1. PRODUCT AND COMPANY IDENTIFICATION

Product name : Ezetimibe / Rosuvastatin 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
Carcinogenicity : Category 1B
Reproductive toxicity : Category 1B
Specific target organ toxicity - single exposure (Oral) : Category 2 (Liver, Kidney, muscle)
Specific target organ toxicity - repeated exposure (Oral) : Category 2 (Eye)
Long-term (chronic) aquatic hazard : Category 2

GHS label elements
Hazard pictograms : 

Signal word : Danger
Hazard statements : H350 May cause cancer.
H360FD May damage fertility. May damage the unborn child.
H371 May cause damage to organs (Liver, Kidney, muscle) if swallowed.
H373 May cause damage to organs (Eye) through prolonged or repeated exposure if swallowed.
H411 Toxic to aquatic life with long lasting effects.
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.
- P264 Wash skin thoroughly after handling.
- P270 Do not eat, drink or smoke when using this product.
- P273 Avoid release to the environment.
- P280 Wear protective gloves/protective clothing/eye protection/face protection.

**Response:**
- P308 + P311 IF exposed or concerned: Call a POISON CENTER/doctor.
- P391 Collect spillage.

**Storage:**
- P405 Store locked up.

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

**Other hazards which do not result in classification**

Important symptoms and outlines of the emergency assumed:
- Dust contact with the eyes can lead to mechanical irritation.
- 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;= 10 - &lt; 20</td>
<td></td>
</tr>
<tr>
<td>Ezetimibe</td>
<td>163222-33-1</td>
<td>&gt;= 2.5 - &lt; 10</td>
<td></td>
</tr>
<tr>
<td>Rosuvastatin</td>
<td>147098-20-2</td>
<td>&gt;= 2.5 - &lt; 10</td>
<td></td>
</tr>
<tr>
<td>Sodium n-dodecyl sulfate</td>
<td>151-21-3</td>
<td>1.43</td>
<td>2-1679</td>
</tr>
<tr>
<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.

**In case of skin contact:**
In case of contact, immediately flush skin with 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.
- Never give anything by mouth to an unconscious person.

Most important symptoms and effects, both acute and delayed:
- May cause cancer.
- May damage fertility. May damage the unborn child.
- May cause damage to organs if swallowed.
- May cause damage to organs through prolonged or repeated exposure if swallowed.
- 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
- Fluorine compounds
- Nitrogen oxides (NOx)
- Sulphur oxides
- Metal oxides

Specific extinguishing methods:
- Use extinguishing measures that are appropriate to local circumstances and the surrounding environment.
- Use water spray to cool unopened containers.
- Remove undamaged containers from fire area if it is safe to do so.
- Evacuate area.

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

6. ACCIDENTAL RELEASE MEASURES

Personal precautions, protective equipment and emergency procedures:
- Use personal protective equipment.
- Follow safe handling advice and personal protective equipment recommendations.
Environmental precautions: Discharge into the environment must be avoided. Prevent further leakage or spillage if safe to do so. Retain and dispose of contaminated wash water. Local authorities should be advised if significant spillages cannot be contained.

Methods and materials for containment and cleaning up: Sweep up or vacuum up spillage and collect in suitable container for disposal. Avoid dispersal of dust in the air (i.e., clearing dust surfaces with compressed air). Dust deposits should not be allowed to accumulate on surfaces, as these may form an explosive mixture if they are released into the atmosphere in sufficient concentration. Local or national regulations may apply to releases and disposal of this material, as well as those materials and items employed in the cleanup of releases. You will need to determine which regulations are applicable. Sections 13 and 15 of this SDS provide information regarding certain local or national requirements.

### 7. HANDLING AND STORAGE

**Handling**

**Technical measures:** Static electricity may accumulate and ignite suspended dust causing an explosion. Provide adequate precautions, such as electrical grounding and bonding, or inert atmospheres.

**Local/Total ventilation:** If sufficient ventilation is unavailable, use with local exhaust ventilation.

**Advice on safe handling:** Do not get on skin or clothing. Do not breathe dust. Do not swallow. Avoid contact with eyes. Handle in accordance with good industrial hygiene and safety practice, based on the results of the workplace exposure assessment. Keep container tightly closed. Minimize dust generation and accumulation. Keep container closed when not in use. Keep away from heat and sources of ignition. Take precautionary measures against static discharges. Take care to prevent spills, waste and minimize release to the environment.

**Avoidance of contact:** Oxidizing agents

**Hygiene measures:** If exposure to chemical is likely during typical use, provide eye flushing systems and safety showers close to the working place. When using do not eat, drink or smoke. Wash contaminated clothing before re-use. The effective operation of a facility should include review of engineering controls, proper personal protective equipment, appropriate degowning and decontamination procedures, industrial hygiene monitoring, medical surveillance and the use of administrative controls.
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>Rosuvastatin</td>
<td>147098-20-2</td>
<td>TWA</td>
<td>20 µg/m³ (OEB 3)</td>
<td>Internal</td>
</tr>
<tr>
<td>Magnesium stearate</td>
<td>557-04-0</td>
<td>Wipe limit (Inhalable fraction)</td>
<td>10 mg/m³</td>
<td>ACGIH</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA (Respirable fraction)</td>
<td>3 mg/m³</td>
<td>ACGIH</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 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
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>white to off-white</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>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>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>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>
</tbody>
</table>
SAFETY DATA SHEET

Ezetimibe / Rosuvastatin Formulation

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 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.

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

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
### Acute Inhalation Toxicity
- LD50 (Mouse): > 5,000 mg/kg
- LD50 (Dog): > 3,000 mg/kg

### 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

### Rosuvastatin
- **Acute oral toxicity**
  - LD50 (Rat): > 2,000 mg/kg
  - Target Organs: Liver, Stomach, muscle, Kidney

### Sodium n-dodecyl sulfate
- **Acute oral toxicity**
  - LD50 (Rat): 1,200 mg/kg
  - Method: OECD Test Guideline 401
- **Acute dermal toxicity**
  - LD50 (Rat): > 2,000 mg/kg
  - Method: OECD Test Guideline 402
  - Remarks: Based on data from similar materials

### 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
Not classified based on available information.

### Components

#### Ezetimibe
- **Species**
  - Rabbit
- **Result**
  - No skin irritation

#### Sodium n-dodecyl sulfate
- **Species**
  - Rabbit
- **Result**
  - Skin irritation

#### Magnesium stearate
### SAFETY DATA SHEET

**Ezetimibe / Rosuvastatin Formulation**

<table>
<thead>
<tr>
<th>Version</th>
<th>Revision Date:</th>
<th>SDS Number:</th>
<th>Date of last issue:</th>
<th>Date of first issue:</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.4</td>
<td>09/13/2019</td>
<td>3177576-00005</td>
<td>2019/04/24</td>
<td>2018/09/18</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Species</th>
<th>Result</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rabbit</td>
<td>No skin irritation</td>
<td>Based on data from similar materials</td>
</tr>
</tbody>
</table>

**Serious eye damage/eye irritation**

Not classified based on available information.

### Components:

**Ezetimibe:**

<table>
<thead>
<tr>
<th>Species</th>
<th>Result</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rabbit</td>
<td>No eye irritation</td>
<td>Based on data from similar materials</td>
</tr>
</tbody>
</table>

**Sodium n-dodecyl sulfate:**

<table>
<thead>
<tr>
<th>Species</th>
<th>Result</th>
<th>Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rabbit</td>
<td>Irreversible effects on the eye</td>
<td>OECD Test Guideline 405</td>
</tr>
</tbody>
</table>

**Magnesium stearate:**

<table>
<thead>
<tr>
<th>Species</th>
<th>Result</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rabbit</td>
<td>No eye irritation</td>
<td>Based on data from similar materials</td>
</tr>
</tbody>
</table>

### Respiratory or skin sensitisation

**Skin sensitisation**

Not classified based on available information.

**Respiratory sensitisation**

Not classified based on available information.

### Components:

**Ezetimibe:**

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

**Sodium n-dodecyl sulfate:**

<table>
<thead>
<tr>
<th>Test Type</th>
<th>Exposure routes</th>
<th>Species</th>
<th>Result</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maximisation Test</td>
<td>Skin contact</td>
<td>Guinea pig</td>
<td>negative</td>
<td>Based on data from similar materials</td>
</tr>
</tbody>
</table>

**Magnesium stearate:**

<table>
<thead>
<tr>
<th>Test Type</th>
<th>Exposure routes</th>
<th>Species</th>
<th>Method</th>
<th>Result</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maximisation Test</td>
<td>Skin contact</td>
<td>Guinea pig</td>
<td>OECD Test Guideline 406</td>
<td>negative</td>
<td>Based on data from similar materials</td>
</tr>
</tbody>
</table>
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

**Rosuvastatin:**
Genotoxicity in vitro: Test Type: Bacterial reverse mutation assay (AMES)  
Test system: Escherichia coli  
Result: negative  
Test Type: Chromosomal aberration  
Test system: Chinese hamster lung cells  
Result: negative

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

**Sodium n-dodecyl sulfate:**
Genotoxicity in vitro: Test Type: Bacterial reverse mutation assay (AMES)  
Method: OECD Test Guideline 471
## SAFETY DATA SHEET

### Ezetimibe / Rosuvastatin Formulation

<table>
<thead>
<tr>
<th>Version</th>
<th>Revision Date</th>
<th>SDS Number</th>
<th>Date of last issue</th>
<th>Date of first issue</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.4</td>
<td>09/13/2019</td>
<td>3177576-00005</td>
<td>2019/04/24</td>
<td>2018/09/18</td>
</tr>
</tbody>
</table>

Result: negative

Test Type: In vitro mammalian cell gene mutation test
Result: negative

**Genotoxicity in vivo**

Test Type: Rodent dominant lethal test (germ cell) (in vivo)
Species: Mouse
Application Route: Ingestion
Result: negative

**Magnesium stearate**

Genotoxicity in vitro
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

May cause cancer.

### Components:

#### Cellulose:

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

#### 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
Rosuvastatin:
Species: Rat
Application Route: Oral
Exposure time: 104 weeks
LOAEL: 80 mg/kg body weight
Result: positive
Symptoms: Tumour
Target Organs: Uterus (including cervix)
Species: Mouse
Application Route: Oral
Exposure time: 107 weeks
LOAEL: 200 mg/kg body weight
Result: positive
Symptoms: liver adenoma, carcinoma
Target Organs: Liver

Sodium n-dodecyl sulfate:
Species: Rat
Application Route: Ingestion
Exposure time: 2 Years
Method: OECD Test Guideline 453
Result: negative
Remarks: Based on data from similar materials

Reproductive toxicity
May damage fertility. 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

Ezetimibe:
Effects on fertility: Test Type: Fertility/early embryonic development
Species: Rat, male and female
Fertility: NOAEL: > 1,000 mg/kg body weight
Result: No effects on fertility, No fetotoxicity

Effects on foetal development: Test Type: Development
Species: Rat
Application Route: Oral
Developmental Toxicity: NOAEL: > 1,000 mg/kg body weight
Result: No adverse effects
SAFETY DATA SHEET

Ezetimibe / Rosuvastatin Formulation

Version 1.4  Revision Date: 09/13/2019  SDS Number: 3177576-00005  Date of last issue: 2019/04/24  Date of first issue: 2018/09/18

Test Type: Development  
Species: Rabbit  
Application Route: Oral  
Developmental Toxicity: NOAEL: > 1,000 mg/kg body weight  
Result: No adverse effects

**Rosuvastatin:**

**Effects on fertility** : Test Type: Fertility  
Species: Rat  
Application Route: Oral  
Fertility: NOAEL: 50 mg/kg body weight

Test Type: Fertility  
Species: Monkey  
Application Route: Oral  
Fertility: LOAEL: 30 mg/kg body weight  
Result: Effects on male and female reproductive organs.

**Effects on foetal development** : Test Type: Development  
Species: Rat  
Application Route: Oral  
Developmental Toxicity: LOAEL: 50 mg/kg body weight  
Result: foetal mortality

Test Type: Development  
Species: Rabbit  
Application Route: Oral  
Developmental Toxicity: LOAEL: 3 mg/kg body weight  
Result: foetal mortality, Maternal toxicity observed.

Reproductive toxicity - Assessment : May damage fertility. May damage the unborn child.

**Sodium n-dodecyl sulfate:**

**Effects on fertility** : Test Type: Two-generation reproduction toxicity study  
Species: Rat  
Application Route: Ingestion  
Method: OECD Test Guideline 416  
Result: negative  
Remarks: Based on data from similar materials

**Effects on foetal development** : Test Type: Embryo-foetal development  
Species: Rat  
Application Route: Ingestion  
Result: negative  
Remarks: Based on data from similar materials

**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
Ezetimibe / Rosuvastatin Formulation

Effects on foetal development
Test Type: Embryo-foetal development
Species: Rat
Application Route: Ingestion
Result: negative
Remarks: Based on data from similar materials

STOT - single exposure
May cause damage to organs (Liver, Kidney, muscle) if swallowed.

Components:
Rosuvastatin:
Exposure routes: Oral
Target Organs: Liver, Kidney, muscle
Assessment: Causes damage to organs.

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

Components:
Rosuvastatin:
Exposure routes: Oral
Target Organs: 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
### Ezetimibe / Rosuvastatin Formulation

<table>
<thead>
<tr>
<th>NOAEL</th>
<th>500 mg/kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Application Route</td>
<td>Oral</td>
</tr>
<tr>
<td>Exposure time</td>
<td>90 d</td>
</tr>
<tr>
<td>Remarks</td>
<td>No significant adverse effects were reported</td>
</tr>
</tbody>
</table>

**Species**: Dog

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

---

**Rosuvastatin**

<table>
<thead>
<tr>
<th>LOAEL</th>
<th>90 mg/kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Application Route</td>
<td>Oral</td>
</tr>
<tr>
<td>Exposure time</td>
<td>24 Days</td>
</tr>
<tr>
<td>Target Organs</td>
<td>Brain</td>
</tr>
<tr>
<td>Symptoms</td>
<td>Oedema, Blood disorders, Necrosis</td>
</tr>
<tr>
<td>Remarks</td>
<td>Based on data from similar materials</td>
</tr>
</tbody>
</table>

**Species**: Dog

**LOAEL**: 6 mg/kg
**Application Route**: Oral
**Exposure time**: 52 Weeks
**Target Organs**: Cornea
**Symptoms**: Corneal opacity
**Remarks**: Based on data from similar materials

**Species**: Dog

**LOAEL**: 30 mg/kg
**Application Route**: Oral
**Exposure time**: 12 Weeks
**Target Organs**: Eye
**Symptoms**: Eye disease
**Remarks**: Based on data from similar materials

**Species**: Dog

**LOAEL**: 90 mg/kg
**Application Route**: Oral
**Exposure time**: 4 Weeks
**Target Organs**: eye - retina
**Symptoms**: Eye disease
**Remarks**: Based on data from similar materials

---

**Sodium n-dodecyl sulfate**

<table>
<thead>
<tr>
<th>NOAEL</th>
<th>488 mg/kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Application Route</td>
<td>Ingestion</td>
</tr>
<tr>
<td>Exposure time</td>
<td>90 Days</td>
</tr>
<tr>
<td>Remarks</td>
<td>Based on data from similar materials</td>
</tr>
</tbody>
</table>

**Species**: Rat

---

**Magnesium stearate**

<table>
<thead>
<tr>
<th>Species</th>
<th>Rat</th>
</tr>
</thead>
</table>

---

15 / 25
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

**Rosuvastatin:**
Ingestion: Target Organs: Kidney
Symptoms: kidney toxicity
Remarks: Based on Human Evidence
Target Organs: muscle
Symptoms: musculoskeletal pain
Remarks: Based on Human Evidence
Target Organs: Liver
Symptoms: liver function change
Remarks: Based on Human Evidence

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

**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 |

| Rosuvastatin: |
| Toxicity to fish | LC50 (Pimephales promelas (fathead minnow)): > 1,000 mg/l  
| Exposure time: 96 hrs  
| Method: FDA 4.11  
| LC50 (Lepomis macrochirus (Bluegill sunfish)): > 1,000 mg/l  
| Exposure time: 96 hrs  
| Method: FDA 4.11 |

| Toxicity to daphnia and other aquatic invertebrates | EC50 (Daphnia magna (Water flea)): 63 mg/l  
| Exposure time: 48 hrs  
| Method: OECD Test Guideline 202 |

| Toxicity to algae/aquatic plants | EC50 (Microcystis aeruginosa (blue-green algae)): > 640 mg/l  
| Exposure time: 96 hrs |
Method: FDA 4.01

NOEC (Microcystis aeruginosa (blue-green algae)): 330 mg/l
Exposure time: 96 hrs
Method: FDA 4.01

EC50 (Pseudokirchneriella subcapitata (green algae)): > 800 mg/l
Exposure time: 96 hrs
Method: FDA 4.01

NOEC (Pseudokirchneriella subcapitata (green algae)): 350 mg/l
Exposure time: 96 hrs
Method: FDA 4.01

Toxicity to fish (Chronic toxicity):
NOEC (Pimephales promelas (fathead minnow)): 1 mg/l
Exposure time: 32 Days
Method: OECD Test Guideline 210

Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity):
NOEC (Daphnia magna (Water flea)): 0.018 mg/l
Exposure time: 21 Days
Method: OECD Test Guideline 211

M-Factor (Chronic aquatic toxicity):
EC50: > 100 mg/l
Exposure time: 3 hrs
Test Type: Respiration inhibition
Method: OECD Test Guideline 209

NOEC: 100 mg/l
Exposure time: 3 hrs
Test Type: Respiration inhibition
Method: OECD Test Guideline 209

**Sodium n-dodecyl sulfate:**

Toxicity to fish:
LC50 (Pimephales promelas (fathead minnow)): 29 mg/l
Exposure time: 96 h

Toxicity to daphnia and other aquatic invertebrates:
EC50 (Ceriodaphnia dubia (water flea)): 5.55 mg/l
Exposure time: 48 h

Toxicity to algae/aquatic plants:
ErC50 (Desmodesmus subspicatus (green algae)): > 120 mg/l
Exposure time: 72 h

NOEC (Desmodesmus subspicatus (green algae)): 30 mg/l
Exposure time: 72 h

Toxicity to fish (Chronic toxicity):
NOEC (Pimephales promelas (fathead minnow)): >= 1.357 mg/l
Exposure time: 42 d

Toxicity to daphnia and other:
NOEC (Ceriodaphnia dubia (water flea)): 0.88 mg/l
aquatic invertebrates (Chronic toxicity)
Toxicity to microorganisms
Exposure time: 7 d
EC50: 135 mg/l
Exposure time: 3 h

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

Toxicity to daphnia and other aquatic invertebrates
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 algae/aquatic plants
EL50 (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
No toxicity at the limit of solubility

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
### Rosuvastatin:
- **Biodegradability**: Biodegradation: < 10 %
  - Exposure time: 28 Days
  - Method: OECD Test Guideline 301F
  - Remarks: Not inherently biodegradable.
- **Stability in water**: Hydrolysis: < 10 % (5 Days)

### Sodium n-dodecyl sulfate:
- **Biodegradability**: Result: Readily biodegradable.
  - Biodegradation: 95 %
  - Exposure time: 28 d
  - Method: OECD Test Guideline 301B

### 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

**Rosuvastatin**
- **Partition coefficient: n-octanol/water**: log Pow: 0.3

**Sodium n-dodecyl sulfate**
- **Partition coefficient: n-octanol/water**: log Pow: 0.83

**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

**Rosuvastatin**
- **Distribution among environmental compartments**: log Koc: 2.15
  - Method: FDA 3.08
11. HAZARDS IDENTIFICATION

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, Rosuvastatin)
Class: 9
Packing group: III
Labels: 9

IATA-DGR
UN/ID No.: UN 3077
Proper shipping name: Environmentally hazardous substance, solid, n.o.s. (Ezetimibe, Rosuvastatin)
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, Rosuvastatin)
Class: 9
Packing group: III
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
Priority Assessment Chemical Substance

<table>
<thead>
<tr>
<th>Chemical name</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium alkyl(C=8-18) sulfate</td>
<td>214</td>
</tr>
</tbody>
</table>

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

Class I Designated Chemical Substances

<table>
<thead>
<tr>
<th>Chemical name</th>
<th>Number</th>
<th>Concentration (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium Lauryl Sulfate</td>
<td>275</td>
<td>1.4</td>
</tr>
</tbody>
</table>

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
SAFETY DATA SHEET

Ezetimibe / Rosuvastatin Formulation

Version 1.4   Revision Date: 09/13/2019   SDS Number: 3177576-00005   Date of last issue: 2019/04/24

16. OTHER INFORMATION

Further information

Date format: yyyy/mm/dd

Full text of other abbreviations
ACGIH: USA. ACGIH Threshold Limit Values (TLV)

ACGIH / TWA: 8-hour, time-weighted average

AICS - 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.
<table>
<thead>
<tr>
<th>Version</th>
<th>Revision Date:</th>
<th>SDS Number:</th>
<th>Date of last issue:</th>
<th>Date of first issue:</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.4</td>
<td>09/13/2019</td>
<td>3177576-00005</td>
<td>2019/04/24</td>
<td>2018/09/18</td>
</tr>
</tbody>
</table>

JP / EN