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

Product Identifier

Material Name: Sinequan (Doxepin hydrochloride) capsules
Trade Name: Sinequan
Chemical Family: Mixture

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

Intended Use: Pharmaceutical product used as antidepressant, antianxiety agent, anti-itch treatment (antipruritus)

Details of the Supplier of the Safety Data Sheet

Pfizer Inc
Pfizer Pharmaceuticals Group
235 East 42nd Street
New York, New York 10017
1-800-879-3477

Pfizer Ltd
Ramsgate Road
Sandwich, Kent
CT13 9NJ
United Kingdom
+00 44 (0)1304 616161

Emergency telephone number:
CHEMTREC (24 hours): 1-800-424-9300
Emergency telephone number:
International CHEMTREC (24 hours): +1-703-527-3887
Contact E-Mail: pfizer-MSDS@pfizer.com

2. HAZARDS IDENTIFICATION

Classification of the Substance or Mixture

GHS - Classification
Reproductive Toxicity: Category 2 : Effects on or via lactation

EU Classification:
EU Indication of danger: Toxic to Reproduction: Category 3

EU Risk Phrases:
R62 - Possible risk of impaired fertility.
R64 - May cause harm to breastfed babies.

Label Elements

Signal Word: Warning
Hazard Statements:
H361f - Suspected of damaging fertility
H362 - May cause harm to breast-fed children

Precautionary Statements:
P202 - Do not handle until all safety precautions have been read and understood
P281 - Use personal protective equipment as required
P260 - Do not breathe dust/fume/gas/mist/vapors/spray
P263 - Avoid contact during pregnancy/while nursing
P308 + P313 - IF exposed or concerned: Get medical attention/advice
P405 - Store locked up
SAFETY DATA SHEET

Material Name: Sinequan (Doxepin hydrochloride) capsules
Revision date: 14-Apr-2015
Version: 4.0

Other Hazards
Australian Hazard Classification (NOHSC):


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>EU Classification</th>
<th>GHS Classification</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Doxepin hydrochloride</td>
<td>1229-29-4</td>
<td>214-966-8</td>
<td>N;R50</td>
<td>Acute Tox.4 (H302)Repr.2 (H261f) Lact. (H362) Aquatic Acute 1 (H400)</td>
<td>15-25</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>CAS Number</th>
<th>EU EINECS/ELINCS List</th>
<th>EU Classification</th>
<th>GHS Classification</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Corn Starch</td>
<td>9005-25-8</td>
<td>232-679-6</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>Not Listed</td>
<td>*</td>
</tr>
<tr>
<td>Sodium Lauryl Sulfate</td>
<td>151-21-3</td>
<td>205-788-1</td>
<td>Not Listed</td>
<td>Not Listed</td>
<td>*</td>
</tr>
<tr>
<td>Magnesium Stearate</td>
<td>557-04-0</td>
<td>209-150-3</td>
<td>Not Listed</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. In accordance with 29 CFR 1910.1200, the exact percentage composition of this mixture has been withheld as a trade secret.

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.

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: 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.

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

Special Hazards Arising from the Substance or Mixture
Hazardous Combustion Products: May emit toxic fumes of carbon monoxide, carbon dioxide, nitrogen oxides, hydrogen chloride and other chlorine-containing compounds.

Advice for Fire-Fighters
During all fire fighting 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. Clean up operations should only be undertaken by trained personnel.

7. HANDLING AND STORAGE

Precautions for Safe Handling
If tablets or capsules are crushed and/or broken, avoid breathing dust and avoid contact with eyes, skin, and clothing. Use only in a well-ventilated area. Minimize dust generation and accumulation.

Conditions for Safe Storage, Including any Incompatibilities
Storage Conditions: Keep container tightly closed when not in use. Store out of direct sunlight in a well ventilated area at room temperature.

Storage Temperature: 15 - 30 °C
Specific end use(s): Pharmaceutical product used as antidepressant, antianxiety agent, anti-itch treatment (antipruritus)

8. EXPOSURE CONTROLS / PERSONAL PROTECTION

Control Parameters
8. EXPOSURE CONTROLS / PERSONAL PROTECTION

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

Doxepin hydrochloride
Pfizer OEL TWA-8 Hr: 600µg/m³

Corn Starch
ACGIH Threshold Limit Value (TWA) 10 mg/m³
Australia TWA 10 mg/m³
Belgium OEL - TWA 10 mg/m³
Bulgaria OEL - TWA 10.0 mg/m³
Czech Republic OEL - TWA 4.0 mg/m³
Greece OEL - TWA 10 mg/m³
       5 mg/m³
Ireland OEL - TWAs 10 mg/m³
       4 mg/m³
OSHA - Final PELS - TWAs: 15 mg/m³
Portugal OEL - TWA 10 mg/m³
Slovakia OEL - TWA 4 mg/m³
Spain OEL - TWA 10 mg/m³
Switzerland OEL -TWAs 3 mg/m³

Magnesium Stearate
ACGIH Threshold Limit Value (TWA) 10 mg/m³
Lithuania OEL - TWA 5 mg/m³
Sweden OEL - TWAs 5 mg/m³

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


Exposure Controls
Engineering Controls: Engineering controls should be used as the primary means to control exposures. Local and general ventilation should be used as necessary, when handling this material in bulk.

Personal Protective Equipment: Refer to applicable national standards and regulations in the selection and use of personal protective equipment (PPE).

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: Not required for the normal use of this product. 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>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical State</td>
<td>Capsule</td>
</tr>
<tr>
<td>Odor</td>
<td>Odorless</td>
</tr>
<tr>
<td>Molecular Formula</td>
<td>Mixture</td>
</tr>
<tr>
<td>Solvent Solubility</td>
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</tr>
<tr>
<td>Water Solubility</td>
<td>No data available</td>
</tr>
<tr>
<td>pH</td>
<td>No data available</td>
</tr>
<tr>
<td>Melting/Freezing Point (°C)</td>
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</tr>
<tr>
<td>Color</td>
<td>White Blue</td>
</tr>
<tr>
<td>Odor Threshold</td>
<td>No data available</td>
</tr>
<tr>
<td>Molecular Weight</td>
<td>Mixture</td>
</tr>
</tbody>
</table>
9. PHYSICAL AND CHEMICAL PROPERTIES

Boiling Point (°C): No data available.
Partition Coefficient: (Method, pH, Endpoint, Value)

Doxepin hydrochloride
No data available
Lactose Monohydrate
No data available
Magnesium Stearate
No data available
Sodium Lauryl Sulfate
No data available
Corn Starch
No data available

Decomposition Temperature (°C): No data available.
Evaporation Rate (Gram/s): No data available
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

Polymerization: Will not occur

10. STABILITY AND REACTIVITY

Reactivity: No data available
Chemical Stability: Stable
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
General Information: The information included in this section describes the potential hazards of the individual ingredients.
Short Term: Harmful if swallowed (based on animal data).
Known Clinical Effects: Ingestion of this material may cause effects similar to those seen in clinical use including dry mouth, drowsiness, headache, dizziness, nausea, vomiting, weakness, anxiety, and dilated pupils. Cases of severe overdose may lead to respiratory depression, hypotension, coma, convulsions, cardiac arrhythmia, and tachycardia.

Acute Toxicity: (Species, Route, End Point, Dose)
Doxepin hydrochloride
11. TOXICOLOGICAL INFORMATION

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. No data available.

Skin Irritation / Sensitization
An IM irritation study conducted in rabbits showed that the compound was moderately irritating when injected into muscle.

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

Doxepin hydrochloride
- 30 Day(s) Dog Oral 25 mg/kg/day NOEL Central nervous system
- 1 Year(s) Rat Oral 25 mg/kg/day NOEL None identified
- 18 Month(s) Rat Oral 50 mg/kg/day NOEL Liver
- 1 Year(s) Dog Oral 5 mg/kg/day NOEL Central Nervous System

Magnesium Stearate
- 13 Week(s) Rat Oral 1092 g/kg LOAEL Liver

Sodium Lauryl Sulfate
- 3 Day(s) Rat Oral 75 mg/kg LOAEL Liver, Blood

Chronic Toxicity:
Chronic toxicity studies were conducted in rats and dogs. Rats treated for 1 year exhibited dose-dependent fatty metamorphosis of the liver, which was moderate to marked at the high dose (200 mg/kg/day). A 1-year study in dogs resulted in ptosis, sedation, tremors, and intermittent emesis at doses of 25 and 50 mg/kg/day.

Chronic Effects/Carcinogenicity
No long-term toxicity studies have been conducted to evaluate the chronic toxicity or carcinogenic potential of this material. A similar drug, amitriptyline, was negative when tested for carcinogenicity.

Subchronic Effects
Subchronic oral toxicity studies were performed in rats at doses up to 200 mg/kg/day and in dogs at doses up to 50 mg/kg/day for five weeks and one month, respectively. In rats, deaths were seen in all high-dose animals and in 1/3 of the mid-dose animals. No necropsies were performed in this study. No gross, histopathological or hematological changes were observed in dogs. The low dose (25 mg/kg/day) animals showed sedation and mild emesis.

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

Doxepin hydrochloride
- Reproductive & Fertility Rat Oral5 mg/kg/day NOEL Fertility
- Embryo / Fetal Development Rat Oral 25 mg/kg/day NOEL Not Teratogenic
- Embryo / Fetal Development Rabbit Oral 25 mg/kg/day NOEL Not Teratogenic
- Embryo / Fetal Development Monkey Oral 18 mg/kg/day NOEL Not Teratogenic

Studies in rats resulted in a reduced conception rate in animals receiving the high dose (25 or 50 mg/kg). No effects on developmental behavior or reproductive performance of the rat offspring were observed in a peri- and post-natal toxicity study.
11. TOXICOLOGICAL INFORMATION

Teratogenicity
No evidence of teratogenicity was observed in rats, rabbits, or monkeys.

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

Lactose Monohydrate
\(\text{In Vitro Bacterial Mutagenicity (Ames)}\)  \(\text{Salmonella, E. coli}\)  Negative

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

Additional Information:
Individuals taking monoamine oxidase inhibitors (MAO) should avoid exposure to this material.

12. ECOLOGICAL INFORMATION

Environmental Overview:
The environmental characteristics of this mixture have not been fully evaluated. Releases to the environment should be avoided.

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

Doxepin hydrochloride
\(\text{Daphnia magna (Water Flea)}\)  EC50  48 Hours  11.1 mg/L
\(\text{Scenedesmus subspicatus (Green Alga)}\)  EC50  72 Hours  0.5-0.73 mg/L

Persistence and Degradability:
No data available

Bio-accumulative Potential:
No data available

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

Canada - WHMIS: Classifications
WHMIS hazard class:
Class D, Division 2, Subdivision A
This product has been classified in accordance with the hazard criteria of the CPR and the SDS contains all of the information required by the CPR.

Doxepin hydrochloride
CERCLA/SARA 313 Emission reporting Not Listed
California Proposition 65 Not Listed
Australia (AICS): Present
EU EINECS/ELINCS List 214-966-8

Corn Starch
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 232-679-6

Lactose Monohydrate
CERCLA/SARA 313 Emission reporting Not Listed
California Proposition 65 Not Listed
Australia (AICS): Present
REACH - Annex IV - Exemptions from the obligations of Register: Present
EU EINECS/ELINCS List Not Listed

Sodium Lauryl Sulfate
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 6
EU EINECS/ELINCS List 205-788-1

Magnesium Stearate
CERCLA/SARA 313 Emission reporting Not Listed
California Proposition 65 Not Listed
Inventory - United States TSCA - Sect. 8(b) Present
SAFETY DATA SHEET

Material Name: Sinequan (Doxepin hydrochloride) capsules
Revision date: 14-Apr-2015

15. REGULATORY INFORMATION

Australia (AICS): Present
EU EINECS/ELINCS List: 209-150-3

16. OTHER INFORMATION

Text of R phrases and GHS Classification abbreviations mentioned in Section 3

Acute toxicity, oral-Cat.4; H302 - Harmful if swallowed
Reproductive toxicity-Cat.2; H361f - Suspected of damaging fertility
Reproductive toxicity, effects on or via lactation; H362 - May cause harm to breast-fed children
Hazardous to the aquatic environment, acute toxicity-Cat.1; H400 - Very toxic to aquatic life

Xn - Harmful
Toxic to Reproduction: Category 2
N - Dangerous for the environment

R22 - Harmful if swallowed.
R62 - Possible risk of impaired fertility.
R64 - May cause harm to breastfed babies.
R50 - Very toxic to aquatic organisms.

Data Sources:
Pfizer proprietary drug development information. Publicly available toxicity information.

Reasons for Revision:
Updated Section 1 - Identification of the Substance/Preparation and the Company/Undertaking.
Updated Section 2 - Hazard Identification. Updated Section 3 - Composition / Information on Ingredients. Updated Section 16 - Other Information.

Revision date: 14-Apr-2015
Prepared by:
Product Stewardship Hazard Communication
Pfizer Global Environment, Health, and Safety Operations

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 a warranty of any kind, expressed or implied.

End of Safety Data Sheet