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

Material Name: Olmesartan Medoximil, Amlodipine Besylate and Hydrochlorothiazide Tablets

Trade Name: CAPENON HCT
Synonyms: OLMETEC TRIPLO
Chemical Family: Mixture
Intended Use: Pharmaceutical product used as Antihypertensive

2. HAZARDS IDENTIFICATION

Appearance: Tablets
Signal Word: DANGER

Statement of Hazard:
Causes severe eye damage.
Suspected of damaging the unborn child.
Toxic to aquatic life with long lasting effects.

Additional Hazard Information:
Short Term: Antihypertensive drug: has blood pressure-lowering properties

Long Term:
In humans, the use of drugs in this class can cause fetal and neonatal toxicity, including low blood pressure and kidney failure, when they are taken during the second and third trimesters of pregnancy.

Known Clinical Effects:
Effects reported during clinical use include dizziness, headache, lethargy, changes in blood pressure, nausea, and abdominal pain. Drugs of this class may cause electrolyte imbalance, dry mouth, muscle cramps, and muscle weakness

EU Indication of danger:
Toxic to Reproduction: Category 3
Dangerous for the Environment

EU Hazard Symbols:

Xn N

EU Risk Phrases:
R41 - Risk of serious damage to eyes.
R63 - Possible risk of harm to the unborn child.
R51/53 - Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment.
2. HAZARDS IDENTIFICATION

Australian Hazard Classification (NOHSC):

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

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>CAS Number</th>
<th>EU EINECS/ELINCS List</th>
<th>EU Classification</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Olmesartan medoxomil</td>
<td>144689-63-4</td>
<td>Not Listed</td>
<td>Repr.Cat.3;R63</td>
<td>3-19</td>
</tr>
<tr>
<td>Amlodipine besylate</td>
<td>111470-99-6</td>
<td>Not Listed</td>
<td>N;R50/53, Xn;R22</td>
<td>3-13</td>
</tr>
<tr>
<td>Hydrochlorothiazide</td>
<td>58-93-5</td>
<td>200-403-3</td>
<td>Not Listed</td>
<td>*</td>
</tr>
<tr>
<td>Starch, pregelatinized</td>
<td>9005-25-8</td>
<td>232-679-6</td>
<td>Not Listed</td>
<td>*</td>
</tr>
<tr>
<td>Microcrystalline cellulose</td>
<td>9004-34-6</td>
<td>232-674-9</td>
<td>Not Listed</td>
<td>*</td>
</tr>
<tr>
<td>Silica colloidal, Ph. Eur.</td>
<td>112945-52-5</td>
<td>Not Listed</td>
<td>Not Listed</td>
<td>*</td>
</tr>
<tr>
<td>Croscarmellose sodium</td>
<td>74811-65-7</td>
<td>Not Listed</td>
<td>Not Listed</td>
<td>*</td>
</tr>
</tbody>
</table>

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.
MATERIAL SAFETY DATA SHEET

Material Name: Olmesartan Medoximil, Amlodipine Besylate and Hydrochlorothiazide Tablets
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Version: 1.0

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. 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/m³

Hydrochlorothiazide
Pfizer OEL TWA-8 Hr: 250µg/m³

Starch, pregelatinized
ACGIH Threshold Limit Value (TWA) 10 mg/m³ TWA
Australia TWA 10 mg/m³
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/m³ total
5 mg/m³
Portugal OEL - TWA Listed
8. EXPOSURE CONTROLS / PERSONAL PROTECTION

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

**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.

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9. PHYSICAL AND CHEMICAL PROPERTIES

**Physical State:** Film-coated tablets

**Molecular Formula:** Mixture

**Color:** Various

**Molecular Weight:** Mixture

**Polymerization:** Will not occur

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10. STABILITY AND REACTIVITY

**Chemical 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)

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

Microcrystalline cellulose
- Rat Oral LD50 > 5000 mg/kg
- Rabbit Dermal LD50 > 2000 mg/kg

Hydrochlorothiazide
- Rat Oral LD50 2750 mg/kg
- Mouse Oral LD50 2830 mg/kg
- Rat Intravenous LD50 990 mg/kg
- Dog Intravenous LD50 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)

Amlodipine besylate
- Eye Irritation Rabbit Severe
- Skin Irritation Rabbit Non-irritating
- Skin Sensitization - GPMT Guinea Pig Negative

Microcrystalline cellulose
- Skin Irritation Rabbit Non-irritating
- Eye Irritation Rabbit Non-irritating

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

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))

Olmesartan medoxomil
- Reproductive & Fertility Rat Oral 1000 mg/kg/day NOAEL No effects at maximum dose

Amlodipine besylate
- Fertility and Embryonic Development Rat Oral 25 mg/kg/day NOAEL Not teratogenic, Maternal toxicity
11. TOXICOLOGICAL INFORMATION

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  

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)

Olmesartan medoxomil  
In Vitro Bacterial Mutagenicity (Ames)  
Salmonella  Negative  
In Vitro Cell Transformation Assay  
Hamster  Negative  
In Vitro Chromosome Aberration  
Hamster  Positive  
In Vitro Mammalian Cell Mutagenicity  
Mouse Lymphoma  Positive
In Vivo  
Micronucleus  Mouse Bone Marrow  Negative

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

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))

Olmesartan medoxomil  
2 Year(s)  
Rat  Oral, in feed  2000 mg/kg/day  NOAEL  Not carcinogenic  
6 Month(s)  
Mouse  Oral, in feed  1000 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

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 components of this formulation are listed as a carcinogen by IARC, NTP or OSHA.

Silica colloidal, Ph. Eur.  
IARC:  
Group 3

Hydrochlorothiazide  
IARC:  
Group 3
11. TOXICOLOGICAL INFORMATION

12. ECOLOGICAL INFORMATION

Environmental Overview: The environmental characteristics of this material have not been fully evaluated. Releases to the environment should be avoided. See Aquatic toxicity data of the active ingredient, below:

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

Amldipine 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

Aquatic Toxicity Comments: A greater than symbol (>) indicates that aquatic toxicity was not observed at the maximum dose tested.

Bacterial Inhibition: (Inoculum, Method, End Point, Result)

Amldipine besylate
- *Nostoc sp.* (Freshwater Cyanobacteria) MIC 20 mg/L
- *Aspergillus Niger* MIC > 100 mg/L
- *Trichoderma viride* MIC > 100 mg/L
- *Clostridium perfringens* MIC >100 mg/L
- *Bacillus subtilis* MIC 80 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: Xn N
EU Indication of danger: Toxic to Reproduction: Category 3
Dangers for the Environment

EU Risk Phrases: R41 - Risk of serious damage to eyes.
R63 - Possible risk of harm to the unborn child.
15. REGULATORY INFORMATION

R51/53 - Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment.

EU Safety Phrases:

S22 - Do not breathe dust.
S36/37 - Wear suitable protective clothing and gloves.
S53 - Avoid exposure - obtain special instructions before use.
S57 - Use appropriate containment to avoid environmental contamination.

OSHA Label:

DANGER
Causes severe eye damage.
Suspected of damaging the unborn child.
Toxic to aquatic life with long lasting effects.

Canada - WHMIS: Classifications

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

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

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

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

Silica colloidal, Ph. Eur.
- Australia (AICS): Listed

Croscarmellose sodium
- Australia (AICS): Listed
16. OTHER INFORMATION

Text of R phrases mentioned in Section 3

R63 - Possible risk of harm to the unborn child.
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.

Data Sources: Publicly available toxicity information. Safety data sheets for individual ingredients.

Prepared by: Product Stewardship Hazard Communications
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