SAFETY DATA SHEET

Lisinopril / Hydrochlorothiazide Formulation

SECTION 1. PRODUCT AND COMPANY IDENTIFICATION

Product name : Lisinopril / Hydrochlorothiazide Formulation

Manufacturer or supplier's details
Company : MSD
Address : 91-105 Harpin Street
          Bendigo 3550, Victoria Australia
Telephone : +1-908-740-4000
Emergency telephone number : 1 800 033 461
E-mail address : EHSDATASTeward@msd.com

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

SECTION 2. HAZARDS IDENTIFICATION

GHS Classification
Reproductive toxicity : Category 1A
Specific target organ toxicity - repeated exposure : Category 1 (Kidney, Parathyroid gland)

GHS label elements
Hazard pictograms : Ᵽ
Signal word : Danger
Hazard statements : H360D May damage the unborn child.
                   H372 Causes damage to organs (Kidney, Parathyroid gland) through prolonged or repeated exposure.
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/ fume/ gas/ mist/ vapours/ spray.
                          P264 Wash skin thoroughly after handling.
                          P270 Do not eat, drink or smoke when using this product.
                          P281 Use personal protective equipment as required.
Response: P308 + P313 IF exposed or concerned: Get medical advice/ attention.
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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
Dust contact with the eyes can lead to mechanical irritation.
Contact with dust can cause mechanical irritation or drying of the skin.
May form combustible dust concentrations in air during processing, handling or other means.

SECTION 3. COMPOSITION/INFORMATION ON INGREDIENTS

<table>
<thead>
<tr>
<th>Substance / Mixture</th>
<th>Components</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mixture</td>
<td>Mixture</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Chemical name</th>
<th>CAS-No.</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Starch</td>
<td>9005-25-8</td>
<td>&gt;= 10 - &lt; 30</td>
</tr>
<tr>
<td>Hydrochlorothiazide</td>
<td>58-93-5</td>
<td>&gt;= 10 - &lt; 30</td>
</tr>
<tr>
<td>Lisinopril</td>
<td>83915-83-7</td>
<td>&gt;= 0.3 - &lt; 10</td>
</tr>
</tbody>
</table>

SECTION 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: If in eyes, rinse well with water.
   Get medical attention if irritation develops and persists.

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 damage the unborn child.
   Causes damage to organs through prolonged or repeated exposure.
   Contact with dust can cause mechanical irritation or drying of the skin.
   Dust contact with the eyes can lead to mechanical irritation.

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.
SECTION 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: Exposure to combustion products may be a hazard to health.

Hazardous combustion products:
- Carbon oxides
- Nitrogen oxides (NOx)
- Chlorine compounds
- Sulphur oxides
- Metal oxides
- Oxides of phosphorus

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.

SECTION 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.

SECTION 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, fume, gas, mist, vapours or spray. Do not swallow. Avoid contact with 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.

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. The effective operation of a facility should include review of engineering controls, proper personal protective equipment, appropriate degowning and decontamination procedures, industrial hygiene monitoring, medical surveillance and the use of administrative controls.

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

SECTION 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>Starch</td>
<td>9005-25-8</td>
<td>TWA</td>
<td>10 mg/m³</td>
<td>AU OEL</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA</td>
<td>10 mg/m³</td>
<td></td>
</tr>
<tr>
<td>Further information: This value is for inhalable dust containing no asbestos and &lt; 1% crystalline silica</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hydrochlorothiazide</td>
<td>58-93-5</td>
<td>TWA</td>
<td>100 µg/m³ (OEB 2)</td>
<td>Internal</td>
</tr>
<tr>
<td>Lisinopril</td>
<td>83915-83-7</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>200 µg/100 cm²</td>
<td>Internal</td>
</tr>
</tbody>
</table>
**Engineering measures**: Use feasible engineering controls to minimize exposure to compound. All engineering controls should be implemented by facility design and operated in accordance with GMP principles to protect products, workers, and the environment.

**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
  - **Material**: Chemical-resistant gloves

- **Eye protection**: Wear safety glasses with side shields or goggles. If the work environment or activity involves dusty conditions, mists or aerosols, wear the appropriate goggles. Wear a faceshield or other full face protection if there is a potential for direct contact to the face with dusts, mists, or aerosols.

- **Skin and body protection**: Work uniform or laboratory coat.

## SECTION 9. PHYSICAL AND CHEMICAL PROPERTIES

- **Appearance**: solid
- **Colour**: No data available
- **Odour**: odourless
- **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**: Not applicable
- **Flammability (solid, gas)**: May form combustible dust concentrations in air 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 : Not applicable
Relative vapour density : Not applicable
Relative density : No data available
Density : No data available
Solubility(ies)
  Water solubility : No data available
Partition coefficient: n-octanol/water : Not applicable
Auto-ignition temperature : No data available
Decomposition temperature : No data available
Viscosity
  Viscosity, kinematic : Not applicable
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

SECTION 10. STABILITY AND REACTIVITY
Reactivity : Not classified as a reactivity hazard.
Chemical stability : Stable under normal conditions.
Possibility of hazardous reac-
tions : May form combustible dust concentrations in air during pro-
  cessing, 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.

SECTION 11. TOXICOLOGICAL INFORMATION
Exposure routes : Inhalation
  Skin contact
  Ingestion
  Eye contact
Acute toxicity
Not classified based on available information.
### Components:

#### Starch:
- **Acute oral toxicity**: LD50 (Rat): > 5,000 mg/kg  
- **Acute dermal toxicity**: LD50 (Rabbit): > 2,000 mg/kg  

#### Hydrochlorothiazide:
- **Acute oral toxicity**: LD50 (Rat): > 2,750 mg/kg  
  - LD50 (Mouse): > 2,830 mg/kg  
- **Acute toxicity (other routes of administration)**:  
  - LD50 (Rat): 990 mg/kg  
  - Application Route: Intravenous  
  - LD50 (Mouse): 590 mg/kg  
  - Application Route: Intravenous  

#### Lisinopril:
- **Acute oral toxicity**: LD50 (Rat): > 20,000 mg/kg  
  - LD50 (Mouse): > 20,000 mg/kg  

### Skin corrosion/irritation
Not classified based on available information.

### Components:

#### Hydrochlorothiazide:
- **Species**: Rabbit  
- **Result**: No skin irritation  

#### Lisinopril:
- **Species**: Rabbit  
- **Result**: Mild skin irritation  

### Serious eye damage/eye irritation
Not classified based on available information.

### Components:

#### Starch:
- **Species**: Rabbit  
- **Result**: No eye irritation  

#### Hydrochlorothiazide:
- **Species**: Rabbit  
- **Result**: Mild eye irritation  

#### Lisinopril:
- **Species**: Rabbit
Result : Mild eye irritation

Respiratory or skin sensitisation

Skin sensitisation
Not classified based on available information.

Respiratory sensitisation
Not classified based on available information.

Components:

Starch:
Test Type : Maximisation Test
Exposure routes : Skin contact
Species : Guinea pig
Result : negative

Lisinopril:
Test Type : Maximisation Test
Exposure routes : Dermal
Result : negative

Chronic toxicity

Germ cell mutagenicity
Not classified based on available information.

Components:

Starch:
Genotoxicity in vitro : Test Type: Bacterial reverse mutation assay (AMES)
Result: negative

Hydrochlorothiazide:
Genotoxicity in vitro : Test Type: Bacterial reverse mutation assay (AMES)
Result: negative

Test Type: Chromosomal aberration
Test system: Chinese hamster ovary cells
Result: negative

Test Type: sister chromatid exchange assay
Test system: Chinese hamster ovary cells
Result: positive

Test Type: in vitro assay
Test system: mouse lymphoma cells
Result: positive

Genotoxicity in vivo : Test Type: Chromosomal aberration
Species: Chinese hamster
Cell type: Bone marrow
Result: negative
<table>
<thead>
<tr>
<th>Test Type:</th>
<th>Germ cell mutagenicity assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Species:</td>
<td>Mouse</td>
</tr>
<tr>
<td>Cell type:</td>
<td>Bone marrow</td>
</tr>
<tr>
<td>Result:</td>
<td>negative</td>
</tr>
</tbody>
</table>

**Lisinopril:**

**Genotoxicity in vitro:**
- Test Type: Bacterial reverse mutation assay (AMES)
  - Result: negative
- Test Type: In vitro mammalian cell gene mutation test
  - Test system: Chinese hamster lung cells
  - Result: negative
- Test Type: Alkaline elution assay
  - Test system: rat hepatocytes
  - Result: negative

**Genotoxicity in vivo:**
- Test Type: Micronucleus test
  - Species: Mouse
  - Application Route: Oral
  - Result: negative

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

**Components:**

**Hydrochlorothiazide:**
- Species: Mouse, female
  - Application Route: Oral
  - Exposure time: 2 Years
  - Result: negative
- Species: Mouse, male
  - Application Route: Oral
  - Exposure time: 2 Years
  - Result: equivocal
- Species: Rat, male and female
  - Application Route: Oral
  - Exposure time: 2 Years
  - Result: negative

**Lisinopril:**
- Species: Rat
  - Application Route: Oral
  - Exposure time: 105 weeks
  - NOAEL: 90 mg/kg body weight
  - Result: negative
Reproductive toxicity
May damage the unborn child.

Components:

Hydrochlorothiazide:
Effects on fertility
Species: Mouse
Application Route: Oral
Exposure time: 92 weeks
NOAEL: 135 mg/kg body weight
Result: negative

Test Type: Fertility
Species: Rat, male and female
Application Route: oral (feed)
Fertility: NOAEL: 4 mg/kg body weight
Result: Effects on fertility

Test Type: Fertility
Species: Mouse, male and female
Application Route: oral (feed)
Fertility: NOAEL: 100 mg/kg body weight
Result: Effects on fertility

Effects on foetal development
Test Type: Development
Species: Mouse
Application Route: Oral
Developmental Toxicity: NOAEL: 3,000 mg/kg body weight
Result: No teratogenic effects

Test Type: Development
Species: Rat
Application Route: Oral
Developmental Toxicity: NOAEL: 1,000 mg/kg body weight
Result: No teratogenic effects

Lisinopril:
Effects on fertility
Test Type: Fertility
Species: Rat
Application Route: Oral
Fertility: NOAEL: 300 mg/kg body weight
Symptoms: No effects on mating performance
Result: Animal testing did not show any effects on fertility.

Effects on foetal development
Test Type: Development
Species: Rat
Application Route: Oral
Developmental Toxicity: LOAEL: 30 mg/kg body weight
Result: positive, No teratogenic effects

Test Type: Development
Species: Mouse
Application Route: Oral
Developmental Toxicity: LOAEL: 100 mg/kg body weight
Symptoms: Total Resorptions / resorption rate
Result: Embryotoxic effects and adverse effects on the offspring were detected.

Test Type: Development
Species: Rabbit
Application Route: Oral
Developmental Toxicity: LOAEL: 0.1 mg/kg body weight
Result: Embryotoxic effects and adverse effects on the offspring were detected.

Reproductive toxicity - Assessment: Positive evidence of adverse effects on development from human epidemiological studies.

STOT - single exposure
Not classified based on available information.

STOT - repeated exposure
Causes damage to organs (Kidney, Parathyroid gland) through prolonged or repeated exposure.

Components:

Hydrochlorothiazide:
Target Organs: Kidney, Parathyroid gland
Assessment: Causes damage to organs through prolonged or repeated exposure.

Lisinopril:
Exposure routes: Ingestion
Target Organs: Kidney
Assessment: May cause damage to organs through prolonged or repeated exposure.

Repeated dose toxicity

Components:

Starch:
Species: Rat
NOAEL: >= 2,000 mg/kg
Application Route: Skin contact
Exposure time: 28 Days
Method: OECD Test Guideline 410

Hydrochlorothiazide:
Species: Rat, male and female
LOAEL: 10 mg/kg
Application Route: Oral
Exposure time: 2 yr
Target Organs: Kidney, Parathyroid gland

Species: Mouse, male and female
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NOAEL: 300 - 550 mg/kg
Application Route: Oral
Exposure time: 2 yr
Remarks: No significant adverse effects were reported
Species: Dog
Application Route: Oral
Exposure time: 9 Months
Target Organs: Parathyroid gland

Lisinopril:
Species: Rat
LOAEL: < 3,650 mg/kg
Application Route: Oral
Exposure time: 1 yr
Target Organs: Kidney
Species: Dog
LOAEL: < 840 mg/kg
Application Route: Oral
Exposure time: 4 Weeks
Target Organs: Kidney

Aspiration toxicity
Not classified based on available information.

Components:

Hydrochlorothiazide:
No aspiration toxicity classification

Experience with human exposure

Components:

Hydrochlorothiazide:
Eye contact: Symptoms: Eye irritation
Ingestion: Symptoms: Dizziness, Headache, Fatigue, Nausea, Abdominal pain, hypotension, dry mouth, electrolyte imbalance, eye pain

Lisinopril:
Ingestion: Symptoms: Dizziness, Headache, Fatigue, Diarrhoea, Nausea, Cough, Lowered blood pressure, electrolyte imbalance
Remarks: May damage the unborn child.

SECTION 12. ECOLOGICAL INFORMATION

Ecotoxicity

Components:

Hydrochlorothiazide:
Toxicity to fish: LC50 (Pimephales promelas (fathead minnow)): > 500 mg/l Exposure time: 96 h

Toxicity to daphnia and other aquatic invertebrates: EC50 (Daphnia magna (Water flea)): > 500 mg/l Exposure time: 48 h

Lisinopril:
Toxicity to daphnia and other aquatic invertebrates: EC50 (Daphnia magna (Water flea)): 20,000 mg/l Exposure time: 48 h Method: OECD Test Guideline 202

Persistence and degradability

Components:

Hydrochlorothiazide:
Stability in water: Hydrolysis: 46.2 % (96 h)

Bioaccumulative potential
No data available

Mobility in soil
No data available

Other adverse effects
No data available

SECTION 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.

SECTION 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

ADG
Not regulated as a dangerous good
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SECTION 15. REGULATORY INFORMATION

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

Prohibition/Licensing Requirements

There is no applicable prohibition, authorisation and restricted use requirements, including for carcinogens referred to in Schedule 10 of the model WHS Act and Regulations.

The components of this product are reported in the following inventories:

- AICS: not determined
- DSL: not determined
- IECSC: not determined

SECTION 16. OTHER INFORMATION

Further information

Revision Date: 10.10.2020

Date format: dd.mm.yyyy

Full text of other abbreviations

- ACGIH: USA. ACGIH Threshold Limit Values (TLV)
- ACGIH / TWA: 8-hour, time-weighted average
- AU OEL / TWA: Exposure standard - time weighted average

AIIC - 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 Civil Aviation Organization; IBC - International Code for the Construction and Equipment of Ships carrying Dangerous Chemicals in Bulk; IC50 - Half maximal inhibitory concentration; ICAO - 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 Con-
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.

AU / EN