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

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Sandwich, Kent
CT13 9NJ
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Emergency telephone number:
CHEMTREC (24 hours): 1-800-424-9300

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

Material Name: Metoprolol Tartrate/Hydrochlorothiazide Tablets

Trade Name: Co-Betaloc
Chemical Family: Mixture
Intended Use: Pharmaceutical product for the treatment of high blood pressure (hypertension)

2. COMPOSITION/INFORMATION ON INGREDIENTS

Hazardous

Ingredient	CAS Number	EU EINECS List	%
Metoprolol Tartrate	56392-17-7	260-148-9	100 mg***
Hydrochlorothiazide	58-93-5	200-403-3	12.5 mg***
Microcrystalline cellulose	9004-34-6	232-674-9	*
Colloidal silicon dioxide	7631-86-9	231-545-4	*
Magnesium Stearate	557-04-0	209-150-3	*

Ingredient	CAS Number	EU EINECS List	%
Sodium starch glycolate	9063-38-1	Not listed	*
Lactose	63-42-3	200-559-2	*
Povidone	9003-39-8	Not listed	*

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

3. HAZARDS IDENTIFICATION

Appearance: Tablets
Signal Word: WARNING

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) .
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

EU Hazard Symbols:

EU Risk Phrases:

R63 - Possible risk of 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: 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: 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. 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/m^3 TWA total = 5 mg/m^3 TWA
ACGIH Threshold Limit Value (TWA)	= 10 mg/m^3 TWA
Australia TWA	= 10 mg/m^3 TWA

Colloidal silicon dioxide

OSHA - Final PELs - Table Z-3 Mineral D:	(80)/(% SiO2) mg/m^3 TWA = 20 mppcf TWA
Australia TWA	= 2 mg/m^3 TWA

Magnesium Stearate

ACGIH Threshold Limit Value (TWA)	= 10 mg/m^3 TWA except stearates of toxic metals
Australia TWA	= 10 mg/m^3 TWA

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

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

Engineering Controls: Engineering controls should be used as the primary means to control exposures. Good general ventilation should be sufficient to control airborne levels.

Personal Protective Equipment:

Hands:	Not required for the normal use of this product. Wear impervious gloves if skin contact is possible.
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:	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: Not determined
Incompatible Materials: As a precautionary measure, keep away from strong oxidizers.

11. TOXICOLOGICAL INFORMATION

General Information: There are no data for this formulation. The information included in this section describes the potential hazards of the individual ingredients.

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

Lactose
Rat Oral LD50 > 10 g/kg

Povidone
Rat Oral LD50 100 g/kg

Microcrystalline cellulose
Rat Oral LD50 > 5000 mg/kg
Rabbit Dermal LD50 > 2000 mg/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 2830 mg/kg
Rat Intravenous LD 50 990 mg/kg
Dog Intravenous LD 50 250 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

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

Magnesium Stearate
13 Week(s) Rat Oral 1092 g/kg LOAEL Liver

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

Carcinogen Status: None of the other components of this mixture are listed as a carcinogen by IARC, NTP or OSHA. See below

Povidone
IARC: Group 3

Hydrochlorothiazide
IARC: Group 3

Colloidal silicon dioxide
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.

14. TRANSPORT INFORMATION

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

15. REGULATORY INFORMATION

EU Symbol: 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 - Wear suitable protective clothing.
S53 - Avoid exposure - obtain special instructions before use.

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

Canada - WHMIS: Classifications

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

Sodium starch glycolate

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

Metoprolol Tartrate

Australia (AICS):	Present
EU EINECS List	260-148-9

Hydrochlorothiazide

Inventory - United States TSCA - Sect. 8(b)	Present
Australia (AICS):	Present
Standard for the Uniform Scheduling for Drugs and Poisons:	Schedule 4
EU EINECS List	200-403-3

Microcrystalline cellulose

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

Lactose

Inventory - United States TSCA - Sect. 8(b)	Present
Australia (AICS):	Present
EU EINECS List	200-559-2

Colloidal silicon dioxide

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

Povidone

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

Magnesium Stearate

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

16. OTHER INFORMATION

Reasons for Revision: Updated Section 2 - Composition / Information on Ingredients. Updated Section 3 - Hazard Identification. Updated Section 6 - Accidental Release Measures. Updated Section 8 - Exposure Controls / Personal Protection. Updated Section 10 - Stability and Reactivity. Updated Section 11 - Toxicology Information.

Prepared by: Toxicology and Hazard Communication
Pfizer Global Environment, Health, and Safety

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End of Safety Data Sheet