SAFETY DATA SHEET

Enalapril Formulation

Version: 2.7  Revision Date: 10.10.2020  SDS Number: 734750-00011  Date of last issue: 23.03.2020  Date of first issue: 07.06.2016

1. PRODUCT AND COMPANY IDENTIFICATION

Product name: Enalapril Formulation

Manufacturer or supplier's details
Company: MSD
Address: 50 Tuas West Drive
          Singapore - Singapore 638408
Telephone: 908-740-4000
Emergency telephone number: 65 6697 2111 (24/7/365)
E-mail address: EHSDATASTEWARD@msd.com
Telefax: 908-735-1496

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 2 (Kidney, Cardio-vascular system)

GHS label elements
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.
P202 Do not handle until all safety precautions have been read and understood.
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/
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Attention.

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

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>Starch</td>
<td></td>
</tr>
<tr>
<td>(S)-1-[N-[1-(Ethoxycarbonyl)-3-phenylpropyl]-L-alanyl]-L-proline maleate</td>
<td>76095-16-4</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.
May cause 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: 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 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

Technical measures: Static electricity may accumulate and ignite suspended dust
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.

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

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>(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></td>
<td>Wipe limit</td>
<td>500 μg/100 cm²</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 expo-
sure assessment demonstrates exposures outside the recommended guidelines, use respiratory protection.

Filter type
Hand protection

Material
Hand protection

Remarks
Eye protection

Skin and body protection
Eye protection

Hygiene measures

9. PHYSICAL AND CHEMICAL PROPERTIES

Appearance
Colour
Odour
Odour Threshold
pH
Melting point/freezing point
Initial boiling point and boiling range
Flash point
Evaporation rate
Flammability (solid, gas)
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.

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: > 2,000 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-(Ethoxycarbonyl)-3-phenylpropyl]-L-alanyl-L-proline maleate:
Species : Rabbit
Result : Severe 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

(S)-1-[N-(Ethoxycarbonyl)-3-phenylpropyl]-L-alanyl-L-proline maleate:
Test Type : Maximisation Test
Exposure routes : 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-(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 cyto genetic 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  
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 foetal development:

Species: Rat  
Application Route: Ingestion  
Developmental Toxicity: NOAEL: 200 mg/kg body weight  
Result: No effects on foetal 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:**

<table>
<thead>
<tr>
<th>Target Organs</th>
<th>Assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kidney, Cardio-vascular system</td>
<td>Causes damage to organs through prolonged or repeated exposure.</td>
</tr>
</tbody>
</table>

**Repeated dose toxicity**

**Components:**

**Starch:**

| Species | Rat |
| 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 | >= 2,000 mg/kg |
| Application Route | Ingestion |
| Exposure time | 1 yr |

**Species**

| Rat |
| NOAEL | 15 mg/kg |
| LOAEL | 30 mg/kg |
| Application Route | Oral |
| Exposure time | 1 yr |
| Target Organs | Kidney |

**Species**

| Rat |
| NOAEL | 90 mg/kg |
| Application Route | Oral |
| Exposure time | 1 yr |

**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, Oedema, Nausea, hyperkalemia, fainting, Weakness, skin rash
- **Remarks:** May cause harm to the unborn child.

### 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

### 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.

15. REGULATORY INFORMATION

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

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
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