1. PRODUCT AND COMPANY IDENTIFICATION

Product name: Lisinopril / Hydrochlorothiazide Formulation

Manufacturer or supplier’s details
Company: MSD
Address: 50 Tuas West Drive
Singapore - Singapore 638408
Telephone: +1-908-740-4000
Emergency telephone number: 65 6697 2111 (24/7/365)
E-mail address: EHSDATASTEWARD@msd.com

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

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:
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.
P280 Wear protective gloves/ protective clothing/ eye protection/ face protection.
Response:
P308 + P313 IF exposed or concerned: Get medical advice/
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Version 1.7 Revision Date: 10.10.2020 SDS Number: 4573763-00008 Date of last issue: 13.04.2020
Date of first issue: 08.07.2019

P405 Store locked up.

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.

3. COMPOSITION/INFORMATION ON INGREDIENTS

Substance / Mixture : Mixture

<table>
<thead>
<tr>
<th>Components</th>
<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; 20</td>
<td></td>
</tr>
<tr>
<td>Hydrochlorothiazide</td>
<td>58-93-5</td>
<td>&gt;= 10 - &lt; 20</td>
<td></td>
</tr>
<tr>
<td>Lisinopril</td>
<td>83915-83-7</td>
<td>&gt;= 1 - &lt; 10</td>
<td></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 : 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.
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.

6. ACCIDENTAL RELEASE MEASURES

Personal precautions, protective equipment and emergency procedures: Use personal protective equipment.
Follow safe handling advice (see section 7) and personal protective equipment recommendations (see section 8).

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

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

7. HANDLING AND STORAGE
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>PEL (long term)</td>
<td>10 mg/m³</td>
<td>SG OEL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA</td>
<td>10 mg/m³</td>
<td>ACGIH</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.
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
### 10. STABILITY AND REACTIVITY

**Reactivity**: Not classified as a reactivity hazard.

**Chemical stability**: Stable under normal conditions.

**Possibility of hazardous reactions**: May form combustible dust concentrations in air 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.

**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

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
  Test Type: in vivo assay
  Species: Mouse
  Cell type: Bone marrow
Germ cell mutagenicity - Assessment : Weight of evidence does not support classification as a germ cell mutagen.

**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:**

<table>
<thead>
<tr>
<th>Species</th>
<th>Application Route</th>
<th>Exposure time</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mouse, female</td>
<td>Oral</td>
<td>2 Years</td>
<td>negative</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Species</th>
<th>Application Route</th>
<th>Exposure time</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mouse, male</td>
<td>Oral</td>
<td>2 Years</td>
<td>equivocal</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Species</th>
<th>Application Route</th>
<th>Exposure time</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rat, male and female</td>
<td>Oral</td>
<td>2 Years</td>
<td>negative</td>
</tr>
</tbody>
</table>

**Lisinopril:**

<table>
<thead>
<tr>
<th>Species</th>
<th>Application Route</th>
<th>Exposure time</th>
<th>NOAEL</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rat</td>
<td>Oral</td>
<td>105 weeks</td>
<td>90 mg/kg body weight</td>
<td>negative</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Species</th>
<th>Application Route</th>
<th>Exposure time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mouse</td>
<td>Oral</td>
<td>92 weeks</td>
</tr>
</tbody>
</table>
**Reproductive toxicity**
May damage the unborn child.

**Components:**

**Hydrochlorothiazide:**

**Effects on fertility**
- Test Type: Fertility
- Species: Rat, male and female
- Application Route: oral (feed)
- Fertility: NOAEL: 4 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

**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.
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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
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.

**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: EC50 (Daphnia magna (Water flea)): > 500 mg/l
aquatic invertebrates: 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

**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.
Workplace Safety and Health Act and Workplace Safety and Health (General Provisions) Regulations: This product is subjected to the SDS, labelling, PEL and other requirements in the Act/Regulations.

Environmental Protection and Management Act and Environmental Protection and Management (Hazardous Substances) Regulations: Not applicable

Fire Safety (Petroleum and Flammable Materials) Regulations: Not applicable

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)
- SG OEL: Singapore. Workplace Safety and Health Act - First Schedule Permissible Exposure Limits of Toxic Substances
- ACGIH / TWA: 8-hour, time-weighted average
- SG OEL / PEL (long term): Permissible Exposure Level (PEL) Long Term
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Version 1.7  Revision Date: 10.10.2020  SDS Number: 4573763-00008  Date of last issue: 13.04.2020

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.

SG / EN