1. PRODUCT AND COMPANY IDENTIFICATION

Product name: Ezetimibe / Simvastatin Formulation

Manufacturer or supplier’s details
Company: MSD
Address: 50 Tuas West Drive
Singapore - Singapore 638408
Telephone: 908-740-4000
Emergency telephone number: 65 6697 2111 (24/7/365)
E-mail address: EHSDATASTEWARD@msd.com
Telefax: 908-735-1496

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)
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.
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 
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>
</tr>
</thead>
<tbody>
<tr>
<td>Cellulose</td>
<td>9004-34-6</td>
<td>&gt;= 10 - &lt; 20</td>
</tr>
<tr>
<td>Ezetimibe</td>
<td>163222-33-1</td>
<td>&gt;= 10 - &lt; 20</td>
</tr>
<tr>
<td>Simvastatin</td>
<td>79902-63-9</td>
<td>&gt;= 10 - &lt; 20</td>
</tr>
<tr>
<td>Magnesium stearate</td>
<td>557-04-0</td>
<td>&gt;= 1 - &lt; 10</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 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 re-
leased 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

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.

Conditions for safe storage: Keep in properly labelled containers.

Materials to avoid: Do not store with the following product types: Strong oxidizing agents

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Components with workplace control parameters

<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>PEL (long term)</td>
<td>10 mg/m³</td>
<td>SG OEL</td>
</tr>
<tr>
<td></td>
<td></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></td>
<td></td>
<td>Wipe limit</td>
<td>250 µg/100 cm²</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></td>
<td></td>
<td>Further information: DSEN</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Wipe limit</td>
<td>250 µg/100 cm²</td>
<td>Internal</td>
</tr>
<tr>
<td>Magnesium stearate</td>
<td>557-04-0</td>
<td>PEL (long term)</td>
<td>10 mg/m³</td>
<td>SG OEL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA (Inhalable fraction)</td>
<td>10 mg/m³</td>
<td>ACGIH</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA (Res-3)</td>
<td>3 mg/m³</td>
<td>ACGIH</td>
</tr>
</tbody>
</table>
SAFETY DATA SHEET

Ezetimibe / Simvastatin Formulation

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: Material: Chemical-resistant gloves

Skin and body protection: Material: 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.

Hygiene measures: Material: 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.

9. PHYSICAL AND CHEMICAL PROPERTIES

Appearance: powder

Colour: No data available

Odour: No data available
# SAFETY DATA SHEET

## Ezetimibe / Simvastatin 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>
</table>

- **Odour Threshold**: No data available
- **pH**: No data available
- **Melting point/freezing point**: No data available
- **Initial boiling point and boiling range**: No data available
- **Flash point**: No data available
- **Evaporation rate**: No data available
- **Flammability (solid, gas)**: May form explosive dust-air mixture during processing, handling or other means.
- **Flammability (liquids)**: No data available
- **Upper explosion limit / Upper flammability limit**: No data available
- **Lower explosion limit / Lower flammability limit**: No data available
- **Vapour pressure**: No data available
- **Relative vapour density**: No data available
- **Relative density**: No data available
- **Solubility(ies)**
  - **Water solubility**: No data available
- **Partition coefficient: n-octanol/water**: No data available
- **Auto-ignition temperature**: No data available
- **Decomposition temperature**: No data available
- **Viscosity**
  - **Viscosity, kinematic**: No data available
- **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.
SAFETY DATA SHEET

Ezetimibe / Simvastatin Formulation

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
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:**
- Test Type: Maximisation Test
- Species: Guinea pig
- Result: negative

**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

<table>
<thead>
<tr>
<th>Test Type</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacterial reverse mutation assay (AMES)</td>
<td>negative</td>
</tr>
<tr>
<td>Alkaline elution assay</td>
<td>negative</td>
</tr>
<tr>
<td>Chromosomal aberration</td>
<td>negative</td>
</tr>
<tr>
<td>In vitro mammalian cell gene mutation test</td>
<td>negative</td>
</tr>
</tbody>
</table>

Genotoxicity in vivo

<table>
<thead>
<tr>
<th>Test Type</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Micronucleus test</td>
<td>negative</td>
</tr>
</tbody>
</table>

Germ cell mutagenicity - Assessment

Weight of evidence does not support classification as a germ cell mutagen.

**Magnesium stearate:**

Genotoxicity in vitro

<table>
<thead>
<tr>
<th>Test Type</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>In vitro mammalian cell gene mutation test</td>
<td>negative</td>
</tr>
</tbody>
</table>

Remarks: Based on data from similar materials

Carcinogenicity

Not classified based on available information.

**Components:**

**Cellulose:**

<table>
<thead>
<tr>
<th>Species</th>
<th>Rat</th>
</tr>
</thead>
<tbody>
<tr>
<td>Application Route</td>
<td>Ingestion</td>
</tr>
<tr>
<td>Exposure time</td>
<td>72 weeks</td>
</tr>
<tr>
<td>Result</td>
<td>negative</td>
</tr>
</tbody>
</table>

**Ezetimibe:**

<table>
<thead>
<tr>
<th>Species</th>
<th>Rat, female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Application Route</td>
<td>oral (feed)</td>
</tr>
<tr>
<td>Exposure time</td>
<td>104 weeks</td>
</tr>
</tbody>
</table>
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
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
Test Type: Development  
Species: Rabbit  
Application Route: Oral  
Developmental Toxicity: NOAEL: > 1,000 mg/kg body weight  
Result: No adverse effects

**Simvastatin:**

<table>
<thead>
<tr>
<th>Test Type</th>
<th>Species</th>
<th>Application Route</th>
<th>Toxicity</th>
<th>Result</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Effects on fertility</td>
<td>Test Type: Fertility</td>
<td>Species: Rat, male</td>
<td>Application Route: Oral</td>
<td>Fertility: LOAEL: 25 mg/kg body weight</td>
<td>No adverse effects</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Test Type</th>
<th>Species</th>
<th>Application Route</th>
<th>Toxicity</th>
<th>Result</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Effects on foetal development</td>
<td>Test Type: Embryo-foetal development</td>
<td>Species: Rat</td>
<td>Application Route: Oral</td>
<td>Embryo-foetal toxicity: NOAEL: 25 mg/kg body weight</td>
<td>No teratogenic effects, No adverse effects</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Test Type</th>
<th>Species</th>
<th>Application Route</th>
<th>Toxicity</th>
<th>Result</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Effects on foetal development</td>
<td>Test Type: Embryo-foetal development</td>
<td>Species: Rabbit</td>
<td>Application Route: Oral</td>
<td>Embryo-foetal toxicity: NOAEL: 10 mg/kg body weight</td>
<td>No teratogenic effects, No adverse effects</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Test Type</th>
<th>Species</th>
<th>Application Route</th>
<th>Toxicity</th>
<th>Result</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Effects on foetal development</td>
<td>Test Type: Embryo-foetal development</td>
<td>Species: Rat</td>
<td>Application Route: Oral</td>
<td>Embryo-foetal toxicity: LOAEL: 60 mg/kg body weight</td>
<td>Teratogenic potential</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Test Type</th>
<th>Species</th>
<th>Application Route</th>
<th>Toxicity</th>
<th>Result</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Embryo-foetal toxicity</td>
<td>Test Type: Embryo-foetal development</td>
<td>Species: Rat</td>
<td>Application Route: Oral</td>
<td>Embryo-foetal toxicity: LOAEL: 10 mg/kg body weight</td>
<td>No teratogenic effects, No adverse effects</td>
</tr>
</tbody>
</table>

**Magnesium stearate:**

<table>
<thead>
<tr>
<th>Test Type</th>
<th>Species</th>
<th>Application Route</th>
<th>Toxicity</th>
<th>Result</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Effects on fertility</td>
<td>Test Type: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test</td>
<td>Species: Rat</td>
<td>Application Route: Ingestion</td>
<td>Method: OECD Test Guideline 422</td>
<td>negative</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Test Type</th>
<th>Species</th>
<th>Application Route</th>
<th>Toxicity</th>
<th>Result</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Effects on foetal development</td>
<td>Test Type: Embryo-foetal development</td>
<td>Species: Rat</td>
<td>Application Route: Ingestion</td>
<td>Result: negative</td>
<td>Remarks: Based on data from similar materials</td>
</tr>
</tbody>
</table>

**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**: $\geq 9,000$ 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
Ezetimibe / Simvastatin Formulation

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
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

Toxicity to algae/aquatic plants

Toxicity to fish (Chronic toxicity)

Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity)

M-Factor (Chronic aquatic toxicity)

Toxicity to microorganisms

Simvastatin:

Toxicity to fish

Toxicity to daphnia and other aquatic invertebrates
Method: OECD Test Guideline 202

**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:**

**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

**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
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: 9

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
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.

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
15. REGULATORY INFORMATION

Safety, health and environmental regulations/legislation specific for the substance or mixture

Workplace Safety and Health Act and Workplace Safety and Health (General Provisions) Regulations: This product is subjected to the SDS, labelling, PEL and other requirements in the Act/Regulations.

Environmental Protection and Management Act and Environmental Protection and Management (Hazardous Substances) Regulations: Not applicable

Fire Safety (Petroleum and Flammable Materials) Regulations: Not applicable

The components of this product are reported in the following inventories:

<table>
<thead>
<tr>
<th>Inventory</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
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<td>DSL</td>
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<tr>
<td>IECSC</td>
<td>not determined</td>
</tr>
</tbody>
</table>

16. OTHER INFORMATION

Further information


Date format: dd.mm.yyyy

Full text of other abbreviations

ACGIH: USA. ACGIH Threshold Limit Values (TLV)
SG OEL: Singapore. Workplace Safety and Health Act - First Schedule Permissible Exposure Limits of Toxic Substances
ACGIH / TWA: 8-hour, time-weighted average
SG OEL / PEL (long term): Permissible Exposure Level (PEL) Long Term

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
SAFETY DATA SHEET

Ezetimibe / Simvastatin 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>
</table>

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.

SG / EN