



MATERIAL SAFETY DATA SHEET

Revision date: 30-Sep-2005

Version: 1.0

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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): 1-800-262-8200

Emergency telephone number:
ChemSafe (24 hours): +44 (0)208 762 8322

Material Name: Metoprolol Tartrate/Hydrochlorothiazide Extended Release Tablets

Trade Name: Co-Betaloc SA
Synonyms: None
Chemical Family: Not determined
Intended Use: Antihypertensive

2. COMPOSITION/INFORMATION ON INGREDIENTS

Hazardous

| Ingredient | CAS Number | EU EINECS List | % |
|----------------------------|------------|----------------|-----------|
| Metoprolol Tartrate | 56392-17-7 | 260-148-9 | 200 mg*** |
| Hydrochlorothiazide | 58-93-5 | 200-403-3 | 25 mg*** |
| Microcrystalline cellulose | 9004-34-6 | 232-674-9 | * |
| Iron oxide | 1309-37-1 | 215-168-2 | * |
| Paraffin | 8002-74-2 | 232-315-6 | * |
| Ethanol | 64-17-5 | 200-578-6 | * |
| Maize starch | 9005-25-8 | 232-679-6 | * |

| Ingredient | CAS Number | EU EINECS List | % |
|-------------------------------|------------|----------------|---|
| Purified water | 7732-18-5 | 231-791-2 | * |
| Hydroxypropyl methylcellulose | 9004-65-3 | Not listed | * |
| Polyethylene glycol | 25322-68-3 | Not listed | * |
| Sodium stearyl fumarate | 4070-80-8 | 223-781-1 | * |
| Povidone | 9003-39-8 | Not listed | * |
| Ethylcellulose | 9004-57-3 | Not listed | * |
| Lactose | 63-42-3 | 200-559-2 | * |
| Sodium aluminosilicate | 1344-00-9 | 215-684-8 | * |
| Riboflavin (Vitamin B2) | 83-88-5 | 201-507-1 | * |
| Magnesium Stearate | 557-04-0 | 209-150-3 | * |

Additional Information:

* Proprietary
*** per tablet/capsule/lozenge/suppository

3. HAZARDS IDENTIFICATION

Appearance: Tablets
Signal Word: WARNING

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Statement of Hazard: Antihypertensive drug: has blood pressure-lowering properties
Suspected of damaging the unborn child.

Additional Hazard Information:
Short Term: Not acutely toxic (based on components) . An Occupational Exposure Limit has been established for one or more of the ingredients (see Section 8).

Known Clinical Effects: The most common adverse effects seen during clinical use of this drug include headache, chest pain, dizziness, gastrointestinal disturbances, and decreased heart rate (bradycardia). Due to intended use, dangerous lowering of blood pressure can occur.

EU Indication of danger: Toxic to Reproduction; Category 3



R63 - Possible risk of harm to the unborn child.

Additional Information: For a more detailed discussion of potential health hazards and toxicity see Section 11.
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: 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. 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.

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: Wipe up with a damp cloth and place in container for disposal. Clean spill area thoroughly.

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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:

Contain the source of the spill or leak if it is safe to do so. Vacuum or sweep material into appropriate container for disposal.

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. Minimize dust generation and accumulation. Use with adequate ventilation.

Storage Conditions:

Store out of direct sunlight in a cool, well ventilated, dry area.

Storage Temperature

Store below 25°C

8. EXPOSURE CONTROLS / PERSONAL PROTECTION

Hydrochlorothiazide

Pfizer OEL TWA-8 Hr: 0.25 mg/m³

Microcrystalline cellulose

OSHA - Final PELs - TWAs 15 mg/m³ total dust
5 mg/m³ respirable fraction
ACGIH Threshold Limit Value (TWA) 10 mg/m³ TWA

Iron oxide

OSHA - Final PELs - TWAs 10 mg/m³
ACGIH Threshold Limit Value (TWA) 5 mg/m³ TWA

Paraffin

ACGIH Threshold Limit Value (TWA) 2 mg/m³ TWA

Ethanol

OSHA - Final PELs - TWAs 1000 ppm
1900 mg/m³
ACGIH Threshold Limit Value (TWA) 1000 ppm TWA

Maize starch

OSHA - Final PELs - TWAs 15 mg/m³ total dust
5 mg/m³ respirable fraction
ACGIH Threshold Limit Value (TWA) 10 mg/m³ TWA

Engineering Controls:

Engineering controls should be used as the primary means to control exposures. Local exhaust ventilation is required unless used in a closed system. For laboratory use, handle in a lab fume hood.

Personal Protective Equipment:

Hands: Wear impervious gloves if skin contact is possible.
Eyes: Safety glasses or goggles
Skin: Use protective clothing (uniforms, lab coats, disposable coveralls, etc.) in both production and laboratory areas.
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.

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9. PHYSICAL AND CHEMICAL PROPERTIES:

| | | | |
|---------------------------|---------|--------------------------|--------------------|
| Physical State: | Tablets | Color: | No data available. |
| Molecular Formula: | Mixture | Molecular Weight: | Mixture |

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: There are no data for this formulation. The following information is available for the individual ingredients.

Acute Toxicity: (Species, Route, End Point, Dose)

Lactose

Rat Oral LD50 > 10 g/kg

Magnesium Stearate

Rat Oral LD 50 1092 gm/kg/13 weeks

Hydroxypropyl methylcellulose

Rat Oral LD50 > 10,000 mg/kg

Microcrystalline cellulose

Rat Oral LD50 > 5000 mg/kg
Rabbit Dermal LD50 > 2000 mg/kg

Ethanol

Mouse Oral LD50 3,450 mg/kg
Rat Oral LD50 7,060mg/kg
Mouse Inhalation LC50 4h 39g/m³
Rat Inhalation LC50 10h 20,000mg/kg

Metoprolol Tartrate

Rat Oral LD50 5500 mg/kg
Rat Intravenous LD50 71.9 mg/kg
Mouse Oral LD50 1500 mg/kg
Mouse Intravenous LD50 62 mg/kg
Mouse Intraperitoneal LD50 > 200 mg/kg

Hydrochlorothiazide

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

Irritation / Sensitization: (Study Type, Species, Severity)

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Microcrystalline cellulose

Skin Irritation Rabbit Non-irritating
Eye Irritation Rabbit Non-irritating

Ethanol

Eye Irritation Rabbit Severe

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

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))

Metoprolol Tartrate

Reproductive & Fertility Rat Oral 430 mg/kg/day NOAEL Fertility
Embryo / Fetal Development Rat Oral 430 mg/kg/day NOAEL Not Teratogenic
Embryo / Fetal Development Rat Oral 430 mg/kg/day LOAEL Fetotoxicity
Embryo / Fetal Development Rabbit Oral 64 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)

Metoprolol Tartrate

Bacterial Mutagenicity (Ames) *Salmonella* Negative with activation
Chromosome Aberration Human Lymphocytes Negative
Dominant Lethal Assay Mouse Negative

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))

Metoprolol Tartrate

2 Year(s) Rat Oral 800 mg/kg/day NOAEL Not carcinogenic
21 Month(s) Mouse Oral 750 mg/kg/day NOAEL Not carcinogenic

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

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Carcinogen Status: Not listed as a carcinogen by IARC, NTP or US OSHA.

Povidone

IARC: Group 3

Hydrochlorothiazide

IARC: Group 3

12. ECOLOGICAL INFORMATION

Environmental Overview: Environmental properties have not been investigated.

Ethanol

| | | | | |
|------------------|-------|------|----------|-------------|
| Fingerling Trout | NPDES | LC50 | 24 Hours | 11,200 mg/L |
| Rainbow Trout | NPDES | LC50 | 96 Hours | 12,900 mg/L |
| Fathead minnow | NPDES | LC50 | 96 Hours | 14,200 mg/L |

13. DISPOSAL CONSIDERATIONS

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

14. TRANSPORT INFORMATION

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

15. REGULATORY INFORMATION

EU Labeling: Xn
EU Indication of danger: Toxic to Reproduction; Category 3
EU Risk Phrases: R63 - Possible risk of harm to the unborn child.

EU Safety Phrases: S22 - Do not breathe dust.
S36/37 - Wear suitable protective clothing and gloves.
S53 - Avoid exposure - obtain special instructions before use.

OSHA Label:
WARNING

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Antihypertensive drug: has blood pressure-lowering properties
Suspected of damaging the unborn child.

Canada - WHMIS: Classifications

WHMIS hazard class:

D2a very toxic materials



| | |
|--|---|
| Metoprolol Tartrate EU EINECS List | 260-148-9 |
| Hydrochlorothiazide EU EINECS List Inventory - United States TSCA - Sect. 8(b) | 200-403-3 Listed |
| Microcrystalline cellulose EU EINECS List Inventory - United States TSCA - Sect. 8(b) | 232-674-9 Listed |
| Purified water EU EINECS List Inventory - United States TSCA - Sect. 8(b) | 231-791-2 Listed |
| Hydroxypropyl methylcellulose Inventory - United States TSCA - Sect. 8(b) | Listed |
| Polyethylene glycol Inventory - United States TSCA - Sect. 8(b) | Listed |
| Iron oxide EU EINECS List Inventory - United States TSCA - Sect. 8(b) | 215-168-2 Listed |
| Paraffin EU EINECS List Inventory - United States TSCA - Sect. 8(b) | 232-315-6 Listed |
| Ethanol California Proposition 65 EU EINECS List Inventory - United States TSCA - Sect. 8(b) | developmental toxicity, initial date 10/1/87 (when in alcoholic beverages) 200-578-6 Listed |
| Maize starch EU EINECS List Inventory - United States TSCA - Sect. 8(b) | 232-679-6 Listed |
| Sodium stearyl fumarate EU EINECS List | 223-781-1 |

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| | | |
|---|--|-----------|
| Povidone | | |
| Inventory - United States TSCA - Sect. 8(b) | | Listed |
| Ethylcellulose | | |
| Inventory - United States TSCA - Sect. 8(b) | | Listed |
| Lactose | | |
| EU EINECS List | | 200-559-2 |
| Inventory - United States TSCA - Sect. 8(b) | | Listed |
| Sodium aluminosilicate | | |
| EU EINECS List | | 215-684-8 |
| Inventory - United States TSCA - Sect. 8(b) | | Listed |
| Riboflavin (Vitamin B2) | | |
| EU EINECS List | | 201-507-1 |
| Inventory - United States TSCA - Sect. 8(b) | | Listed |
| Magnesium Stearate | | |
| EU EINECS List | | 209-150-3 |
| Inventory - United States TSCA - Sect. 8(b) | | Listed |

16. OTHER INFORMATION

Prepared by: Corporate Occupational Toxicology & Hazard Assessment

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.

End of Safety Data Sheet