1. PRODUCT AND COMPANY IDENTIFICATION

Product name: Losartan / Amlodipine Besylate Formulation

Manufacturer or supplier’s details
Company name of supplier: MSD
Address: Kumagaya, Saitama Prefecture, Xicheng 810 MSD Co., Ltd.
Menuma factory
Telephone: 048-588-8411
E-mail address: EHSDATASTEWARD@msd.com
Emergency telephone number: 1-908-423-6000

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

2. HAZARDS IDENTIFICATION

GHS Classification
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/ 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

Components

<table>
<thead>
<tr>
<th>Chemical name</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
Special protective equipment for firefighters: In the event of fire, wear self-contained breathing apparatus. Use personal protective equipment.

6. ACCIDENTAL RELEASE MEASURES

Personal precautions, protective equipment and emergency procedures: Use personal protective equipment. Follow safe handling advice and personal protective equipment recommendations.

Environmental precautions: Discharge into the environment must be avoided. 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: Do not get on skin or clothing. Do not breathe dust. Do not swallow. Do not get in eyes. 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. 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. 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></td>
<td>4 mg/m³ (Titanium)</td>
<td>JP OEL JSOH</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Further information: Class 2 Dust</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>OEL-M (Total dust)</td>
<td></td>
<td></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 rec-
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

Appearance: powder
Colour: No data available
Odour: No data available
Odour Threshold: No data available
pH: No data available
Melting point/freezing point: No data available
Initial boiling point and boiling range: No data available
Flash point: Not applicable
Evaporation rate: No data available
Flammability (solid, gas): May form explosive dust-air mixture during processing, handling or other means.
Flammability (liquids): No data available
Upper explosion limit / Upper flammability limit: No data available
Lower explosion limit / Lower flammability limit: No data available
10. STABILITY AND REACTIVITY

Reactivity: Not classified as a reactivity hazard.
Chemical stability: Stable under normal conditions.
Possibility of hazardous reactions:
- May form explosive dust-air mixture during processing, handling or other means.
- Can react with strong oxidizing agents.

Conditions to avoid: Heat, flames and sparks.
Avoid dust formation.

Incompatible materials: Oxidizing agents

Hazardous decomposition products: No hazardous decomposition products are known.

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 toxicity

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
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  
Application Route: Ingestion  
Result: negative

**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:
- Test Type: Development
  - Species: Rat
  - Application Route: Oral
  - Developmental Toxicity: LOAEL: 10 mg/kg body weight
  - Result: Fetotoxicity, No teratogenic effects

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

- Test Type: Fertility/early embryonic development
  - Species: Rabbit
  - Application Route: Ingestion
  - Fertility: NOAEL: 25 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
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: 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

**Titanium dioxide:**
- Toxicity to fish: LC50 (Oncorhynchus mykiss (rainbow trout)): > 100 mg/l
  - Exposure time: 96 h
  - Method: OECD Test Guideline 203
Toxicity to daphnia and other aquatic invertebrates: EC50 (Daphnia magna (Water flea)): > 100 mg/l
Exposure time: 48 h

Toxicity to algae/aquatic plants: EC50 (Skeletonema costatum (marine diatom)): > 10,000 mg/l
Exposure time: 72 h

Toxicity to microorganisms: EC50: > 1,000 mg/l
Exposure time: 3 h
Method: OECD Test Guideline 209

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

M-Factor (Chronic aquatic toxicity): 1

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

<table>
<thead>
<tr>
<th>Chemical name</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>2,6-Di-tert-butyl-4-methylphenol</td>
<td>64</td>
</tr>
</tbody>
</table>

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)

<table>
<thead>
<tr>
<th>Chemical name</th>
<th>Number</th>
<th>Concentration (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Titanium(IV) oxide</td>
<td>191</td>
<td>&gt;=0.1 - &lt;1</td>
</tr>
</tbody>
</table>

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
DSL : not determined
IECSC : not determined

16. OTHER INFORMATION

Further information
Date format : yyyy/mm/dd

Full text of other abbreviations
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 material 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 appropriateness of the SDS material in the user’s end product, if applicable.