SAFETY DATA SHEET

Ezetimibe / Rosuvastatin Formulation

SECTION 1. PRODUCT AND COMPANY IDENTIFICATION

Product name : Ezetimibe / Rosuvastatin 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 3
Carcinogenicity : Category 1B
Reproductive toxicity : Category 1B
Specific target organ toxicity - single exposure (Oral) : Category 2 (Liver, Kidney, muscle)
Specific target organ toxicity - repeated exposure (Oral) : Category 2 (Eye)
Long-term (chronic) aquatic hazard : Category 2

GHS label elements
Hazard pictograms :

Signal Word : Danger
Hazard Statements : H316 Causes mild skin irritation.
                      H350 May cause cancer.
                      H360FD May damage fertility. May damage the unborn child.
Precautionary Statements:

H371 May cause damage to organs (Liver, Kidney, muscle) if swallowed.
H373 May cause damage to organs (Eye) through prolonged or repeated exposure if swallowed.
H411 Toxic to aquatic life with long lasting effects.

Prevention:
P201 Obtain special instructions before use.
P202 Do not handle until all safety precautions have been read and understood.
P260 Do not breathe dust.
P264 Wash skin thoroughly after handling.
P270 Do not eat, drink or smoke when using this product.
P273 Avoid release to the environment.
P280 Wear protective gloves/ protective clothing/ eye protection/ face protection.

Response:
P308 + P311 IF exposed or concerned: Call a POISON CENTER/doctor.
P332 + P313 If skin irritation occurs: Get medical advice/ attention.
P391 Collect spillage.

Storage:
P405 Store locked up.

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

Other hazards which do not result in classification
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>Mixture</th>
</tr>
</thead>
</table>

Components

<table>
<thead>
<tr>
<th>Chemical name</th>
<th>CAS-No.</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cellulose</td>
<td>9004-34-6</td>
<td>&gt;= 10 - &lt; 20</td>
</tr>
<tr>
<td>Ezetimibe</td>
<td>163222-33-1</td>
<td>&gt;= 2,5 - &lt; 5</td>
</tr>
<tr>
<td>Rosuvastatin</td>
<td>147098-20-2</td>
<td>&gt;= 1 - &lt; 2,5</td>
</tr>
<tr>
<td>Sodium n-dodecyl sulfate</td>
<td>151-21-3</td>
<td>&gt;= 1 - &lt; 2,5</td>
</tr>
<tr>
<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.
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If inhaled
: If inhaled, remove to fresh air. Get medical attention.

In case of skin contact
: In case of contact, immediately flush skin with plenty of water. Remove contaminated clothing and shoes. Get medical attention. Wash clothing before reuse. Thoroughly clean shoes before reuse.

In case of eye contact
: If in eyes, rinse well with water. Get medical attention if irritation develops and persists.

If swallowed
: If swallowed, DO NOT induce vomiting. Get medical attention. Rinse mouth thoroughly with water. Never give anything by mouth to an unconscious person.

Most important symptoms and effects, both acute and delayed
: Causes mild skin irritation. May cause cancer. May damage fertility. May damage the unborn child. May cause damage to organs if swallowed. May cause damage to organs through prolonged or repeated exposure if swallowed. Dust contact with the eyes can lead to mechanical irritation.

Protection of first-aiders
: First Aid responders should pay attention to self-protection, and use the recommended personal protective equipment when the potential for exposure exists (see section 8).

Notes to physician
: Treat symptomatically and supportively.

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
   Fluorine compounds
   Nitrogen oxides (NOx)
   Sulfur oxides
   Metal oxides

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

Special protective equipment for 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:
If sufficient ventilation is unavailable, use with local exhaust ventilation.

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

Conditions for safe storage:
Keep in properly labeled containers.
Store locked up.
Keep tightly closed.
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
## 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><strong>Further information:</strong> Irritation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>TWA</strong></td>
<td></td>
<td>10 mg/m³</td>
<td>ACGIH</td>
<td></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><strong>Wipe limit</strong></td>
<td></td>
<td>250 µg/100 cm²</td>
<td>Internal</td>
<td></td>
</tr>
<tr>
<td>Rosuvastatin</td>
<td>147098-20-2</td>
<td>TWA</td>
<td>20 µg/m³ (OEB 3)</td>
<td>Internal</td>
</tr>
<tr>
<td><strong>Wipe limit</strong></td>
<td></td>
<td>200 µg/100 cm²</td>
<td>Internal</td>
<td></td>
</tr>
<tr>
<td>Magnesium stearate</td>
<td>557-04-0</td>
<td>CMP</td>
<td>10 mg/m³</td>
<td>AR OEL</td>
</tr>
<tr>
<td><strong>Further information:</strong> A4 - 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.,</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Irritation</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>TWA</strong></td>
<td></td>
<td>10 mg/m³</td>
<td>ACGIH</td>
<td></td>
</tr>
<tr>
<td><strong>TWA (Inhalable fraction)</strong></td>
<td></td>
<td>10 mg/m³</td>
<td>ACGIH</td>
<td></td>
</tr>
<tr>
<td><strong>TWA (Respirable fraction)</strong></td>
<td></td>
<td>3 mg/m³</td>
<td>ACGIH</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**: Chemical-resistant gloves
- **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.

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

### SECTION 9. PHYSICAL AND CHEMICAL PROPERTIES

**Appearance**: powder

**Color**: white to off-white

**Odor**: No data available

**Odor 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**: Not applicable

**Evaporation rate**: Not applicable

**Flammability (solid, gas)**: May form explosive dust-air mixture during processing, handling or other means.

**Flammability (liquids)**: No data available

**Upper explosion limit / Upper flammability limit**: No data available

**Lower explosion limit / Lower flammability limit**: No data available

**Vapor pressure**: Not applicable

**Relative vapor density**: Not applicable
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.

Product:
Acute oral toxicity: Acute toxicity estimate: > 5.000 mg/kg
Method: Calculation method
Components:

Cellulose:
- Acute oral toxicity: LD50 (Rat): > 5.000 mg/kg
- Acute inhalation toxicity: LC50 (Rat): > 5.8 mg/l
  Exposure time: 4 h
  Test atmosphere: dust/mist
- Acute dermal toxicity: LD50 (Rabbit): > 2.000 mg/kg

Ezetimibe:
- Acute oral toxicity: LD50 (Rat): > 5.000 mg/kg
  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

Rosuvastatin:
- Acute oral toxicity: LD50 (Rat): > 2.000 mg/kg
  Target Organs: Liver, Stomach, muscle, Kidney

Sodium n-dodecyl sulfate:
- Acute oral toxicity: LD50 (Rat): 1.200 mg/kg
  Method: OECD Test Guideline 401
- Acute dermal toxicity: LD50 (Rat): > 2.000 mg/kg
  Method: OECD Test Guideline 402
  Remarks: Based on data from similar materials

Magnesium stearate:
- Acute oral toxicity: LD50 (Rat): > 2.000 mg/kg
  Method: OECD Test Guideline 423
  Assessment: The substance or mixture has no acute oral toxicity
  Remarks: Based on data from similar materials
- Acute dermal toxicity: LD50 (Rabbit): > 2.000 mg/kg
  Remarks: Based on data from similar materials
Skin corrosion/irritation
Causes mild skin irritation.

**Components:**

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

**Sodium n-dodecyl sulfate:**
Species: Rabbit
Result: 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

**Sodium n-dodecyl sulfate:**
Species: Rabbit
Result: Irreversible effects on the eye
Method: OECD Test Guideline 405

**Magnesium stearate:**
Species: Rabbit
Result: No eye irritation
Remarks: Based on data from similar materials

Respiratory or skin sensitization

Skin sensitization
Not classified based on available information.

Respiratory sensitization
Not classified based on available information.

**Components:**

**Ezetimibe:**
Test Type: Maximization Test
Species: Guinea pig
Result: negative
Sodium n-dodecyl sulfate:
Test Type: Maximization Test
Routes of exposure: Skin contact
Species: Guinea pig
Result: negative
Remarks: Based on data from similar materials

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

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

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

Sodium n-dodecyl sulfate:
Genotoxicity in vitro:
Test Type: Bacterial reverse mutation assay (AMES)  
Method: OECD Test Guideline 471  
Result: negative

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

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

Magnesium stearate:
Genotoxicity in vitro:
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:
May cause cancer.

Components:

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

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

Species: Mouse
Application Route: oral (feed)
Exposure time: 104 weeks
Result: negative

**Rosuvastatin:**
Species: Rat
Application Route: Oral
Exposure time: 104 weeks
LOAEL: 80 mg/kg body weight
Result: positive
Symptoms: Tumor
Target Organs: Uterus (including cervix)

Species: Mouse
Application Route: Oral
Exposure time: 107 weeks
LOAEL: 200 mg/kg body weight
Result: positive
Symptoms: liver adenoma, carcinoma
Target Organs: Liver

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

**Reproductive toxicity**
May damage fertility. May damage the unborn child.

**Components:**

**Cellulose:**
Effects on fertility: Test Type: One-generation reproduction toxicity study
Species: Rat
Application Route: Ingestion
Result: negative

Effects on 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.

Rosuvastatin:

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

Effects on fetal development:
- Test Type: Development
  - Species: Rabbit
  - Application Route: Oral
  - Developmental Toxicity: LOAEL: 3 mg/kg body weight
  - Result: Fetal mortality., Maternal toxicity observed.

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

Sodium n-dodecyl sulfate:

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

Magnesium stearate:
Effects on fertility: Test Type: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test
Species: Rat
Application Route: Ingestion
Method: OECD Test Guideline 422
Result: negative
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
May cause damage to organs (Liver, Kidney, muscle) if swallowed.

Components:
Rosuvastatin:
Routes of exposure: Oral
Target Organs: Liver, Kidney, muscle
Assessment: Causes damage to organs.

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

Components:
Rosuvastatin:
Routes of exposure: Oral
Target Organs: Eye
Assessment: Causes damage to organs through prolonged or repeated exposure.

Repeated dose toxicity

Components:
Cellulose:
Species: Rat
NOAEL: $\geq 9.000$ mg/kg
Application Route: Ingestion
Exposure time: 90 Days

Ezetimibe:
### Species:

<table>
<thead>
<tr>
<th>Species</th>
<th>NOAEL</th>
<th>Application Route</th>
<th>Exposure time</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dog</td>
<td>1.000 mg/kg</td>
<td>Oral</td>
<td>90 d</td>
<td>No significant adverse effects were reported</td>
</tr>
<tr>
<td>Rat</td>
<td>1.500 mg/kg</td>
<td>Oral</td>
<td>90 d</td>
<td>No significant adverse effects were reported</td>
</tr>
<tr>
<td>Mouse</td>
<td>500 mg/kg</td>
<td>Oral</td>
<td>90 d</td>
<td>No significant adverse effects were reported</td>
</tr>
<tr>
<td>Dog</td>
<td>300 mg/kg</td>
<td>Oral</td>
<td>1 y</td>
<td>No significant adverse effects were reported</td>
</tr>
</tbody>
</table>

### Rosuvastatin:

<table>
<thead>
<tr>
<th>Species</th>
<th>LOAEL</th>
<th>Application Route</th>
<th>Exposure time</th>
<th>Target Organs</th>
<th>Symptoms</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dog</td>
<td>90 mg/kg</td>
<td>Oral</td>
<td>24 Days</td>
<td>Brain</td>
<td>Edema, Blood disorders, Necrosis</td>
<td>Based on data from similar materials</td>
</tr>
<tr>
<td>Dog</td>
<td>6 mg/kg</td>
<td>Oral</td>
<td>52 Weeks</td>
<td>Cornea</td>
<td>Corneal opacity</td>
<td>Based on data from similar materials</td>
</tr>
<tr>
<td>Dog</td>
<td>30 mg/kg</td>
<td>Oral</td>
<td>12 Weeks</td>
<td>Eye</td>
<td>Eye disease</td>
<td>Based on data from similar materials</td>
</tr>
</tbody>
</table>

### Remarks:

- Based on data from similar materials.
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Symptoms : Eye disease
Remarks : Based on data from similar materials

Sodium n-dodecyl sulfate:
Species : Rat
NOAEL : 488 mg/kg
Application Route : Ingestion
Exposure time : 90 Days
Remarks : Based on data from similar materials

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

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

SECTION 12. ECOLOGICAL INFORMATION

Ecotoxicity

Components:
Cellulose:
Toxicity to fish : LC50 (Oryzias latipes (Japanese medaka)): > 100 mg/l
Ezetimibe:

**Toxicity to fish**
- LC50 (Pimephales promelas (fathead minnow)): > 0.125 mg/l
  - Exposure time: 96 h
  - Method: OECD Test Guideline 203
  - Remarks: No toxicity at the limit of solubility.

**Toxicity to daphnia and other aquatic invertebrates**
- EC50 (Daphnia magna (Water flea)): > 4 mg/l
  - Exposure time: 48 h
  - Method: OECD Test Guideline 202
  - Remarks: No toxicity at the limit of solubility.

**Toxicity to algae/aquatic plants**
- EC50 (Pseudokirchneriella subcapitata (green algae)): > 0.317 mg/l
  - Exposure time: 96 h
  - Method: OECD Test Guideline 201
  - Remarks: No toxicity at the limit of solubility.

  NOEC (Pseudokirchneriella subcapitata (green algae)): 0.317 mg/l
  - Exposure time: 96 h
  - Method: OECD Test Guideline 201
  - Remarks: No toxicity at the limit of solubility.

**Toxicity to fish (Chronic toxicity)**
- NOEC (Pimephales promelas (fathead minnow)): 0.051 mg/l
  - Exposure time: 33 d
  - Method: OECD Test Guideline 210

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

**Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity)**
- NOEC (Daphnia magna (Water flea)): 0.282 mg/l
  - Exposure time: 21 d
  - Remarks: No toxicity at the limit of solubility.

**M-Factor (Chronic aquatic toxicity)**
- 1

**Toxicity to microorganisms**
- EC50: > 4.4 mg/l
  - Exposure time: 3 h
  - Test Type: Respiration inhibition
  - Method: OECD Test Guideline 209
  - Remarks: No toxicity at the limit of solubility.

  NOEC: 4.4 mg/l
  - Exposure time: 3 h
  - Test Type: Respiration inhibition
  - Method: OECD Test Guideline 209
  - Remarks: No toxicity at the limit of solubility.

Rosuvastatin:

**Toxicity to fish**
- LC50 (Pimephales promelas (fathead minnow)): > 1.000 mg/l
Exposure time: 96 hrs
Method: FDA 4.11

LC50 (Lepomis macrochirus (Bluegill sunfish)): > 1.000 mg/l
Exposure time: 96 hrs
Method: FDA 4.11

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

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

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

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

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

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

Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity):
- NOEC (Daphnia magna (Water flea)): 0,018 mg/l
  Exposure time: 21 Days
  Method: OECD Test Guideline 211

M-Factor (Chronic aquatic toxicity):
- 1

Toxicity to microorganisms:
- EC50: > 100 mg/l
  Exposure time: 3 hrs
  Test Type: Respiration inhibition
  Method: OECD Test Guideline 209

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

Sodium n-dodecyl sulfate:
- Toxicity to fish:
  LC50 (Pimephales promelas (fathead minnow)): 29 mg/l
  Exposure time: 96 h

- Toxicity to daphnia and other:
  EC50 (Ceriodaphnia dubia (water flea)): 5,55 mg/l
<table>
<thead>
<tr>
<th>Component</th>
<th>Toxicity to algae/aquatic plants</th>
<th>Toxicity to fish (Chronic toxicity)</th>
<th>Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity)</th>
<th>Toxicity to microorganisms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Magnesium stearate</td>
<td>LC50 (Leuciscus idus (Golden orfe)): &gt; 100 mg/l Exposure time: 48 h Method: DIN 38412 Remarks: Based on data from similar materials</td>
<td>NOEC (Pimephales promelas (fathead minnow)): &gt;= 1,357 mg/l Exposure time: 42 d</td>
<td>NOEC (Ceriodaphnia dubia (water flea)): 0,88 mg/l Exposure time: 7 d</td>
<td>EC50: 135 mg/l Exposure time: 3 h</td>
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<td>Elle (Pseudokirchneriella subcapitata (green algae)): &gt; 1 mg/l Exposure time: 72 h Test substance: Water Accommodated Fraction Method: OECD Test Guideline 201 Remarks: Based on data from similar materials No toxicity at the limit of solubility.</td>
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<td></td>
<td>NOELR (Pseudokirchneriella subcapitata (green algae)): &gt; 1 mg/l Exposure time: 72 h Test substance: Water Accommodated Fraction Method: OECD Test Guideline 201 Remarks: Based on data from similar materials</td>
<td></td>
</tr>
<tr>
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<td></td>
<td>EC10 (Pseudomonas putida): &gt; 100 mg/l Exposure time: 16 h Test substance: Water Accommodated Fraction Remarks: Based on data from similar materials</td>
<td></td>
</tr>
</tbody>
</table>

**Exposure time:** 48 h

**Toxicity to algae/aquatic plants**
- ErC50 (Desmodesmus subspicatus (green algae)): > 120 mg/l Exposure time: 72 h
- NOEC (Desmodesmus subspicatus (green algae)): 30 mg/l Exposure time: 72 h

**Test substance:** Water Accommodated Fraction

**Method:** OECD Test Guideline 201

**Remarks:** Based on data from similar materials

No toxicity at the limit of solubility.
Persistence and degradability

**Components:**

**Cellulose:**
Biodegradability: Readily biodegradable.

**Ezetimibe:**
Biodegradability: Not readily biodegradable.
Biodegradation: 6.8%
Exposure time: 28 d
Stability in water: Hydrolysis: 50%(4,5 d)
Method: OECD Test Guideline 111

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

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

**Magnesium stearate:**
Biodegradability: Not biodegradable.
Remarks: Based on data from similar materials

Bioaccumulative potential

**Components:**

**Ezetimibe:**
Bioaccumulation: Species: Lepomis macrochirus (Bluegill sunfish)
Bioconcentration factor (BCF): 173
Exposure time: 97 d
Method: OECD Test Guideline 305
Partition coefficient: n-octanol/water: log Pow: 4,36

**Rosuvastatin:**
Partition coefficient: n-octanol/water: log Pow: 0,3

**Sodium n-dodecyl sulfate:**
Partition coefficient: n-octanol/water: log Pow: 0,83
octanol/water

**Magnesium stearate:**
Partition coefficient: n-octanol/water : log Pow: > 4

**Mobility in soil**

**Components:**

**Ezetimibe:**
Distribution among environmental compartments : log Koc: 4,35 Method: OECD Test Guideline 106

**Rosuvastatin:**
Distribution among environmental compartments : log Koc: 2,15 Method: FDA 3.08

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

**IATA-DGR**
UN/ID No. : UN 3077
Proper shipping name : Environmentally hazardous substance, solid, n.o.s. (Ezetimibe, Rosuvastatin)
Class : 9
Packing group : III
Labels : Miscellaneous
Packing instruction (cargo aircraft) : 956
Packing instruction (passenger aircraft) : 956
Environmentally hazardous : yes
SAFETY DATA SHEET

Ezetimibe / Rosuvastatin Formulation

IMDG-Code
UN number : UN 3077
Proper shipping name : ENVIRONMENTALLY HAZARDOUS SUBSTANCE, SOLID, N.O.S. (Ezetimibe, Rosuvastatin)
Class : 9
Packing group : III
Labels : 9
EmS Code : F-A, S-F
Marine pollutant : yes

Transport in bulk according to Annex II of MARPOL 73/78 and the IBC Code
Not applicable for product as supplied.

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
IECSC : 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
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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