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

<table>
<thead>
<tr>
<th>Pfizer Inc</th>
<th>Pfizer Ltd</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pfizer Pharmaceuticals Group</td>
<td>Ramsgate Road</td>
</tr>
<tr>
<td>235 East 42nd Street</td>
<td>Sandwich, Kent</td>
</tr>
<tr>
<td>New York, New York 10017</td>
<td>CT13 9NJ</td>
</tr>
<tr>
<td>1-212-573-2222</td>
<td>United Kingdom</td>
</tr>
<tr>
<td>Emergency telephone number:</td>
<td>+00 44 (0)1304 616161</td>
</tr>
<tr>
<td>CHEMTREC (24 hours): 1-800-424-9300</td>
<td>Emergency telephone number: International CHEMTREC (24 hours): +1-703-527-3887</td>
</tr>
<tr>
<td>Contact E-Mail: <a href="mailto:pfizer-MSDS@pfizer.com">pfizer-MSDS@pfizer.com</a></td>
<td></td>
</tr>
</tbody>
</table>

**Material Name:** Caduet (Amlodipine besylate/Atorvastatin calcium) tablets-
2.5 mg/10 mg, 5 mg/20 mg and 10 mg/40 mg

| Trade Name: | CADUET |
| Chemical Family: | Mixture |
| Intended Use: | Pharmaceutical product for the treatment of high blood pressure (hypertension), high cholesterol (hyperlipidemia). |

## 2. HAZARDS IDENTIFICATION

**Appearance:** 5 mg/20 mg: White film-coated tablets 10 mg/40 mg: Blue film-coated tablets

**Signal Word:** WARNING

**Statement of Hazard:** Toxic to aquatic life with long-lasting effects.

**Additional Hazard Information:**

**Short Term:** May cause eye irritation; May be harmful if swallowed. (based on components).

**Long Term:** May cause eye irritation; May be harmful if swallowed. (based on components).

**Antihypertensive drug:** has blood pressure-lowering properties

**Known Clinical Effects:**

**Repetitive dose studies in animals have shown a potential to cause adverse effects on liver.**

**Adverse effects associated with therapeutic use of amlodipine include headache, swelling, dizziness, flushing, and palpitations.**

The most common adverse effects seen with the therapeutic use of atorvastatin include constipation, flatulence, upset stomach, and abdominal pain. Therapeutic use of atorvastatin has been associated with changes in liver function and muscle aches or weakness.

**EU Classification**

**EU Indication of danger:** Dangerous for the Environment

**EU Hazard Symbols:** N

**EU Risk Phrases:** R51/53 - Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment.

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

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>Ingredient</th>
<th>CAS Number</th>
<th>EU EINECS/ELINCS List</th>
<th>EU Classification</th>
<th>%</th>
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</thead>
<tbody>
<tr>
<td>Amlodipine besylate</td>
<td>111470-99-6</td>
<td>Not Listed</td>
<td>N;R50/53</td>
<td>3.47</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Xn;R22</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Xi;R41</td>
<td></td>
</tr>
<tr>
<td>Atorvastatin calcium</td>
<td>134523-03-8</td>
<td>Not Listed</td>
<td>R52/53</td>
<td>10.85</td>
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<tr>
<td>Calcium carbonate</td>
<td>471-34-1</td>
<td>207-439-9</td>
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<tr>
<td>Magnesium stearate</td>
<td>557-04-0</td>
<td>209-150-3</td>
<td>Not Listed</td>
<td>*</td>
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<tr>
<td>Microcrystalline cellulose</td>
<td>9004-34-6</td>
<td>232-674-9</td>
<td>Not Listed</td>
<td>*</td>
</tr>
<tr>
<td>Silicon dioxide, NF</td>
<td>7631-86-9</td>
<td>231-545-4</td>
<td>Not Listed</td>
<td>*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>418-260-2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Starch, pregelatinized</td>
<td>9005-25-8</td>
<td>232-679-6</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: 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.

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.

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. When handling, use appropriate personal protective equipment (see Section 8). Wash hands and any exposed skin after removal of PPE. Refer to Section 12 - Ecological Information, for information on potential effects on the environment. 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. Releases to the environment should be avoided.

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.

Amlodipine besylate
Pfizer OEL TWA-8 Hr: 100µg/m³

Atorvastatin calcium
Pfizer OEL TWA-8 Hr: 50 µg/m³

Calcium carbonate
Bulgaria OEL - TWA 10.0 mg/m³
France OEL - TWA 10 mg/m³
# 8. EXPOSURE CONTROLS / PERSONAL PROTECTION

## Magnesium stearate
- ACGIH Threshold Limit Value (TWA): 10 mg/m³
- Lithuania OEL - TWA: 5 mg/m³
- Sweden OEL - TWA: 5 mg/m³

## Microcrystalline cellulose
- ACGIH Threshold Limit Value (TWA): 10 mg/m³
- Australia TWA: 10 mg/m³
- Belgium OEL - TWA: 10 mg/m³
- Estonia OEL - TWA: 10 mg/m³
- France OEL - TWA: 10 mg/m³
- Ireland OEL - TWAs: 4 mg/m³
- Latvia OEL - TWA: 2 mg/m³
- OSHA - Final PELS - TWAs: 15 mg/m³
- Portugal OEL - TWA: 10 mg/m³
- Romania OEL - TWA: 10 mg/m³
- Spain OEL - TWA: 10 mg/m³

## Silicon dioxide, NF
- Australia TWA: 2 mg/m³
- Austria OEL - MAKs: 4 mg/m³
- Czech Republic OEL - TWA: 0.1 mg/m³
- Estonia OEL - TWA: 2 mg/m³
- Germany - TRGS 900 - TWAs: 4 mg/m³
- Germany (DFG) - MAK: 4 mg/m³ inhalable fraction
- Ireland OEL - TWAs: 6 mg/m³
- Latvia OEL - TWA: 1 mg/m³
- OSHA - Final PELs - Table Z-3 Mineral D: Listed
- Slovakia OEL - TWA: 4.0 mg/m³
- Slovenia OEL - TWA: 4 mg/m³

## Starch, pregelatinized
- 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
- Ireland OEL - TWAs: 10 mg/m³
- OSHA - Final PELS - TWAs: 15 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.

Environmental Exposure Controls: Refer to specific Member State legislation for requirements under Community environmental legislation.

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: 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

Physical State: Tablet
Molecular Formula: Mixture
Color: Blue White
Molecular Weight: Mixture

Polymerization: Will not occur

10. STABILITY AND REACTIVITY

Chemical Stability: Stable under normal conditions of use.
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

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)

Calcium carbonate
Rat Oral LD50 6450 mg/kg

Magnesium stearate
Rat Oral LD50 > 2000 mg/kg
Rat Inhalation LC50 > 2000 mg/m³
11. TOXICOLOGICAL INFORMATION

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

**Polysorbate 80**
- Rat Oral LD50 25 g/kg

**Silicon dioxide, NF**
- Rat Oral LD50 10 g/kg

**Amlodipine besylate**
- Rat (M) Oral LD50 393 mg/kg
- Rat (F) Oral LD50 686 mg/kg

**Atorvastatin calcium**
- Rat/Mouse Oral LD50 > 5000 mg/kg
- Rabbit Dermal LD50 > 2000 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

**Amlodipine besylate**
- Eye Irritation Rabbit Severe
- Skin Irritation Rabbit Non-irritating
- Skin Sensitization - GPMT Guinea Pig Negative

**Atorvastatin calcium**
- Skin Sensitization - Beuhler Guinea Pig Negative
- Skin Irritation Rabbit Non-irritating
- Eye Irritation Rabbit Mild

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

**Amlodipine besylate**
- 3 Month(s) Rat Oral 3 mg/kg/day NOAEL Adrenal gland, Heart
- 1 Month(s) Rat Oral 3.5 mg/kg/day LOEL Heart
- 1 Year(s) Rat Oral 2 mg/kg/day NOAEL Adrenal gland, Heart

**Atorvastatin calcium**
- 104 Week(s) Dog Oral 10 mg/kg/day LOAEL Liver
- 13 Week(s) Mouse Oral 100 mg/kg/day LOAEL Liver
- 52 Week(s) Rat Oral 5 mg/kg/day NOAEL Liver
- 13 Week(s) Rat Oral 5 (male); 20 (female) mg/kg/day NOAEL Liver

**Reproduction & Developmental Toxicity: (Study Type, Species, Route, Dose, End Point, Effect(s))**
11. TOXICOLOGICAL INFORMATION

Amlodipine besylate
Fertility and Embryonic Development  Rat  Oral  25 mg/kg/day  NOAEL  Not teratogenic, Maternal toxicity
Peri-/Postnatal Development  Rat  Oral  4 mg/kg/day  NOAEL  Fetotoxicity, Fetal mortality
Prenatal & Postnatal Development  Rat  Oral  25 mg/kg/day  NOAEL  Not Teratogenic
Prenatal & Postnatal Development  Rabbit  Oral  25 mg/kg/day  NOAEL  Not Teratogenic

Amlodipine besylate
Fertility and Embryonic Development  Rat  Oral  20 mg/kg/day  NOAEL  Negative
Reproductive & Fertility  Rat  Oral  200 mg/kg/day  NOAEL  Negative
Embryo / Fetal Development  Rat  Oral  100 mg/kg/day  NOAEL  Not Teratogenic, Maternal Toxicity
Embryo / Fetal Development  Rabbit  Oral  10 mg/kg/day  NOAEL  Not Teratogenic, Maternal Toxicity, Fetotoxicity
Peri-/Postnatal Development  Rat  Oral  20 mg/kg/day  NOAEL  Fetotoxicity

Atorvastatin calcium
Reproductive & Fertility  Rat  Oral  20 mg/kg/day  NOAEL  Negative
Fertility and Embryonic Development  Rat  Oral  100 mg/kg/day  NOAEL  Negative
Embryo / Fetal Development  Rat  Oral  100 mg/kg/day  NOAEL  Not Teratogenic, Maternal Toxicity
Embryo / Fetal Development  Rabbit  Oral  10 mg/kg/day  NOAEL  Not Teratogenic, Maternal Toxicity, Fetotoxicity
Peri-/Postnatal Development  Rat  Oral  20 mg/kg/day  NOAEL  Fetotoxicity

Atorvastatin calcium
Reproductive & Fertility  Rat  Oral  20 mg/kg/day  NOAEL  Negative
Fertility and Embryonic Development  Rat  Oral  100 mg/kg/day  NOAEL  Negative
Embryo / Fetal Development  Rat  Oral  100 mg/kg/day  NOAEL  Not Teratogenic, Maternal Toxicity
Embryo / Fetal Development  Rabbit  Oral  10 mg/kg/day  NOAEL  Not Teratogenic, Maternal Toxicity, Fetotoxicity
Peri-/Postnatal Development  Rat  Oral  20 mg/kg/day  NOAEL  Fetotoxicity

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

Amlodipine besylate
In Vitro Bacterial Mutagenicity (Ames)  Salmonella, E. coli  Negative
In Vivo Cytogenetics  Mouse Bone Marrow  Negative
In Vitro Chromosome Aberration  Human Lymphocytes  Negative

Atorvastatin calcium
In Vitro Bacterial Mutagenicity (Ames)  Salmonella, E. coli  Negative
In Vivo Micronucleus  Mouse Bone Marrow  Negative

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

Amlodipine besylate
24 Month(s)  Rat  Oral, in feed  2.5 mg/kg/day  NOAEL  Not carcinogenic, No effects at maximum dose
24 Month(s)  Mouse  Oral, in feed  0.5 mg/kg/day  NOAEL  Not carcinogenic

Atorvastatin calcium
104 Week(s)  Mouse  Oral  200 mg/kg/day  NOAEL  Not carcinogenic
104 Week(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.

Silicon dioxide, NF  
IARC:  Group 3 (Not Classifiable)

At increase risk from exposure:  Individuals with a known history of hypersensitivity to this material or other materials in its chemical class and individuals with liver conditions and/or impaired liver function may be more susceptible to toxicity in cases of overexposure. Atorvastatin calcium as a HMG-CoA reductase inhibitor is contraindicated during pregnancy and in nursing mothers. Women of childbearing age or nursing mothers should exercise caution regarding exposure.

Additional Information:  There have been rare reports of persistent elevations of liver function enzymes or myopathy resulting from therapeutic use of atorvastatin calcium.
12. ECOLOGICAL INFORMATION

Environmental Overview: This formulation has not been tested as a whole, the following apply to component substance(s):

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

Amlodipine besylate
- *Daphnia magna* (Water Flea) **OECD** EC50 48 Hours 9.9 mg/L
- *Oncorhynchus mykiss* (Rainbow Trout) **OECD** LC50 96 Hours 14 mg/L
- Green algae **OECD** EbC50 72 Hours 0.28 mg/L
- Green Algae **OECD** ErC50 72 Hours > 0.91 mg/L

Atorvastatin calcium
- *Daphnia magna* (Water Flea) **EC50** 48 Hours 200 mg/L
- *Oncorhynchus mykiss* (Rainbow Trout) **OECD** LC50 96 Hours > 92 mg/L
- *Pseudokirchneriella subcapitata* (Green Alga) **OECD** EbC50 72 Hours 75 mg/L
- *Daphnia magna* (Water Flea) **OECD** NOEC 21 Days 0.14 mg/L
- *Pimephales promelas* (Fathead Minnow) **OECD** NOEC 32 Days 0.45 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)

Amlodipine besylate
- *Nostoc sp.* (Freshwater Cyanobacteria) **MIC** 20 mg/L
- *Aspergillus Niger* **MIC** > 100 mg/L
- *Trichoderma viride* **MIC** > 100 mg/L
- *Clostridium perfingens* **MIC** > 100 mg/L
  - *Bacillus subtilis* **MIC** 80 mg/L

Atorvastatin calcium
- *Aspergillus niger* (Fungus) **MIC** > 1000 mg/L
- *Trichoderma viride* (Fungus) **MIC** > 1000 mg/L
- *Clostridium perfingens* (Bacterium) **MIC** 100 mg/L
- Activated sludge **OECD** EC50 > 1000 mg/L

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**

| EU Symbol: | N |
| EU Indication of danger: | Dangerous for the Environment |
| EU Risk Phrases: | R51/53 - Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment. |
| EU Safety Phrases: | S57 - Use appropriate containment to avoid environmental contamination. |

**OSHA Label:**

**WARNING**

Toxic to aquatic life with long lasting effects.

**Canada - WHMIS: Classifications**

**WHMIS hazard class:**

Class D, Division 2, Subdivision B

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**Calcium carbonate**

- Inventory - United States TSCA - Sect. 8(b): Present
- Australia (AICS): Present
- EU EINECS/ELINCS List: 207-439-9

**Crocarmellose sodium**

- Australia (AICS): Present

**Hydroxypropyl cellulose**

- Inventory - United States TSCA - Sect. 8(b): Present
- Australia (AICS): Present

**Magnesium stearate**

- Inventory - United States TSCA - Sect. 8(b): Present
- Australia (AICS): Present
15. REGULATORY INFORMATION

<table>
<thead>
<tr>
<th>Material</th>
<th>EU EINECS/ELINCS List</th>
</tr>
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<tbody>
<tr>
<td>Polysorbate 80</td>
<td>209-150-3</td>
</tr>
<tr>
<td>Starch, pregelatinized</td>
<td>232-674-9</td>
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<tr>
<td>Silicon dioxide, NF</td>
<td>232-679-6</td>
</tr>
<tr>
<td>Microcrystalline cellulose</td>
<td>231-545-4</td>
</tr>
<tr>
<td></td>
<td>418-260-2</td>
</tr>
</tbody>
</table>

16. OTHER INFORMATION

Text of R phrases mentioned in Section 3

R22 - Harmful if swallowed.
R41 - Risk of serious damage to eyes.
R50/53 - Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment.
R52/53 - Harmful to aquatic organisms, may cause long-term adverse effects in the aquatic environment.

Data Sources: Pfizer proprietary drug development information. Safety data sheets for individual ingredients.
Reasons for Revision: Updated Section 1 - Identification of the Substance/Preparation and the Company/Undertaking.
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 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