SAFETY DATA SHEET

Enalapril Formulation

Version 2.5  Revision Date: 09/13/2019  SDS Number: 734745-00009  Date of last issue: 2019/04/24  Date of first issue: 2016/06/07

1. PRODUCT AND COMPANY IDENTIFICATION

Product name : Enalapril Formulation

Manufacturer or supplier’s details

Company name of supplier : MSD
Address : Kumagaya, Saitama Prefecture, Xicheng 810 MSD Co., Ltd. Menuma factory
Telephone : 048-588-8411
E-mail address : EHSDATASTEWARD@msd.com
Emergency telephone number : 1-908-423-6000

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/ attention.
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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
Important symptoms and outlines of the emergency assumed:
- 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

Substance / Mixture: Mixture

Components

<table>
<thead>
<tr>
<th>Chemical name</th>
<th>CAS-No.</th>
<th>Concentration (% w/w)</th>
<th>ENCS No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Starch</td>
<td>9005-25-8</td>
<td>&gt;= 10 - &lt; 20</td>
<td>8-98</td>
</tr>
<tr>
<td>(S)-1-[N-[1-(Ethoxycarbonyl)-3-phenylpropyl]-L-alanyl]-L-proline maleate</td>
<td>76095-16-4</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.
- 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 and personal protective equipment recommendations.

**Environmental precautions**
- 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.

**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

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.
- 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.

Avoidance of contact:
- Oxidizing agents

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.

Storage

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

Packaging material:
- Unsuitable material: None known.

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Threshold limit value and permissible exposure limits for each component in the work environment

<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>


### 5. PHYSICAL AND CHEMICAL PROPERTIES

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Appearance</strong></td>
<td>powder</td>
</tr>
<tr>
<td><strong>Colour</strong></td>
<td>white</td>
</tr>
<tr>
<td><strong>Odour</strong></td>
<td>No data available</td>
</tr>
<tr>
<td><strong>Odour Threshold</strong></td>
<td>No data available</td>
</tr>
<tr>
<td><strong>pH</strong></td>
<td>No data available</td>
</tr>
<tr>
<td><strong>Melting point/freezing point</strong></td>
<td>No data available</td>
</tr>
<tr>
<td><strong>Initial boiling point and boiling range</strong></td>
<td>No data available</td>
</tr>
</tbody>
</table>
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
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.
Particle size : No data available

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.
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 (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 sensitisation

Skin sensitisation
Not classified based on available information.

Respiratory sensitisation
Not classified based on available information.

Components:

(S)-1-[(N-[(1-(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:

(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
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:
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:
Species: Dog
NOAEL: 15 mg/kg
LOAEL: 30 mg/kg
Application Route: Ingestion
Exposure time: 1 yr
Target Organs: Kidney

Species: Rat
NOAEL: 90 mg/kg
Application Route: Oral
Exposure time: 1 yr
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, 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

Hazardous to the ozone layer
Not applicable

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.

### National Regulations
Refer to section 15 for specific national regulation.

### 15. REGULATORY INFORMATION

#### Related Regulations

**Fire Service Law**
Not applicable to dangerous materials / designated flammables.

**Chemical Substance Control Law**
Not applicable for Specified Chemical Substance, Monitoring Chemical Substance and Priority Assessment Chemical Substance.

**Industrial Safety and Health Law**

- **Harmful Substances Prohibited from Manufacture**
  Not applicable

- **Harmful Substances Required Permission for Manufacture**
  Not applicable

- **Substances Prevented From Impairment of Health**
  Not applicable

- **Circular concerning Information on Chemicals having Mutagenicity - Annex 2: Information on Existing Chemicals having Mutagenicity**
  Not applicable

- **Circular concerning Information on Chemicals having Mutagenicity - Annex 1: Information on Notified Substances having Mutagenicity**
  Not applicable

- **Substances Subject to be Notified Names**
  Not applicable

- **Substances Subject to be Indicated Names**
  Not applicable

- **Ordinance on Prevention of Hazards Due to Specified Chemical Substances**
  Not applicable

- **Ordinance on Prevention of Lead Poisoning**
  Not applicable

- **Ordinance on Prevention of Tetraalkyl Lead Poisoning**
  Not applicable

- **Ordinance on Prevention of Organic Solvent Poisoning**
  Not applicable

- **Enforcement Order of the Industrial Safety and Health Law - Attached table 1 (Dangerous Substances)**
  Not applicable
Poisonous and Deleterious Substances Control Law
Not applicable

Act on Confirmation, etc. of Release Amounts of Specific Chemical Substances in the Environment and Promotion of Improvements to the Management Thereof
Not applicable

High Pressure Gas Safety Act
Not applicable

Explosive Control Law
Not applicable

Vessel Safety Law
Not regulated as a dangerous good

Aviation Law
Not regulated as a dangerous good

Marine Pollution and Sea Disaster Prevention etc Law
Bulk transportation : Not classified as noxious liquid substance
Pack transportation : Not classified as marine pollutant

Narcotics and Psychotropics Control Act
Narcotic or Psychotropic Raw Material (Export / Import Permission)
Not applicable
Specific Narcotic or Psychotropic Raw Material (Export / Import permission)
Not applicable

Waste Disposal and Public Cleansing Law
Industrial waste

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 : yyyy/mm/dd

Full text of other abbreviations
ACGIH : 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.

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