Ramipril Formulation

1. PRODUCT AND COMPANY IDENTIFICATION

Product name: Ramipril Formulation

Manufacturer or supplier’s details
Company: MSD
Address: No. 485 Jing Tai Road, Pu Tuo District - Shanghai - China 200331
Telephone: +1-908-740-4000
Emergency telephone number: 86-571-87268110
E-mail address: EHSDATASTEWARD@msd.com

Recommended use of the chemical and restrictions on use
Recommended use: Veterinary product

2. HAZARDS IDENTIFICATION

Emergency Overview
Appearance: powder
Colour: No data available
Odour: No data available

May cause an allergic skin reaction. May damage the unborn child. May cause damage to organs through prolonged or repeated exposure.

GHS Classification
Skin sensitisation: Category 1
Reproductive toxicity: Category 1A
Specific target organ toxicity - repeated exposure: Category 2

GHS label elements
Hazard pictograms:

Signal word: Danger
Hazard statements: H317 May cause an allergic skin reaction. 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.
P202 Do not handle until all safety precautions have been read and understood.
P260 Do not breathe dust.
P272 Contaminated work clothing should not be allowed out of the workplace.
P280 Wear protective gloves/protective clothing/eye protection/face protection.

Response:
P302 + P352 IF ON SKIN: Wash with plenty of water.
P308 + P313 IF exposed or concerned: Get medical advice/attention.
P333 + P313 If skin irritation or rash occurs: Get medical advice/attention.
P362 + P364 Take off contaminated clothing and wash it before reuse.

Storage:
P405 Store locked up.

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

Physical and chemical hazards
Not classified based on available information.

Health hazards
May cause an allergic skin reaction. May damage the unborn child. May cause damage to organs through prolonged or repeated exposure.

Environmental hazards
Not classified based on available information.

Additional Labelling
The following percentage of the mixture consists of ingredient(s) with unknown hazards to the aquatic environment: 10 %

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

Substance / Mixture: Mixture

<table>
<thead>
<tr>
<th>Components</th>
<th>Chemical name</th>
<th>CAS-No.</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Starch</td>
<td>9005-25-8</td>
<td>&gt;= 30 - &lt; 50</td>
<td></td>
</tr>
<tr>
<td>Cellulose</td>
<td>9004-34-6</td>
<td>&gt;= 30 - &lt; 50</td>
<td></td>
</tr>
<tr>
<td>Ramipril</td>
<td>87333-19-5</td>
<td>&gt;= 10 - &lt; 20</td>
<td></td>
</tr>
</tbody>
</table>
SAFETY DATA SHEET
according to GB/T 16483 and GB/T 17519

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</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 cause an allergic skin reaction. 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

Specific extinguishing method: Use extinguishing measures that are appropriate to local cir-
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

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.
SAFETY DATA SHEET
according to GB/T 16483 and GB/T 17519

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<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>TWA</td>
<td>10 mg/m³</td>
<td>ACGIH</td>
</tr>
<tr>
<td>Cellulose</td>
<td>9004-34-6</td>
<td>PC-TWA</td>
<td>10 mg/m³</td>
<td>CN OEL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA</td>
<td>10 mg/m³</td>
<td>ACGIH</td>
</tr>
<tr>
<td>Ramipril</td>
<td>87333-19-5</td>
<td>TWA</td>
<td>3 µg/m³ (OEB 4)</td>
<td>Internal</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Wipe limit</td>
<td>30 µg/100cm²</td>
<td>Internal</td>
</tr>
</tbody>
</table>

Engineering measures: Containment technologies suitable for controlling compounds are required to control at source and to prevent migration of the compound to uncontrolled areas (e.g., vacuum conveying from a closed system, packout head with inflatable seal from stationary container, ventilated enclosure, etc.). All engineering controls should be implemented by facility design and operated in accordance with GMP principles to protect products, workers, and the environment. Essentially no open handling permitted. Use closed processing systems or containment technologies.

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

Eye/face 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 face shield 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, dis-
Hand protection

Material: Chemical-resistant gloves

Remarks: Consider double gloving.

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.
Contaminated work clothing should not be allowed out of the workplace.
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.

9. PHYSICAL AND CHEMICAL PROPERTIES

Appearance: powder

Colour: No data available

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

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.
Molecular weight : No data available
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 products : No hazardous decomposition products are known.
Components:

Starch:
- Acute oral toxicity: LD50 (Rat): > 5,000 mg/kg
- Acute dermal toxicity: LD50 (Rabbit): > 2,000 mg/kg

Cellulose:
- Acute oral toxicity: LD50 (Rat): > 5,000 mg/kg
- Acute inhalation toxicity: LC50 (Rat): > 5.8 mg/l
  Exposure time: 4 h
  Test atmosphere: dust/mist
- Acute dermal toxicity: LD50 (Rabbit): > 2,000 mg/kg

Ramipril:
- Acute oral toxicity: LD50 (Rat): > 10,000 mg/kg
  LD50 (Dog): > 1,000 mg/kg
- Acute toxicity (other routes of administration):
  LD50 (Dog): > 250 mg/kg
  Application Route: Intravenous
  LD50 (Rat): 600 mg/kg
  Application Route: Intravenous

Skin corrosion/irritation
Not classified based on available information.

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

Components:

Starch:
- Species: Rabbit
- Result: No eye irritation

Respiratory or skin sensitisation

Skin sensitisation
May cause an allergic skin reaction.

Respiratory sensitisation
Not classified based on available information.

Components:

Starch:
- Test Type: Maximisation Test
- Exposure routes: Skin contact
- Species: Guinea pig
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**Result**: negative

**Natural Pork Flavor**:
Assessment: The product is a skin sensitiser, sub-category 1B.

**Germ cell mutagenicity**
Not classified based on available information.

**Components**:

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

**Cellulose**:
Genotoxicity in vitro: Test Type: Bacterial reverse mutation assay (AMES) Result: negative
Test Type: In vitro mammalian cell gene mutation test Result: negative
Genotoxicity in vivo: Test Type: Mammalian erythrocyte micronucleus test (in vivo cytogenetic assay) Species: Mouse Application Route: Ingestion Result: negative

**Ramipril**:
Genotoxicity in vitro: Test Type: Bacterial reverse mutation assay (AMES) Result: negative
Test Type: unscheduled DNA synthesis assay Result: negative
Test Type: In vitro mammalian cell gene mutation test Test system: Chinese hamster ovary cells Result: negative
Genotoxicity in vivo: Test Type: Micronucleus test Species: mice Result: negative

**Carcinogenicity**
Not classified based on available information.

**Components**:

**Cellulose**:
Species: Rat Application Route: Ingestion Exposure time: 72 weeks
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**Result**: negative

<table>
<thead>
<tr>
<th>Species</th>
<th>Rat</th>
</tr>
</thead>
<tbody>
<tr>
<td>Application Route</td>
<td>Oral</td>
</tr>
<tr>
<td>Exposure time</td>
<td>24 month(s)</td>
</tr>
<tr>
<td>NOAEL</td>
<td>500 mg/kg body weight</td>
</tr>
<tr>
<td>Result</td>
<td>negative</td>
</tr>
</tbody>
</table>

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<tr>
<th>Species</th>
<th>Rat</th>
</tr>
</thead>
<tbody>
<tr>
<td>Application Route</td>
<td>Oral</td>
</tr>
<tr>
<td>Exposure time</td>
<td>18 month(s)</td>
</tr>
<tr>
<td>NOAEL</td>
<td>1,000 mg/kg body weight</td>
</tr>
<tr>
<td>Result</td>
<td>negative</td>
</tr>
</tbody>
</table>

### Reproductive toxicity

May damage the unborn child.

### Components:

#### Cellulose:

- **Effects on fertility**: Test Type: One-generation reproduction toxicity study
  - Species: Rat
  - Application Route: Ingestion
  - Result: negative

- **Effects on foetal development**: Test Type: Fertility/early embryonic development
  - Species: Rat
  - Application Route: Ingestion
  - Result: negative

#### Ramipril:

- **Effects on fertility**: Test Type: Fertility
  - Species: Rat
  - Application Route: Oral
  - Fertility: NOAEL: 500 mg/kg body weight
  - Result: No adverse effects

- **Effects on foetal development**: Test Type: Development
  - Species: Rat
  - Application Route: Oral
  - Developmental Toxicity: NOAEL: 10 mg/kg body weight
  - Result: Malformations were observed.

  Test Type: Development
  - Species: Rat
  - Application Route: Oral
  - Developmental Toxicity: LOAEL: 50 mg/kg body weight
  - Result: Malformations were observed.

  Test Type: Development
  - Species: Rabbit
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Application Route: Oral
Developmental Toxicity: NOAEL: 0.4 mg/kg body weight
Result: Maternal toxicity observed.

Test Type: Development
Species: Rabbit
Application Route: Oral
Developmental Toxicity: LOAEL: 1 mg/kg body weight
Result: Maternal toxicity observed.

Test Type: Development
Species: Monkey
Application Route: Oral
Developmental Toxicity: NOAEL: 5 mg/kg body weight
Result: Maternal toxicity observed.

Test Type: Development
Species: Monkey
Application Route: Oral
Developmental Toxicity: LOAEL: 50 mg/kg body weight
Result: Maternal toxicity observed.

Reproductive toxicity - Assessment: May damage the unborn child.

STOT - single exposure
Not classified based on available information.

STOT - repeated exposure
May cause damage to organs through prolonged or repeated exposure.

Components:

Ramipril:
Exposure routes: Oral
Target Organs: Kidney
Assessment: May cause 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

Cellulose:
Species: Rat
NOAEL: >= 9,000 mg/kg
Application Route: Ingestion
Exposure time: 90 Days

**Ramipril:**

Species: Mouse  
LOAEL: 100 mg/kg  
Application Route: Oral  
Target Organs: Blood, Kidney  
Symptoms: kidney effects

Species: Rat  
NOAEL: 2 mg/kg  
Application Route: Oral

Species: Dog  
NOAEL: 2.5 mg/kg  
LOAEL: 250 mg/kg  
Application Route: Oral  
Target Organs: Blood, Kidney  
Symptoms: kidney effects

Species: Monkey  
NOAEL: 8 mg/kg  
LOAEL: 250 mg/kg  
Application Route: Oral  
Target Organs: Blood, Kidney  
Symptoms: kidney effects

**Aspiration toxicity**  
Not classified based on available information.

**Experience with human exposure**

**Components:**

**Ramipril:**

Ingestion  
Symptoms: Allergic reactions, Kidney disorders, liver function change, Rash, Cough, Dizziness, Nausea, Headache, Vomiting

**12. ECOLOGICAL INFORMATION**

**Ecotoxicity**

**Components:**

**Cellulose:**

Toxicity to fish: LC50 (Oryzias latipes (Japanese medaka)): > 100 mg/l  
Exposure time: 48 h  
Remarks: Based on data from similar materials

**Ramipril:**

Toxicity to fish: LC50 (Brachydanio rerio (zebrafish)): > 100 mg/l
Exposure time: 96 h
Method: OECD Test Guideline 203

Toxicity to daphnia and other aquatic invertebrates
EC50 (Daphnia magna (Water flea)): > 100 mg/l
Exposure time: 48 h
Method: OECD Test Guideline 202

Toxicity to algae/aquatic plants
EC50 (Pseudokirchneriella subcapitata (green algae)): > 100 mg/l
Exposure time: 72 h
Method: OECD Test Guideline 201

Hydrolyzed Vegetable Protein:
Ecotoxicology Assessment
Acute aquatic toxicity: Toxic effects cannot be excluded
Chronic aquatic toxicity: Toxic effects cannot be excluded

Natural Pork Flavor:
Ecotoxicology Assessment
Acute aquatic toxicity: Toxic effects cannot be excluded
Chronic aquatic toxicity: Toxic effects cannot be excluded

Hydrogenated Vegetable Oil:
Ecotoxicology Assessment
Acute aquatic toxicity: Toxic effects cannot be excluded
Chronic aquatic toxicity: Toxic effects cannot be excluded

Persistence and degradability

Components:

Cellulose:
Biodegradability: Result: Readily biodegradable.

Ramipril:
Biodegradability: Result: Not readily biodegradable.
Biodegradation: 20 - 50 %
Exposure time: 28 d
Method: OECD Test Guideline 301A

Bioaccumulative potential
No data available

Mobility in soil
No data available
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according to GB/T 16483 and GB/T 17519

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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
GB 6944/12268
Not regulated as a dangerous good

Special precautions for user
Not applicable

15. REGULATORY INFORMATION

National regulatory information
Law on the Prevention and Control of Occupational Diseases

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
Sources of key data used to : Internal technical data, data from raw material SDSs, OECD
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Full text of other abbreviations
ACGIH  : USA. ACGIH Threshold Limit Values (TLV)
CN OEL  : Occupational exposure limits for hazardous agents in the workplace - Chemical hazardous agents.

ACGIH / TWA  : 8-hour, time-weighted average
CN OEL / PC-TWA  : Permissible concentration - time weighted average

All abbreviations are defined in the introductory section of the SDS.

Disclaimer
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.