1. PRODUCT AND COMPANY IDENTIFICATION

   **Product name**: Losartan / Amlodipine Besylate Formulation

   **Manufacturer or supplier’s details**
   - **Company**: MSD
   - **Address**: Briahnager - Off Pune Nagar Road, Wagholi - Pune - India 412 207
   - **Telephone**: 908-740-4000
   - **Emergency telephone number**: 1-908-423-6000
   - **E-mail address**: EHSDATASTEWARD@msd.com
   - **Telefax**: 908-735-1496

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

2. HAZARDS IDENTIFICATION

   **Manufacture, Storage and Import of Hazardous Chemicals Rules 1989**

   **Classification**
   Not classified as hazardous according to criteria laid down in Part I of Schedule-1.

   **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.
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:

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>
</tr>
</thead>
<tbody>
<tr>
<td>Cellulose</td>
<td>9004-34-6</td>
<td>&gt;= 50 - &lt; 70</td>
</tr>
<tr>
<td>Losartan</td>
<td>124750-99-8</td>
<td>&gt;= 10 - &lt; 20</td>
</tr>
<tr>
<td>Amlodipine Besylate</td>
<td>652969-01-2</td>
<td>&gt;= 1 - &lt; 2.5</td>
</tr>
<tr>
<td>Titanium dioxide</td>
<td>13463-67-7</td>
<td>&gt;= 0.1 - &lt; 1</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 so. Evacuate area.

**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**

**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...
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

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Components with workplace control parameters

<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>TWA</td>
<td>10 mg/m³ (Titanium dioxide)</td>
<td>ACGIH</td>
</tr>
</tbody>
</table>

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 re-
Sistance data and an assessment of the local exposure potential. Skin contact must be avoided by using impervious protective clothing (gloves, aprons, boots, etc).

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.

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
Vapour pressure : No data available
Relative vapour density : No data available
Relative density : No data available
Density : No data available
Solubility(ies)
   Water solubility : No data available
Partition coefficient: n-octanol/water : No data available
Auto-ignition temperature : No data available
Decomposition temperature : No data available

Viscosity
  Viscosity, kinematic : No data available

Explosive properties : Not explosive

Oxidizing properties : The substance or mixture is not classified as oxidizing.

Molecular weight : No data available

Particle size : 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 / Amlodipine Besylate Formulation

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

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

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
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

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

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

**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
### 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.

### 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: Oral  
  Result: Female reproductive effects

#### 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

  Test Type: Development  
  Species: Rat  
  Application Route: Oral  
  Developmental Toxicity: LOAEL: 10 mg/kg body weight
Result: Fetotoxicity, 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

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.

**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.
Repeated dose toxicity

**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 days
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

**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: 10 mg/l
Exposure time: 32 d
Species: Pimephales promelas (fathead minnow)
Method: OECD Test Guideline 210

Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity): NOEC: 100 mg/l
Exposure time: 21 d
Species: Daphnia magna (Water flea)
**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

**Persistence and degradability**

**Components:**

**Cellulose:**

- Biodegradability: Result: Readily biodegradable.

**Losartan:**

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

**Bioaccumulative potential**

**Components:**

**Losartan:**

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

**Amlodipine Besylate:**

- Partition coefficient: n-octanol/water: log Pow: 3
Mobility in soil
No data available

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 IMO instruments
Not applicable for product as supplied.

15. REGULATORY INFORMATION

Safety, health and environmental regulations/legislation specific for the substance or mixture

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 : dd.mm.yyyy
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.

IN / EN