SECTION 1. PRODUCT AND COMPANY IDENTIFICATION

Product name : Ezetimibe / Simvastatin Formulation

Manufacturer or supplier’s details
Company : MSD
Address : Rua Treze de Maio, 1161
Campinas, São Paulo, Brazil 13106-054
Telephone : 908-740-4000
Emergency telephone : 55 19 3758 2000
E-mail address : EHSDATASTEWARD@msd.com
Telefax : 908-735-1496

Recommended use of the chemical and restrictions on use
Recommended use : Pharmaceutical

SECTION 2. HAZARDS IDENTIFICATION

GHS Classification in accordance with ABNT NBR 14725 Standard
Skin irritation : Category 2
Skin sensitization : 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 in accordance with ABNT NBR 14725 Standard
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.
  - P273 Avoid release to the environment.
  - P280 Wear protective gloves.
- Response:
  - P314 Get medical advice/attention if you feel unwell.
  - P391 Collect spillage.

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.

**SECTION 3. COMPOSITION/INFORMATION ON INGREDIENTS**

<table>
<thead>
<tr>
<th>Substance / Mixture</th>
<th>Components</th>
<th>Chemical name</th>
<th>CAS-No.</th>
<th>Classification</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mixture</td>
<td>Cellulose</td>
<td>9004-34-6</td>
<td></td>
<td></td>
<td>&gt;= 10 - &lt; 20</td>
</tr>
<tr>
<td></td>
<td>Ezetimibe</td>
<td>163222-33-1</td>
<td>Long-term (chronic) aquatic hazard, Category 1</td>
<td>&gt;= 10 - &lt; 20</td>
<td></td>
</tr>
</tbody>
</table>
|                     | Simvastatin| 79902-63-9    | Skin irritation, Category 2
Skin sensitization, Category 1
Specific target organ toxicity - repeated exposure (Liver, muscle, optic nerve, Eye), Category 1
Short-term (acute) aquatic hazard, Category 2
Long-term (chronic) aquatic hazard, Category 2 | >= 10 - < 20 |
| Magnesium stearate  | 557-04-0   |               |         |               | >= 1 - < 5            |

**SECTION 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.
In case of skin contact: Get medical attention if symptoms occur. 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.

SECTION 5. FIRE-FIGHTING MEASURES

Suitable extinguishing media: Water spray
Alcohol-resistant foam
Carbon dioxide (CO2)
Dry chemical

Unsuitable extinguishing media: None known.

Specific hazards during fire fighting: 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 fire-fighters: In the event of fire, wear self-contained breathing apparatus. Use personal protective equipment.

SECTION 6. ACCIDENTAL RELEASE MEASURES

Personal precautions, protective equipment and emergency procedures: Use personal protective equipment. Follow safe handling advice (see section 7) and personal protective equipment recommendations (see section 8).
Environmental precautions: Avoid release to the environment. Prevent further leakage or spillage if safe to do so. Retain and dispose of contaminated wash water. Local authorities should be advised if significant spillages cannot be contained.

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

SECTION 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. Wash skin thoroughly after handling. 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. Do not eat, drink or smoke when using this product. Take care to prevent spills, waste and minimize release to the environment.

Hygiene measures: If exposure to chemical is likely during typical use, provide eye flushing systems and safety showers close to the working place. When using do not eat, drink or smoke. Contaminated work clothing should not be allowed out of the workplace. Wash contaminated clothing before re-use. The effective operation of a facility should include review of engineering controls, proper personal protective equipment, appropriate degowning and decontamination procedures, industrial hygiene monitoring, medical surveillance and the use of administrative controls.
SAFETY DATA SHEET

Ezetimibe / Simvastatin Formulation

Version 6.1  Revision Date: 16.10.2020  SDS Number: 28108-00016  Date of last issue: 23.03.2020
Date of first issue: 04.11.2014

Conditions for safe storage: Keep in properly labeled containers. Store in accordance with the particular national regulations.

Materials to avoid: Do not store with the following product types:
Strong oxidizing agents
Organic peroxides
Explosives
Gases

SECTION 8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Ingredients 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>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 particulate matter)</td>
<td>10 mg/m³</td>
<td>ACGIH</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA (Respirable particulate matter)</td>
<td>3 mg/m³</td>
<td>ACGIH</td>
</tr>
</tbody>
</table>

Further information: DSEN
Wipe limit 250 µg/100 cm² Internal

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 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.

### SECTION 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>Color</td>
<td>No data available</td>
</tr>
<tr>
<td>Odor</td>
<td>No data available</td>
</tr>
<tr>
<td>Odor 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>Vapor pressure</td>
<td>No data available</td>
</tr>
<tr>
<td>Relative vapor 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>Water solubility</td>
</tr>
<tr>
<td>Partition coefficient: n-octanol/water</td>
<td>No data available</td>
</tr>
<tr>
<td>Autoignition temperature</td>
<td>No data available</td>
</tr>
</tbody>
</table>
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

SECTION 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.

SECTION 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 sensitization

Skin sensitization
May cause an allergic skin reaction.

Respiratory sensitization
Not classified based on available information.

Components:

Ezetimibe:
Test Type: Maximization Test
Species: Guinea pig
Result: negative

Simvastatin:
Assessment: Probability or evidence of skin sensitization in humans
Result: positive

Magnesium stearate:
Test Type: Maximization Test
Routes of exposure: 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
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

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
Effects on fetal 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 fetal 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:**

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

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

Test Type: Embryo-fetal development
Species: Rabbit
Application Route: Oral
Embryo-fetal toxicity: NOAEL: 10 mg/kg body weight
Result: No teratogenic effects., No adverse effects.

Test Type: Embryo-fetal development
Species: Rat
Application Route: Oral
Embryo-fetal toxicity: LOAEL: 60 mg/kg body weight
Result: Teratogenic potential.
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
Remarks: Based on data from similar materials

Effects on fetal development:
Test Type: Embryo-fetal development
Species: Rat
Application Route: Ingestion
Result: negative
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
## Ezetimibe / Simvastatin Formulation

<table>
<thead>
<tr>
<th>Exposure time</th>
<th>90 d</th>
</tr>
</thead>
<tbody>
<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 y

**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, Diarrhea, 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

**SECTION 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)  
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
- Exposure time: 96 h
- Method: OECD Test Guideline 203

Toxicity to daphnia and other aquatic invertebrates:

- EC50 (Daphnia magna (Water flea)): 3.5 mg/l
- Exposure time: 48 h
- 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:

- EL50 (Pseudokirchneriella subcapitata (green algae)): > 1
plants
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

**SECTION 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.

**SECTION 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
SAFETY DATA SHEET

Ezetimibe / Simvastatin Formulation

Environmen tally 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.

Domestic regulation

ANTT
UN number : UN 3077
Proper shipping name : ENVIRONMENTALLY HAZARDOUS SUBSTANCE, SOLID, N.O.S. (Ezetimibe, Simvastatin)

Class : 9
Packing group : III
Labels : 9
Hazard Identification Number : 90

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.

SECTION 15. REGULATORY INFORMATION

Safety, health and environmental regulations/legislation specific for the substance or mixture
National List of Carcinogenic Agents for Humans - (LINACH) : Not applicable

Brazil, List of chemicals controlled by the Federal Police : Not applicable

International Regulations

The ingredients of this product are reported in the following inventories:
AICS : not determined
DSL : not determined
IECSC : not determined
SECTION 16. OTHER INFORMATION

Further information

Full text of other abbreviations
ACGIH : USA. ACGIH Threshold Limit Values (TLV)
ACGIH / TWA : 8-hour, time-weighted average

AIIIC - Australian Inventory of Industrial Chemicals; 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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