SAFETY DATA SHEET

Enalapril Formulation

SECTION 1. PRODUCT AND COMPANY IDENTIFICATION

Product name: Enalapril Formulation

Manufacturer or supplier’s details
Company name of supplier: MSD
Address: Avenida 16 de Septiembre No. 301, Xaltocan - Xochimilco Mexico 16090
Telephone: 52 55 57284444
Telefax: 908-735-1496
Emergency telephone: 1-908-423-6000
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, Cardio-vascular system)

GHS label elements
Hazard pictograms:

Signal Word: Danger
Hazard Statements:
H360D May damage the unborn child.
H372 Causes damage to organs (Kidney, Cardio-vascular system) 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.
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/ attention.

Storage:
P405 Store locked up.
SAFETY DATA SHEET

Enalapril Formulation

Version 4.2  Revision Date: 09/13/2019  SDS Number: 734747-00009  Date of last issue: 24.04.2019

Disposal:
P501 Dispose of contents/container to an approved waste disposal plant.

Other hazards
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

<table>
<thead>
<tr>
<th>Substance / Mixture</th>
<th>Components</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Chemical name</td>
</tr>
<tr>
<td>Mixture</td>
<td>Starch</td>
</tr>
<tr>
<td></td>
<td>(S)-1-[N-[1-(Ethoxycarbonyl)-3-phenylpropyl]-L-alanyl]-L-proline maleate</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.

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. FIRE-FIGHTING MEASURES

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

None known.

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.

Carbon oxides
Metal oxides

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.

In the event of fire, wear self-contained breathing apparatus. Use personal protective equipment.

Use personal protective equipment. Follow safe handling advice and personal protective equipment recommendations.

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.

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.

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.
- 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.
- 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>
<tbody>
<tr>
<td>Starch</td>
<td>9005-25-8</td>
<td>VLE-PPT</td>
<td>10 mg/m³</td>
<td>NOM-010-STPS-2014</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA</td>
<td>10 mg/m³</td>
<td>ACGIH</td>
</tr>
<tr>
<td>(S)-1-[N-{1-(Ethoxycarbonyl)-3-phenylpropyl]-L-alanyl}-L-proline maleate</td>
<td>76095-16-4</td>
<td>TWA</td>
<td>50 µg/m³ (OEB 3)</td>
<td>Internal</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Wipe limit</td>
<td>500 µg/100 cm²</td>
<td>Internal</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.
- 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

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appearance</td>
<td>powder</td>
</tr>
<tr>
<td>Color</td>
<td>white</td>
</tr>
<tr>
<td>Odor</td>
<td>No data available</td>
</tr>
<tr>
<td>Odor Threshold</td>
<td>No data available</td>
</tr>
<tr>
<td>pH</td>
<td>No data available</td>
</tr>
<tr>
<td>Melting point/freezing point</td>
<td>No data available</td>
</tr>
<tr>
<td>Initial boiling point and boiling range</td>
<td>No data available</td>
</tr>
<tr>
<td>Flash point</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Evaporation rate</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Flammability (solid, gas)</td>
<td>May form explosive dust-air mixture during processing, handling or other means.</td>
</tr>
<tr>
<td>Flammability (liquids)</td>
<td>No data available</td>
</tr>
</tbody>
</table>
### 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 products**: No hazardous decomposition products are known.

### SECTION 11. TOXICOLOGICAL INFORMATION

**Information on likely routes of exposure**

- **Inhalation**
- **Skin contact**
- **Ingestion**
- **Eye contact**
SAFETY DATA SHEET

Enalapril Formulation

Version 4.2  Revision Date: 09/13/2019  SDS Number: 734747-00009  Date of last issue: 24.04.2019  Date of first issue: 07.06.2016

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 (Mouse): > 5,000 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:**

(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:
(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:
(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:
Species: Rat
Application Route: Ingestion
Exposure time: 106 weeks
NOAEL: 90 mg/kg body weight
Result: negative
Species: Mouse
Application Route: Ingestion
Exposure time: 94 weeks
NOAEL: 90 - 180 mg/kg body weight
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
Causes 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:**

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

<table>
<thead>
<tr>
<th>Species</th>
<th>Dog</th>
</tr>
</thead>
<tbody>
<tr>
<td>NOAEL</td>
<td>15 mg/kg</td>
</tr>
<tr>
<td>LOAEL</td>
<td>30 mg/kg</td>
</tr>
<tr>
<td>Application Route</td>
<td>Ingestion</td>
</tr>
<tr>
<td>Exposure time</td>
<td>1 y</td>
</tr>
<tr>
<td>Target Organs</td>
<td>Kidney</td>
</tr>
</tbody>
</table>

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
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.

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
SAFETY DATA SHEET

Enalapril Formulation

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
NOM-002-SCT
Not regulated as a dangerous good

Special precautions for user
Not applicable

SECTION 15. REGULATORY INFORMATION

Safety, health and environmental regulations/legislation specific for the substance or mixture
Federal Law for the control of chemical precursors, essential chemical products and machinery for producing capsules, tablets and pills. : Not applicable
The ingredients of this product are reported in the following inventories:

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

SECTION 16. OTHER INFORMATION

Full text of other abbreviations

- ACGIH: USA. ACGIH Threshold Limit Values (TLV)
- ACGIH / TWA: 8-hour, time-weighted average
- NOM-010-STPS-2014 / VLE-PPT: Time weighted average limit value

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 Organisation 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

Sources of key data used to compile the Material Safety: Internal technical data, data from raw material SDSs, OECD eChem Portal search results and European Chemicals Agen-
SAFETY DATA SHEET

Enalapril Formulation

Version 4.2  Revision Date: 09/13/2019  SDS Number: 734747-00009  Date of last issue: 24.04.2019
Date of first issue: 07.06.2016

The information is considered as correct, but not exhaustive, and will be used only as a guide, which is based in the current knowledge of the substance or mixture, and is applicable to proper safety precautions for the product.

MX / Z8