Enalapril Formulation

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

1.1 Product identifier
   Trade name : Enalapril 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
             Innishannon
             County Cork - Ireland
   Telephone : 353 214329300
   Telefax : 908-735-1496
   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 2 : H373: May cause damage to organs through pro-
   longed 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.
                       H373 May cause damage to organs 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.

Storage:
P405  Store locked up.

Hazardous components which must be listed on the label:
(S)-1-[N-[1-(Ethoxycarbonyl)-3-phenylpropyl]-L-alanyl]-L-proline maleate

2.3 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

3.2 Mixtures

<table>
<thead>
<tr>
<th>Components</th>
<th>CAS-No.</th>
<th>EC-No.</th>
<th>Classification</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(S)-1-[N-[1-(Ethoxycarbonyl)-3-phenylpropyl]-L-alanyl]-L-proline maleate</td>
<td>76095-16-4 278-375-7</td>
<td></td>
<td>Acute Tox. 4; H302 Eye Irrit. 2; H319 Repr. 1A; H360D STOT RE 1; H372</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.
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.

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:
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

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

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 and personal protective equipment recommendations.

6.2 Environmental precautions

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.

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 to 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. 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.

**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>OELV - 8 hrs (TWA) (Respirable dust)</td>
<td>4 mg/m³</td>
<td>IE OEL</td>
</tr>
<tr>
<td>(S)-1-][N-[1- (Ethoxycarbonyl)-</td>
<td>76095-16-4</td>
<td>TWA</td>
<td>50 µg/m³ (OEB 3)</td>
<td>Internal</td>
</tr>
</tbody>
</table>

Further information: Where no specific short-term exposure limit is listed, a figure three times the long-term exposure limit value should be used.
8.2 Exposure controls

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
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
Remarks: Consider double gloving.

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.

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: powder
Colour: white
Odour: No data available
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
### Enalapril Formulation

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<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>Upper explosion limit / Upper flammability limit</td>
<td>No data available</td>
</tr>
<tr>
<td>Lower explosion limit / Lower flammability limit</td>
<td>No data available</td>
</tr>
<tr>
<td>Vapour pressure</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Relative vapour density</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Relative density</td>
<td>No data available</td>
</tr>
<tr>
<td>Density</td>
<td>No data available</td>
</tr>
<tr>
<td>Solubility(ies)</td>
<td></td>
</tr>
<tr>
<td>Water solubility</td>
<td>No data available</td>
</tr>
<tr>
<td>Partition coefficient: n-octanol/water</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Auto-ignition temperature</td>
<td>No data available</td>
</tr>
<tr>
<td>Decomposition temperature</td>
<td>No data available</td>
</tr>
<tr>
<td>Viscosity</td>
<td></td>
</tr>
<tr>
<td>Viscosity, kinematic</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Explosive properties</td>
<td>Not explosive</td>
</tr>
<tr>
<td>Oxidizing properties</td>
<td>The substance or mixture is not classified as oxidizing.</td>
</tr>
</tbody>
</table>

#### 9.2 Other information
- Flammability (liquids) : 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 explosive dust-air mixture 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

<table>
<thead>
<tr>
<th>Information on likely routes of exposure</th>
<th>Inhalation</th>
<th>Skin contact</th>
<th>Ingestion</th>
<th>Eye contact</th>
</tr>
</thead>
</table>

**Acute toxicity**

Not classified based on available information.

**Product:**

- **Acute oral toxicity**: Acute toxicity estimate: > 2,000 mg/kg
  
  Method: Calculation method

**Components:**

- (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

Components:
(S)-1-[N-[1-(Ethoxycarbonyl)-3-phenylpropyl]-L-alanyl]-L-proline maleate:
Species: Rat, male and female
Application Route: Ingestion
Fertility: NOAEL: 90 mg/kg body weight
Result: No effects on fertility

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: Rabbit
Application Route: Ingestion
Developmental Toxicity: LOAEL: 30 mg/kg body weight
Result: Effects on postnatal development, Effects on newborn, No teratogenic effects
SAFETY DATA SHEET
according to Regulation (EC) No. 1907/2006

Enalapril Formulation

Version 3.2  Revision Date: 09/13/2019  SDS Number: 746057-00009  Date of last issue: 24.04.2019
Date of first issue: 07.06.2016

General Toxicity Maternal:
LOAEL: 1 mg/kg body weight
Developmental Toxicity: LOAEL: 1 mg/kg body weight
Result: Fetal toxicity, 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 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
Enalapril Formulation

Symptoms: hypotension, Cough, Dizziness, Headache, Blurred vision, Fatigue, Oedema, Nausea, hyperkalemia, fainting, Weakness, skin rash
Remarks: May cause harm to the unborn child.

SECTION 12: Ecological information

12.1 Toxicity

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

12.2 Persistence and degradability
No data available

12.3 Bioaccumulative potential
No data available

12.4 Mobility in soil
No data available

12.5 Results of PBT and vPvB assessment
Not relevant

12.6 Other adverse effects
No data available

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

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
REACH - Candidate List of Substances of Very High Concern for Authorisation (Article 59). : Not applicable
REACH - List of substances subject to authorisation (Annex XIV) : Not applicable
Regulation (EC) No 1005/2009 on substances that deplete the ozone layer : Not applicable
Regulation (EC) No 850/2004 on persistent organic pollutants : Not applicable
Regulation (EC) No 649/2012 of the European Parliament and the Council concerning the export and import of dangerous chemicals : Not applicable
REACH - Restrictions on the manufacture, placing on the market and use of certain dangerous substances, preparations and articles (Annex XVII) : Not applicable

Other regulations:
Take note of Directive 92/85/EEC regarding maternity protection or stricter national regulations, where applicable.
Take note of Directive 94/33/EC on the protection of young people at work or stricter national regulations, where applicable.

The components of this product are reported in the following inventories:
AICS : not determined
**Enalapril Formulation**

**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**

- **H302**: Harmful if swallowed.
- **H319**: Causes serious eye irritation.
- **H360D**: May damage the unborn child.
- **H372**: Causes damage to organs through prolonged or repeated exposure.

**Full text of other abbreviations**

- **Acute Tox.**: Acute toxicity
- **Eye Irrit.**: Eye irritation
- **Repr.**: Reproductive toxicity
- **STOT RE**: Specific target organ toxicity - repeated exposure
- **IE OEL**: Ireland. List of Chemical Agents and Occupational Exposure Limit Values - Schedule 1
- **IE OEL / OELV - 8 hrs (TWA)**: Occupational exposure limit value (8-hour reference period)

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; AICS - Australian Inventory of Chemical Substances; 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 - 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; KECl - 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; NO(A)EC - No Observed (Adverse) Effect Concentration; NO(A)EL - No Observed (Adverse) Effect Level; NOELR - No Observable Effect Loading Rate; NZIoC - New Zealand Inventory of Chemicals; OECD - Organization for Economic Co-operation and Development; OPPTS - Office of Chemical Safety and Pollution Prevention; PBT - Persistent, Bioaccumu-
Enalapril Formulation

Further information

Sources of key data used to compile the Safety Data Sheet:

Classification of the mixture:

<table>
<thead>
<tr>
<th>Repr. 1A</th>
<th>STOT RE 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>H360D</td>
<td>H373</td>
</tr>
</tbody>
</table>

Classification procedure:
Calculation method
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.