SECTION 1. PRODUCT AND COMPANY IDENTIFICATION

Product name : Enalapril Formulation

Manufacturer or supplier’s details
Company : MSD
Address : Rua Treze de Maio, 1161
          Campinas, São Paulo, Brazil 13106-054
Telephone : 908-740-4000
Emergency telephone : 55 19 3758 2000
E-mail address : EHSDATASTEWARD@msd.com
Telefax : 908-735-1496

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

SECTION 2. HAZARDS IDENTIFICATION

GHS Classification in accordance with ABNT NBR 14725 Standard
Reproductive toxicity : Category 1A
Specific target organ toxicity - repeated exposure : Category 2 (Kidney, Cardio-vascular system)

GHS label elements in accordance with ABNT NBR 14725 Standard
Hazard pictograms :

Signal Word : Danger
Hazard Statements : H360D May damage the unborn child.
                  H373 May cause damage to organs (Kidney, Cardio-vascular system) through prolonged or repeated exposure.

Precautionary Statements : Prevention:
                       P201 Obtain special instructions before use.
                       P260 Do not breathe dust.
                       P280 Wear protective gloves/ protective clothing/ eye protection/ face protection.
Response: P308 + P313 IF exposed or concerned: Get medical advice/ attention.
SAFETY DATA SHEET
Enalapril Formulation

Version 5.1  Revision Date: 10.10.2020  SDS Number: 734735-00011  Date of last issue: 23.03.2020
Date of first issue: 07.06.2016

Storage:
P405 Store locked up.

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 explosive dust-air mixture during processing, handling or other means.

SECTION 3. COMPOSITION/INFORMATION ON INGREDIENTS

Substance / Mixture: Mixture

Components

<table>
<thead>
<tr>
<th>Chemical name</th>
<th>CAS-No.</th>
<th>Classification</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Starch</td>
<td>9005-25-8</td>
<td>Acute toxicity (Oral), Eye irritation, Reproductive toxicity</td>
<td>&gt;= 10 - &lt; 20</td>
</tr>
<tr>
<td>(S)-1-[N-[1-(Ethoxycarbonyl)-3-phenylpropyl]-L-alanyl]-L-proline maleate</td>
<td>76095-16-4</td>
<td>Eye irritation, Reproductive toxicity, Specific target organ toxicity - repeated exposure (Kidney, Cardio-vascular system), Category 1</td>
<td>&gt;= 5 - &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.
May cause damage to organs through prolonged or repeated exposure.
Contact with dust can cause mechanical irritation or drying of the skin.
Protection of first-aiders: Dust contact with the eyes can lead to mechanical irritation. 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. FIRE-FIGHTING 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
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.

Special protective equipment for fire-fighters: 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...
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. 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 labeled 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 Organic peroxides Explosives Gases

SECTION 8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Ingredients 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>
</table>

4 / 13
SAFETY DATA SHEET
Enalapril Formulation

Version 5.1  Revision Date: 10.10.2020  SDS Number: 734735-00011  Date of last issue: 23.03.2020

Date of first issue: 07.06.2016

<table>
<thead>
<tr>
<th>Starch</th>
<th>9005-25-8</th>
<th>(S)-1-[N-[1-(Ethoxycarbonyl)-3-phenylpropyl]-L-alanyl]-L-proline maleate</th>
<th>76095-16-4</th>
<th>TWA</th>
<th>10 mg/m³</th>
<th>ACeGHI (N-[1-(Ethoxycarbonyl)-3-phenylpropyl]-L-alanyl]-L-proline maleate</th>
<th>Wipe limit 500 µg/100 cm²</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>TWA</td>
<td>50 µg/m³ (OEB 3)</td>
<td>Internal</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Engineering measures**: All engineering controls should be implemented by facility design and operated in accordance with GMP principles to protect products, workers, and the environment. Containment technologies suitable for controlling compounds are required to control at source and to prevent migration of the compound to uncontrolled areas (e.g., open-face containment devices). Minimize open handling.

**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**: Consider double gloving.

**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. Additional body garments should be used based upon the task being performed (e.g., sleevelets, apron, gauntlets, disposable suits) to avoid exposed skin surfaces. Use appropriate degowning techniques to remove potentially contaminated clothing.

**SECTION 9. PHYSICAL AND CHEMICAL PROPERTIES**

- **Appearance**: powder
- **Color**: white
- **Odor**: No data available
- **Odor 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 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
Vapor pressure : Not applicable
Relative vapor 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
Autoignition 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.
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 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 : No hazardous decomposition products are known.
SAFETY DATA SHEET

Enalapril Formulation

SECTION 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: Calculation method

Components:
Starch:
Acute oral toxicity: LD50 (Rat): > 5.000 mg/kg
Acute dermal toxicity: LD50 (Rabbit): > 2.000 mg/kg

(S)-1-[N-[1-(Ethoxycarbonyl)-3-phenylpropyl]-L-alanyl]-L-proline maleate:
Acute oral toxicity: LD50 (Rat): 2.000 - 3.500 mg/kg
- LDLo (Rat): 1.775 mg/kg
- LD50 (Mouse): 2.000 - 3.500 mg/kg
- LDLo (Mouse): 1.000 mg/kg

Acute toxicity (other routes of administration): LD50 (Rat): 850 mg/kg
Application Route: Intravenous
- LD50 (Mouse): 750 mg/kg
Application Route: Intravenous
- LD50 (Dog): > 100 mg/kg
- LDLo (Dog): 200 mg/kg

Skin corrosion/irritation
Not classified based on available information.

Components:
(S)-1-[N-[1-(Ethoxycarbonyl)-3-phenylpropyl]-L-alanyl]-L-proline maleate:
Species: Rabbit
Result: No skin irritation

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

Starch:
Species: Rabbit
Result: No eye irritation

(S)-1-[N-[1-(Ethoxycarbonyl)-3-phenylpropyl]-L-alanyl]-L-proline maleate:
Species: Rabbit
Result: Severe irritation

Respiratory or skin sensitization
Skin sensitization
Not classified based on available information.

Respiratory sensitization
Not classified based on available information.

Components:

Starch:
Test Type: Maximization Test
Routes of exposure: Skin contact
Species: Guinea pig
Result: negative

(S)-1-[N-[1-(Ethoxycarbonyl)-3-phenylpropyl]-L-alanyl]-L-proline maleate:
Test Type: Maximization Test
Routes of exposure: Skin contact
Species: Guinea pig
Result: Not a skin sensitizer.

Germ cell mutagenicity
Not classified based on available information.

Components:

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

(S)-1-[N-[1-(Ethoxycarbonyl)-3-phenylpropyl]-L-alanyl]-L-proline maleate:
Genotoxicity in vitro: Test Type: Bacterial reverse mutation assay (AMES)
Result: negative

Test Type: In vitro sister chromatid exchange assay in mammalian cells
Result: negative

Test Type: Alkaline elution assay
Result: negative

Genotoxicity in vivo: Test Type: Mammalian erythrocyte micronucleus test (in vivo
cytogenetic assay)  
Species: Mouse  
Application Route: Ingestion  
Result: negative

Test Type: Mutagenicity (in vivo mammalian bone-marrow cytogenetic test, chromosomal analysis)  
Species: Mouse  
Application Route: Ingestion  
Result: negative

Carcinogenicity  
Not classified based on available information.

Components:

(S)-1-[N-[1-(Ethoxycarbonyl)-3-phenylpropyl]-L-alanyl]-L-proline maleate:

<table>
<thead>
<tr>
<th>Species</th>
<th>Rat</th>
</tr>
</thead>
<tbody>
<tr>
<td>Application Route</td>
<td>Ingestion</td>
</tr>
<tr>
<td>Exposure time</td>
<td>106 weeks</td>
</tr>
<tr>
<td>NOAEL</td>
<td>90 mg/kg body weight</td>
</tr>
<tr>
<td>Result</td>
<td>negative</td>
</tr>
</tbody>
</table>

Species: Mouse  
Application Route: Ingestion  
Exposure time: 94 weeks  
NOAEL: 90 - 180 mg/kg body weight  
Result: negative

Reproductive toxicity  
May damage the unborn child.

Components:

(S)-1-[N-[1-(Ethoxycarbonyl)-3-phenylpropyl]-L-alanyl]-L-proline maleate:

Effects on fertility  
Test Type: Fertility  
Species: Rat, male and female  
Application Route: Ingestion  
Fertility: NOAEL: 90 mg/kg body weight  
Result: No effects on fertility.

Effects on fetal development  
Species: Rat  
Application Route: Ingestion  
Developmental Toxicity: NOAEL: 200 mg/kg body weight  
Result: No effects on fetal development.

Species: Rat  
Application Route: Ingestion  
Developmental Toxicity: LOAEL: 1.200 mg/kg body weight  
Result: Fetotoxicity.

Species: Rat  
Application Route: Ingestion  
Developmental Toxicity: LOAEL: 30 mg/kg body weight
Result: Effects on postnatal development., Effects on newborn., No teratogenic effects.

Species: Rabbit
Application Route: Ingestion
General Toxicity Maternal: LOAEL: 1 mg/kg body weight
Developmental Toxicity: LOAEL: 1 mg/kg body weight
Result: Fetotoxicity., Maternal toxicity observed., No teratogenic effects.

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
May cause damage to organs (Kidney, Cardio-vascular system) through prolonged or repeated exposure.

Components:
(S)-1-[N-[1-(Ethoxycarbonyl)-3-phenylpropyl]-L-alanyl]-L-proline maleate:
Target Organs : Kidney, Cardio-vascular system
Assessment : Causes 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

(S)-1-[N-[1-(Ethoxycarbonyl)-3-phenylpropyl]-L-alanyl]-L-proline maleate:
Species : Dog
NOAEL : 15 mg/kg
LOAEL : 30 mg/kg
Application Route : Ingestion
Exposure time : 1 y
Target Organs : Kidney

Species : Rat
NOAEL : 90 mg/kg
Application Route : Oral
Exposure time : 1 y
Remarks : No significant adverse effects were reported

Species : Monkey
NOAEL : 30 mg/kg
SAFETY DATA SHEET

Enalapril Formulation

Application Route: Oral
Exposure time: 1 Months
Remarks: No significant adverse effects were reported

Aspiration toxicity
Not classified based on available information.

Experience with human exposure

Components:

(S)-1-[N-[1-(Ethoxycarbonyl)-3-phenylpropyl]-L-alanyl]-L-proline maleate:

Ingestion:
Target Organs: Cardio-vascular system
Symptoms: hypotension, Cough, Dizziness, Headache, Blurred vision, Fatigue, Edema, Nausea, hyperkalemia, fainting, Weakness, skin rash
Remarks: May cause harm to the unborn child.

SECTION 12. ECOLOGICAL INFORMATION

Ecotoxicity

Components:

(S)-1-[N-[1-(Ethoxycarbonyl)-3-phenylpropyl]-L-alanyl]-L-proline maleate:

Toxicity to fish: LC50 (Pimephales promelas (fathead minnow)): > 1.000 mg/l
Exposure time: 96 h
Method: OECD Test Guideline 203

Toxicity to daphnia and other aquatic invertebrates: EC50 (Daphnia magna (Water flea)): 346 mg/l
Exposure time: 48 h
Method: OECD Test Guideline 202

Toxicity to microorganisms: EC50 (Natural microorganism): > 1.000 mg/l
Exposure time: 3 h
Test Type: Respiration inhibition
Method: OECD Test Guideline 209

Persistence and degradability
No data available

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.

Domestic regulation

ANTT
Not regulated as a dangerous good

SECTION 15. REGULATORY INFORMATION

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

National List of Carcinogenic Agents for Humans - (LINACH): Not applicable

Brazil. List of chemicals controlled by the Federal Police: Sodium hydrogen carbonate

International Regulations

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

AICS: not determined

DSL: not determined

IECSC: not determined

SECTION 16. OTHER INFORMATION

Further information


Full text of other abbreviations
SAFETY DATA SHEET

Enalapril Formulation

Version: 5.1
Revision Date: 10.10.2020
SDS Number: 734735-00011
Date of last issue: 23.03.2020
Date of first issue: 07.06.2016

ACGIH / TWA: USA. ACGIH Threshold Limit Values (TLV)

ACGIH / TWA: 8-hour, time-weighted average

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.

BR / Z8