MATERIAL SAFETY DATA SHEET

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

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Pfizer Pharmaceuticals Group
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Emergency telephone number:
CHEMTREC (24 hours): 1-800-424-9300
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Material Name: Caduet® (amlodipine besylate/atorvastatin calcium) Tablets- 2.5 mg/40 mg, 5 mg/40 mg, 5 mg/80 mg, and 10 mg/80 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:	2.5 mg/40 mg: White film-coated tablets 5 mg/40 mg: White film-coated tablets 5 mg/80 mg: White film-coated tablets 10 mg/80 mg: Blue film-coated tablets
Statement of Hazard:	Non-hazardous in accordance with international standards for workplace safety.
Additional Hazard Information:	
Short Term:	May 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 Indication of danger:	Not classified
Australian Hazard Classification (NOHSC):	Non-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

3. COMPOSITION/INFORMATION ON INGREDIENTS

Ingredient	CAS Number	EU EINECS/ELINCS List	Classification	%
Amlodipine besylate	111470-99-6	Not listed	N;R51 Xn;R22 Xi;R41	0.87-1.74
Atorvastatin calcium	134523-03-8	Not listed	Not Listed	10.85
Starch, pregelatinized	9005-25-8	232-679-6	Not Listed	*
Silicon dioxide, NF	7631-86-9	231-545-4	Not Listed	*
Microcrystalline cellulose	9004-34-6	232-674-9	Not Listed	*
Calcium carbonate	471-34-1	207-439-9	Not Listed	*
Magnesium stearate	557-04-0	209-150-3	Not Listed	*

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

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. 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. 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

No Occupational Exposure Limit (OEL) or Short Term Exposure Limit (STEL) has been identified.

Amlodipine besylate

Pfizer OEL TWA-8 Hr:	100µg/m^3

Atorvastatin calcium

Pfizer OEL TWA-8 Hr:	50 µg/m^3

Starch, pregelatinized

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

Silicon dioxide, NF

Australia TWA	2 mg/m^3

8. EXPOSURE CONTROLS / PERSONAL PROTECTION

Austria OEL - MAKs	Listed
Czech Republic OEL - TWA	Listed
Estonia OEL - TWA	Listed
Germany - TRGS 900 - TWAs	4 mg/m^3
Germany (DFG) - MAK	4 mg/m^3 MAK
Ireland OEL - TWAs	Listed
Latvia OEL - TWA	Listed
OSHA - Final PELs - Table Z-3 Mineral D:	- (80)/(% SiO2) mg/m^3 TWA TWA-20 mppcf
Slovenia OEL - TWA	Listed

Microcrystalline cellulose

ACGIH Threshold Limit Value (TWA)	10 mg/m^3 TWA
Australia TWA	10 mg/m^3
Belgium OEL - TWA	Listed
Estonia OEL - TWA	Listed
France OEL - TWA	Listed
Ireland OEL - TWAs	Listed
Latvia OEL - TWA	Listed
OSHA - Final PELS - TWAs:	15 mg/m^3 total 5 mg/m^3
Portugal OEL - TWA	Listed
Romania OEL - TWA	Listed
Spain OEL - TWA	Listed

Calcium carbonate

Australia TWA	10 mg/m^3
Belgium OEL - TWA	Listed
Bulgaria OEL - TWA	Listed
Czech Republic OEL - TWA	Listed
Estonia OEL - TWA	Listed
France OEL - TWA	Listed
Greece OEL - TWA	Listed
Hungary OEL - TWA	Listed
Ireland OEL - TWAs	Listed
Latvia OEL - TWA	Listed
OSHA - Final PELS - TWAs:	15 mg/m^3 total 5 mg/m^3
Poland OEL - TWA	Listed
Portugal OEL - TWA	Listed
Spain OEL - TWA	Listed

Magnesium stearate

ACGIH Threshold Limit Value (TWA)	10 mg/m^3 TWA
Australia TWA	10 mg/m^3
Belgium OEL - TWA	Listed
Ireland OEL - TWAs	Listed
Lithuania OEL - TWA	Listed
Portugal OEL - TWA	Listed
Spain OEL - TWA	Listed
Sweden OEL - TWAs	Listed

8. EXPOSURE CONTROLS / PERSONAL PROTECTION

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

Analytical Method: Analytical method available for Amlopidine, 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: 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:	Film-coated tablets	**Color:**	White Blue
Molecular Formula:	Mixture	**Molecular Weight:**	Mixture

Polymerization: Will not occur

10. STABILITY AND REACTIVITY

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)

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

Calcium carbonate
Rat Oral LD50 6450 mg/kg

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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/m^3

Silicon dioxide, NF
Rat Oral LD50 10 g/kg

Polysorbate 80
Rat Oral LD50 25 g/kg

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

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

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

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

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

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

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

11. TOXICOLOGICAL INFORMATION

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

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

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

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

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

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

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

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

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

12. ECOLOGICAL INFORMATION

Environmental Overview: This formulation has not been tested as a whole, the following apply to component substance(s): Based on the concentration of the active ingredient in the formulation, No harmful effects to aquatic organisms are expected.

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

Atorvastatin calcium
Daphnia magna (Water Flea) EC50 48 Hours 200 mg/L

12. ECOLOGICAL INFORMATION

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 LOEC 21 Days 0.27 mg/L
Pimephales promelas (Fathead Minnow) OECD LOEC 32 Days 0.92 mg/L

Amlodipine besylate
Daphnia Magna OECD EC50 48 Hours 9.9 mg/L
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

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)

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

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

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. 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

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

15. REGULATORY INFORMATION

EU Indication of danger: Not classified

15. REGULATORY INFORMATION

OSHA Label:
Non-hazardous in accordance with international standards for workplace safety.

Canada - WHMIS: Classifications

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

Starch, pregelatinized

Inventory - United States TSCA - Sect. 8(b)	Listed
Australia (AICS):	Listed
REACH - Annex IV - Exemptions from the obligations of Register:	Present
EU EINECS/ELINCS List	232-679-6

Silicon dioxide, NF

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

Polysorbate 80

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

Croscarmellose sodium

Australia (AICS):	Listed

Microcrystalline cellulose

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

Hydroxypropyl cellulose

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

Calcium carbonate

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

15. REGULATORY INFORMATION

REACH - Annex IV - Exemptions from the obligations of Register:	Present
EU EINECS/ELINCS List	207-439-9

Magnesium stearate

Inventory - United States TSCA - Sect. 8(b)	Listed
Australia (AICS):	Listed
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.
R51 - Toxic to aquatic organisms.

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 4 - First Aid Measures. Updated Section 5 - Fire Fighting Measures. Updated Section 7 - Handling and Storage. Updated Section 8 - Exposure Controls / Personal Protection. Updated Section 12 - Ecological Information. Updated Section 13 - Disposal Considerations. Updated Section 15 - Regulatory Information.

Prepared by: Toxicology and 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