1. PRODUCT AND COMPANY IDENTIFICATION

Product name : Losartan 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
Acute toxicity (Oral) : Category 4
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:

- H302 Harmful if swallowed.
- 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:
  - P301 + P312 + P330 IF SWALLOWED: Call a POISON CENTER/doctor if you feel unwell. Rinse mouth.
  - 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:
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. Never give anything by mouth to an unconscious person.

Most important symptoms and effects, both acute and delayed: Harmful if swallowed. 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)

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.

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

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 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 as-
sessment
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.

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>Starch</td>
<td>9005-25-8</td>
<td>TWA</td>
<td>10 mg/m³</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:
SAFETY DATA SHEET

Losartan Formulation

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).

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: White to light yellow

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: No data available

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: 1 g/cm³

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
Minimum ignition energy: > 300 mJ
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
Harmful if swallowed.

Product:
Acute oral toxicity: Acute toxicity estimate: 1,502 mg/kg
Method: Calculation method

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

Starch:
Acute oral toxicity: LD50 (Mouse): > 5,000 mg/kg

Skin corrosion/irritation
Not classified based on available information.

Components:

Losartan:
Species: Rabbit
Result: Mild skin irritation

Serious eye damage/eye irritation
Causes serious eye damage.

Components:

Losartan:
Species: Rabbit
Result: Severe 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
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

**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
**SAFETY DATA SHEET**

**Losartan Formulation**

<table>
<thead>
<tr>
<th>Version</th>
<th>Revision Date</th>
<th>SDS Number</th>
<th>Date of last issue</th>
<th>Date of first issue</th>
</tr>
</thead>
</table>

**Species**

- Species: Rat  
- Application Route: Oral  
- Exposure time: 105 weeks  
- Dose: 270 mg/kg body weight  
- 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  
| 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.
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

Components:

Cellulose:
- Species: Rat
- NOAEL: \( \geq 9,000 \text{ mg/kg} \)
- 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

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

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)
  Method: OECD Test Guideline 211

Persistence and degradability

Components:

Cellulose:
- Biodegradability: Result: Readily biodegradable.
Losartan Formulation

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

Bioaccumulative potential

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

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

UN RTDG
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

Full text of other abbreviations
ACGIH: USA. ACGIH Threshold Limit Values (TLV)
ACGIH / TWA: 8-hour, time-weighted average

AICS - Australian Inventory of Chemical Substances; 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 Organization 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 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