SAFETY DATA SHEET
according to Regulation (EC) No. 1907/2006

Ezetimibe / Simvastatin Formulation

SECTION 1: Identification of the substance/mixture and of the company/undertaking

1.1 Product identifier
Trade name : Ezetimibe / Simvastatin Formulation

1.2 Relevant identified uses of the substance or mixture and uses advised against
Use of the Substance/Mixture : Pharmaceutical

1.3 Details of the supplier of the safety data sheet
Company : Organon & Co.
Shotton Lane
NE23 3JU Cramlington NU - Great Britain

Telephone : 44 1 670 59 30 00
E-mail address of person responsible for the SDS : EHSSTEWARD@organon.com

1.4 Emergency telephone number
215-631-6999

SECTION 2: Hazards identification

2.1 Classification of the substance or mixture

Classification (REGULATION (EC) No 1272/2008)

<table>
<thead>
<tr>
<th>Classification</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin irritation, Category 2</td>
<td>H315: Causes skin irritation.</td>
</tr>
<tr>
<td>Skin sensitisation, Category 1</td>
<td>H317: May cause an allergic skin reaction.</td>
</tr>
<tr>
<td>Specific target organ toxicity - repeated exposure, Category 1</td>
<td>H372: Causes damage to organs through prolonged or repeated exposure.</td>
</tr>
<tr>
<td>Long-term (chronic) aquatic hazard, Category 2</td>
<td>H411: Toxic to aquatic life with long lasting effects.</td>
</tr>
</tbody>
</table>

2.2 Label elements

Labelling (REGULATION (EC) No 1272/2008)

Hazard pictograms : ![Chemical Hazard Pictograms]

Signal word : Danger

Hazard statements : 
- H315 Causes skin irritation.
- H317 May cause an allergic skin reaction.
- H372 Causes damage to organs 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.
- P273 Avoid release to the environment.
- P280 Wear protective gloves.

**Response:**
- P314 Get medical advice/attention if you feel unwell.
- P391 Collect spillage.

**Hazardous components which must be listed on the label:**
Simvastatin

**2.3 Other hazards**
This substance/mixture contains no components considered to be either persistent, bioaccumulative and toxic (PBT), or very persistent and very bioaccumulative (vPvB) at levels of 0.1% or higher.
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**

**3.2 Mixtures**

<table>
<thead>
<tr>
<th>Components</th>
<th>Chemical name</th>
<th>CAS-No.</th>
<th>EC-No.</th>
<th>Index-No.</th>
<th>Registration number</th>
<th>Classification</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Ezetimibe</td>
<td>163222-33-1</td>
<td></td>
<td></td>
<td></td>
<td>Aquatic Chronic 1; H410</td>
<td>&gt;= 10 - &lt; 20</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>M-Factor (Chronic aquatic toxicity): 1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Simvastatin</td>
<td>79902-63-9</td>
<td></td>
<td></td>
<td></td>
<td>Skin Irrit. 2; H315 Skin Sens. 1; H317 STOT RE 1; H372 (Liver, muscle, optic nerve, Eye) Aquatic Chronic 2; H411</td>
<td>&gt;= 10 - &lt; 20</td>
</tr>
</tbody>
</table>

For explanation of abbreviations see section 16.

**SECTION 4: First aid measures**

**4.1 Description of 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.
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).

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.

4.2 Most important symptoms and effects, both acute and delayed

Risks: 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.

4.3 Indication of any immediate medical attention and special treatment needed

Treatment: Treat symptomatically and supportively.

SECTION 5: Firefighting measures

5.1 Extinguishing media

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

Unsuitable extinguishing media: None known.

5.2 Special hazards arising from the substance or mixture

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

5.3 Advice for firefighters

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

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.

SECTION 6: Accidental release measures

6.1 Personal precautions, protective equipment and emergency procedures

Personal precautions:
- Use personal protective equipment.
- Follow safe handling advice (see section 7) and personal protective equipment recommendations (see section 8).

6.2 Environmental precautions

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.

6.3 Methods and material for containment and cleaning up

Methods for 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.

6.4 Reference to other sections

See sections: 7, 8, 11, 12 and 13.
SECTION 7: Handling and storage

7.1 Precautions for safe handling

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

Local/Total ventilation: Use only with adequate ventilation.

Advice on safe handling: Do not get on skin or clothing. Do not breathe dust. Do not swallow. Avoid contact with eyes. 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.

7.2 Conditions for safe storage, including any incompatibilities

Requirements for storage areas and containers: Keep in properly labelled containers. Store in accordance with the particular national regulations.

Advice on common storage: Do not store with the following product types: Strong oxidizing agents Organic peroxides Explosives Gases

7.3 Specific end use(s)

Specific use(s): No data available
SECTION 8: Exposure controls/personal protection

8.1 Control parameters

### Occupational Exposure Limits

<table>
<thead>
<tr>
<th>Components</th>
<th>CAS-No.</th>
<th>Value type (Form of exposure)</th>
<th>Control parameters</th>
<th>Basis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cellulose</td>
<td>9004-34-6</td>
<td>TWA (inhalable dust)</td>
<td>10 mg/m³</td>
<td>GB EH40</td>
</tr>
</tbody>
</table>

Further information: For the purposes of these limits, respirable dust and inhalable dust are those fractions of airborne dust which will be collected when sampling is undertaken in accordance with the methods described in MDHS14/4 General methods for sampling and gravimetric analysis or respirable, thoracic and inhalable aerosols. The COSHH definition of a substance hazardous to health includes dust of any kind when present at a concentration in air equal to or greater than 10 mg.m⁻³ 8-hour TWA of inhalable dust or 4 mg.m⁻³ 8-hour TWA of respirable dust. This means that any dust will be subject to COSHH if people are exposed to dust above these levels. Some dusts have been assigned specific WELs and exposure to these must comply with the appropriate limits. Most industrial dusts contain particles of a wide range of sizes. The behaviour, deposition and fate of any particular particle after entry into the human respiratory system, and the body response that it elicits, depend on the nature and size of the particle. HSE distinguishes two size fractions for limit-setting purposes termed ‘inhalable’ and ‘respirable’. Inhalable dust approximates to the fraction of airborne material that enters the nose and mouth during breathing and is therefore available for deposition in the respiratory tract. Respirable dust approximates to the fraction that penetrates to the gas exchange region of the lung. Fuller definitions and explanatory material are given in MDHS14/4. Where dusts contain components that have their own assigned WEL, all the relevant limits should be complied with.

<table>
<thead>
<tr>
<th></th>
<th>TWA (Respirable dust)</th>
<th>4 mg/m³</th>
<th>GB EH40</th>
</tr>
</thead>
</table>

Further information: For the purposes of these limits, respirable dust and inhalable dust are those fractions of airborne dust which will be collected when sampling is undertaken in accordance with the methods described in MDHS14/4 General methods for sampling and gravimetric analysis or respirable, thoracic and inhalable aerosols. The COSHH definition of a substance hazardous to health includes dust of any kind when present at a concentration in air equal to or greater than 10 mg.m⁻³ 8-hour TWA of inhalable dust or 4 mg.m⁻³ 8-hour TWA of respirable dust. This means that any dust will be subject to COSHH if people are exposed to dust above these levels. Some dusts have been assigned specific WELs and exposure to these must comply with the appropriate limits. Most industrial dusts contain particles of a wide range of sizes. The behaviour, deposition and fate of any particular particle after entry into the human respiratory system, and the body response that it elicits, depend on the nature and size of the particle. HSE distinguishes two size fractions for limit-setting purposes termed ‘inhalable’ and ‘respirable’. Inhalable dust approximates to the fraction of airborne material that enters the nose and mouth during breathing and is therefore available for deposition in the respiratory tract. Respirable dust approximates to the fraction that penetrates to the gas exchange region of the lung. Fuller definitions and explanatory material are given in MDHS14/4. Where dusts contain components that have their own assigned WEL, all the relevant limits should be complied with.
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<table>
<thead>
<tr>
<th>STEL (inhalable dust)</th>
<th>20 mg/m³</th>
<th>GB EH40</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ezetimibe</td>
<td>163222-33-1</td>
<td>TWA</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Wipe limit</td>
</tr>
<tr>
<td>Simvastatin</td>
<td>79902-63-9</td>
<td>TWA</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Wipe limit</td>
</tr>
</tbody>
</table>

Further information: For the purposes of these limits, respirable dust and inhalable dust are those fractions of airborne dust which will be collected when sampling is undertaken in accordance with the methods described in MDHS14/4 General methods for sampling and gravimetric analysis or respirable, thoracic and inhalable aerosols. The COSHH definition of a substance hazardous to health includes dust of any kind when present at a concentration in air equal to or greater than 10 mg.m⁻³ 8-hour TWA of inhalable dust or 4 mg.m⁻³ 8-hour TWA of respirable dust. This means that any dust will be subject to COSHH if people are exposed to dust above these levels. Some dusts have been assigned specific WELs and exposure to these must comply with the appropriate limits. Most industrial dusts contain particles of a wide range of sizes. The behaviour, deposition and fate of any particular particle after entry into the human respiratory system, and the body response that it elicits, depend on the nature and size of the particle. HSE distinguishes two size fractions for limit-setting purposes termed 'inhalable' and 'respirable'. Inhalable dust approximates to the fraction of airborne material that enters the nose and mouth during breathing and is therefore available for deposition in the respiratory tract. Respirable dust approximates to the fraction that penetrates to the gas exchange region of the lung. Fuller definitions and explanatory material are given in MDHS14/4. Where dusts contain components that have their own assigned WEL, all the relevant limits should be complied with.

8.2 Exposure controls

**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**

**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.

**Hand protection**

**Material**: Chemical-resistant gloves
Remarks : Consider double gloving.
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, dis-
posable suits) to avoid exposed skin surfaces.
Use appropriate degowning techniques to remove potentially
contaminated clothing.
Respiratory protection : If adequate local exhaust ventilation is not available or expo-
sure assessment demonstrates exposures outside the rec-
ommended guidelines, use respiratory protection.
Equipment should conform to BS EN 143
Filter type : Particulates type (P)

SECTION 9: Physical and chemical properties

9.1 Information on basic physical and chemical properties

Appearance : powder
Colour : No data available
Odour : No data available
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, han-
dling 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.

9.2 Other information
  Molecular weight : No data available
  Particle size : No data available

SECTION 10: Stability and reactivity

10.1 Reactivity
  Not classified as a reactivity hazard.

10.2 Chemical stability
  Stable under normal conditions.

10.3 Possibility of hazardous reactions
  Hazardous reactions : May form explosive dust-air mixture during processing, handling or other means. Can react with strong oxidizing agents.

10.4 Conditions to avoid
  Conditions to avoid : Heat, flames and sparks. Avoid dust formation.

10.5 Incompatible materials
  Materials to avoid : Oxidizing agents

10.6 Hazardous decomposition products
  No hazardous decomposition products are known.

SECTION 11: Toxicological information

11.1 Information on toxicological effects
  Information on likely routes of exposure : Inhalation
  Skin contact
  Ingestion
  Eye contact

  Acute toxicity
  Not classified based on available information.
Components:

**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

Skin corrosion/irritation
Causes skin irritation.

Components:

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

**Simvastatin:**
- **Species:** Rabbit
- **Remarks:** Moderate skin irritation

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
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

Germ cell mutagenicity
Not classified based on available information.

Components:

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
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<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>

Species: Mouse  
Application Route: Oral  
Result: negative

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

Carcinogenicity
Not classified based on available information.

**Components:**

**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>
<tr>
<td>Result</td>
<td>negative</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Species</th>
<th>Rat, male</th>
</tr>
</thead>
<tbody>
<tr>
<td>Application Route</td>
<td>oral (feed)</td>
</tr>
<tr>
<td>Exposure time</td>
<td>104 weeks</td>
</tr>
<tr>
<td>Result</td>
<td>negative</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Species</th>
<th>Mouse</th>
</tr>
</thead>
<tbody>
<tr>
<td>Application Route</td>
<td>oral (feed)</td>
</tr>
<tr>
<td>Exposure time</td>
<td>104 weeks</td>
</tr>
<tr>
<td>Result</td>
<td>negative</td>
</tr>
</tbody>
</table>

**Simvastatin:**

<table>
<thead>
<tr>
<th>Species</th>
<th>Mouse</th>
</tr>
</thead>
<tbody>
<tr>
<td>Application Route</td>
<td>Oral</td>
</tr>
<tr>
<td>Exposure time</td>
<td>&lt; 92 weeks</td>
</tr>
<tr>
<td>Target Organs</td>
<td>Harderian gland</td>
</tr>
<tr>
<td>Tumor Type</td>
<td>Liver, Lungs</td>
</tr>
<tr>
<td>Remarks</td>
<td>The significance of these findings for humans is not certain.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Species</th>
<th>Rat</th>
</tr>
</thead>
<tbody>
<tr>
<td>Application Route</td>
<td>Oral</td>
</tr>
<tr>
<td>Exposure time</td>
<td>2 Years</td>
</tr>
<tr>
<td>Tumor Type</td>
<td>Liver, Thyroid</td>
</tr>
<tr>
<td>Remarks</td>
<td>The significance of these findings for humans is not certain.</td>
</tr>
</tbody>
</table>

Reproductive toxicity
Not classified based on available information.

**Components:**

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

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

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

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

STOT - single exposure
Not classified based on available information.

STOT - repeated exposure
Causes damage to organs 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:**

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

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

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

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

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

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

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

**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

SECTION 12: Ecological information

12.1 Toxicity

Components:

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 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

Toxicity to fish (Chronic toxicity):

NOEC: 0.051 mg/l
Exposure time: 33 d
Species: Pimephales promelas (fathead minnow)
Method: OECD Test Guideline 210

NOEC: 4 mg/l
Exposure time: 7 d
Species: Cyprinodon variegatus (sheepshead minnow)
Remarks: No toxicity at the limit of solubility

Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity):

NOEC: 0.282 mg/l
Exposure time: 21 d
Species: Daphnia magna (Water flea)
Remarks: No toxicity at the limit of solubility

M-Factor (Chronic aquatic toxicity): 1

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
12.2 Persistence and degradability

**Components:**

**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)

12.3 Bioaccumulative potential

**Components:**

**Ezetimibe:**
- Bioaccumulation: Species: Lepomis macrochirus (Bluegill sunfish) Exposure time: 97 d Bioconcentration factor (BCF): 173 Method: OECD Test Guideline 305
- Partition coefficient: n-octanol/water: log Pow: 4.36

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

12.4 Mobility in soil

**Components:**

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

12.5 Results of PBT and vPvB assessment

**Product:**
- Assessment: This substance/mixture contains no components considered to be either persistent, bioaccumulative and toxic (PBT), or very persistent and very bioaccumulative (vPvB) at levels of 0.1% or higher.

12.6 Other adverse effects

**Product:**
Endocrine disrupting potential: The substance/mixture does not contain components considered to have endocrine disrupting properties according to REACH Article 57(f) or Commission Delegated regulation (EU) 2017/2100 or Commission Regulation (EU) 2018/605 at levels of 0.1% or higher.

SECTION 13: Disposal considerations

13.1 Waste treatment methods

Product: Dispose of in accordance with local regulations. According to the European Waste Catalogue, Waste Codes are not product specific, but application specific. Waste codes should be assigned by the user, preferably in discussion with the waste disposal authorities.

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

14.1 UN number

<table>
<thead>
<tr>
<th>ADN</th>
<th>ADR</th>
<th>RID</th>
<th>IMDG</th>
<th>IATA</th>
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</thead>
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14.2 UN proper shipping name

<table>
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<th>ADN</th>
<th>ADR</th>
<th>RID</th>
<th>IMDG</th>
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<td>ENVIRONMENTALLY HAZARDOUS SUBSTANCE, SOLID, N.O.S. (Ezetimibe, Simvastatin)</td>
<td>ENVIRONMENTALLY HAZARDOUS SUBSTANCE, SOLID, N.O.S. (Ezetimibe, Simvastatin)</td>
<td>ENVIRONMENTALLY HAZARDOUS SUBSTANCE, SOLID, N.O.S. (Ezetimibe, Simvastatin)</td>
<td>ENVIRONMENTALLY HAZARDOUS SUBSTANCE, SOLID, N.O.S. (Ezetimibe, Simvastatin)</td>
<td>Environmentally hazardous substance, solid, n.o.s. (Ezetimibe, Simvastatin)</td>
</tr>
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</table>

14.3 Transport hazard class(es)

<table>
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<tr>
<th>ADN</th>
<th>ADR</th>
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<tbody>
<tr>
<td>9</td>
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</tr>
</tbody>
</table>
14.4 Packing group

**ADN**
- Packing group: III
- Classification Code: M7
- Hazard Identification Number: 90
- Labels: 9

**ADR**
- Packing group: III
- Classification Code: M7
- Hazard Identification Number: 90
- Labels: 9
- Tunnel restriction code: (-)

**RID**
- Packing group: III
- Classification Code: M7
- Hazard Identification Number: 90
- Labels: 9

**IMDG**
- Packing group: III
- Labels: 9
- EmS Code: F-A, S-F

**IATA (Cargo)**
- Packing instruction (cargo aircraft): 956
- Packing instruction (LQ): Y956
- Packing group: III
- Labels: Miscellaneous

**IATA (Passenger)**
- Packing instruction (passenger aircraft): 956
- Packing instruction (LQ): Y956
- Packing group: III
- Labels: Miscellaneous

14.5 Environmental hazards

**ADN**
- Environmentally hazardous: yes

**ADR**
- Environmentally hazardous: yes

**RID**
- Environmentally hazardous: yes

**IMDG**
- Marine pollutant: yes
14.6 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.

14.7 Transport in bulk according to Annex II of Marpol and the IBC Code
Remarks: Not applicable for product as supplied.

SECTION 15: Regulatory information

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

<table>
<thead>
<tr>
<th>Regulation</th>
<th>Description</th>
<th>Not applicable</th>
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</thead>
<tbody>
<tr>
<td>REACH</td>
<td>Restrictions on the manufacture, placing on the market and use of certain dangerous substances, preparations and articles (Annex XVII)</td>
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<tr>
<td>REACH</td>
<td>Candidate List of Substances of Very High Concern for Authorisation (Article 59).</td>
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<tr>
<td>REACH</td>
<td>List of substances subject to authorisation (Annex XIV)</td>
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<tr>
<td>Regulation (EC) No 1005/2009 on substances that deplete the ozone layer</td>
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<tr>
<td>Regulation (EU) 2019/1021 on persistent organic pollutants (recast)</td>
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<tr>
<td>Regulation (EC) No 649/2012 of the European Parliament and the Council concerning the export and import of dangerous chemicals</td>
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</tbody>
</table>

Other regulations:
Take note of Directive 94/33/EC on the protection of young people at work or stricter national regulations, where applicable.

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

<table>
<thead>
<tr>
<th>Inventory</th>
<th>Description</th>
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</tr>
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<tbody>
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<tr>
<td>DSL</td>
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<tr>
<td>IECSC</td>
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</tbody>
</table>

15.2 Chemical safety assessment
A Chemical Safety Assessment has not been carried out.

SECTION 16: Other information
## Ezetimibe / Simvastatin Formulation

### SAFETY DATA SHEET
according to Regulation (EC) No. 1907/2006

**Version** 3.5  
**SDS Number:** 28119-00017  
**Date of last issue:** 16.10.2020  
**Date of first issue:** 04.11.2014

### Full text of H-Statements

| H315 | Causes skin irritation. |
| H317 | May cause an allergic skin reaction. |
| H372 | Causes damage to organs through prolonged or repeated exposure. |
| H410 | Very toxic to aquatic life with long lasting effects. |
| H411 | Toxic to aquatic life with long lasting effects. |

### Full text of other abbreviations

- **Aquatic Chronic**: Long-term (chronic) aquatic hazard
- **Skin Irrit.**: Skin irritation
- **Skin Sens.**: Skin sensitisation
- **STOT RE**: Specific target organ toxicity - repeated exposure
- **GB EH40**: UK. EH40 WEL - Workplace Exposure Limits
- **GB EH40 / TWA**: Long-term exposure limit (8-hour TWA reference period)
- **GB EH40 / STEL**: Short-term exposure limit (15-minute reference period)

ADN - European Agreement concerning the International Carriage of Dangerous Goods by Inland Waterways; ADR - European Agreement concerning the International Carriage of Dangerous Goods by Road; AIIC - Australian Inventory of Industrial Chemicals; ASTM - American Society for the Testing of Materials; bw - Body weight; CLP - Classification Labelling Packaging Regulation; Regulation (EC) No 1272/2008; CMR - Carcinogen, Mutagen or Reproductive Toxicant; DIN - Standard of the German Institute for Standardisation; DSL - Domestic Substances List (Canada); ECHA - European Chemicals Agency; EC-Number - European Community number; 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; 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; NO(A)EC - No Observed (Adverse) Effect Concentration; NO(A)EL - No Observed (Adverse) Effect Level; NOELR - No Observable Effect Loading Rate; 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; RID - Regulations concerning the International Carriage of Dangerous Goods by Rail; SADT - Self-Accelerating Decomposition Temperature; SDS - Safety Data Sheet; SVHC - Substance of Very High Concern; TCSI - Taiwan Chemical Substance Inventory; TRGS - Technical Rule for Hazardous Substances; TSCA - Toxic Substances Control Act (United States); UN - United Nations; vPvB - Very Persistent and Very Bioaccumulative
SAFETY DATA SHEET
according to Regulation (EC) No. 1907/2006

Ezetimibe / Simvastatin Formulation

Version: 3.5
Revision Date: 09.04.2021
SDS Number: 28119-00017
Date of last issue: 16.10.2020
Date of first issue: 04.11.2014

Further information

Classification of the mixture:
Skin Irrit. 2 H315 Calculation method
Skin Sens. 1 H317 Calculation method
STOT RE 1 H372 Calculation method
Aquatic Chronic 2 H411 Calculation method

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.

GB / EN