



# MATERIAL SAFETY DATA SHEET

Revision date: 05-Jan-2007

Version: 1.1

Page 1 of 9

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

**Pfizer Inc**  
**Pfizer Pharmaceuticals Group**  
**235 East 42nd Street**  
**New York, New York 10017**  
**1-212-573-2222**

**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:**  
**ChemSafe (24 hours): +44 (0)208 762 8322**

### Material Name: Spironolactone and Hydrochlorothiazide Tablets

**Trade Name:** Aldactazide(R)  
**Chemical Family:** Mixture  
**Intended Use:** Pharmaceutical product used as antihypertensive, diuretic

## 2. COMPOSITION/INFORMATION ON INGREDIENTS

### Hazardous

Ingredient	CAS Number	EU EINECS List	%
Spironolactone	52-01-7	200-133-6	25 / 50 mg ***
Magnesium stearate	557-04-0	209-150-3	*
Titanium dioxide	13463-67-7	236-675-5	*
Hydrochlorothiazide	58-93-5	200-403-3	25 / 50 mg ***
Corn Starch	9005-25-8	232-679-6	*
Calcium sulfate	7778-18-9	231-900-3	*
Iron oxide	1309-37-1	215-168-2	*

Ingredient	CAS Number	EU EINECS List	%
Povidone	9003-39-8	Not listed	*
Hypromellose	9004-65-3	Not listed	*
Hydroxypropyl cellulose	9004-64-2	Not listed	*
Polyethylene glycol	25322-68-3	Not listed	*
Flavor	NOT ASSIGNED	Not listed	*

**Additional Information:** \*\*\* per tablet/capsule/lozenge/suppository  
\* Proprietary  
Ingredient(s) indicated as hazardous have been assessed under standards for workplace safety.

## 3. HAZARDS IDENTIFICATION

**Appearance:** Tan film-coated tablets  
**Signal Word:** DANGER

## MATERIAL SAFETY DATA SHEET

Material Name: Spironolactone and Hydrochlorothiazide  
Tablets

Page 2 of 9

Revision date: 05-Jan-2007

Version: 1.1

**Statement of Hazard:** Antihypertensive drug: has blood pressure-lowering properties  
May damage fertility or the unborn child.  
Suspected of causing cancer.  
May cause damage to: blood and blood forming organs through prolonged or repeated exposure.

**Additional Hazard Information:**  
**Long Term:** Repeat-dose studies in animals have shown a potential to cause adverse effects on blood, kidneys, reproductive system.

**Known Clinical Effects:** Signs and symptoms might include nausea, vomiting, cramps, dizziness, headache, vertigo, low blood pressure on standing, rash, urticaria, photosensitivity, electrolyte imbalance, muscle spasm, weakness, and restlessness. Hypersensitivity reactions may also occur in susceptible individuals. Effects on blood and blood-forming organs have also occurred. May cause adverse effects on the developing fetus.

**EU Indication of danger:** Harmful  
Toxic to reproduction: Category 1  
Carcinogenic: Category 3

**EU Hazard Symbols:**



**EU Risk Phrases:**  
R40 - Limited evidence of a carcinogenic effect  
R48/22 - Harmful: danger of serious damage to health by prolonged exposure if swallowed.  
R60 - May impair fertility.  
R61 - May cause harm to the unborn child.

**Note:** This document has been prepared in accordance with standards for workplace safety, which require the inclusion of all known hazards of the active substance or its intermediates 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.

### 4. FIRST AID MEASURES

**Eye Contact:** Rinse immediately with plenty of water, also under the eyelids, for at least 15 minutes. If irritation occurs or persists, get medical attention.

**Skin Contact:** Wash skin with soap and water. If irritation occurs or persists, get 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.

### 5. FIRE FIGHTING MEASURES

**Extinguishing Media:** Use carbon dioxide, dry chemical, or water spray.

**Hazardous Combustion Products:** Toxic or corrosive gases including oxides of carbon and oxides of sulfur

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

# MATERIAL SAFETY DATA SHEET

Material Name: Spironolactone and Hydrochlorothiazide  
Tablets  
Revision date: 05-Jan-2007

Page 3 of 9

Version: 1.1

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:** If tablets or capsules are crushed and/or broken, avoid breathing dust and avoid contact with eyes, skin, and clothing. Avoid generating airborne dust.

**Storage Conditions:** Store as directed by product packaging.

## 8. EXPOSURE CONTROLS / PERSONAL PROTECTION

**Spironolactone**  
Pfizer OEL TWA-8 Hr: 0.09 mg/m<sup>3</sup>, Skin

**Magnesium stearate**  
ACGIH Threshold Limit Value (TWA) = 10 mg/m<sup>3</sup> TWA except stearates of toxic metals  
Australia TWA = 10 mg/m<sup>3</sup> TWA

**Titanium dioxide**  
OSHA - Final PELS - TWAs: = 15 mg/m<sup>3</sup> TWA total  
ACGIH Threshold Limit Value (TWA) = 10 mg/m<sup>3</sup> TWA  
Australia TWA = 10 mg/m<sup>3</sup> TWA

**Hydrochlorothiazide**  
Pfizer OEL TWA-8 Hr: 0.25 mg/m<sup>3</sup>

**Corn Starch**  
OSHA - Final PELS - TWAs: = 15 mg/m<sup>3</sup> TWA total  
= 5 mg/m<sup>3</sup> TWA  
ACGIH Threshold Limit Value (TWA) = 10 mg/m<sup>3</sup> TWA  
Australia TWA = 10 mg/m<sup>3</sup> TWA

**Calcium sulfate**  
OSHA - Final PELS - TWAs: = 15 mg/m<sup>3</sup> TWA total  
= 5 mg/m<sup>3</sup> TWA  
ACGIH Threshold Limit Value (TWA) = 10 mg/m<sup>3</sup> TWA  
Australia TWA = 10 mg/m<sup>3</sup> TWA

**Iron oxide**  
OSHA - Final PELS - TWAs: = 10 mg/m<sup>3</sup> TWA

# MATERIAL SAFETY DATA SHEET

Material Name: Spironolactone and Hydrochlorothiazide  
Tablets

Page 4 of 9

Revision date: 05-Jan-2007

Version: 1.1

ACGIH Threshold Limit Value (TWA) = 5 mg/m<sup>3</sup> TWA

Australia TWA = 5 mg/m<sup>3</sup> TWA

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

**Analytical Method:** Analytical method available for Spironolactone. Contact Pfizer Inc for further information.

**Engineering Controls:** Engineering controls should be used as the primary means to control exposures.

## Personal Protective Equipment:

**Hands:** Not required for the normal use of this product. Wear protective gloves when working with large quantities.

**Eyes:** Not required under normal conditions of use. Wear safety glasses or goggles if eye contact is possible.

**Skin:** Not required for the normal use of this product. Wear protective clothing when working with large quantities.

**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:

**Physical State:** Film-coated tablets

**Color:** Tan

**Molecular Formula:** Mixture

**Molecular Weight:** Mixture

## 10. STABILITY AND REACTIVITY

**Stability:** Stable under normal conditions of use.

**Conditions to Avoid:** None known

**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)

#### Spironolactone

Rat Oral LD 50 4121 mg/kg

Mouse Oral LD 50 >1000 mg/kg

Rabbit Oral LD 50 >1000 mg/kg

Rat Intraperitoneal LD 50 786 mg/kg

#### Povidone

Rat Oral LD50 100 g/kg

#### Magnesium stearate

Rat Oral LD50 > 2000 mg/kg

Rat Inhalation LC50 > 2000 mg/m<sup>3</sup>

## MATERIAL SAFETY DATA SHEET

Material Name: Spironolactone and Hydrochlorothiazide  
Tablets

Page 5 of 9

Revision date: 05-Jan-2007

Version: 1.1

### Titanium dioxide

Rat Oral LD50 > 7500 mg/kg  
Rat Subcutaneous LD 50 50 mg/kg

### Hydrochlorothiazide

Rat Oral LD 50 2750 mg/kg  
Mouse Oral LD 50 2830 mg/kg  
Rat Intravenous LD 50 990 mg/kg  
Dog Intravenous LD 50 250 mg/kg

### Hypromellose

Rat Oral LD50 > 10,000 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)

#### Spironolactone

Skin Sensitization - GPMT Guinea Pig No effect

#### Polyethylene glycol

Eye Irritation Rabbit Mild  
Skin Irritation Rabbit Mild

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

#### Spironolactone

13 Week(s) Rat Oral 50 mg/kg LOAEL Blood  
78 Week(s) Rat Oral 50 mg/kg/day LOAEL Liver, Male reproductive system

#### Hydrochlorothiazide

30 Day(s) Rat Oral 1 g/kg/day LOAEL Blood  
13 Week(s) Mouse Oral 12,500 ppm LOAEL Bladder  
9 Month(s) Dog Oral 50 mg/kg/day LOAEL Endocrine system  
1 Year(s) Rat Oral 2000 ppm LOAEL Kidney  
2 Year(s) Rat Oral 250 ppm LOAEL Kidney

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

#### Spironolactone

Reproductive & Fertility Rat Oral 15 mg/kg/day NOAEL Fetotoxicity  
Reproductive & Fertility Rat Intraperitoneal 100 mg/kg/day LOAEL Fertility  
Embryo / Fetal Development Mouse Intraperitoneal 100 mg/kg/day LOAEL Maternal Toxicity  
Embryo / Fetal Development Rat Oral 50 mg/kg/day LOAEL Fetotoxicity  
Embryo / Fetal Development Rabbit Oral 20 mg/kg/day LOAEL Fetotoxicity

#### Hydrochlorothiazide

Reproductive & Fertility Rat Oral 1000 mg/kg LOAEL Maternal toxicity  
Reproductive & Fertility Mouse Oral 3000 mg/kg/day NOEL No effects at maximum dose  
Embryo / Fetal Development Rat Oral 1000 mg/kg/day NOEL Not Teratogenic  
Embryo / Fetal Development Mouse Oral 3000 mg/kg/day NOEL Not Teratogenic

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

## MATERIAL SAFETY DATA SHEET

Material Name: Spironolactone and Hydrochlorothiazide  
Tablets  
Revision date: 05-Jan-2007

Page 6 of 9

Version: 1.1

### Spironolactone

Bacterial Mutagenicity (Ames) *Salmonella*, *E. coli* Negative  
Mammalian Cell Mutagenicity Negative without activation

### Hydrochlorothiazide

Bacterial Mutagenicity (Ames) *Salmonella* Negative  
*In Vitro* Sister Chromatid Exchange Chinese Hamster Ovary (CHO) cells Positive  
*In Vitro* Chromosome Aberration Chinese Hamster Ovary (CHO) cells Negative  
Dominant Lethal Assay *Drosophila* Negative  
Mammalian Cell Mutagenicity Mouse Lymphoma Positive

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

#### Spironolactone

104 Week(s) Rat Oral 10 mg/kg/day LOAEL Benign tumors  
52 Week(s) Non-human Primate Oral 20 mg/kg/day LOAEL Reproductive System

#### Hydrochlorothiazide

2 Year(s) Rat Oral 2000 ppm NOAEL Not carcinogenic  
2 Year(s) Female Mouse Oral 5000 ppm NOAEL Not carcinogenic  
2 Year(s) Male Mouse Oral 5000 ppm LOAEL Malignant tumors, Liver

**Carcinogen Status:** See below

#### Spironolactone

**IARC:** Group 3

#### Povidone

**IARC:** Group 3

#### Iron oxide

**IARC:** Group 3

#### Titanium dioxide

**IARC:** Group 2B  
**OSHA:** Present

#### Hydrochlorothiazide

**IARC:** Group 3

## 12. ECOLOGICAL INFORMATION

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

## 13. DISPOSAL CONSIDERATIONS

**Disposal Procedures:** Dispose of waste in accordance with all applicable laws and regulations.

# MATERIAL SAFETY DATA SHEET

Material Name: Spironolactone and Hydrochlorothiazide  
Tablets  
Revision date: 05-Jan-2007

Page 7 of 9

Version: 1.1

## 14. TRANSPORT INFORMATION

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

## 15. REGULATORY INFORMATION

**EU Symbol:** T  
**EU Indication of danger:** Harmful  
Toxic to reproduction: Category 1  
Carcinogenic: Category 3

**EU Risk Phrases:**

R40 - Limited evidence of a carcinogenic effect  
R48/22 - Harmful: danger of serious damage to health by prolonged exposure if swallowed.  
R60 - May impair fertility.  
R61 - May cause harm to the unborn child.

**EU Safety Phrases:**

S22 - Do not breathe dust.  
S24 - Avoid contact with skin.  
S53 - Avoid exposure - obtain special instructions before use.

**OSHA Label:**

DANGER

Antihypertensive drug: has blood pressure-lowering properties

May damage fertility or the unborn child.

Suspected of causing cancer.

May cause damage to: blood and blood forming organs through prolonged or repeated exposure.

**Canada - WHMIS: Classifications**

**WHMIS hazard class:**

Class D, Division 2, Subdivision A



**Spironolactone**

California Proposition 65

Inventory - United States TSCA - Sect. 8(b)

Australia (AICS):

Standard for the Uniform Scheduling  
for Drugs and Poisons:

EU EINECS List

carcinogen, initial date 5/1/97

Present

Present

Schedule 4

200-133-6

Povidone

# MATERIAL SAFETY DATA SHEET

Material Name: Spironolactone and Hydrochlorothiazide  
Tablets

Page 8 of 9

Revision date: 05-Jan-2007

Version: 1.1

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Inventory - United States TSCA - Sect. 8(b) Australia (AICS):	XU Present
<b>Hypromellose</b>	
Inventory - United States TSCA - Sect. 8(b) Australia (AICS): Standard for the Uniform Scheduling for Drugs and Poisons:	XU Present Schedule 4
<b>Magnesium stearate</b>	
Inventory - United States TSCA - Sect. 8(b) Australia (AICS): EU EINECS List	Present Present 209-150-3
<b>Titanium dioxide</b>	
Inventory - United States TSCA - Sect. 8(b) Australia (AICS): EU EINECS List	Present Present 236-675-5
<b>Hydrochlorothiazide</b>	
Inventory - United States TSCA - Sect. 8(b) Australia (AICS): Standard for the Uniform Scheduling for Drugs and Poisons: EU EINECS List	Present Present Schedule 4 200-403-3
<b>Corn Starch</b>	
Inventory - United States TSCA - Sect. 8(b) Australia (AICS): EU EINECS List	XU Present 232-679-6
<b>Hydroxypropyl cellulose</b>	
Inventory - United States TSCA - Sect. 8(b) Australia (AICS):	XU Present
<b>Calcium sulfate</b>	
Inventory - United States TSCA - Sect. 8(b) Australia (AICS): EU EINECS List	Present Present 231-900-3
<b>Polyethylene glycol</b>	
Inventory - United States TSCA - Sect. 8(b) Australia (AICS):	XU Present
<b>Iron oxide</b>	
Inventory - United States TSCA - Sect. 8(b) Australia (AICS): EU EINECS List	Present Present 215-168-2

## 16. OTHER INFORMATION

Reasons for Revision: Updated Section 3 - Hazard Identification. Updated Section 8 - Exposure Controls / Personal Protection. Updated Section 11 - Toxicology Information.

Prepared by: Corporate Occupational Toxicology & Hazard Assessment



## MATERIAL SAFETY DATA SHEET

**Material Name: Spironolactone and Hydrochlorothiazide  
Tablets**

**Page 9 of 9**

**Revision date: 05-Jan-2007**

**Version: 1.1**

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**End of Safety Data Sheet**