td>Mixture</td>
<td>Molecular Weight:</td>
<td>Mixture</td>
</tr>
</tbody>
</table>

| Solvent Solubility:   | No data available |
| Water Solubility:     | No data available |
| pH:                   | No data available |
| Melting/Freezing Point (°C): | No data available |
| Boiling Point (°C):   | No data available |
| Partition Coefficient: Method, pH, Endpoint, Value | No data available |
| Calcium phosphate dibasic, anhydrous | No data available |
| Microcrystalline cellulose | No data available |
| Magnesium stearate    | No data available |
| Croscarmellose sodium | No data available |
| Sildenafil citrate    | Predicted 7.4 Log D 2.26 |
| Hydroxypropyl methylcellulose | No data available |
| Titanium dioxide      | No data available |
| Lactose Monohydrate   | No data available |
| Triacetin             | No data available |
| Decomposition Temperature (°C): | No data available |
| Evaporation Rate (Gram/s): | No data available |
| Vapor Pressure (kPa):  | No data available |
SAFETY DATA SHEET

Material Name: Sildenafil citrate tablets
Revision date: 08-Mar-2018

Vapor Density (g/ml): No data available
Relative Density: No data available
Viscosity: No data available

Flammability:
- Autoignition Temperature (Solid) (°C): No data available
- Flammability (Solids): No data available
- Flash Point (Liquid) (°C): No data available
- Upper Explosive Limits (Liquid) (% by Vol.): No data available
- Lower Explosive Limits (Liquid) (% by Vol.): No data available

10. STABILITY AND REACTIVITY

Reactivity: No data available
Chemical Stability: Stable under normal conditions of use.
Possibility of Hazardous Reactions
- Oxidizing Properties: No data available
- Conditions to Avoid: None known
- Incompatible Materials: As a precautionary measure, keep away from strong oxidizers
- Hazardous Decomposition Products: No data available

11. TOXICOLOGICAL INFORMATION

Information on Toxicological Effects
General Information: The information included in this section describes the potential hazards of the individual ingredients.
Short Term: Active ingredient 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.

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

**Microcrystalline cellulose**
- Rat Oral LD50 > 5000 mg/kg
- Rabbit Dermal LD50 > 2000 mg/kg

**Magnesium stearate**
- Rat Oral LD50 > 2000 mg/kg
- Rat Inhalation LC50 > 2000 mg/m³

**Sildenafil citrate**
- Rat Oral LDmin. 300-500 mg/kg
- Mouse Oral LDmin. 500-1000 mg/kg
- Rat Dermal LD50 > 2000 mg/kg

**Hydroxypropyl methylcellulose**
- Rat Oral LD50 > 10,000 mg/kg
11. TOXICOLOGICAL INFORMATION

Titanium dioxide
Rat  Oral  LD50  > 7500 mg/kg
Rat  Subcutaneous  LD50  50 mg/kg

Lactose Monohydrate
Rat  Oral  LD50  29700 mg/kg

Triacetin
Rat  Oral  LD 50  3000 mg/kg
Mouse  Oral  LD 50  1100mg/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)

Microcrystalline cellulose
Skin Irritation  Rabbit  Non-irritating
Eye Irritation  Rabbit  Non-irritating

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

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

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

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

Lactose Monohydrate
*In Vitro* Bacterial Mutagenicity (Ames)  *Salmonella*, *E. coli*  Negative

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

Sildenafil citrate
11. TOXICOLOGICAL INFORMATION

Carcinogen Status: See below

Titanium dioxide
IARC: Group 2B (Possibly Carcinogenic to Humans)

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.

Toxicity:

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

Sildenafil citrate
*Daphnia magna* (Water Flea) TAD OECD 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: (Inoculum, Method, End Point, Result)

Sildenafil citrate
Activated sludge OECD EC50 > 1000 mg/L

Persistence and Degradability: No data available

Bio-accumulative Potential:
Partition Coefficient: (Method, pH, Endpoint, Value)
Sildenafil citrate
Predicted 7.4 Log D 2.26

Mobility in Soil: No data available

13. DISPOSAL CONSIDERATIONS

Waste Treatment Methods: 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

The following refers to all modes of transportation unless specified below.

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

15. REGULATORY INFORMATION

Safety, Health and Environmental Regulations/Legislation Specific for the Substance or Mixture

Lactose Monohydrate
- CERCLA/SARA 313 Emission reporting: Not Listed
- California Proposition 65: Not Listed
- Australia (AICS): Present
- EU EINECS/ELINCS List: Not Listed

Triacetin
- CERCLA/SARA 313 Emission reporting: Not Listed
- California Proposition 65: Not Listed
- Inventory - United States TSCA - Sect. 8(b): Present
- Australia (AICS): Present
- EU EINECS/ELINCS List: 203-051-9

Hydroxypropyl methylcellulose
- CERCLA/SARA 313 Emission reporting: Not Listed
- California Proposition 65: Not Listed
- Inventory - United States TSCA - Sect. 8(b): Present
- Australia (AICS): Present
- Standard for the Uniform Scheduling for Drugs and Poisons: Schedule 4
- EU EINECS/ELINCS List: Not Listed

Crocarmellose sodium
- CERCLA/SARA 313 Emission reporting: Not Listed
- California Proposition 65: Not Listed
- Australia (AICS): Present
- EU EINECS/ELINCS List: Not Listed

Sildenafil citrate
- CERCLA/SARA 313 Emission reporting: Not Listed
- California Proposition 65: Not Listed
- EU EINECS/ELINCS List: Not Listed

Titanium dioxide
- CERCLA/SARA 313 Emission reporting: Not Listed
15. REGULATORY INFORMATION

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<tr>
<th>Substance/Preparation</th>
<th>California Proposition 65</th>
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16. OTHER INFORMATION

Text of CLP/GHS Classification abbreviations mentioned in Section 3

- Acute toxicity, oral-Cat.4; H302 - Harmful if swallowed
- Serious eye damage/eye irritation-Cat. 2B; H320 - Causes eye irritation
- Hazardous to the aquatic environment, acute toxicity-Cat.3; H402 - Harmful to aquatic life
- Hazardous to the aquatic environment, chronic toxicity-Cat.3; H412 - Harmful to aquatic life with long lasting effects

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

Reasons for Revision: Updated Section 2 - Hazard Identification. Updated Section 1 - Identification of the Substance/Preparation and the Company/Undertaking. Updated Section 8 - Exposure Controls / Personal Protection.

Revision date: 08-Mar-2018

Prepared by: Product Stewardship Hazard Communication

Pfizer Inc believes that the information contained in this Material Safety Data Sheet is accurate, and while it is provided in good faith, it is without warranty of any kind, expressed or implied. If data for a hazard are not included in this document there is no known information at this time.

End of Safety Data Sheet