SAFETY DATA SHEET

Ertugliflozin (< 5%) / Sitagliptin Formulation

Version 1.6
Revision Date: 2020/09/28
SDS Number: 2400320-00007
Date of last issue: 2020/03/23
Date of first issue: 2018/02/01

1. PRODUCT AND COMPANY IDENTIFICATION

Product name : Ertugliflozin (< 5%) / Sitagliptin Formulation

Manufacturer or supplier's details
Company : MSD
Address : JL Raya Pandaan KM. 48
Pandaan, Jawa Timur - Indonesia
Telephone : 908-740-4000
Emergency telephone number : 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

2. HAZARDS IDENTIFICATION

GHS Classification
Skin corrosion/irritation : Category 2
Serious eye damage/eye irritation : Category 1

GHS label elements
Hazard pictograms : 
Signal word : Danger
Hazard statements : H315 Causes skin irritation.
H318 Causes serious eye damage.

Precautionary statements : Prevention:
P264 Wash skin thoroughly after handling.
P280 Wear protective gloves/ eye protection/ face protection.

Response:
P302 + P352 IF ON SKIN: Wash with plenty of water.
P305 + P351 + P338 + P310 IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. Immediately call a POISON CENTER/ doctor.
P332 + P313 IF skin irritation occurs: Get medical advice/ atten-
Other hazards which do not result in classification
May form explosive dust-air mixture during processing, handling or other means.

3. COMPOSITION/INFORMATION ON INGREDIENTS

<table>
<thead>
<tr>
<th>Substance / Mixture</th>
<th>Components</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Chemical name</td>
</tr>
<tr>
<td></td>
<td>Sitagliptin</td>
</tr>
<tr>
<td></td>
<td>Cellulose</td>
</tr>
<tr>
<td></td>
<td>Ertugliflozin</td>
</tr>
<tr>
<td></td>
<td>Magnesium stearate</td>
</tr>
</tbody>
</table>

4. FIRST AID MEASURES

General advice:
In the case of accident or if you feel unwell, seek medical advice immediately.
When symptoms persist or in all cases of doubt seek medical advice.

If inhaled:
If inhaled, remove to fresh air.
Get medical attention if symptoms occur.

In case of skin contact:
In case of contact, immediately flush skin with plenty of water for at least 15 minutes while removing contaminated clothing and shoes.
Get medical attention.
Wash clothing before reuse.
Thoroughly clean shoes before reuse.

In case of eye contact:
In case of contact, immediately flush eyes with plenty of water for at least 15 minutes.
If easy to do, remove contact lens, if worn.
Get medical attention immediately.

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.
Causes serious eye damage.

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

Notes to physician:
Treat symptomatically and supportively.

5. FIREFIGHTING MEASURES

Suitable extinguishing media:
Water spray
Alcohol-resistant foam
Carbon dioxide (CO2)
Dry chemical
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Unsuitable extinguishing media: None known.
Specific hazards during firefighting: Avoid generating dust; fine dust dispersed in air in sufficient concentrations, and in the presence of an ignition source is a potential dust explosion hazard. Exposure to combustion products may be a hazard to health.

Hazardous combustion products: Carbon oxides, Metal oxides, Oxides of phosphorus
Specific extinguishing methods: Use extinguishing measures that are appropriate to local circumstances and the surrounding environment. Use water spray to cool unopened containers. Remove undamaged containers from fire area if it is safe to do so. Evacuate area.

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

6. ACCIDENTAL RELEASE MEASURES

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

Environmental precautions: Avoid release to the environment. Prevent further leakage or spillage if safe to do so. Retain and dispose of contaminated wash water. Local authorities should be advised if significant spillages cannot be contained.

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

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.
Do not get in 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
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 labelled containers.
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

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Components with workplace control parameters

<table>
<thead>
<tr>
<th>Components</th>
<th>CAS-No.</th>
<th>Value type (Form of exposure)</th>
<th>Control parameters / Permissible concentration</th>
<th>Basis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sitagliptin</td>
<td>654671-77-9</td>
<td>TWA</td>
<td>0.5 mg/m³ (OEB 2)</td>
<td>Internal</td>
</tr>
<tr>
<td>Cellulose</td>
<td>9004-34-6</td>
<td>TWA</td>
<td>10 mg/m³</td>
<td>ACGIH</td>
</tr>
<tr>
<td>Ertugliflozin</td>
<td>1210344-83-4</td>
<td>TWA</td>
<td>10 µg/m³ (OEB 3)</td>
<td>Internal</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Wipe limit 100 µg/100 cm²</td>
<td>Internal</td>
</tr>
<tr>
<td>Magnesium stearate</td>
<td>557-04-0</td>
<td>NAB</td>
<td>10 mg/m³</td>
<td>ID OEL</td>
</tr>
</tbody>
</table>

Further information: Adopted in Year 1996, Not classified as carcinogenic to humans. Not enough data to classify these materials as carcinogenic to humans or animals

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

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.

9. 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: Not applicable

Evaporation rate: Not applicable

Flammability (solid, gas): May form explosive dust-air mixture during processing, han-
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.

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: > 2,000 mg/kg
Method: Calculation method

**Components:**

**Sitagliptin:**
Acute oral toxicity: LD50 (Rat): > 3,000 mg/kg
LD50 (Mouse): 3,000 mg/kg

**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

**Ertugliflozin:**
Acute oral toxicity: LD50 (Rat): 500 mg/kg
Acute inhalation toxicity: Remarks: No data available
Acute dermal toxicity: Remarks: No data available

**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:**

**Sitagliptin:**
Species: Rabbit
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Method  Result:
Draize Test  No skin irritation

Ertugliflozin:
Result: Corrosive

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

Serious eye damage/eye irritation
Causes serious eye damage.

Components:

Sitagliptin:
Species: Rabbit
Result: Irritating to eyes.
Method: Draize Test

Ertugliflozin:
Result: Severe irritation

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

Respiratory or skin sensitisation

Skin sensitisation
Not classified based on available information.

Respiratory sensitisation
Not classified based on available information.

Components:

Sitagliptin:
Test Type: Local lymph node assay (LLNA)
Species: Mouse
Method: OECD Test Guideline 429
Result: Not a skin sensitizer.

Ertugliflozin:
Test Type: Local lymph node assay (LLNA)
Result: Not a skin sensitizer.
Magnesium stearate:
- **Test Type**: Maximisation Test
- **Exposure routes**: Skin contact
- **Species**: Guinea pig
- **Method**: OECD Test Guideline 406
- **Result**: negative
- **Remarks**: Based on data from similar materials

**Germ cell mutagenicity**
Not classified based on available information.

**Components**

**Sitagliptin**
- **Genotoxicity in vitro**
  - **Test Type**: Ames test
  - **Result**: negative

  - **Test Type**: Chromosome aberration test in vitro
  - **Test system**: Chinese hamster ovary cells
  - **Result**: negative

  - **Test Type**: DNA damage and repair, unscheduled DNA synthesis in mammalian cells (in vitro)
  - **Test system**: rat hepatocytes
  - **Result**: negative

- **Genotoxicity in vivo**
  - **Test Type**: Micronucleus test
  - **Species**: Mouse
  - **Application Route**: Oral
  - **Result**: negative

**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

**Ertugliflozin**
- **Genotoxicity in vitro**
  - **Test Type**: Bacterial reverse mutation assay (AMES)
  - **Result**: negative

  - **Test Type**: Chromosome aberration test in vitro
  - **Result**: negative

- **Genotoxicity in vivo**
  - **Test Type**: Mammalian erythrocyte micronucleus test (in vivo cytogenetic assay)
Species: Rat
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
Not classified based on available information.

Components:

Sitagliptin:
Species: Mouse
Application Route: Oral
Exposure time: 2 Years
Result: negative

Species: Rat
Application Route: oral (drinking water)
Exposure time: 2 Years
Result: positive
Target Organs: Liver
Remarks: Significant toxicity observed in testing

Carcinogenicity - Assessment: Weight of evidence does not support classification as a carcinogen

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

Ertugliflozin:
Species: Mouse
Application Route: Oral
Exposure time: 2 Years
Result: negative

Species: Rat
Application Route: Oral
Exposure time: 2 Years
Result: negative

Carcinogenicity - Assessment: Weight of evidence does not support classification as a carcinogen

Reproductive toxicity
Not classified based on available information.

Components:

Sitagliptin:
- **Effects on fertility**
  - Test Type: Fertility/early embryonic development
  - Species: Rat
  - Application Route: Oral
  - Fertility: NOAEL Parent: 1,000 mg/kg body weight
  - Result: Animal testing did not show any effects on fertility.

- **Effects on foetal development**
  - Test Type: Embryo-foetal development
  - Species: Rat
  - Application Route: Oral
  - Teratogenicity: LOAEL: 250 mg/kg body weight
  - Result: Embryotoxic effects and adverse effects on the offspring were detected, No teratogenic effects

  - Test Type: Embryo-foetal development
  - Species: Rabbit
  - Teratogenicity: NOAEL: 125 mg/kg body weight
  - Result: No teratogenic effects

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

- **Effects on foetal development**
  - Test Type: Fertility/early embryonic development
  - Species: Rat
  - Application Route: Ingestion
  - Result: negative

Ertugliflozin:
- **Effects on fertility**
  - Test Type: Fertility/early embryonic development
  - Species: Rat
  - Application Route: Oral
  - Fertility: NOAEL: 250 mg/kg body weight
  - Remarks: Maternal toxicity observed. No significant adverse effects were reported

  - Test Type: Fertility/early embryonic development
  - Species: Rabbit
  - Application Route: Oral
  - Fertility: NOAEL: 200 mg/kg body weight
Remarks: No significant adverse effects were reported

Effects on foetal development
: Test Type: Embryo-foetal development
  Species: Rat
  Application Route: Oral
  Developmental Toxicity: NOAEL: 50 mg/kg body weight
  Remarks: Adverse developmental effects were observed

  Test Type: Embryo-foetal development
  Species: Rabbit
  Application Route: Oral
  Developmental Toxicity: NOAEL: 250 mg/kg body weight
  Remarks: No significant adverse effects were reported

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 foetal development
: Test Type: Embryo-foetal development
  Species: Rat
  Application Route: Ingestion
  Result: negative
  Remarks: Based on data from similar materials

STOT - single exposure
Not classified based on available information.

STOT - repeated exposure
Not classified based on available information.

Components:

Ertugliflozin:
Exposure routes : Oral
Target Organ(s) : Kidney, Stomach, Prostate
Assessment : May cause damage to organs through prolonged or repeated exposure.

Repeated dose toxicity

Components:

Sitagliptin:
Species : Mouse
NOAEL : 500 mg/kg
LOAEL : 1,000 mg/kg
Application Route : Oral
Exposure time : > 2yr
Target Organ(s) : Kidney
<table>
<thead>
<tr>
<th>Species</th>
<th>Rat</th>
<th>500 mg/kg</th>
<th>Oral</th>
<th>14 Weeks</th>
<th>Liver, Kidney, Heart, Teeth</th>
</tr>
</thead>
<tbody>
<tr>
<td>NOAEL</td>
<td>500 mg/kg</td>
<td>1,000 mg/kg</td>
<td>Oral</td>
<td>14 Weeks</td>
<td>Liver, Kidney, Heart, Teeth</td>
</tr>
<tr>
<td>LOAEL</td>
<td>1,000 mg/kg</td>
<td>Oral</td>
<td>14 Weeks</td>
<td>Liver, Kidney, Heart, Teeth</td>
<td></td>
</tr>
<tr>
<td>Application Route</td>
<td>Oral</td>
<td>Oral</td>
<td>Oral</td>
<td>Oral</td>
<td>Oral</td>
</tr>
<tr>
<td>Exposure time</td>
<td>14 Weeks</td>
<td>14 Weeks</td>
<td>14 Weeks</td>
<td>14 Weeks</td>
<td>14 Weeks</td>
</tr>
<tr>
<td>Target Organs</td>
<td>Liver, Kidney, Heart, Teeth</td>
<td>Liver, Kidney, Heart, Teeth</td>
<td>Liver, Kidney, Heart, Teeth</td>
<td>Liver, Kidney, Heart, Teeth</td>
<td>Liver, Kidney, Heart, Teeth</td>
</tr>
</tbody>
</table>

**Species: Dog**

<table>
<thead>
<tr>
<th>NOAEL</th>
<th>10 mg/kg</th>
<th>50 mg/kg</th>
<th>Oral</th>
<th>53 Weeks</th>
<th>Central nervous system</th>
</tr>
</thead>
<tbody>
<tr>
<td>LOAEL</td>
<td>50 mg/kg</td>
<td>10 mg/kg</td>
<td>Oral</td>
<td>53 Weeks</td>
<td>Central nervous system</td>
</tr>
<tr>
<td>Application Route</td>
<td>Oral</td>
<td>Oral</td>
<td>Oral</td>
<td>Oral</td>
<td>Oral</td>
</tr>
<tr>
<td>Exposure time</td>
<td>53 Weeks</td>
<td>53 Weeks</td>
<td>53 Weeks</td>
<td>53 Weeks</td>
<td>53 Weeks</td>
</tr>
<tr>
<td>Target Organs</td>
<td>Central nervous system</td>
<td>Central nervous system</td>
<td>Central nervous system</td>
<td>Central nervous system</td>
<td>Central nervous system</td>
</tr>
<tr>
<td>Symptoms</td>
<td>Loss of balance</td>
<td>Loss of balance</td>
<td>Loss of balance</td>
<td>Loss of balance</td>
<td>Loss of balance</td>
</tr>
<tr>
<td>Remarks</td>
<td>The mechanism or mode of action may not be relevant in humans.</td>
<td>The mechanism or mode of action may not be relevant in humans.</td>
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<td>The mechanism or mode of action may not be relevant in humans.</td>
<td>The mechanism or mode of action may not be relevant in humans.</td>
</tr>
</tbody>
</table>

**Species: Monkey**

<table>
<thead>
<tr>
<th>NOAEL</th>
<th>100 mg/kg</th>
<th>10 mg/kg</th>
<th>Oral</th>
<th>14 Weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Application Route</td>
<td>Oral</td>
<td>Oral</td>
<td>Oral</td>
<td>Oral</td>
</tr>
<tr>
<td>Exposure time</td>
<td>14 Weeks</td>
<td>14 Weeks</td>
<td>14 Weeks</td>
<td>14 Weeks</td>
</tr>
<tr>
<td>Remarks</td>
<td>No significant adverse effects were reported</td>
<td>No significant adverse effects were reported</td>
<td>No significant adverse effects were reported</td>
<td>No significant adverse effects were reported</td>
</tr>
</tbody>
</table>

**Cellulose:**

<table>
<thead>
<tr>
<th>Species</th>
<th>Rat</th>
<th>&gt;= 9,000 mg/kg</th>
<th>Oral</th>
<th>90 Days</th>
</tr>
</thead>
<tbody>
<tr>
<td>NOAEL</td>
<td>&gt;= 9,000 mg/kg</td>
<td>Oral</td>
<td>90 Days</td>
<td></td>
</tr>
<tr>
<td>Application Route</td>
<td>Oral</td>
<td>Oral</td>
<td>Oral</td>
<td>Oral</td>
</tr>
<tr>
<td>Exposure time</td>
<td>90 Days</td>
<td>90 Days</td>
<td>90 Days</td>
<td>90 Days</td>
</tr>
</tbody>
</table>

**Ertugliflozin:**

<table>
<thead>
<tr>
<th>Species</th>
<th>Rat</th>
<th>500 mg/kg</th>
<th>Oral</th>
<th>30 d</th>
</tr>
</thead>
<tbody>
<tr>
<td>NOAEL</td>
<td>500 mg/kg</td>
<td>Oral</td>
<td>30 d</td>
<td></td>
</tr>
<tr>
<td>Application Route</td>
<td>Oral</td>
<td>Oral</td>
<td>Oral</td>
<td>Oral</td>
</tr>
<tr>
<td>Exposure time</td>
<td>30 d</td>
<td>30 d</td>
<td>30 d</td>
<td>30 d</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Species</th>
<th>Rat</th>
<th>250 mg/kg</th>
<th>Oral</th>
<th>30 d</th>
</tr>
</thead>
<tbody>
<tr>
<td>NOAEL</td>
<td>250 mg/kg</td>
<td>Oral</td>
<td>30 d</td>
<td></td>
</tr>
<tr>
<td>Application Route</td>
<td>Oral</td>
<td>Oral</td>
<td>Oral</td>
<td>Oral</td>
</tr>
<tr>
<td>Exposure time</td>
<td>30 d</td>
<td>30 d</td>
<td>30 d</td>
<td>30 d</td>
</tr>
<tr>
<td>Target Organs</td>
<td>Kidney</td>
<td>Kidney</td>
<td>Kidney</td>
<td>Kidney</td>
</tr>
<tr>
<td>Species</td>
<td>Rat</td>
<td>25 mg/kg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NOAEL</td>
<td>25 mg/kg</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
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</tbody>
</table>

- **Application Route**: Oral
- **Exposure time**: 180 d
- **Target Organs**: Kidney, Bone, Stomach

- **Species**: Rat
- **LOAEL**: 25 mg/kg
- **Exposure time**: 90 d
- **Target Organs**: Kidney, Gastrointestinal tract, Prostate

- **Species**: Dog
- **NOAEL**: 150 mg/kg
- **Application Route**: Oral
- **Exposure time**: 270 d
- **Remarks**: No significant adverse effects were reported

- **Species**: Mouse
- **NOAEL**: 100 mg/kg
- **Application Route**: Oral
- **Exposure time**: 90 d
- **Remarks**: No significant adverse effects were reported

- **Species**: Mouse
- **NOAEL**: 100 mg/kg
- **Application Route**: Oral
- **Exposure time**: 28 d
- **Target Organs**: Bone
- **Remarks**: No significant adverse effects were reported

**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.

**Experience with human exposure**

**Components:**

**Sitagliptin:**

- **Inhalation**: Symptoms: upper respiratory tract infection, pharyngitis, Headache
- **Ingestion**: Symptoms: upper respiratory tract infection, nasopharyngitis, Headache, Nausea, Abdominal pain, Diarrhoea

**Ertugliflozin:**

- **Ingestion**: Symptoms: The most common side effects are; Headache, constipation, Diarrhoea, Nausea, urinary tract infection, muscle pain, upper respiratory tract infection
12. ECOLOGICAL INFORMATION

Ecotoxicity

Components:

Sitagliptin:
Toxicity to fish: LC50 (Pimephales promelas (fathead minnow)): > 100 mg/l
  Exposure time: 96 h
  Method: OECD Test Guideline 203

Toxicity to daphnia and other aquatic invertebrates: EC50 (Daphnia magna (Water flea)): 60 mg/l
  Exposure time: 48 h
  Method: OECD Test Guideline 202

Toxicity to algae/aquatic plants: EC50 (Pseudokirchneriella subcapitata (green algae)): > 39 mg/l
  Exposure time: 96 h
  Method: OECD Test Guideline 201

  NOEC (Pseudokirchneriella subcapitata (green algae)): 2.2 mg/l
  Exposure time: 96 h
  Method: OECD Test Guideline 201

Toxicity to fish (Chronic toxicity): NOEC (Pimephales promelas (fathead minnow)): 9.2 mg/l
  Exposure time: 33 d
  Method: OECD Test Guideline 210

Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity): NOEC (Daphnia magna (Water flea)): 9.8 mg/l
  Exposure time: 21 d
  Method: OECD Test Guideline 211

Toxicity to microorganisms: EC50: > 150 mg/l
  Exposure time: 3 h
  Test Type: Respiration inhibition
  Method: OECD Test Guideline 209

  NOEC: 150 mg/l
  Exposure time: 3 h
  Test Type: Respiration inhibition

Cellulose:
Toxicity to fish: LC50 (Oryzias latipes (Japanese medaka)): > 100 mg/l
  Exposure time: 48 h
  Remarks: Based on data from similar materials

Ertugliflozin:
Toxicity to algae/aquatic plants: EC50 (Pseudokirchneriella subcapitata (green algae)): 77 mg/l
  Exposure time: 72 h
  Method: OECD Test Guideline 201

  NOEC (Pseudokirchneriella subcapitata (green algae)): 50
Toxicity to fish (Chronic toxicity):
- NOEC (Pimephales promelas (fathead minnow)): 1 mg/l
  - Exposure time: 32 d
  - Method: OECD Test Guideline 210
  - Remarks: No toxicity at the limit of solubility

Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity):
- NOEC (Daphnia magna (Water flea)): 2.14 mg/l
  - Exposure time: 21 d
  - Method: OECD Test Guideline 211
  - Remarks: No toxicity at the limit of solubility

Toxicity to microorganisms:
- EC50: > 1,000 mg/l
  - Exposure time: 3 h
  - Test Type: Respiration inhibition
  - Method: OECD Test Guideline 209

Magnesium stearate:
Toxicity to fish:
- LC50 (Leuciscus idus (Golden orfe)): > 100 mg/l
  - Exposure time: 48 h
  - Method: DIN 38412
  - Remarks: Based on data from similar materials

Toxicity to daphnia and other aquatic invertebrates:
- EL50 (Daphnia magna (Water flea)): > 1 mg/l
  - Exposure time: 47 h
  - Test substance: Water Accommodated Fraction
  - Remarks: Based on data from similar materials
  - No toxicity at the limit of solubility

Toxicity to algae/aquatic plants:
- EL50 (Pseudokirchneriella subcapitata (green algae)): > 1 mg/l
  - Exposure time: 72 h
  - Test substance: Water Accommodated Fraction
  - Method: OECD Test Guideline 201
  - Remarks: Based on data from similar materials
  - No toxicity at the limit of solubility

  NOELR (Pseudokirchneriella subcapitata (green algae)): > 1 mg/l
  - Exposure time: 72 h
  - Test substance: Water Accommodated Fraction
  - Method: OECD Test Guideline 201
  - Remarks: Based on data from similar materials

Toxicity to microorganisms:
- EC10 (Pseudomonas putida): > 100 mg/l
  - Exposure time: 16 h
Test substance: Water Accommodated Fraction
Remarks: Based on data from similar materials

Persistence and degradability

Components:

Sitagliptin:
Biodegradability: Result: not rapidly degradable
Biodegradation: 39.7 %
Exposure time: 28 d
Method: OECD Test Guideline 314

Stability in water: Hydrolysis: 50 % (401 d)
Method: OECD Test Guideline 111

Cellulose:
Biodegradability: Result: Readily biodegradable.

Ertugliflozin:
Biodegradability: Result: Not readily biodegradable.
Biodegradation: 40.8 %
Exposure time: 28 d

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

Bioaccumulative potential

Components:

Sitagliptin:
Partition coefficient: n-octanol/water: log Pow: -0.03

Ertugliflozin:
Partition coefficient: n-octanol/water: log Pow: 2.47

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

Mobility in soil

Components:

Sitagliptin:
Distribution among environmental compartments: log Koc: 4.37

Ertugliflozin:
**SAFETY DATA SHEET**

**Ertugliflozin (< 5%) / Sitagliptin Formulation**

<table>
<thead>
<tr>
<th>Version</th>
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Distribution among environmental compartments: \( \log K_{oc} = 2.88 \)

**Other adverse effects**
No data available

### 13. DISPOSAL CONSIDERATIONS

**Disposal methods**
- **Waste from residues**: Dispose of in accordance with local regulations.
- **Contaminated packaging**: Empty containers should be taken to an approved waste handling site for recycling or disposal. If not otherwise specified: Dispose of as unused product.

### 14. TRANSPORT INFORMATION

**International Regulations**

**UNRTDG**
Not regulated as a dangerous good

**IATA-DGR**
Not regulated as a dangerous good

**IMDG-Code**
Not regulated as a dangerous good

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

### 15. REGULATORY INFORMATION

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

**Minister of Industry Regulation No. 23/M-IND/PER/4/2013 concerning the Revision of Minister of Industry Regulation No. 87/M-IND/PER/9/2009 concerning Globally Harmonized System of Classification and Labelling of Chemicals.**

**Regulation of the Minister of Health No. 472 of 1996 on the Safeguarding of Substances Hazardous to Health**
- Hazardous substances that must be registered: Not applicable

**Government Regulation No. 74 of 2001 on the Management of Hazardous and Toxic Substances**
- Hazardous substances approved for use: Not applicable
- Prohibited substances: Not applicable
- Restricted substances: Not applicable
SAFETY DATA SHEET

Ertugliflozin (< 5%) / Sitagliptin Formulation

Version 1.6
Revision Date: 2020/09/28
SDS Number: 2400320-00007
Date of last issue: 2020/03/23
Date of first issue: 2018/02/01

Regulation of the Minister of Trade No. 44 of 2009 on Procurement, Distribution and Supervision of Hazardous Materials
Type of Hazardous Materials Restricted to Import, Distribution and Supervision: Not applicable

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

AICS: not determined
DSL: not determined
IECSC: not determined

16. OTHER INFORMATION

Further information

Date format: yyyy/mm/dd

Full text of other abbreviations
ACGIH: USA. ACGIH Threshold Limit Values (TLV)
ID OEL: Indonesia. Occupational Exposure Limits

ACGIH / TWA: 8-hour, time-weighted average
ID OEL / NAB: Long term exposure limit

AIIC - Australian Inventory of Industrial Chemicals; ANTT - National Agency for Transport by Land of Brazil; ASTM - American Society for the Testing of Materials; bw - Body weight; CMR - Carcinogen, Mutagen or Reproductive Toxicant; DIN - Standard of the German Institute for Standardisation; DSL - Domestic Substances List (Canada); ECx - Concentration associated with x% response; ELx - Loading rate associated with x% response; EmS - Emergency Schedule; ENCS - Existing and New Chemical Substances (Japan); ErCx - Concentration associated with x% growth rate response; ERG - Emergency Response Guide; GHS - Globally Harmonized System; GLP - Good Laboratory Practice; IARC - International Agency for Research on Cancer; IATA - International Air Transport Association; IBC - International Code for the Construction and Equipment of Ships carrying Dangerous Chemicals in Bulk; IC50 - Half maximal inhibitory concentration; ICAO - International Civil Aviation Organization; IECSC - Inventory of Existing Chemical Substances in China; IMDG - International Maritime Dangerous Goods; IMO - International Maritime Organization; ISHL - Industrial Safety and Health Law (Japan); ICAR - International Organisation for Standardization; KECI - Korea Existing Chemicals Inventory; LC50 - Lethal Concentration to 50 % of a test population; LD50 - Lethal Dose to 50% of a test population (Median Lethal Dose); MARPOL - International Convention for the Prevention of Pollution from Ships; n.o.s. - Not Otherwise Specified; Nch - Chilean Norm; NO(A)EC - No Observed (Adverse) Effect Concentration; NO(A)EL - No Observed (Adverse) Effect Level; NOELR - No Observable Effect Loading Rate; NOM - Official Mexican Norm; NTP - National Toxicology Program; NZIoC - New Zealand Inventory of Chemicals; OECD - Organization for Economic Co-operation and Development; OPPTS - Office of Chemical Safety and Pollution Prevention; PBT - Persistent, Bioaccumulative and Toxic substance; PICCS - Philippines Inventory of Chemicals and Chemical Substances; (Q)SAR - (Quantitative) Structure Activity Relationship; REACH - Regulation (EC) No 1907/2006 of the European Parliament and of the Council concerning the Registration, Evalua-
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.