1. PRODUCT AND COMPANY IDENTIFICATION

Chemical product name: Losartan / Amlodipine Besylate Formulation

Supplier’s company name, address and phone number
Company name of supplier: Organon & Co.
Address: 30 Hudson Street, 33nd floor
Jersey City, New Jersey, U.S.A 07302
Telephone: 551-430-6000
E-mail address: EHSSTEWARD@organon.com
Emergency telephone number: 215-631-6999

Recommended use of the chemical and restrictions on use
Recommended use: Pharmaceutical

2. HAZARDS IDENTIFICATION

GHS classification of chemical product
Serious eye damage/eye irritation: Category 1
Skin sensitisation: Category 1
Reproductive toxicity: Category 1B
Effects on or via lactation
Specific target organ toxicity - repeated exposure (Oral): Category 2 (Blood, Cardio-vascular system, Stomach, Kidney)

GHS label elements
Hazard pictograms:
Signal word: Danger
Hazard statements:
H317 May cause an allergic skin reaction.
H318 Causes serious eye damage.
H360D May damage the unborn child.
H362 May cause harm to breast-fed children.
H373 May cause damage to organs (Blood, Cardio-vascular system, Stomach, Kidney) through prolonged or repeated exposure if swallowed.

Precautionary statements:
Prevention:
P201 Obtain special instructions before use.
P202 Do not handle until all safety precautions have been read and understood.
P260 Do not breathe dust.
P263 Avoid contact during pregnancy and while nursing.
P264 Wash skin thoroughly after handling.
P270 Do not eat, drink or smoke when using this product.
P272 Contaminated work clothing should not be allowed out of the workplace.
P280 Wear protective gloves/ protective clothing/ eye protection/ face protection.

Response:
P302 + P352 IF ON SKIN: Wash with plenty of water.
P305 + P351 + P338 + P310 IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. Immediately call a POISON CENTER/ doctor.
P308 + P313 IF exposed or concerned: Get medical advice/ attention.
P333 + P313 If skin irritation or rash occurs: Get medical advice/ attention.
P362 + P364 Take off contaminated clothing and wash it before reuse.

Storage:
P405 Store locked up.

Disposal:
P501 Dispose of contents/ container to an approved waste disposal plant.

Other hazards which do not result in classification
Important symptoms and outlines of the emergency assumed:
Contact with dust can cause mechanical irritation or drying of the skin.
May form explosive dust-air mixture during processing, handling or other means.

3. COMPOSITION/INFORMATION ON INGREDIENTS

Substance / Mixture: Mixture

<table>
<thead>
<tr>
<th>Components</th>
<th>CAS-No.</th>
<th>Concentration (% w/w)</th>
<th>ENCS No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cellulose</td>
<td>9004-34-6</td>
<td>&gt;= 60 - &lt; 70</td>
<td></td>
</tr>
<tr>
<td>Losartan</td>
<td>124750-99-8</td>
<td>&gt;= 10 - &lt; 20</td>
<td></td>
</tr>
<tr>
<td>Amlodipine Besylate</td>
<td>652969-01-2</td>
<td>&gt;= 1 - &lt; 2.5</td>
<td></td>
</tr>
<tr>
<td>Titanium dioxide</td>
<td>13463-67-7</td>
<td>&gt;= 0.1 - &lt; 1</td>
<td>1-558, 5-5225</td>
</tr>
<tr>
<td>2,6-Di-tert-butyl-p-cresol</td>
<td>128-37-0</td>
<td>&gt;= 0.0025 - &lt; 0.025</td>
<td>3-540, 9-1805</td>
</tr>
</tbody>
</table>

4. FIRST AID MEASURES
General advice: In the case of accident or if you feel unwell, seek medical advice immediately. When symptoms persist or in all cases of doubt seek medical advice.

If inhaled: If inhaled, remove to fresh air. Get medical attention.

In case of skin contact: In case of contact, immediately flush skin with soap and plenty of water. Remove contaminated clothing and shoes. Get medical attention. Wash clothing before reuse. Thoroughly clean shoes before reuse.

In case of eye contact: In case of contact, immediately flush eyes with plenty of water for at least 15 minutes. If easy to do, remove contact lens, if worn. Get medical attention immediately.

If swallowed: If swallowed, DO NOT induce vomiting. Get medical attention. Rinse mouth thoroughly with water.

Most important symptoms and effects, both acute and delayed: May cause an allergic skin reaction. Causes serious eye damage. May damage the unborn child. May cause harm to breast-fed children. May cause damage to organs through prolonged or repeated exposure if swallowed. Contact with dust can cause mechanical irritation or drying of the skin.

Protection of first-aiders: First Aid responders should pay attention to self-protection, and use the recommended personal protective equipment when the potential for exposure exists (see section 8).

Notes to physician: Treat symptomatically and supportively.

5. FIREFIGHTING MEASURES

Suitable extinguishing media: Water spray
Alcohol-resistant foam
Carbon dioxide (CO2)
Dry chemical

Unsuitable extinguishing media: None known.

Specific hazards during firefighting: Avoid generating dust; fine dust dispersed in air in sufficient concentrations, and in the presence of an ignition source is a potential dust explosion hazard. Exposure to combustion products may be a hazard to health.

Hazardous combustion products: Carbon oxides
Chlorine compounds
Nitrogen oxides (NOx)
Metal oxides

Specific extinguishing methods: Use extinguishing measures that are appropriate to local circumstances and the surrounding environment. Use water spray to cool unopened containers. Remove undamaged containers from fire area if it is safe to do
6. ACCIDENTAL RELEASE MEASURES

Personal precautions, protective equipment and emergency procedures

- Use personal protective equipment.
- Follow safe handling advice (see section 7) and personal protective equipment recommendations (see section 8).

Environmental precautions

- Avoid release to the environment.
- Prevent further leakage or spillage if safe to do so.
- Retain and dispose of contaminated wash water.
- Local authorities should be advised if significant spillages cannot be contained.

Methods and materials for containment and cleaning up

- Sweep up or vacuum up spillage and collect in suitable container for disposal.
- Avoid dispersal of dust in the air (i.e., clearing dust surfaces with compressed air).
- Dust deposits should not be allowed to accumulate on surfaces, as these may form an explosive mixture if they are released into the atmosphere in sufficient concentration.
- Local or national regulations may apply to releases and disposal of this material, as well as those materials and items employed in the cleanup of releases. You will need to determine which regulations are applicable.
- Sections 13 and 15 of this SDS provide information regarding certain local or national requirements.

7. HANDLING AND STORAGE

Handling

Technical measures

- Static electricity may accumulate and ignite suspended dust causing an explosion.
- Provide adequate precautions, such as electrical grounding and bonding, or inert atmospheres.

Local/Total ventilation

- If sufficient ventilation is unavailable, use with local exhaust ventilation.

Advice on safe handling

- Avoid contact during pregnancy and while nursing.
- Do not get on skin or clothing.
- Do not breathe dust.
- Do not swallow.
- Do not get in eyes.
- Wash skin thoroughly after handling.
- Handle in accordance with good industrial hygiene and safety practice, based on the results of the workplace exposure assessment.
- Keep container tightly closed.
- Minimize dust generation and accumulation.
- Keep container closed when not in use.
- Keep away from heat and sources of ignition.
- Take precautionary measures against static discharges.
Do not eat, drink or smoke when using this product.
Take care to prevent spills, waste and minimize release to the environment.

Avoidance of contact:
Oxidizing agents

Hygiene measures:
If exposure to chemical is likely during typical use, provide eye flushing systems and safety showers close to the working place.
When using do not eat, drink or smoke.
Contaminated work clothing should not be allowed out of the workplace.
Wash contaminated clothing before re-use.

Storage
Conditions for safe storage:
Keep in properly labelled containers.
Store locked up.
Keep tightly closed.
Store in accordance with the particular national regulations.

Materials to avoid:
Do not store with the following product types:
Strong oxidizing agents

Packaging material:
Unsuitable material: None known.

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Threshold limit value and permissible exposure limits for each component in the work environment

<table>
<thead>
<tr>
<th>Components</th>
<th>CAS-No.</th>
<th>Value type (Form of exposure)</th>
<th>Control parameters / Permissible concentration</th>
<th>Basis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cellulose</td>
<td>9004-34-6</td>
<td>TWA</td>
<td>10 mg/m3</td>
<td>ACGIH</td>
</tr>
<tr>
<td>Losartan</td>
<td>124750-99-8</td>
<td>TWA</td>
<td>100 µg/m3 (OEB 2)</td>
<td>Internal</td>
</tr>
<tr>
<td>Amlodipine Besylate</td>
<td>652969-01-2</td>
<td>TWA</td>
<td>20 µg/m3 (OEB 3)</td>
<td>Internal</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Wipe limit</td>
<td>100 µg/100 cm²</td>
<td>Internal</td>
</tr>
<tr>
<td>Titanium dioxide</td>
<td>13463-67-7</td>
<td>OEL-M (Respirable dust)</td>
<td>1 mg/m3 (Titanium)</td>
<td>JP OEL JSOH</td>
</tr>
<tr>
<td></td>
<td></td>
<td>OEL-M (Total dust)</td>
<td>4 mg/m3 (Titanium)</td>
<td>JP OEL JSOH</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA</td>
<td>10 mg/m3 (Titanium dioxide)</td>
<td>ACGIH</td>
</tr>
<tr>
<td>2,6-Di-tert-butyl-p-cresol</td>
<td>128-37-0</td>
<td>TWA (Inhalable fraction and vapor)</td>
<td>2 mg/m3</td>
<td>ACGIH</td>
</tr>
</tbody>
</table>

Further information: Class 2 Dust

Further information: Class 2 Dust

Engineering measures:
Minimize workplace exposure concentrations.
Apply measures to prevent dust explosions.
Ensure that dust-handling systems (such as exhaust ducts, dust collectors, vessels, and processing equipment) are designed in a manner to prevent the escape of dust into the work area (i.e., there is no leakage from the equipment).
If sufficient ventilation is unavailable, use with local exhaust ventilation.

### Personal protective equipment

**Respiratory protection:**
- If adequate local exhaust ventilation is not available or exposure assessment demonstrates exposures outside the recommended guidelines, use respiratory protection.
- **Filter type:** Particulates type

**Hand protection:**
- Material: Chemical-resistant gloves
- **Remarks:** Choose gloves to protect hands against chemicals depending on the concentration and quantity of the hazardous substance and specific to place of work. Breakthrough time is not determined for the product. Change gloves often! For special applications, we recommend clarifying the resistance to chemicals of the aforementioned protective gloves with the glove manufacturer.
- Wash hands before breaks and at the end of workday.

**Eye protection:**
- Wear the following personal protective equipment:
  - Chemical resistant goggles must be worn.
  - If splashes are likely to occur, wear: Face-shield

**Skin and body protection:**
- Select appropriate protective clothing based on chemical resistance data and an assessment of the local exposure potential.
- Skin contact must be avoided by using impervious protective clothing (gloves, aprons, boots, etc).

### 9. PHYSICAL AND CHEMICAL PROPERTIES

- **Physical state:** powder
- **Colour:** No data available
- **Odour:** No data available
- **Odour Threshold:** No data available
- **Melting point/freezing point:** No data available
- **Boiling point, initial boiling point and boiling range:** No data available
- **Flammability (solid, gas):** May form explosive dust-air mixture during processing, handling or other means.
- **Flammability (liquids):** No data available
- **Lower explosion limit and upper explosion limit / flammability limit**
  - **Upper explosion limit / Upper flammability limit:** No data available
  - **Lower explosion limit / Lower flammability limit:** No data available
<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flammability limit</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Flash point</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Decomposition temperature</td>
<td>No data available</td>
</tr>
<tr>
<td>pH</td>
<td>No data available</td>
</tr>
<tr>
<td>Evaporation rate</td>
<td>No data available</td>
</tr>
<tr>
<td>Auto-ignition temperature</td>
<td>No data available</td>
</tr>
<tr>
<td>Viscosity</td>
<td>No data available</td>
</tr>
<tr>
<td>Viscosity, kinematic</td>
<td>No data available</td>
</tr>
<tr>
<td>Solubility(ies)</td>
<td>No data available</td>
</tr>
<tr>
<td>Water solubility</td>
<td>No data available</td>
</tr>
<tr>
<td>Partition coefficient: n-octanol/water</td>
<td>No data available</td>
</tr>
<tr>
<td>Vapour pressure</td>
<td>No data available</td>
</tr>
<tr>
<td>Density and/or relative density</td>
<td>No data available</td>
</tr>
<tr>
<td>Relative density</td>
<td>No data available</td>
</tr>
<tr>
<td>Density</td>
<td>No data available</td>
</tr>
<tr>
<td>Relative vapour density</td>
<td>No data available</td>
</tr>
<tr>
<td>Explosive properties</td>
<td>Not explosive</td>
</tr>
<tr>
<td>Oxidizing properties</td>
<td>The substance or mixture is not classified as oxidizing.</td>
</tr>
<tr>
<td>Molecular weight</td>
<td>No data available</td>
</tr>
<tr>
<td>Particle characteristics</td>
<td>No data available</td>
</tr>
<tr>
<td>Particle size</td>
<td>No data available</td>
</tr>
</tbody>
</table>

**10. STABILITY AND REACTIVITY**

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reactivity</td>
<td>Not classified as a reactivity hazard.</td>
</tr>
<tr>
<td>Chemical stability</td>
<td>Stable under normal conditions.</td>
</tr>
<tr>
<td>Possibility of hazardous reactions</td>
<td>May form explosive dust-air mixture during processing, handling or other means. Can react with strong oxidizing agents.</td>
</tr>
<tr>
<td>Conditions to avoid</td>
<td>Heat, flames and sparks.</td>
</tr>
<tr>
<td>Incompatible materials</td>
<td>Avoid dust formation.</td>
</tr>
<tr>
<td>Oxidizing agents</td>
<td></td>
</tr>
<tr>
<td>Hazardous decomposition products</td>
<td>No hazardous decomposition products are known.</td>
</tr>
</tbody>
</table>
11. TOXICOLOGICAL INFORMATION

Information on likely routes of exposure:
- Inhalation
- Skin contact
- Ingestion
- Eye contact

Acute toxicity:
Not classified based on available information.

Product:
- Acute oral toxicity: Acute toxicity estimate: > 5,000 mg/kg
  Method: Expert judgement

Components:

**Cellulose:**
- Acute oral toxicity: LD50 (Rat): > 5,000 mg/kg
- Acute inhalation toxicity: LC50 (Rat): > 5.8 mg/l
  Exposure time: 4 h
  Test atmosphere: dust/mist
- Acute dermal toxicity: LD50 (Rabbit): > 2,000 mg/kg

**Losartan:**
- Acute oral toxicity:
  - LD50 (Mouse): 1,257 - 1,590 mg/kg
  - LDLo (Rat): 200 mg/kg
  - LDLo (Mouse): 400 mg/kg

**Amlodipine Besylate:**
- Acute oral toxicity: LD50 (Rat): 393 mg/kg

**Titanium dioxide:**
- Acute oral toxicity: LD50 (Rat): > 5,000 mg/kg
- Acute inhalation toxicity:
  - LC50 (Rat): > 6.82 mg/l
  - Exposure time: 4 h
  - Test atmosphere: dust/mist
  - Assessment: The substance or mixture has no acute inhalation toxicity

**2,6-Di-tert-butyl-p-cresol:**
- Acute oral toxicity:
  - LD50 (Rat): > 6,000 mg/kg
  - Method: OECD Test Guideline 401
- Acute dermal toxicity:
  - LD50 (Rat): > 2,000 mg/kg
  - Method: OECD Test Guideline 402
  - Assessment: The substance or mixture has no acute dermal
**Skin corrosion/irritation**
Not classified based on available information.

**Components:**

**Losartan:**
Species: Rabbit  
Result: Mild skin irritation

**Titanium dioxide:**
Species: Rabbit  
Result: No skin irritation

**2,6-Di-tert-butyl-p-cresol:**
Species: Rabbit  
Method: OECD Test Guideline 404  
Result: No skin irritation  
Remarks: Based on data from similar materials

**Serious eye damage/eye irritation**
Causes serious eye damage.

**Components:**

**Losartan:**
Species: Rabbit  
Result: Severe irritation

**Amlodipine Besylate:**
Species: Rabbit  
Result: Severe irritation

**Titanium dioxide:**
Species: Rabbit  
Result: No eye irritation

**2,6-Di-tert-butyl-p-cresol:**
Species: Rabbit  
Result: No eye irritation  
Method: OECD Test Guideline 405  
Remarks: Based on data from similar materials

**Respiratory or skin sensitisation**

**Skin sensitisation**
May cause an allergic skin reaction.
Respiratory sensitisation
Not classified based on available information.

**Components:**

**Losartan:**
- Test Type: Maximisation Test
- Exposure routes: Skin contact
- Species: Guinea pig
- Assessment: Probability or evidence of skin sensitisation in humans
- Result: positive

**Titanium dioxide:**
- Test Type: Local lymph node assay (LLNA)
- Exposure routes: Skin contact
- Species: Mouse
- Result: negative

**2,6-Di-tert-butyl-p-cresol:**
- Test Type: Human repeat insult patch test (HRIPT)
- Exposure routes: Skin contact
- Species: Humans
- Result: negative

**Germ cell mutagenicity**
Not classified based on available information.

**Components:**

**Cellulose:**
- Genotoxicity in vitro: Test Type: Bacterial reverse mutation assay (AMES) Result: negative
  - Test Type: In vitro mammalian cell gene mutation test Result: negative
- Genotoxicity in vivo: Test Type: Mammalian erythrocyte micronucleus test (in vivo cytogenetic assay)
  - Species: Mouse
  - Application Route: Ingestion
  - Result: negative

**Losartan:**
- Genotoxicity in vitro: Test Type: in vitro assay Result: negative
  - Test Type: In vitro mammalian cell gene mutation test
    - Test system: Chinese hamster ovary cells
    - Result: negative
  - Test Type: Alkaline elution assay
    - Result: negative
Test Type: Chromosomal aberration
Result: negative

Genotoxicity in vivo
: Test Type: Chromosomal aberration
Result: negative

**Amlodipine Besylate:**
Genotoxicity in vitro :
: Test Type: Bacterial reverse mutation assay (AMES)
Result: negative

Test Type: Chromosome aberration test in vitro
Result: negative

**Titanium dioxide:**
Genotoxicity in vitro :
: Test Type: Bacterial reverse mutation assay (AMES)
Result: negative

Genotoxicity in vivo :
: Test Type: In vivo micronucleus test
Species: Mouse
Result: negative

**2,6-Di-tert-butyl-p-cresol:**
Genotoxicity in vitro :
: Test Type: Bacterial reverse mutation assay (AMES)
Result: negative

Test Type: In vitro mammalian cell gene mutation test
Result: negative

Test Type: Chromosome aberration test in vitro
Result: negative

Genotoxicity in vivo :
: Test Type: Mutagenicity (in vivo mammalian bone-marrow cytogenetic test, chromosomal analysis)
Species: Rat
Application Route: Ingestion
Result: negative

**Carcinogenicity**
Not classified based on available information.

**Components:**

**Cellulose:**
Species :
: Rat
Application Route :
: Ingestion
Exposure time :
: 72 weeks
Result :
: negative

**Losartan:**
Species :
: Mouse
Application Route :
: Oral
Exposure time :
: 92 weeks
Dose: 200 mg/kg body weight
Result: negative

Species: Rat
Application Route: Oral
Exposure time: 105 weeks
Dose: 270 mg/kg body weight
Result: negative

**Amlodipine Besylate:**
Species: Mouse
Application Route: Oral
Exposure time: 2 Years
Result: negative

Species: Rat
Application Route: Oral
Exposure time: 2 Years
Result: negative

**Titanium dioxide:**
Species: Rat
Application Route: inhalation (dust/mist/fume)
Exposure time: 2 Years
Method: OECD Test Guideline 453
Result: positive
Remarks: The mechanism or mode of action may not be relevant in humans.

Carcinogenicity - Assessment: Limited evidence of carcinogenicity in inhalation studies with animals.

**2,6-Di-tert-butyl-p-cresol:**
Species: Rat
Application Route: Ingestion
Exposure time: 22 Months
Result: negative

**Reproductive toxicity**
May damage the unborn child.
May cause harm to breast-fed children.

**Components:**

**Cellulose:**
Effects on fertility: Test Type: One-generation reproduction toxicity study
Species: Rat
Application Route: Ingestion
Result: negative

Effects on foetal development: Test Type: Fertility/early embryonic development
Species: Rat
**Losartan:**

**Effects on fertility**
- Test Type: Fertility
- Species: Rat, female
- Application Route: Oral
- Fertility: LOAEL: 200 mg/kg body weight
- Result: female reproductive effects
- Remarks: Maternal toxicity observed.

**Effects on foetal development**
- Test Type: Development
- Species: Rabbit
- Application Route: Oral
- General Toxicity Maternal: NOAEL: 10 mg/kg body weight
- Developmental Toxicity: NOAEL F1: 20 mg/kg body weight
- Result: Embryotoxic effects and adverse effects on the offspring were detected only at high maternally toxic doses, No teratogenic effects

**Reproductive toxicity - Assessment**
- Clear evidence of adverse effects on development, based on animal experiments.
- Studies indicating a hazard to babies during the lactation period

**Amlodipine Besylate:**

**Effects on fertility**
- Test Type: Fertility/early embryonic development
- Species: Rat
- Application Route: Ingestion
- Fertility: NOAEL: 10 mg/kg body weight
- Result: No effects on fertility

**Effects on foetal development**
- Test Type: Embryo-foetal development
- Species: Rat
- Application Route: Ingestion
- Developmental Toxicity: LOAEL: 10 mg/kg body weight
- Result: Effects on foetal development

Test Type: Embryo-foetal development
- Species: Rabbit
- Application Route: Ingestion
### Developmental Toxicity

**NOAEL**: 10 mg/kg body weight  
**Result**: No effects on foetal development

**Test Type**: Embryo-foetal development  
**Species**: Mouse  
**Application Route**: Ingestion

**Developmental Toxicity**: LOAEL: 1.6 mg/kg body weight  
**Result**: Effects on foetal development  
**Remarks**: Maternal toxicity observed.

#### 2,6-Di-tert-butyl-p-cresol:

**Effects on fertility**:  
**Test Type**: Two-generation reproduction toxicity study  
**Species**: Rat  
**Application Route**: Ingestion  
**Result**: negative

**Effects on foetal development**:  
**Test Type**: Embryo-foetal development  
**Species**: Rat  
**Application Route**: Ingestion  
**Result**: negative

### STOT - single exposure

Not classified based on available information.

### STOT - repeated exposure

May cause damage to organs (Blood, Cardio-vascular system, Stomach, Kidney) through prolonged or repeated exposure if swallowed.

### Components:

#### Losartan:

- **Exposure routes**: Ingestion  
- **Target Organs**: Blood, Cardio-vascular system, Stomach, Kidney  
- **Assessment**: May cause damage to organs through prolonged or repeated exposure.

#### 2,6-Di-tert-butyl-p-cresol:

- **Assessment**: No significant health effects observed in animals at concentrations of 100 mg/kg bw or less.

### Repeated dose toxicity

#### Components:

#### Cellulose:

- **Species**: Rat  
- **NOAEL**: >= 9,000 mg/kg  
- **Application Route**: Ingestion  
- **Exposure time**: 90 Days

#### Losartan:

- **Species**: Rat
LOAEL: 15 mg/kg  
Application Route: Oral  
Exposure time: 309 d  
Number of exposures: daily  
Target Organs: Blood, Kidney, Cardio-vascular system, Stomach  
Species: Dog  
NOAEL: 5 mg/kg  
Application Route: Oral  
Exposure time: 1 Months  
Symptoms: Salivation, Vomiting  
Number of exposures: daily  
Species: Dog  
LOAEL: 25 mg/kg  
Application Route: Oral  
Exposure time: 53 Weeks  
Number of exposures: daily  
Symptoms: Salivation, Vomiting

**Amlodipine Besylate:**  
Species: Rat  
NOAEL: 15 mg/kg  
Application Route: Oral  
Exposure time: 90 d  
Remarks: No significant adverse effects were reported

**Titanium dioxide:**  
Species: Rat  
NOAEL: 24,000 mg/kg  
Application Route: Ingestion  
Exposure time: 28 Days  
Species: Rat  
NOAEL: 10 mg/m3  
Application Route: inhalation (dust/mist/fume)  
Exposure time: 2 yr

**2,6-Di-tert-butyl-p-cresol:**  
Species: Rat  
NOAEL: 25 mg/kg  
Application Route: Ingestion  
Exposure time: 22 Months

**Aspiration toxicity**  
Not classified based on available information.

**Components:**  
**Losartan:**  
No aspiration toxicity classification
Experience with human exposure

**Components:**

**Losartan:**
- **Eye contact**: Symptoms: Eye irritation
- **Ingestion**: Symptoms: hypotension, tachycardia

**Amlodipine Besylate:**
- **Eye contact**: Symptoms: Severe irritation
- **Ingestion**: Symptoms: Nausea, Abdominal pain, Fatigue, Headache, Oedema, Palpitation

### 12. ECOLOGICAL INFORMATION

**Ecotoxicity**

**Components:**

**Cellulose:**
- **Toxicity to fish**: LC50 (Oryzias latipes (Japanese medaka)): > 100 mg/l
  - Exposure time: 48 h
  - Remarks: Based on data from similar materials

**Losartan:**
- **Toxicity to fish**: LC50 (Oncorhynchus mykiss (rainbow trout)): > 929 mg/l
  - Exposure time: 96 h
  - Method: FDA 4.11

- **Toxicity to daphnia and other aquatic invertebrates**: EC50 (Daphnia magna (Water flea)): 331 mg/l
  - Exposure time: 48 h
  - Method: OECD Test Guideline 202

- **Toxicity to algae/aquatic plants**: NOEC (Microcystis aeruginosa (blue-green algae)): 949 mg/l
  - Exposure time: 10 d
  - Method: FDA 4.01

  NOEC (Selenastrum capricornutum (green algae)): 143 mg/l
  - Exposure time: 10 d
  - Method: FDA 4.01

- **Toxicity to fish (Chronic toxicity)**: NOEC (Pimephales promelas (fathead minnow)): 10 mg/l
  - Exposure time: 32 d
  - Method: OECD Test Guideline 210

- **Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity)**: NOEC (Daphnia magna (Water flea)): 100 mg/l
  - Exposure time: 21 d
  - Method: OECD Test Guideline 211

**Amlodipine Besylate:**
### Toxicity to Fish
- **Titanium dioxide**
  - Toxicity to fish: LC50 (Pimephales promelas (fathead minnow)): 2.7 mg/l
    - Exposure time: 96 h
  - Toxicity to daphnia and other aquatic invertebrates: EC50 (Daphnia magna (Water flea)): 3.2 mg/l
    - Exposure time: 48 h
  - Toxicity to algae/aquatic plants: IC50 (Pseudokirchneriella subcapitata (green algae)): 5.6 mg/l
    - Exposure time: 72 h
    - Method: OECD Test Guideline 201

- **2,6-Di-tert-butyl-p-cresol**
  - Toxicity to fish: LC50 (Danio rerio (zebra fish)): > 0.57 mg/l
    - Exposure time: 96 h
  - Toxicity to daphnia and other aquatic invertebrates: EC50 (Daphnia magna (Water flea)): 0.48 mg/l
    - Exposure time: 48 h
    - Method: OECD Test Guideline 202
  - Toxicity to algae/aquatic plants: ErC50 (Pseudokirchneriella subcapitata (green algae)): > 0.24 mg/l
    - Exposure time: 72 h
    - Method: OECD Test Guideline 201
  - NOEC (Pseudokirchneriella subcapitata (green algae)): 0.24 mg/l
    - Exposure time: 72 h
    - Method: OECD Test Guideline 201

- **M-Factor (Acute aquatic toxicity)**: 1

- **Toxicity to fish (Chronic toxicity)**: NOEC (Oryzias latipes (Japanese medaka)): 0.053 mg/l
  - Exposure time: 30 d
  - Method: OECD Test Guideline 210

- **Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity)**
  - NOEC (Daphnia magna (Water flea)): 0.316 mg/l
    - Exposure time: 21 d
  - Method: OECD Test Guideline 202
toxicity)
Toxicity to microorganisms : EC50: > 10,000 mg/l
Exposure time: 3 h
Method: OECD Test Guideline 209

Persistence and degradability

Components:

Cellulose:
Biodegradability : Result: Readily biodegradable.

Losartan:
Stability in water : Hydrolysis: < 10 % (5 d)

2,6-Di-tert-butyl-p-cresol:
Biodegradability : Result: Not readily biodegradable.
Biodegradation: 4.5 %
Exposure time: 28 d
Method: OECD Test Guideline 301C

Bioaccumulative potential

Components:

Losartan:
Partition coefficient: n-octanol/water : log Pow: 1.2

Amlodipine Besylate:
Partition coefficient: n-octanol/water : log Pow: 3

2,6-Di-tert-butyl-p-cresol:
Bioaccumulation : Species: Cyprinus carpio (Carp)
Bioconcentration factor (BCF): 330 - 1,800
Partition coefficient: n-octanol/water : log Pow: 5.1

Mobility in soil
No data available

Hazardous to the ozone layer
Not applicable

Other adverse effects
No data available

13. DISPOSAL CONSIDERATIONS

Disposal methods
Waste from residues : Dispose of in accordance with local regulations.
**Contaminated packaging**: Empty containers should be taken to an approved waste handling site for recycling or disposal. If not otherwise specified: Dispose of as unused product.

**14. TRANSPORT INFORMATION**

**International Regulations**

- **UNRTDG**: Not regulated as a dangerous good
- **IATA-DGR**: Not regulated as a dangerous good
- **IMDG-Code**: Not regulated as a dangerous good

**Transport in bulk according to Annex II of MARPOL 73/78 and the IBC Code**
- Not applicable for product as supplied.

**National Regulations**
- Refer to section 15 for specific national regulation.

**15. REGULATORY INFORMATION**

**Related Regulations**

- **Fire Service Law**: Not applicable to dangerous materials / designated flammables.
- **Chemical Substance Control Law**
  - **Priority Assessment Chemical Substance**
    | Chemical name                      | Number |
    |-----------------------------------|--------|
    | 2,6-Di-tert-butyl-4-methylphenol  | 64     |

- **Industrial Safety and Health Law**
  - **Harmful Substances Prohibited from Manufacture**: Not applicable
  - **Harmful Substances Required Permission for Manufacture**: Not applicable
  - **Substances Prevented From Impairment of Health**: Not applicable
  - **Circular concerning Information on Chemicals having Mutagenicity - Annex 2: Information on Existing Chemicals having Mutagenicity**: Not applicable
  - **Circular concerning Information on Chemicals having Mutagenicity - Annex 1: Information on Notified Substances having Mutagenicity**: Not applicable

- **Substances Subject to be Notified Names**
  - **Article 57-2 (Enforcement Order Table 9)**
    | Chemical name | Number | Concentration (%) |
    |---------------|--------|-------------------|

Titanium(IV) oxide  |  191  |  >=0.1 - <1

**Substances Subject to be Indicated Names**
Not applicable

**Ordinance on Prevention of Hazards Due to Specified Chemical Substances**
Not applicable

**Ordinance on Prevention of Lead Poisoning**
Not applicable

**Ordinance on Prevention of Tetraalkyl Lead Poisoning**
Not applicable

**Ordinance on Prevention of Organic Solvent Poisoning**
Not applicable

**Enforcement Order of the Industrial Safety and Health Law - Attached table 1 (Dangerous Substances)**
Not applicable

**Poisonous and Deleterious Substances Control Law**
Not applicable

**Act on Confirmation, etc. of Release Amounts of Specific Chemical Substances in the Environment and Promotion of Improvements to the Management Thereof**
Not applicable

**High Pressure Gas Safety Act**
Not applicable

**Explosive Control Law**
Not applicable

**Vessel Safety Law**
Not regulated as a dangerous good

**Aviation Law**
Not regulated as a dangerous good

**Marine Pollution and Sea Disaster Prevention etc Law**
- Bulk transportation: Not classified as noxious liquid substance
- Pack transportation: Not classified as marine pollutant

**Narcotics and Psychotropics Control Act**
- Narcotic or Psychotropic Raw Material (Export / Import Permission)
  Not applicable
- Specific Narcotic or Psychotropic Raw Material (Export / Import permission)
  Not applicable

**Waste Disposal and Public Cleansing Law**
Industrial waste

**The components of this product are reported in the following inventories:**
- AICS: not determined
SAFETY DATA SHEET

Losartan / Amlodipine Besylate Formulation

Version 5.1
Revision Date: 2020/10/10
SDS Number: 49939-00016
Date of last issue: 2020/03/23
Date of first issue: 2015/01/26

DSL : not determined
IECSC : not determined

16. OTHER INFORMATION

Further information
Date format: yyyy/mm/dd

Full text of other abbreviations
ACGIH : USA. ACGIH Threshold Limit Values (TLV)

ACGIH / TWA : 8-hour, time-weighted average
JP OEL JSOH / OEL-M : Occupational Exposure Limit-Mean

AICL - Australian Inventory of Industrial Chemicals; ANTT - National Agency for Transport by Land of Brazil; ASTM - American Society for the Testing of Materials; bw - Body weight; CMR - Carcinogen, Mutagen or Reproductive Toxicant; DIN - Standard of the German Institute for Standardisation; DSL - Domestic Substances List (Canada); ECx - Concentration associated with x% response; ELx - Loading rate associated with x% response; EmS - Emergency Schedule; ENCS - Existing and New Chemical Substances (Japan); ErCx - Concentration associated with x% growth rate response; ERG - Emergency Response Guide; GHS - Globally Harmonized System; GLP - Good Laboratory Practice; IARC - International Agency for Research on Cancer; IATA - International Air Transport Association; IBC - International Code for the Construction and Equipment of Ships carrying Dangerous Chemicals in Bulk; IC50 - Half maximal inhibitory concentration; ICAO - International Civil Aviation Organization; IECSC - Inventory of Existing Chemical Substances in China; IMDG - International Maritime Dangerous Goods; IMO - International Maritime Organization; ISHL - Industrial Safety and Health Law (Japan); ISO - International Organisation for Standardization; KECI - Korea Existing Chemicals Inventory; LC50 - Lethal Concentration to 50% of a test population; LD50 - Lethal Dose to 50% of a test population (Median Lethal Dose); MARPOL - International Convention for the Prevention of Pollution from Ships; n.o.s. - Not Otherwise Specified; Nch - Chilean Norm; NO(A)EC - No Observed (Adverse) Effect Concentration; NO(A)EL - No Observed (Adverse) Effect Level; NOELR - No Observable Effect Loading Rate; NOM - Official Mexican Norm; NTP - National Toxicology Program; NZIoC - New Zealand Inventory of Chemicals; OECD - Organization for Economic Co-operation and Development; OPPTS - Office of Chemical Safety and Pollution Prevention; PBT - Persistent, Bioaccumulative and Toxic substance; PICCS - Philippines Inventory of Chemicals and Chemical Substances; (Q)SAR - (Quantitative) Structure Activity Relationship; REACH - Regulation (EC) No 1907/2006 of the European Parliament and of the Council concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals; SADT - Self-Accelerating Decomposition Temperature; SDS - Safety Data Sheet; TCSI - Taiwan Chemical Substance Inventory; TDG - Transportation of Dangerous Goods; TSCA - Toxic Substances Control Act (United States); UN - United Nations; UNRTDG - United Nations Recommendations on the Transport of Dangerous Goods; vPvB - Very Persistent and Very Bioaccumulative; WHMIS - Workplace Hazardous Materials Information System

The information provided in this Safety Data Sheet is correct to the best of our knowledge, information and belief at the date of its publication. The information is designed only as a guidance for
safe handling, use, processing, storage, transportation, disposal and release and shall not be
considered a warranty or quality specification of any type. The information provided relates only
to the specific material identified at the top of this SDS and may not be valid when the SDS mate-
rial is used in combination with any other materials or in any process, unless specified in the text.
Material users should review the information and recommendations in the specific context of their
intended manner of handling, use, processing and storage, including an assessment of the ap-
propriateness of the SDS material in the user’s end product, if applicable.

JP / EN