



A Pfizer Company

SAFETY DATA SHEET

Revision date: 07-Nov-2018

Version: 1.1

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

Product Identifier

Material Name: Diltiazem Hydrochloride for Injection (Hospira, Inc.)

Trade Name: Not established

Chemical Family: Calcium channel blocker

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

Intended Use: Pharmaceutical product for the treatment of high blood pressure (hypertension), angina

Details of the Supplier of the Safety Data Sheet

Hospira, A Pfizer Company
275 North Field Drive
Lake Forest, Illinois 60045
1-800-879-3477

Hospira UK Limited
Horizon
Honey Lane
Hurley
Maidenhead, SL6 6RJ
United Kingdom

Emergency telephone number:

CHEMTREC (24 hours): 1-800-424-9300

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

Emergency telephone number:

International CHEMTREC (24 hours): +1-703-527-3887

2. HAZARDS IDENTIFICATION

Classification of the Substance or Mixture

GHS - Classification

Acute Oral Toxicity: Category 4

Reproductive Toxicity: Category 1B

US OSHA Specific - Classification

Physical Hazard: Combustible Dust

Label Elements

Signal Word: Danger

Hazard Statements: H302 - Harmful if swallowed

H360D - May damage the unborn child

May form combustible dust concentrations in air

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Precautionary Statements:

P201 - Obtain special instructions before use
P202 - Do not handle until all safety precautions have been read and understood
P264 - Wash hands thoroughly after handling
P270 - Do not eat, drink or smoke when using this product
P281 - Use personal protective equipment as required
P301+ P312 - IF SWALLOWED: Call a POISON CENTRE or doctor/physician if you feel unwell
P330 - Rinse mouth
P308 + P313 - IF exposed or concerned: Get medical attention/advice
P405 - Store locked up
P501 - Dispose of contents/container in accordance with all local and national regulations



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 requires the inclusion of all known hazards of the product or its ingredients regardless of the potential risk. The precautionary statements and warning 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 | GHS Classification | % |
|-------------------------|------------|-----------------------|---------------------------------------|----|
| Diltiazem Hydrochloride | 33286-22-5 | 251-443-3 | Acute Tox.4 (H302) Repr.1B (H360D) | 57 |

| Ingredient | CAS Number | EU EINECS/ELINCS List | GHS Classification | % |
|------------|------------|-----------------------|--------------------|----|
| Mannitol | 69-65-8 | 200-711-8 | Not Listed | 43 |

Additional Information:

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

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:

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

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- Skin Contact:** Remove clothing and wash affected skin with soap and water. This material may not be completely removed by conventional laundering. Consult professional laundry service. Do not home launder. If irritation occurs or persists, get medical attention.
- Ingestion:** Do not induce vomiting unless directed by medical personnel. Never give anything by mouth to an unconscious person. Get medical attention.
- Inhalation:** Remove to fresh air. If not breathing, give artificial respiration. Get medical attention.

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: Emits toxic fumes of carbon monoxide, carbon dioxide, nitrogen oxides, sulfur oxides, hydrogen chloride and other chlorine- and sulfur-containing compounds.

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.

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

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.

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. Avoid breathing dust. Avoid contact with eyes, skin and clothing. When handling, use appropriate personal protective equipment (see Section 8). Wash thoroughly after handling. 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.

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Conditions for Safe Storage, Including any Incompatibilities

Storage Conditions: Store as directed by product packaging.
Specific end use(s): Pharmaceutical active

8. EXPOSURE CONTROLS / PERSONAL PROTECTION

Control Parameters

Diltiazem Hydrochloride

Pfizer OEL TWA-8 Hr: 70µg/m³

Exposure Controls

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: 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

Physical State: Lyophilized powder
Odor: No data available.
Molecular Formula: Mixture

Color: Off-white
Odor Threshold: No data available.
Molecular Weight: Mixture

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)

Diltiazem Hydrochloride

No data available

Mannitol

No data available

Decomposition Temperature (°C): No data available.

Evaporation Rate (Gram/s): No data available

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Vapor Pressure (kPa): No data available
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: Fine particles (such as dust and mists) may fuel fires/explosions.
Incompatible Materials: As a precautionary measure, keep away from strong oxidizers
Hazardous Decomposition Products: No data available

11. TOXICOLOGICAL INFORMATION

Information on Toxicological Effects

Short Term: May be harmful if swallowed. (based on animal data) . Drugs of this class have been associated with rare, but potentially serious cardiac events. These events have not been observed from occupational exposures, however, those with preexisting cardiovascular illnesses may be at increased risk from exposure.

Long Term: Animal studies have shown a potential to cause adverse effects on the fetus.

Known Clinical Effects: Ingestion of this material may cause effects similar to those seen in clinical use including dizziness, fatigue, hypotension (low blood pressure), edema and dyspnea.

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

Diltiazem Hydrochloride

Rat Oral LD50 560 mg/kg
Rat Para-periosteal LD50 38mg/kg
Rat Subcutaneous LD50 520mg/kg
Mouse Oral LD50 508mg/kg
Mouse Intravenous LD50 58mg/kg

Mannitol

Rat Oral LD 50 13500 mg/kg
Mouse Oral LD 50 22 g/kg

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

Diltiazem Hydrochloride

1 Month(s) Rat Oral 100 mg/kg/day NOEL Liver, Blood, Heart
1 Month(s) Dog Oral 5 mg/kg/day NOEL Kidney, Heart

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11. TOXICOLOGICAL INFORMATION

6 Month(s) Dog Oral 10 mg/kg/day LOEL Heart, Liver, Cardiovascular system
1 Year(s) Dog Oral 5 mg/kg/day LOEL Cardiovascular system, Heart

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

Diltiazem Hydrochloride

| | | | | | |
|----------------------------|--------|-----------------|----------------|-------|---------------------------|
| Reproductive & Fertility | Rat | Oral | 50 mg/kg/day | NOAEL | Fertility |
| Embryo / Fetal Development | Mouse | Oral | 25 mg/kg/day | LOAEL | Embryotoxicity |
| Embryo / Fetal Development | Rat | Oral | 100 mg/kg/day | NOAEL | Fetotoxicity |
| Embryo / Fetal Development | Rabbit | Intraperitoneal | 6.3 mg/kg/day | LOAEL | Fetotoxicity, Teratogenic |
| Embryo / Fetal Development | Rabbit | Oral | 17.5 mg/kg/day | NOAEL | Fetotoxicity, Teratogenic |

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

Diltiazem Hydrochloride

Bacterial Mutagenicity (Ames) *Salmonella*, *E. coli* Negative
In Vivo Mammalian Cell Mutagenicity Negative
In Vitro Mammalian Cell Mutagenicity Negative

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

Diltiazem Hydrochloride

21 Month(s) Mouse Oral 30 mg/kg/day NOAEL Not carcinogenic
24 Month(s) Rat Oral 100 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.

12. ECOLOGICAL INFORMATION

Environmental Overview: Environmental properties have not been investigated. Releases to the environment should be avoided.

Toxicity: No data available

Persistence and Degradability: No data available

Bio-accumulative Potential: No data available

Mobility in Soil: No data available

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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

Diltiazem Hydrochloride

| | |
|------------------------------------|----------------------------------|
| CERCLA/SARA 313 Emission reporting | Not Listed |
| California Proposition 65 | developmental toxicity 2/27/2001 |
| Australia (AICS): | Present |
| EU EINECS/ELINCS List | 251-443-3 |

Mannitol

| | |
|---|------------|
| CERCLA/SARA 313 Emission reporting | Not Listed |
| California Proposition 65 | Not Listed |
| Inventory - United States TSCA - Sect. 8(b) | Present |
| Australia (AICS): | Present |
| REACH - Annex IV - Exemptions from the obligations of Register: | Present |
| EU EINECS/ELINCS List | 200-711-8 |

16. OTHER INFORMATION

Text of CLP/GHS Classification abbreviations mentioned in Section 3

Acute toxicity, oral-Cat.4; H302 - Harmful if swallowed
Reproductive toxicity-Cat.1B; H360D - May damage the unborn child

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Data Sources: Pfizer proprietary drug development information.

Reasons for Revision: Updated Section 2 - Hazard Identification. Updated Section 1 - Identification of the Substance/Preparation and the Company/Undertaking. Updated Section 10 - Stability and Reactivity.

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Product Stewardship Hazard Communication

Prepared by: Pfizer Global Environment, Health, and Safety Operations

Pfizer Inc believes that the information contained in this 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