SAFETY DATA SHEET
Ezetimibe / Simvastatin Formulation

SECTION 1. PRODUCT AND COMPANY IDENTIFICATION

Product name : Ezetimibe / Simvastatin Formulation

Manufacturer or supplier’s details
Company : MSD
Address : 855 Leandro N. Alem St., 8 Floor
          Buenos Aires, Argentina  C1001AFB
Telephone : 908-740-4000
Emergency telephone : 1-908-423-6000
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
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
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.
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.

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>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mixture</td>
<td>Cellulose</td>
<td>9004-34-6</td>
<td>&gt;= 10 - &lt; 20</td>
</tr>
<tr>
<td></td>
<td>Mixture</td>
<td>Ezetimibe</td>
<td>163222-33-1</td>
<td>&gt;= 10 - &lt; 20</td>
</tr>
<tr>
<td></td>
<td>Mixture</td>
<td>Simvastatin</td>
<td>79902-63-9</td>
<td>&gt;= 10 - &lt; 20</td>
</tr>
<tr>
<td></td>
<td>Mixture</td>
<td>Magnesium stearate</td>
<td>557-04-0</td>
<td>&gt;= 1 - &lt; 5</td>
</tr>
</tbody>
</table>

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.
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.
In case of eye contact: Thoroughly clean shoes before reuse.
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 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.

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.
- 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 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>CMP</td>
<td>10 mg/m³</td>
<td>AR OEL</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ezetimibe</td>
<td>163222-33-1</td>
<td>TWA</td>
<td>10 mg/m³</td>
<td>ACGIH</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>25 µg/m³ (OEB 3)</td>
<td></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

### Eye protection

- **Remarks**: Consider double gloving.
- **Material**: Safety glasses with side shields or goggles.
- **Remarks**: 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

- **Material**: Work uniform or laboratory coat.
- **Remarks**: 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

### Wipe limits

<table>
<thead>
<tr>
<th>Material</th>
<th>Wipe limit</th>
<th>TWA</th>
<th>TWA (Inhale)</th>
<th>TWA (Respir)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Simvastatin</td>
<td>250 µg/100 cm²</td>
<td>25 µg/m³ (OEB 3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Magnesium stearate</td>
<td>250 µg/100 cm²</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Further information:**
- DSEN: Not classifiable as a human carcinogen: Agents which cause concern that they could be carcinogenic for humans but which cannot be assessed conclusively because of a lack of data. In vitro or animal studies do not provide indications of carcinogenicity which are sufficient to classify the agent into one of the other categories.
- Irritation: TWA (Inhalable fraction) 10 mg/m³, ACGIH
- Irritation: TWA (Respirable fraction) 3 mg/m³, ACGIH

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**Version**: 5.2  
**Revision Date**: 09/13/2019  
**SDS Number**: 28100-00014  
**Date of last issue**: 24.04.2019  
**Date of first issue**: 04.11.2014
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.

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></td>
</tr>
<tr>
<td>Water solubility</td>
<td>No data available</td>
</tr>
<tr>
<td>Partition coefficient: n-octanol/water</td>
<td>No data available</td>
</tr>
<tr>
<td>Autoignition temperature</td>
<td>No data available</td>
</tr>
<tr>
<td>Decomposition temperature</td>
<td>No data available</td>
</tr>
</tbody>
</table>
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
SAFETY DATA SHEET

Ezetimibe / Simvastatin Formulation

Version: 5.2  Revision Date: 09/13/2019  SDS Number: 28100-00014  Date of last issue: 24.04.2019  Date of first issue: 04.11.2014

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:**

<table>
<thead>
<tr>
<th>Genotoxicity in vitro</th>
<th>Test Type: Bacterial reverse mutation assay (AMES)</th>
<th>Result: negative</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Metabolic activation: with and without metabolic activation</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Result: negative</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Test Type: Chromosomal aberration</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Test system: Human lymphocytes</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Result: negative</td>
<td></td>
</tr>
</tbody>
</table>

Genotoxicity in vivo:

<table>
<thead>
<tr>
<th>Test Type: Micronucleus test</th>
<th>Species: Mouse</th>
<th>Cell type: Bone marrow</th>
</tr>
</thead>
<tbody>
<tr>
<td>Result: negative</td>
<td>Oral</td>
<td></td>
</tr>
</tbody>
</table>

**Simvastatin:**

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

Genotoxicity in vivo:

<table>
<thead>
<tr>
<th>Test Type: Micronucleus test</th>
<th>Species: Mouse</th>
<th>Cell type: Bone marrow</th>
</tr>
</thead>
<tbody>
<tr>
<td>Result: negative</td>
<td>Oral</td>
<td></td>
</tr>
</tbody>
</table>

**Germs cell mutagenicity - Assessment**

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

**Magnesium stearate:**

<table>
<thead>
<tr>
<th>Genotoxicity in vitro</th>
<th>Test Type: In vitro mammalian cell gene mutation test</th>
<th>Result: negative</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Remarks: Based on data from similar materials</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Test Type: Chromosome aberration test in vitro Method: OECD Test Guideline 473</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Result: negative</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Remarks: Based on data from similar materials</td>
<td></td>
</tr>
</tbody>
</table>

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
Species: Rat
Application Route: Ingestion
Result: negative
Effects on fetal development: Test Type: Fertility/early embryonic development
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
Results

Effects on fetal development

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
Exposure time: 90 d
Remarks: No significant adverse effects were reported

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
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 toxicity): 1

Toxicity to microorganisms: EC50: > 4,4 mg/l
Exposure time: 3 h
Test Type: Respiration inhibition
Method: OECD Test Guideline 209

Target Organs: Musculo-skeletal system
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**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
<th>Exposure Time</th>
<th>Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>LC50</td>
<td>2.91 mg/l</td>
<td>96 h</td>
<td>OECD Test Guideline 203</td>
</tr>
</tbody>
</table>

**Toxicity to daphnia and other aquatic invertebrates**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
<th>Exposure Time</th>
<th>Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>EC50</td>
<td>3.5 mg/l</td>
<td>48 h</td>
<td>OECD Test Guideline 202</td>
</tr>
</tbody>
</table>

**Toxicity to algae/aquatic plants**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
<th>Exposure Time</th>
<th>Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>EC50</td>
<td>&gt; 25 mg/l</td>
<td>96 h</td>
<td>OECD Test Guideline 209</td>
</tr>
<tr>
<td>NOEC</td>
<td>25 mg/l</td>
<td>96 h</td>
<td>OECD Test Guideline 209</td>
</tr>
</tbody>
</table>

**Toxicity to microorganisms**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
<th>Exposure Time</th>
<th>Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>EC50</td>
<td>&gt; 30 mg/l</td>
<td>3 h</td>
<td>OECD Test Guideline 209</td>
</tr>
<tr>
<td>NOEC</td>
<td>21 mg/l</td>
<td>3 h</td>
<td>OECD Test Guideline 209</td>
</tr>
</tbody>
</table>

### Magnesium stearate:

**Toxicity to fish**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
<th>Exposure Time</th>
<th>Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>LC50</td>
<td>&gt; 100 mg/l</td>
<td>48 h</td>
<td>DIN 38412</td>
</tr>
</tbody>
</table>

**Toxicity to daphnia and other aquatic invertebrates**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
<th>Exposure Time</th>
<th>Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>Remarks</td>
<td></td>
<td></td>
<td>Based on data from similar materials</td>
</tr>
</tbody>
</table>

**Toxicity to algae/aquatic plants**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
<th>Exposure Time</th>
<th>Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>EL50</td>
<td>&gt; 1 mg/l</td>
<td>72 h</td>
<td>OECD Test Guideline 201</td>
</tr>
<tr>
<td>Remarks</td>
<td></td>
<td></td>
<td>Based on data from similar materials</td>
</tr>
</tbody>
</table>
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:
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>

Partition coefficient: n-octanol/water

**Magnesium stearate:**  
Partition coefficient: n-octanol/water

**Mobility in soil**

**Components:**

**Ezetimibe:**  
Distribution among environmental compartments

**: log Koc: 4,35  
Method: OECD Test Guideline 106**

**Other adverse effects**

No data available

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**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.

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**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  
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 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
Argentina. Carcinogenic Substances and Agents Registry: Not applicable

Control of precursors and essential chemicals for the preparation of drugs: Not applicable

International Regulations
The ingredients of this product are reported in the following inventories:
AICS: not determined
DSL: not determined
IECS: not determined

SECTION 16. OTHER INFORMATION

Further information

Full text of other abbreviations
ACGIH: USA. ACGIH Threshold Limit Values (TLV)
AR OEL: Argentina. Occupational Exposure Limits
ACGIH / TWA: 8-hour, time-weighted average
AR OEL / CMP: TLV (Threshold Limit Value)
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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