SECTION 1: Identification of the substance/mixture and of the company/undertaking

1.1 Product identifier
   Trade name: Lisinopril / Hydrochlorothiazide Formulation

1.2 Relevant identified uses of the substance or mixture and uses advised against
   Use of the Substance/Mixture: Pharmaceutical

1.3 Details of the supplier of the safety data sheet
   Company: MSD
   117 16th Road
   1685 Halfway house, Midrand, South Africa
   Telephone: +27 11 655 3000
   E-mail address of person responsible for the SDS: EHSDATASTEWARD@msd.com

1.4 Emergency telephone number
   +1-908-423-6000

SECTION 2: Hazards identification

2.1 Classification of the substance or mixture
   Classification (REGULATION (EC) No 1272/2008)
   Reproductive toxicity, Category 1A: H360D: May damage the unborn child.
   Specific target organ toxicity - repeated exposure, Category 1: H372: Causes damage to organs through prolonged or repeated exposure.

2.2 Label elements
   Labelling (REGULATION (EC) No 1272/2008)
   Hazard pictograms: ❱ ⟱
   Signal word: Danger
   Hazard statements: H360D May damage the unborn child.
   H372 Causes damage to organs through prolonged or repeated exposure.
   Precautionary statements: Prevention:
   P201 Obtain special instructions before use.
   P264 Wash skin thoroughly after handling.
   P270 Do not eat, drink or smoke when using this product.
   P280 Wear protective gloves/ protective clothing/ eye protec-
SECTION 3: Composition/information on ingredients

3.2 Mixtures

<table>
<thead>
<tr>
<th>Components</th>
<th>CAS-No.</th>
<th>EC-No.</th>
<th>Index-No.</th>
<th>Registration number</th>
<th>Classification</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydrochlorothiazide</td>
<td>58-93-5</td>
<td>200-403-3</td>
<td></td>
<td></td>
<td>STOT RE 1; H372 (Kidney, Parathyroid gland)</td>
<td>&gt;= 10 &lt; 20</td>
</tr>
<tr>
<td>Lisinopril</td>
<td>83915-83-7</td>
<td></td>
<td></td>
<td></td>
<td>Repr. 1A; H360D STOT RE 2; H373 (Kidney)</td>
<td>&gt;= 1 &lt; 10</td>
</tr>
</tbody>
</table>

For explanation of abbreviations see section 16.

SECTION 4: First aid measures

4.1 Description of 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.

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).

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.

4.2 Most important symptoms and effects, both acute and delayed

Risks:
- 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.

4.3 Indication of any immediate medical attention and special treatment needed

Treatment: Treat symptomatically and supportively.

SECTION 5: Firefighting measures

5.1 Extinguishing media

Suitable extinguishing media:
- Water spray
- Alcohol-resistant foam
- Carbon dioxide (CO2)
- Dry chemical

Unsuitable extinguishing media: None known.

5.2 Special hazards arising from the substance or mixture

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

5.3 Advice for firefighters

Special protective equipment: In the event of fire, wear self-contained breathing apparatus.
for firefighters

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.

SECTION 6: Accidental release measures

6.1 Personal precautions, protective equipment and emergency procedures

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

6.2 Environmental precautions

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.

6.3 Methods and material for containment and cleaning up

Methods for 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.

6.4 Reference to other sections

See sections: 7, 8, 11, 12 and 13.

SECTION 7: Handling and storage

7.1 Precautions for safe 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, 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.

7.2 Conditions for safe storage, including any incompatibilities
Requirements for storage areas and containers:
Keep in properly labelled containers. Store locked up. Keep tightly closed. Store in accordance with the particular national regulations.

Advice on common storage:
Do not store with the following product types:
- Strong oxidizing agents
- Organic peroxides
- Explosives
- Gases

7.3 Specific end use(s)
Specific use(s):
No data available

SECTION 8: Exposure controls/personal protection

8.1 Control parameters

### Occupational Exposure Limits

<table>
<thead>
<tr>
<th>Components</th>
<th>CAS-No.</th>
<th>Value type (Form of exposure)</th>
<th>Control parameters</th>
<th>Basis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Starch</td>
<td>9005-25-8</td>
<td>TWA OEL-RL (Respirable dust)</td>
<td>5 mg/m³</td>
<td>ZA OEL</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Further information: Recommended Limit

<table>
<thead>
<tr>
<th></th>
<th>TWA OEL-RL (inhalable dust)</th>
<th>10 mg/m³</th>
<th>ZA OEL</th>
</tr>
</thead>
</table>

Further information: Recommended Limit

<table>
<thead>
<tr>
<th>Hydrochlorothiazide</th>
<th>58-93-5</th>
<th>TWA</th>
<th>100 µg/m³ (OEB 2)</th>
<th>Internal</th>
</tr>
</thead>
</table>
SAFETY DATA SHEET

Lisinopril / Hydrochlorothiazide Formulation

<table>
<thead>
<tr>
<th>zide</th>
<th>TWA</th>
<th>20 µg/m³ (OEB 3)</th>
<th>Internal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lisinopril 83915-83-7</td>
<td>Wipe limit</td>
<td>200 µg/100 cm²</td>
<td>Internal</td>
</tr>
</tbody>
</table>

8.2 Exposure controls

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

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.

Hand protection

Material: Chemical-resistant gloves

Skin and body protection: Work uniform or laboratory coat.

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 (P)

SECTION 9: Physical and chemical properties

9.1 Information on basic 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.

Upper explosion limit / Upper flammability limit: No data available

Lower explosion limit / Lower flammability limit: No data available
SAFETY DATA SHEET

Lisinopril / Hydrochlorothiazide Formulation

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.

9.2 Other information
  Flammability (liquids) : No data available
  Molecular weight : No data available
  Particle size : No data available

SECTION 10: Stability and reactivity

10.1 Reactivity
  Not classified as a reactivity hazard.

10.2 Chemical stability
  Stable under normal conditions.

10.3 Possibility of hazardous reactions
  Hazardous reactions : May form combustible dust concentrations in air during processing, handling or other means. Can react with strong oxidizing agents.

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

10.5 Incompatible materials
  Materials to avoid : Oxidizing agents

10.6 Hazardous decomposition products
  No hazardous decomposition products are known.
SECTION 11: Toxicological information

11.1 Information on toxicological effects

Information on likely routes of exposure:
- Inhalation
- Skin contact
- Ingestion
- Eye contact

Acute toxicity
Not classified based on available information.

Components:

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:

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:**

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

**Germ cell mutagenicity**
Not classified based on available information.

**Components:**

**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
  - Result: negative

**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:
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

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

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

  - 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 off-
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 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:**

**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.

SECTION 12: Ecological information

12.1 Toxicity

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

12.2 Persistence and degradability

Components:

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

12.3 Bioaccumulative potential
No data available

12.4 Mobility in soil
No data available

12.5 Results of PBT and vPvB assessment

**Product:**
Assessment: This substance/mixture contains no components considered to be either persistent, bioaccumulative and toxic (PBT), or very persistent and very bioaccumulative (vPvB) at levels of 0.1% or higher.

12.6 Other adverse effects

**Product:**
Endocrine disrupting potential: The substance/mixture does not contain components considered to have endocrine disrupting properties according to REACH Article 57(f) or Commission Delegated regulation (EU) 2017/2100 or Commission Regulation (EU) 2018/605 at levels of 0.1% or higher.

SECTION 13: Disposal considerations

13.1 Waste treatment methods

**Product:**
Dispose of in accordance with local regulations. According to the European Waste Catalogue, Waste Codes are not product specific, but application specific. Waste codes should be assigned by the user, preferably in discussion with the waste disposal authorities.

**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

14.1 UN number
Not regulated as a dangerous good

14.2 UN proper shipping name
Not regulated as a dangerous good

14.3 Transport hazard class(es)
Not regulated as a dangerous good

14.4 Packing group
Not regulated as a dangerous good

14.5 Environmental hazards
Not regulated as a dangerous good
SAFETY DATA SHEET

Lisinopril / Hydrochlorothiazide Formulation

Version: 1.7
Revision Date: 09.04.2021
SDS Number: 4573765-00008
Date of last issue: 10.10.2020
Date of first issue: 08.07.2019

14.6 Special precautions for user
Not applicable

14.7 Transport in bulk according to Annex II of Marpol and the IBC Code
Remarks: Not applicable for product as supplied.

SECTION 15: Regulatory information

15.1 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

15.2 Chemical safety assessment
A Chemical Safety Assessment has not been carried out.

SECTION 16: Other information

Other information: Items where changes have been made to the previous version are highlighted in the body of this document by two vertical lines.

Full text of H-Statements
H360D: May damage the unborn child.
H372: Causes damage to organs through prolonged or repeated exposure.
H373: May cause damage to organs through prolonged or repeated exposure if swallowed.

Full text of other abbreviations
Repr.: Reproductive toxicity
STOT RE: Specific target organ toxicity - repeated exposure
ZA OEL: South Africa. Hazardous Chemical Substances Regulations, Occupational Exposure Limits
ZA OEL / TWA OEL-RL: Long term occupational exposure limits - recommended limit

ADN - European Agreement concerning the International Carriage of Dangerous Goods by Inland Waterways; ADR - European Agreement concerning the International Carriage of Dangerous Goods by Road; AIIC - Australian Inventory of Industrial Chemicals; ASTM - American Society for the Testing of Materials; bw - Body weight; CLP - Classification Labelling Packaging Regulation; Regulation (EC) No 1272/2008; CMR - Carcinogen, Mutagen or Reproductive Toxicant; DIN - Standard of the German Institute for Standardisation; DSL - Domestic Substances List (Canada); ECHA - European Chemicals Agency; EC-Number - European Community number; 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; 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
Further information


Classification of the mixture:

<table>
<thead>
<tr>
<th>Repr. 1A</th>
<th>STOT RE 1</th>
</tr>
</thead>
<tbody>
<tr>
<td>H360D</td>
<td>H372</td>
</tr>
</tbody>
</table>

Classification procedure:

Calculation method

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.

ZA / EN