SAFETY DATA SHEET

Ramipril Formulation

Version 2.0  Revision Date: 2020/03/23  SDS Number: 3517203-00004  Date of last issue: 2019/09/13  Date of first issue: 2018/10/11

1. PRODUCT AND COMPANY IDENTIFICATION

Chemical product name : Ramipril Formulation

Supplier’s company name, address and phone number

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 : Veterinary product

2. HAZARDS IDENTIFICATION

GHS classification of chemical product

Skin sensitisation : Category 1
Reproductive toxicity : Category 1A
Specific target organ toxicity - repeated exposure (Oral) : Category 2 (Kidney)

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 (Kidney) through prolonged or repeated exposure if swallowed.

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 protec-
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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
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>Cellulose</td>
<td>9004-34-6</td>
<td>&gt;= 40 - &lt; 50</td>
<td></td>
</tr>
<tr>
<td>Starch</td>
<td>9005-25-8</td>
<td>&gt;= 40 - &lt; 50</td>
<td>8-98</td>
</tr>
<tr>
<td>Ramipril</td>
<td>87333-19-5</td>
<td>&gt;= 10 - &lt; 20</td>
<td></td>
</tr>
<tr>
<td>Hydrolyzed Vegetable Protein</td>
<td>Not Assigned</td>
<td>&gt;= 1 - &lt; 10</td>
<td></td>
</tr>
<tr>
<td>Natural Pork Flavor</td>
<td>Not Assigned</td>
<td>&gt;= 1 - &lt; 10</td>
<td></td>
</tr>
<tr>
<td>Hydrogenated Vegetable Oil</td>
<td>Not Assigned</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 cause an allergic skin reaction.
May damage the unborn child.
May cause damage to organs through prolonged or repeated exposure if swallowed.
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 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

<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>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

Hand protection

Material : Chemical-resistant gloves

Remarks : Consider double gloving.

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.

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.
9. PHYSICAL AND CHEMICAL PROPERTIES

Physical state : powder
Colour : No data available
Odour : No data available
Odour Threshold : No data available
Melting point/freezing point : No data available
Boiling point, initial boiling point and boiling range : No data available
Flammability (solid, gas) : May form explosive dust-air mixture during processing, handling or other means.
Flammability (liquids) : No data available

Lower explosion limit and upper explosion limit / flammability limit
Upper explosion limit / Upper flammability limit : No data available
Lower explosion limit / Lower flammability limit : No data available
Flash point : Not applicable
Decomposition temperature : No data available
pH : No data available
Evaporation rate : Not applicable
Auto-ignition temperature : No data available
Viscosity
Viscosity, kinematic : Not applicable

Solubility(ies)
Water solubility : No data available
Partition coefficient: n-octanol/water : Not applicable
Vapour pressure : Not applicable

Density and / or relative density
Relative density : No data available
Density : No data available
Relative vapour density : Not applicable
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Explosive properties : Not explosive

Oxidizing properties : The substance or mixture is not classified as oxidizing.

Molecular weight : No data available

Particle characteristics
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 reac-
tions : May form explosive dust-air mixture during processing, han-
dling 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.

Components:

<table>
<thead>
<tr>
<th>Component</th>
<th>Acute oral toxicity</th>
<th>Acute inhalation toxicity</th>
<th>Acute dermal toxicity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cellulose</td>
<td>LD50 (Rat): &gt; 5,000 mg/kg</td>
<td>LC50 (Rat): &gt; 5.8 mg/l Exposure time: 4 h Test atmosphere: dust/mist</td>
<td>LD50 (Rabbit): &gt; 2,000 mg/kg</td>
</tr>
<tr>
<td>Starch</td>
<td>LD50 (Rat): &gt; 5,000 mg/kg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ramipril</td>
<td>LD50 (Rat): &gt; 10,000 mg/kg</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Acute toxicity (other routes of administration):  
LD50 (Dog): > 1,000 mg/kg

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

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
Result: negative

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

Germ cell mutagenicity:  
Not classified based on available information.

Components:

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

Genotoxicity in vivo: Test Type: Mammalian erythrocyte micronucleus test (in vivo cytogenetic assay)  
Species: Mouse
Application Route: Ingestion
Result: negative

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

**Ramipril:**
- Species: Rat
- Application Route: Oral
- Exposure time: 24 month(s)
- NOAEL: 500 mg/kg body weight
- Result: negative

- Species: Rat
  Application Route: Oral
  Exposure time: 18 month(s)
  NOAEL: 1,000 mg/kg body weight
  Result: negative

**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: Rabbit, 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 - As: May damage the unborn child.
Assessment

STOT - single exposure
Not classified based on available information.

STOT - repeated exposure
May cause damage to organs (Kidney) through prolonged or repeated exposure if swallowed.

Components:

Ramipril:
- Exposure routes: Oral
- Target Organs: Kidney
- Assessment: May cause damage to organs through prolonged or repeated exposure.

Repeated dose toxicity

Components:

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

Starch:
- Species: Rat
- NOAEL: >= 2,000 mg/kg
- Application Route: Skin contact
- Exposure time: 28 Days
- Method: OECD Test Guideline 410

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
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

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

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

Items where changes have been made to the previous version are highlighted in the body of this document by two vertical lines.
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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.

JP / EN