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

Material Name: Sildenafil citrate tablets

Trade Name: Revatio
Synonyms: Sildenafil citrate tablets
Chemical Family: Mixture
Intended Use: Pharmaceutical product used for Treatment of pulmonary arterial hypertension

2. HAZARDS IDENTIFICATION

Appearance: White, film-coated, round biconvex tablets

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

Additional Hazard Information: May be harmful if swallowed. May cause eye irritation. (based on components).
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


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

<table>
<thead>
<tr>
<th>Hazardous Ingredient</th>
<th>CAS Number</th>
<th>EU EINECS/ELINCS List</th>
<th>Classification</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sildenafil citrate</td>
<td>171599-83-0</td>
<td>Not listed</td>
<td>Xn,R22</td>
<td>23</td>
</tr>
</tbody>
</table>
3. COMPOSITION/INFORMATION ON INGREDIENTS

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>CAS Number</th>
<th>EU EINECS/ELINCS List</th>
<th>Classification</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Magnesium stearate</td>
<td>557-04-0</td>
<td>209-150-3</td>
<td>Not Listed</td>
<td>*</td>
</tr>
<tr>
<td>Microcrystalline cellulose</td>
<td>9004-34-6</td>
<td>232-674-9</td>
<td>Not Listed</td>
<td>*</td>
</tr>
<tr>
<td>Titanium dioxide</td>
<td>13463-67-7</td>
<td>236-675-5</td>
<td>Not Listed</td>
<td>*</td>
</tr>
<tr>
<td>Calcium phosphate dibasic, anhydrous</td>
<td>7757-93-9</td>
<td>231-826-1</td>
<td>Not Listed</td>
<td>*</td>
</tr>
<tr>
<td>Croscarmellose sodium</td>
<td>74811-65-7</td>
<td>Not listed</td>
<td>Not Listed</td>
<td>*</td>
</tr>
<tr>
<td>Hypromellose</td>
<td>9004-65-3</td>
<td>Not listed</td>
<td>Not Listed</td>
<td>*</td>
</tr>
<tr>
<td>Lactose Monohydrate</td>
<td>64044-51-5</td>
<td>Not listed</td>
<td>Not Listed</td>
<td>*</td>
</tr>
<tr>
<td>Triacetin</td>
<td>102-76-1</td>
<td>203-051-9</td>
<td>Not Listed</td>
<td>*</td>
</tr>
</tbody>
</table>

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

Eye Contact: Immediately flush eyes with water for at least 15 minutes. If irritation occurs or persists, get medical attention.

Skin Contact: Wash skin with soap and water. Remove contaminated clothing and shoes. If irritation occurs or persists, get medical attention. This material may not be completely removed by conventional laundering. Consult professional laundry service. Do not home launder.

Ingestion: Get medical attention immediately. Do not induce vomiting unless directed by medical personnel. Never give anything by mouth to an unconscious person.

Inhalation: Remove to fresh air. If not breathing, give artificial respiration. Get medical attention immediately.

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.

5. FIRE FIGHTING MEASURES

Extinguishing Media: Use carbon dioxide, dry chemical, or water spray.

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

Fire Fighting Procedures: During all fire fighting activities, wear appropriate protective equipment, including self-contained breathing apparatus.

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

Additional Information: Not applicable

6. ACCIDENTAL RELEASE MEASURES

Health and Safety Precautions: Personnel involved in clean-up should wear appropriate personal protective equipment (see Section 8). Minimize exposure.
Measures for Cleaning / 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.

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. If tablets or capsules are crushed and/or broken, avoid breathing dust and avoid contact with eyes, skin, and clothing. Refer to Section 12 - Ecological Information, for information on potential effects on the environment.

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/m³

Calcium phosphate dibasic, anhydrous
Latvia OEL - TWA = 10 mg/m³ TWA

Magnesium stearate
ACGIH Threshold Limit Value (TWA) = 10 mg/m³ TWA except stearates of toxic metals
Australia TWA = 10 mg/m³ TWA
Belgium OEL - TWA = 10 mg/m³ TWA
Ireland OEL - TWAs = 10 mg/m³ TWA except lead stearate
Lithuania OEL - TWA = 3 mg/m³ IPRV
Portugal OEL - TWA = 10 mg/m³ TWA does not include stearates of toxic metals
Spain OEL - TWA = 10 mg/m³ VLA-ED not including stearates of toxic metals
Swedish OEL - TWAs = 5 mg/m³ LLV

Microcrystalline cellulose
ACGIH Threshold Limit Value (TWA) = 10 mg/m³ TWA
Australia TWA = 10 mg/m³ TWA
Belgium OEL - TWA = 10 mg/m³ TWA
Estonia OEL - TWA = 10 mg/m³ TWA
France OEL - TWA = 10 mg/m³ VME
Ireland OEL - TWAs = 10 mg/m³ TWA
Latvia OEL - TWA = 2 mg/m³ TWA
OSHA - Final PELS - TWAs: = 15 mg/m³ TWA total
= 5 mg/m³ TWA
Portugal OEL - TWA = 10 mg/m³ TWA
Romania OEL - TWA = 10 mg/m³ TWA
Spain OEL - TWA = 10 mg/m³ VLA-ED

Titanium dioxide
ACGIH Threshold Limit Value (TWA) = 10 mg/m³ TWA
Australia TWA = 10 mg/m³ TWA
Austria OEL - MAKs = 6 mg/m³ MAK
Belgium OEL - TWA = 10 mg/m³ TWA
Bulgaria OEL - TWA = 10.0 mg/m³ TWA
Denmark OEL - TWA = 6 mg/m³ TWA
Estonia OEL - TWA = 5 mg/m³ TWA
France OEL - TWA = 10 mg/m³ VME
Greece OEL - TWA = 10 mg/m³ TWA
= 5 mg/m³ TWA
Ireland OEL - TWAs = 10 mg/m³ TWA
= 4 mg/m³ TWA
Latvia OEL - TWA = 10 mg/m³ TWA
Lithuania OEL - TWA = 5 mg/m³ IPRV
Netherlands OEL - TWA = 10 mg/m³ MAC
OSHA - Final PELS - TWAs: = 15 mg/m³ TWA total
Poland OEL - TWA = 10.0 mg/m³ NDS <2% free crystalline silica and containing no asbestos

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

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.

Personal Protective Equipment:

Hands: Impervious gloves are recommended if skin contact with drug product is possible and for bulk processing operations.
Eyes: Wear safety glasses or goggles if eye contact is possible.
Skin: Impervious protective clothing is recommended if skin contact with drug product is possible and for bulk processing operations.
Respiratory protection: 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:

<table>
<thead>
<tr>
<th>Physical State:</th>
<th>Tablet</th>
<th>Color:</th>
<th>White</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular Formula:</td>
<td>Mixture</td>
<td>Molecular Weight:</td>
<td>Mixture</td>
</tr>
</tbody>
</table>

10. STABILITY AND REACTIVITY

Stability: Stable under normal conditions of use.
Conditions to Avoid: None known
Incompatible Materials: 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)**

**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

**Hypermellose**
- Rat Oral LD50 > 10,000 mg/kg

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

**Lactose Monohydrate**
- Rat Oral LD 50 29700 mg/kg

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

**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))**
11. TOXICOLOGICAL INFORMATION

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
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))

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 present in this material at concentrations equal to or greater than 0.1% are listed by IARC, NTP, OSHA, or ACGIH as a carcinogen.

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

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

<table>
<thead>
<tr>
<th>Species</th>
<th>Method</th>
<th>End Point</th>
<th>Duration</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daphnia Magna</td>
<td>TAD</td>
<td>EC50</td>
<td>48 Hours</td>
<td>14 mg/L</td>
</tr>
<tr>
<td>Oncorhynchus mykiss</td>
<td>OECD</td>
<td>LC50</td>
<td>96 Hours</td>
<td>&gt; 9.5 mg/L</td>
</tr>
<tr>
<td>Pseudokirchneriella subcapitata</td>
<td>OECD EC50</td>
<td>72 Hours</td>
<td>20 mg/L</td>
<td></td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Species</th>
<th>Method</th>
<th>End Point</th>
<th>Duration</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Activated sludge</td>
<td>OECD</td>
<td>EC50</td>
<td>3 Hours</td>
<td>&gt; 1000 mg/L</td>
</tr>
</tbody>
</table>

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.

14. TRANSPORT INFORMATION

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

Calcium phosphate dibasic, anhydrous
Inventory - United States TSCA - Sect. 8(b) Present
Australia (AICS): Present
EU EINECS/ELINCS List 231-826-1

Crocarmellose sodium
Australia (AICS): Present

Magnesium stearate
Inventory - United States TSCA - Sect. 8(b) Present
Australia (AICS): Present
EU EINECS/ELINCS List 209-150-3

Microcrystalline cellulose
Inventory - United States TSCA - Sect. 8(b) XU
Australia (AICS): Present
EU EINECS/ELINCS List 232-674-9

Hypromellose
Inventory - United States TSCA - Sect. 8(b) XU
Australia (AICS): Present
Standard for the Uniform Scheduling for Drugs and Poisons: Schedule 4

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

Lactose Monohydrate
Australia (AICS): Present

Triacetin
Inventory - United States TSCA - Sect. 8(b) Present
16. OTHER INFORMATION

Text of R phrases mentioned in Section 3

R22 - Harmful if swallowed.

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

Reasons for Revision: Updated Section 3 - Composition / Information on Ingredients. Updated Section 2 - Hazard Identification. Updated Section 6 - Accidental Release Measures. Updated Section 8 - Exposure Controls / Personal Protection. Updated Section 13 - Disposal Considerations. Updated Section 15 - Regulatory Information. Updated Section 12 - Ecological Information. Updated Section 7 - Handling and Storage. Updated Section 4 - First Aid Measures.

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

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End of Safety Data Sheet