1. PRODUCT AND COMPANY IDENTIFICATION

Product name: Ezetimibe / Simvastatin 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
Skin corrosion/irritation: Category 2
Skin sensitisation: Category 1
Specific target organ toxicity - repeated exposure: Category 1 (Liver, muscle, optic nerve, Eye)
Short-term (acute) aquatic hazard: Category 3
Long-term (chronic) aquatic hazard: Category 2

GHS label elements
Hazard pictograms:

Signal word: Danger
Hazard statements:
H315 Causes skin irritation.
H317 May cause an allergic skin reaction.
H372 Causes damage to organs (Liver, muscle, optic nerve, Eye) through prolonged or repeated exposure.
H402 Harmful to aquatic life.
H411 Toxic to aquatic life with long lasting effects.

Precautionary statements:
Prevention:
P260 Do not breathe dust.  
P264 Wash skin thoroughly after handling.  
P270 Do not eat, drink or smoke when using this product.  
P272 Contaminated work clothing should not be allowed out of the workplace.  
P273 Avoid release to the environment.  
P280 Wear protective gloves.  

**Response:**  
P302 + P352 IF ON SKIN: Wash with plenty of water.  
P314 Get medical advice/attention if you feel unwell.  
P333 + P313 If skin irritation or rash occurs: Get medical advice/attention.  
P362 + P364 Take off contaminated clothing and wash it before reuse.  
P391 Collect spillage.  

**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.  
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>
<th>ENCS No.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cellulose</td>
<td>9004-34-6</td>
<td>&gt;= 10 - &lt; 20</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ezetimibe</td>
<td>163222-33-1</td>
<td>&gt;= 10 - &lt; 20</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Simvastatin</td>
<td>79902-63-9</td>
<td>&gt;= 10 - &lt; 20</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Magnesium stearate</td>
<td>557-04-0</td>
<td>&gt;= 1 - &lt; 10</td>
<td>2-611</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 if symptoms occur.  

**In case of skin contact:** In case of contact, immediately flush skin with plenty of water for at least 15 minutes while removing 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 if symptoms occur.
- Rinse mouth thoroughly with water.

### Most important symptoms and effects, both acute and delayed:
- Causes skin irritation.
- May cause an allergic skin reaction.
- Causes damage to organs through prolonged or repeated exposure.
- 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
- Nitrogen oxides (NOx)
- Fluorine compounds
- 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:
- Sweep up or vacuum up spillage and collect in suitable con-
containment and cleaning up the material 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: Use only with adequate 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. 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 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>
<tbody>
<tr>
<td>Cellulose</td>
<td>9004-34-6</td>
<td>TWA</td>
<td>10 mg/m³</td>
<td>ACGIH</td>
</tr>
<tr>
<td>Ezetimibe</td>
<td>163222-33-1</td>
<td>TWA</td>
<td>25 µg/m³ (OEB 3)</td>
<td>Internal</td>
</tr>
<tr>
<td>Simvastatin</td>
<td>79902-63-9</td>
<td>TWA</td>
<td>25 µg/m³ (OEB 3)</td>
<td>Internal</td>
</tr>
<tr>
<td>Magnesium stearate</td>
<td>557-04-0</td>
<td>TWA (Inhalable fraction)</td>
<td>10 mg/m³</td>
<td>ACGIH</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>TWA (Respirable fraction)</td>
<td></td>
</tr>
</tbody>
</table>

Further information: DSEN

<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></td>
<td></td>
<td></td>
<td>Wipe limit 250 µg/100 cm²</td>
<td>Internal</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 exposure assessment demonstrates exposures outside the recommended guidelines, use respiratory protection.

Filter type: Particulates type

Hand protection: Chemical-resistant gloves

Eye protection:
Consider double gloving.
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

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appearance</td>
<td>powder</td>
</tr>
<tr>
<td>Colour</td>
<td>No data available</td>
</tr>
<tr>
<td>Odour</td>
<td>No data available</td>
</tr>
<tr>
<td>Odour Threshold</td>
<td>No data available</td>
</tr>
<tr>
<td>pH</td>
<td>No data available</td>
</tr>
<tr>
<td>Melting point/freezing point</td>
<td>No data available</td>
</tr>
<tr>
<td>Initial boiling point and boiling range</td>
<td>No data available</td>
</tr>
<tr>
<td>Flash point</td>
<td>No data available</td>
</tr>
<tr>
<td>Evaporation rate</td>
<td>No data available</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>Flammability (liquids)</td>
<td>No data available</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>No data available</td>
</tr>
<tr>
<td>Relative vapour density</td>
<td>No data available</td>
</tr>
<tr>
<td>Relative 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>No data available</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>No data available</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>
<tr>
<td>Molecular weight</td>
<td>No data available</td>
</tr>
</tbody>
</table>
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.

Components:
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

Ezetimibe:
Acute oral toxicity: LD50 (Rat): > 5,000 mg/kg
LD50 (Mouse): > 5,000 mg/kg
LD50 (Dog): > 3,000 mg/kg
Acute inhalation toxicity: Remarks: No data available
Acute dermal toxicity: Remarks: No data available
Acute toxicity (other routes of administration): LD50 (Rat): > 2,000 mg/kg
Application Route: Intraperitoneal
LD50 (Mouse): > 1,000 - < 2,000 mg/kg
Application Route: Intraperitoneal
Simvastatin:
Acute oral toxicity: LD50 (Rat): 5,000 mg/kg
LD50 (Mouse): 3,800 mg/kg

Magnesium stearate:
Acute oral toxicity: LD50 (Rat): > 2,000 mg/kg
Method: OECD Test Guideline 423
Assessment: The substance or mixture has no acute oral toxicity
Remarks: Based on data from similar materials

Acute dermal toxicity:
LD50 (Rabbit): > 2,000 mg/kg
Remarks: Based on data from similar materials

Skin corrosion/irritation
Causes skin irritation.

Components:

Ezetimibe:
Species: Rabbit
Result: No skin irritation

Simvastatin:
Species: Rabbit
Remarks: Moderate skin irritation

Magnesium stearate:
Species: Rabbit
Result: No skin irritation
Remarks: Based on data from similar materials

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

Components:

Ezetimibe:
Species: Rabbit
Result: No eye irritation

Simvastatin:
Species: Rabbit
Remarks: slight irritation

Magnesium stearate:
Species: Rabbit
Result: No eye irritation
SAFETY DATA SHEET

Ezetimibe / Simvastatin Formulation

Remarks : Based on data from similar materials

**Respiratory or skin sensitisation**

**Skin sensitisation**
May cause an allergic skin reaction.

**Respiratory sensitisation**
Not classified based on available information.

**Components:**

**Ezetimibe:**
<table>
<thead>
<tr>
<th>Test Type</th>
<th>Maximisation Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Species</td>
<td>Guinea pig</td>
</tr>
<tr>
<td>Result</td>
<td>negative</td>
</tr>
</tbody>
</table>

**Simvastatin:**
| Assessment                             | Probability or evidence of skin sensitisation in humans |
| Result                                 | positive                                                 |

**Magnesium stearate:**
| Test Type                      | Maximisation Test |
| Exposure routes                | Skin contact     |
| Species                        | Guinea pig       |
| Method                         | OECD Test Guideline 406 |
| Result                         | negative         |
| Remarks                        | Based on data from similar materials                     |

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

**Components:**

**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 |

**Ezetimibe:**
| Genotoxicity in vitro | Test Type: Bacterial reverse mutation assay (AMES) |
|                       | Metabolic activation: with and without metabolic activation |
|                       | Result: negative |
|                       | Test Type: Chromosomal aberration |
Test system: Human lymphocytes
Result: negative

Genotoxicity in vivo: Test Type: Micronucleus test
Species: Mouse
Cell type: Bone marrow
Application Route: Oral
Result: negative

Simvastatin:
Genotoxicity in vitro: Test Type: Bacterial reverse mutation assay (AMES)
Result: negative
Test Type: Alkaline elution assay
Result: negative
Test Type: Chromosomal aberration
Result: negative
Test Type: In vitro mammalian cell gene mutation test
Result: negative

Genotoxicity in vivo: Test Type: Micronucleus test
Species: Mouse
Application Route: Oral
Result: negative

Germ cell mutagenicity - Assessment: Weight of evidence does not support classification as a germ cell mutagen.

Magnesium stearate:
Genotoxicity in vitro: Test Type: In vitro mammalian cell gene mutation test
Result: negative
Remarks: Based on data from similar materials
Test Type: Chromosome aberration test in vitro
Method: OECD Test Guideline 473
Result: negative
Remarks: Based on data from similar materials
Test Type: Bacterial reverse mutation assay (AMES)
Result: negative
Remarks: Based on data from similar materials

Carcinogenicity
Not classified based on available information.

Components:

Cellulose:
Species: Rat
Application Route: Ingestion
Exposure time: 72 weeks
Ezetimibe:
Species: Rat, female
Application Route: oral (feed)
Exposure time: 104 weeks
Result: negative

Species: Rat, male
Application Route: oral (feed)
Exposure time: 104 weeks
Result: negative

Species: Mouse
Application Route: oral (feed)
Exposure time: 104 weeks
Result: negative

Simvastatin:
Species: Mouse
Application Route: Oral
Exposure time: < 92 weeks
Target Organs: Harderian gland
Tumor Type: Liver, Lungs
Remarks: The significance of these findings for humans is not certain.

Species: Rat
Application Route: Oral
Exposure time: 2 Years
Tumor Type: Liver, Thyroid
Remarks: The significance of these findings for humans is not certain.

Reproductive toxicity
Not classified based on available information.

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

Effects on foetal development:
Species: Rat
Application Route: Ingestion
Result: negative

Ezetimibe:
Effects on fertility:
Species: Rat, male and female
Fertility: NOAEL: > 1,000 mg/kg body weight
### Effects on foetal development

**Simvastatin:**

**Effects on fertility**
- **Test Type:** Fertility
- **Species:** Rat, male
- **Application Route:** Oral
- **Fertility:** LOAEL: 25 mg/kg body weight

**Effects on foetal development**
- **Test Type:** Embryo-foetal development
- **Species:** Rat
- **Application Route:** Oral
  - **Embryo-foetal toxicity:** NOAEL: 25 mg/kg body weight
  - Result: No teratogenic effects, No adverse effects

**Magnesium stearate:**

**Effects on fertility**
- **Test Type:** Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test
- **Species:** Rat
- **Application Route:** Ingestion
- **Method:** OECD Test Guideline 422
- **Result:** negative
- **Remarks:** Based on data from similar materials

**Effects on foetal development**
- **Test Type:** Embryo-foetal development
- **Species:** Rat
- **Application Route:** Ingestion
  - **Embryo-foetal toxicity:** LOAEL: 60 mg/kg body weight
  - Result: Teratogenic potential
  - **Remarks:** Based on data from similar materials
STOT - single exposure
Not classified based on available information.

STOT - repeated exposure
Causes damage to organs (Liver, muscle, optic nerve, Eye) through prolonged or repeated exposure.

Components:

Simvastatin:
Target Organs: Liver, muscle, optic nerve, Eye
Assessment: Causes 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

Ezetimibe:
Species: Dog
NOAEL: 1,000 mg/kg
Application Route: Oral
Exposure time: 90 d
Remarks: No significant adverse effects were reported

Species: Rat
NOAEL: 1,500 mg/kg
Application Route: Oral
Exposure time: 90 d
Remarks: No significant adverse effects were reported

Species: Mouse
NOAEL: 500 mg/kg
Application Route: Oral
Exposure time: 90 d
Remarks: No significant adverse effects were reported

Species: Dog
NOAEL: 300 mg/kg
Application Route: Oral
Exposure time: 1 yr
Remarks: No significant adverse effects were reported

Simvastatin:
Species: Rat
NOAEL: 5 mg/kg
LOAEL: 30 mg/kg
Application Route: Oral
Exposure time: 14 - 104 Weeks
Target Organs: Liver, Testis, Musculo-skeletal system, Eye

Species: Dog
LOAEL: 10 mg/kg
Application Route: Oral
Exposure time: 14 - 104 Weeks
Target Organs: Liver, Testis, Eye

Species: Rabbit
NOAEL: 30 mg/kg
LOAEL: 50 mg/kg
Application Route: Oral
Target Organs: Liver, Kidney

Magnesium stearate:
Species: Rat
NOAEL: > 100 mg/kg
Application Route: Ingestion
Exposure time: 90 Days
Remarks: Based on data from similar materials

Aspiration toxicity
Not classified based on available information.

Components:
Ezetimibe:
Not applicable

Experience with human exposure

Components:
Ezetimibe:
Ingestion: Symptoms: Headache, Nausea, Vomiting, Diarrhoea, flatulence, muscle pain, upper respiratory tract infection, Back pain, joint pain

Simvastatin:
Skin contact: Remarks: May produce an allergic reaction.
Ingestion: Target Organs: Liver
Symptoms: upper respiratory tract infection, Headache, Abdominal pain, constipation, Nausea
Target Organs: Musculo-skeletal system

12. ECOLOGICAL INFORMATION

Ecotoxicity

Components:
Cellulose:
Toxicity to fish: LC50 (Oryzias latipes (Japanese medaka)): > 100 mg/l
Ezetimibe:

Toxicity to fish:
- LC50 (Pimephales promelas (fathead minnow)): > 0.125 mg/l
- Exposure time: 96 h
- Method: OECD Test Guideline 203
- Remarks: No toxicity at the limit of solubility

Toxicity to daphnia and other aquatic invertebrates:
- EC50 (Daphnia magna (Water flea)): > 4 mg/l
- Exposure time: 48 h
- Method: OECD Test Guideline 202
- Remarks: No toxicity at the limit of solubility

Toxicity to algae/aquatic plants:
- EC50 (Pseudokirchneriella subcapitata (green algae)): > 0.317 mg/l
- Exposure time: 96 h
- Method: OECD Test Guideline 201
- Remarks: No toxicity at the limit of solubility
- NOEC (Pseudokirchneriella subcapitata (green algae)): 0.317 mg/l
- Exposure time: 96 h
- Method: OECD Test Guideline 201
- Remarks: No toxicity at the limit of solubility

Toxicity to fish (Chronic toxicity):
- NOEC (Pimephales promelas (fathead minnow)): 0.051 mg/l
- Exposure time: 33 d
- Method: OECD Test Guideline 210
- NOEC (Cyprinodon variegatus (sheepshead minnow)): 4 mg/l
- Exposure time: 7 d
- Remarks: No toxicity at the limit of solubility

Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity):
- NOEC (Daphnia magna (Water flea)): 0.282 mg/l
- Exposure time: 21 d
- Remarks: No toxicity at the limit of solubility

M-Factor (Chronic aquatic toxicity):
- 1

Toxicity to microorganisms:
- EC50: > 4.4 mg/l
- Exposure time: 3 h
- Test Type: Respiration inhibition
- Method: OECD Test Guideline 209
- Remarks: No toxicity at the limit of solubility
- NOEC: 4.4 mg/l
- Exposure time: 3 h
- Test Type: Respiration inhibition
- Method: OECD Test Guideline 209
- Remarks: No toxicity at the limit of solubility

Simvastatin:

Toxicity to fish:
- LC50 (Pimephales promelas (fathead minnow)): 2.91 mg/l
### Toxicity to daphnia and other aquatic invertebrates
- **EC50 (Daphnia magna (Water flea)):** 3.5 mg/l
  - Exposure time: 48 h
  - Method: OECD Test Guideline 203

### Toxicity to algae/aquatic plants
- **EC50 (Pseudokirchneriella subcapitata (green algae)):** > 25 mg/l
  - Exposure time: 96 h
- **NOEC (Pseudokirchneriella subcapitata (green algae)):** 25 mg/l
  - Exposure time: 96 h

### Toxicity to microorganisms
- **EC50:** > 30 mg/l
  - Exposure time: 3 h
  - Test Type: Respiration inhibition
  - Method: OECD Test Guideline 209
- **NOEC:** 21 mg/l
  - Exposure time: 3 h
  - Test Type: Respiration inhibition
  - Method: OECD Test Guideline 209

### Magnesium stearate:
- **LC50 (Leuciscus idus (Golden orfe)):** > 100 mg/l
  - Exposure time: 48 h
  - Method: DIN 38412
  - Remarks: Based on data from similar materials

### Toxicty to fish
- **EL50 (Daphnia magna (Water flea)):** > 1 mg/l
  - Exposure time: 47 h
  - Test substance: Water Accommodated Fraction
  - Remarks: Based on data from similar materials
  - No toxicity at the limit of solubility

### Toxicity to daphnia and other aquatic invertebrates
- **EL50 (Daphnia magna (Water flea)):** > 1 mg/l
  - Exposure time: 72 h
  - Test substance: Water Accommodated Fraction
  - Method: OECD Test Guideline 201
  - Remarks: Based on data from similar materials
  - No toxicity at the limit of solubility

### Toxicity to algae/aquatic plants
- **NOELR (Pseudokirchneriella subcapitata (green algae)):** > 1 mg/l
  - Exposure time: 72 h
  - Test substance: Water Accommodated Fraction
  - Method: OECD Test Guideline 201
  - Remarks: Based on data from similar materials

### Toxicity to microorganisms
- **EC10 (Pseudomonas putida):** > 100 mg/l
Exposure time: 16 h
Test substance: Water Accommodated Fraction
Remarks: Based on data from similar materials

Persistence and degradability

Components:

Cellulose:
Biodegradability: Result: Readily biodegradable.

Ezetimibe:
Biodegradability: Result: Not readily biodegradable.
Biodegradation: 6.8 %
Exposure time: 28 d

Stability in water: Hydrolysis: 50 % (4.5 d)
Method: OECD Test Guideline 111

Simvastatin:
Biodegradability: Result: rapidly degradable
Stability in water: Hydrolysis: 50 % (3.2 d)

Magnesium stearate:
Biodegradability: Result: Not biodegradable
Remarks: Based on data from similar materials

Bioaccumulative potential

Components:

Ezetimibe:
Bioaccumulation: Species: Lepomis macrochirus (Bluegill sunfish)
Bioconcentration factor (BCF): 173
Exposure time: 97 d
Method: OECD Test Guideline 305

Partition coefficient: n-octanol/water: log Pow: 4.36

Simvastatin:
Partition coefficient: n-octanol/water: log Pow: > 4.07

Magnesium stearate:
Partition coefficient: n-octanol/water: log Pow: > 4
Mobility in soil

Components:

Ezetimibe:
Distribution among environmental compartments: log Koc: 4.35
Method: OECD Test Guideline 106

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
UN number: UN 3077
Proper shipping name: ENVIRONMENTALLY HAZARDOUS SUBSTANCE, SOLID, N.O.S. (Ezetimibe, Simvastatin)
Class: 9
Packing group: III
Labels: Miscellaneous

IATA-DGR
UN/ID No.: UN 3077
Proper shipping name: Environmentally hazardous substance, solid, n.o.s. (Ezetimibe, Simvastatin)
Class: 9
Packing group: III
Labels: Miscellaneous
Packing instruction (cargo aircraft): 956
Packing instruction (passenger aircraft): 956
Environmentally hazardous: yes

IMDG-Code
UN number: UN 3077
Proper shipping name: ENVIRONMENTALLY HAZARDOUS SUBSTANCE, SOLID, N.O.S. (Ezetimibe, Simvastatin)
Class: 9
Packing group: III
SAFETY DATA SHEET

Ezetimibe / Simvastatin Formulation

Version 5.5  Revision Date: 09/13/2019  SDS Number: 28126-00014  Date of last issue: 2019/04/24  Date of first issue: 2014/11/04

Labels: 9
EmS Code: F-A, S-F
Marine pollutant: yes

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.

Special precautions for user
The transport classification(s) provided herein are for informational purposes only, and solely based upon the properties of the unpackaged material as it is described within this Safety Data Sheet. Transportation classifications may vary by mode of transportation, package sizes, and variations in regional or country regulations.

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
Article 57-2 (Enforcement Order Table 9)

<table>
<thead>
<tr>
<th>Chemical name</th>
<th>Number</th>
<th>Concentration (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Magnesium stearate</td>
<td>327</td>
<td>&gt;=1 - &lt;10</td>
</tr>
</tbody>
</table>

Substances Subject to be Indicated Names
Article 57 (Enforcement Order Article 18)

<table>
<thead>
<tr>
<th>Chemical name</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Magnesium stearate</td>
<td>327</td>
</tr>
</tbody>
</table>
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
Miscellaneous dangerous substances and articles (Article 2 and 3 of rules on shipping and storage of dangerous goods and its Attached Table 1)

Aviation Law
Miscellaneous dangerous substances and articles (Article 194 of The Enforcement Rules of Aviation Law and its Attached Table 1)

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

Sources of key data used to compile the Safety Data Sheet

Date format
yyyymm/dd

Full text of other abbreviations

ACGIH : USA. ACGIH Threshold Limit Values (TLV)
ACGIH / TWA : 8-hour, time-weighted average

AlCS - Australian Inventory of Chemical Substances; ANTT - National Agency for Transport by Land of Brazil; ASTM - American Society for the Testing of Materials; bw - Body weight; CMR - Carcinogen, Mutagen or Reproductive Toxicant; DIN - Standard of the German Institute for Standardisation; DSL - Domestic Substances List (Canada); 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; ERG - Emergency Response Guide; 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; KECI - 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; Nch - Chilean Norm; NO(A)EC - No Observed (Adverse) Effect Concentration; NO(A)EL - No Observed (Adverse) Effect Level; NOELR - No Observable Effect Loading Rate; NOM - Official Mexican Norm; NTP - National Toxicology Program; NZIoC - New Zealand Inventory of Chemicals; OECD - Organization for Economic Co-operation and Development; OPPTS - Office of Chemical Safety and Pollution Prevention; PBT - Persistent, Bioaccumulative and Toxic substance; PICCS - Philippines Inventory of Chemicals and Chemical Substances; (Q)SAR - (Quantitative) Structure Activity Relationship; REACH - Regulation (EC) No 1907/2006 of the European Parliament and of the Council concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals; SADT - Self-Accelerating Decomposition Temperature; SDS - Safety Data Sheet; TCSI - Taiwan Chemical Substance Inventory; TDG - Transportation of Dangerous Goods; TSCA - Toxic Substances Control Act (United States); UN - United Nations; UNRTDG - United Nations Recommendations on the Transport of Dangerous Goods; vPvB - Very Persistent and Very Bioaccumulative; WHMIS - Workplace Hazardous Materials Information System

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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