MATERIAL SAFETY DATA SHEET

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

Pfizer Inc
Pfizer Pharmaceuticals Group
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1-212-573-2222

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

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Material Name: Caduet (Amlodipine besylate/Atorvastatin calcium) tablets- 10 mg/10 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: Blue film-coated tablets
Signal Word: WARNING

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

Additional Hazard Information:
Short Term: Can cause eye irritation ; May be harmful if swallowed. (based on components) . Antihypertensive drug: has blood pressure-lowering properties

Long Term: Repeat-dose studies in animals have shown a potential to cause adverse effects on liver.
Known Clinical Effects: 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.

2. HAZARDS IDENTIFICATION

Australian Hazard Classification (NOHSC): Hazardous Substance. Non-Dangerous Goods.

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

Ingredient	CAS Number	EU EINECS/ELINCS List	EU Classification	%
Amlodipine besylate	111470-99-6	Not Listed	N;R50/53 Xn;R22 Xi;R41	13.9
Atorvastatin calcium	134523-03-8	Not Listed	R52/53	10.85
Silicon dioxide, NF	7631-86-9	231-545-4 418-260-2	Not Listed	*
Calcium carbonate	471-34-1	207-439-9	Not Listed	*
Microcrystalline cellulose	9004-34-6	232-674-9	Not Listed	*
Starch, pregelatinized	9005-25-8	232-679-6	Not Listed	*
Magnesium stearate	557-04-0	209-150-3	Not Listed	*

Ingredient	CAS Number	EU EINECS/ELINCS List	EU Classification	%
Opadry blue	NOT ASSIGNED	Not Listed	Not Listed	*
Opadry clear	NOT ASSIGNED	Not Listed	Not Listed	*
Hydroxypropyl cellulose	9004-64-2	Not Listed	Not Listed	*
Croscarmellose sodium	74811-65-7	Not Listed	Not Listed	*
Polysorbate 80	9005-65-6	Not Listed	Not Listed	*

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: Carbon monoxide, carbon dioxide, oxides of nitrogen, oxides of sulfur, hydrochloride, and other chlorine-containing compounds

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

Fire / Explosion Hazards: 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. 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. 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.

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/m^3

Atorvastatin calcium
Pfizer OEL TWA-8 Hr: 50 µg/m^3

8. EXPOSURE CONTROLS / PERSONAL PROTECTION

Silicon dioxide, NF

Australia TWA	2 mg/m^3
Austria OEL - MAKs	4 mg/m^3
Czech Republic OEL - TWA	0.1 mg/m^3 4.0 mg/m^3
Estonia OEL - TWA	2 mg/m^3
Germany - TRGS 900 - TWAs	4 mg/m^3
Germany (DFG) - MAK	4 mg/m^3 inhalable fraction
Ireland OEL - TWAs	6 mg/m^3 2.4 mg/m^3
Latvia OEL - TWA	1 mg/m^3
OSHA - Final PELs - Table Z-3 Mineral D:	20 mppcf Listed
Slovakia OEL - TWA	4.0 mg/m^3
Slovenia OEL - TWA	4 mg/m^3

Calcium carbonate

Bulgaria OEL - TWA	10.0 mg/m^3
France OEL - TWA	10 mg/m^3
Latvia OEL - TWA	6 mg/m^3
Poland OEL - TWA	10 mg/m^3
Portugal OEL - TWA	10 mg/m^3
Spain OEL - TWA	10 mg/m^3

Microcrystalline cellulose

ACGIH Threshold Limit Value (TWA)	10 mg/m^3
Australia TWA	10 mg/m^3
Belgium OEL - TWA	10 mg/m^3
Estonia OEL - TWA	10 mg/m^3
France OEL - TWA	10 mg/m^3
Ireland OEL - TWAs	10 mg/m^3 4 mg/m^3
Latvia OEL - TWA	2 mg/m^3
OSHA - Final PELS - TWAs:	15 mg/m^3
Portugal OEL - TWA	10 mg/m^3
Romania OEL - TWA	10 mg/m^3
Spain OEL - TWA	10 mg/m^3

Starch, pregelatinized

ACGIH Threshold Limit Value (TWA)	10 mg/m^3
Australia TWA	10 mg/m^3
Belgium OEL - TWA	10 mg/m^3
Bulgaria OEL - TWA	10.0 mg/m^3
Czech Republic OEL - TWA	4.0 mg/m^3
Greece OEL - TWA	10 mg/m^3 5 mg/m^3
Ireland OEL - TWAs	10 mg/m^3 4 mg/m^3
OSHA - Final PELS - TWAs:	15 mg/m^3
Portugal OEL - TWA	10 mg/m^3

8. EXPOSURE CONTROLS / PERSONAL PROTECTION

Slovakia OEL - TWA	4 mg/m^3
Spain OEL - TWA	10 mg/m^3

Magnesium stearate

ACGIH Threshold Limit Value (TWA)	10 mg/m^3
Lithuania OEL - TWA	5 mg/m^3
Sweden OEL - TWAs	5 mg/m^3

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

Analytical Method: Analytical method available for Amlodipine, Atorvastatin. Contact Pfizer Inc for further information.

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: Wear impervious gloves if skin contact is possible.

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: Film-coated tablets **Color:** Blue
Molecular Formula: Mixture **Molecular Weight:** Mixture

Polymerization: Will not occur

10. STABILITY AND REACTIVITY

Chemical Stability: Stable under normal conditions of use.
Conditions to Avoid: None known
Incompatible Materials: As a precautionary measure, keep away from strong oxidizers
Hazardous Decomposition Products: None known

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)

11. TOXICOLOGICAL INFORMATION

Calcium carbonate
Rat Oral LD50 6450 mg/kg

Magnesium stearate
Rat Oral LD50 > 2000 mg/kg
Rat Inhalation LC50 > 2000 mg/m^3

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

11. TOXICOLOGICAL INFORMATION

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
Subchronic toxicity of amlodipine besylate was evaluated in rats at oral doses up to 30 mg/kg/day for three months. Drug-related changes included increased heart and adrenal gland weights and were reversed one month after cessation of treatment. These changes are considered to be the result of the desired effect of the drug, however, they are considered potential hazards in the workplace. Amlodipine besylate was evaluated in rats orally at doses up to 25 mg/kg/day for twelve months. Effects similar to those reported in the subchronic study were reported. The No Observed Adverse Effect Level (NOAEL) in this study was 2 mg/kg/day.

Chronic Effects/Carcinogenicity Amlodipine showed no carcinogenic potential when tested in mice at dose levels up to 2.5 mg/kg/day for 2 years. Atorvastatin calcium was not carcinogenic in rats. In a 2-year study in mice, the incidence of liver tumors, benign in males and malignant in females, was increased at the highest dose used. Similar results have been reported with other drugs in the same chemical class, but due to the mechanism of tumor development, these results are not considered to be relevant to humans.

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

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

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

Reproductive Effects No effects on fertility or reproductive performance were observed for amlodipine besylate or amlodipine maleate in the rat. Amlodipine besylate was reported to prolong gestation and duration of labor in rats. This effect has been similarly reported for other calcium channel blockers. No adverse effects on fertility or reproduction were observed in rats given atorvastatin calcium at doses up to 175 mg/kg/day in males or up to 225 mg/kg/day in females. Also, atorvastatin did not cause adverse effects on sperm or semen parameters, or on reproductive organ histology in dogs given doses of 10, 40, or 120 mg/kg/day for 2 years.

Teratogenicity No evidence of embryotoxicity, fetotoxicity or teratogenicity was seen in rats or rabbits when amlodipine besylate was administered at dose levels up to 25 mg/kg. No birth defects were observed in rats or rabbits when atorvastatin calcium was given at maternally and fetally toxic doses. However, rare reports of birth defects have been linked to drugs of this class. Liver Adrenal glands Cardiovascular system

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

11. TOXICOLOGICAL INFORMATION

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

Mutagenicity Amlodipine showed No evidence of mutagenic activity in bacterial or mammalian cells in vitro, or clastogenic activity in vitro or in vivo. Atorvastatin showed No evidence of mutagenic or clastogenic activity in in vitro or in vivo tests.

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): Harmful effects to aquatic organisms could occur.

Bioaccumulation and Toxicity: Moderate acute toxicity to aquatic organisms could occur. See aquatic toxicity data, below.

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.

12. ECOLOGICAL INFORMATION

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.

15. REGULATORY INFORMATION

OSHA Label:
WARNING
Toxic to aquatic life with long lasting effects.

Canada - WHMIS: Classifications

WHMIS hazard class:
Class D, Division 2, Subdivision B

Silicon dioxide, NF

Inventory - United States TSCA - Sect. 8(b)	Present
Australia (AICS):	Present
EU EINECS/ELINCS List	231-545-4 418-260-2

Hydroxypropyl cellulose

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

Calcium carbonate

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

Croscarmellose sodium

Australia (AICS):	Present

Polysorbate 80

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

Microcrystalline cellulose

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

Starch, pregelatinized

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

15. REGULATORY INFORMATION

Magnesium stearate

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

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 2 - Hazard Identification. Updated Section 3 - Composition / Information on Ingredients. Updated Section 12 - Ecological Information. Updated Section 15 - Regulatory Information.

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