SAFETY DATA SHEET

Ertugliflozin / Metformin Formulation

1. PRODUCT AND COMPANY IDENTIFICATION

Product name : Ertugliflozin / Metformin 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
Acute toxicity (Oral) : Category 4

GHS label elements
Hazard pictograms : !

Signal word : Warning
Hazard statements : H302 Harmful if swallowed.
Precautionary statements : Prevention:
P264 Wash skin thoroughly after handling.
P270 Do not eat, drink or smoke when using this product.

Response:
P301 + P312 + P330 IF SWALLOWED: Call a POISON CENTER/doctor if you feel unwell. Rinse mouth.

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.
Contact with dust can cause mechanical irritation or drying of the skin.
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>metformin hydrochloride</td>
</tr>
<tr>
<td></td>
<td>Cellulose</td>
</tr>
<tr>
<td></td>
<td>Magnesium stearate</td>
</tr>
<tr>
<td></td>
<td>Ertugliflozin</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
Wash with water and soap.
Get medical attention if symptoms occur.

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 unless directed to do so by medical personnel.
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
Harmful if swallowed.
Contact with dust can cause mechanical irritation or drying of the skin.
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.

5. FIREFIGHTING MEASURES

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

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
- Nitrogen oxides (NOx)
- 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 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 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.

### 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 breathe dust.
- Do not swallow.
- Avoid contact with eyes.
- Avoid prolonged or repeated contact with skin.
- Handle in accordance with good industrial hygiene and safety practice, based on the results of the workplace exposure as-
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.
- 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>Metformin hydrochloride</td>
<td>1115-70-4</td>
<td>TWA</td>
<td>2 mg/m³ (OEB 1)</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>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>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>Ertugliflozin</td>
<td>1210344-83-4</td>
<td>TWA</td>
<td>10 µg/m³ (OEB 3)</td>
<td>Internal</td>
</tr>
</tbody>
</table>

Wipe limit 100 µg/100 cm² Internal

Engineering measures:
- All engineering controls should be implemented by facility design and operated in accordance with GMP principles to protect products, workers, and the environment.
- Containment technologies suitable for controlling compounds are required to control at source and to prevent migration of the compound to uncontrolled areas (e.g., open-face containment devices).
- Minimize open handling.

Personal protective equipment

Respiratory protection:
- If adequate local exhaust ventilation is not available or exposure assessment demonstrates exposures outside the recommended guidelines, use respiratory protection.
  - Filter type: Particulates type
  - Material: Chemical-resistant gloves

Remarks:
- Consider double gloving.
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Date of first issue: 2016/04/01

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, 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

Vapour pressure : Not applicable
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Relative vapour density : Not applicable
Relative density : No data available
Density : No data available
Solubility(ies) : No data available
  Water solubility : No data available
Partition coefficient: n-octanol/water : Not applicable
Auto-ignition temperature : No data available
Decomposition temperature : No data available
Viscosity : Not applicable
  Viscosity, kinematic : Not applicable
Explosive properties : Not explosive
Oxidizing properties : The substance or mixture is not classified as oxidizing.
Particle size : No data available

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
Harmful if swallowed.

Product:
Acute oral toxicity : Acute toxicity estimate: 1,337 mg/kg
Method: Calculation method
### Components:

**metformin hydrochloride:**

- **Acute oral toxicity:**
  - LD50 (Rat): 1,000 mg/kg
  - LD50 (Mouse): 1,450 - 3,500 mg/kg
  - LD50 (Monkey): 463 mg/kg
  - LD50 (Rabbit): 350 mg/kg
  - LD50 (Guinea pig): 500 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

**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

**Ertugliflozin:**

- **Acute oral toxicity:**
  - LD50 (Rat): 500 mg/kg

- **Acute inhalation toxicity:**
  - Remarks: No data available

- **Acute dermal toxicity:**
  - Remarks: No data available

**Skin corrosion/irritation**

Not classified based on available information.

### Components:

**metformin hydrochloride:**

- **Species:** Rabbit
- **Result:** Mild skin irritation

**Magnesium stearate:**

- **Species:** Rabbit
- **Result:** No skin irritation
- **Remarks:** Based on data from similar materials
**SAFETY DATA SHEET**

**Ertugliflozin / Metformin Formulation**

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**Ertugliflozin:**  
Result: Corrosive

**Serious eye damage/eye irritation**  
Not classified based on available information.

**Components:**

**metformin hydrochloride:**  
Species: Rabbit  
Result: Mild eye irritation

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

**Ertugliflozin:**  
Result: Severe irritation

**Respiratory or skin sensitisation**

**Skin sensitisation**  
Not classified based on available information.

**Respiratory sensitisation**  
Not classified based on available information.

**Components:**

**Magnesium stearate:**

<table>
<thead>
<tr>
<th>Test Type</th>
<th>Maximisation Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exposure routes</td>
<td>Skin contact</td>
</tr>
<tr>
<td>Species</td>
<td>Guinea pig</td>
</tr>
<tr>
<td>Method</td>
<td>OECD Test Guideline 406</td>
</tr>
<tr>
<td>Result</td>
<td>negative</td>
</tr>
<tr>
<td>Remarks</td>
<td>Based on data from similar materials</td>
</tr>
</tbody>
</table>

**Ertugliflozin:**

<table>
<thead>
<tr>
<th>Test Type</th>
<th>Local lymph node assay (LLNA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Result</td>
<td>Not a skin sensitizer.</td>
</tr>
</tbody>
</table>

**Germ cell mutagenicity**

Not classified based on available information.

**Components:**

**metformin hydrochloride:**

<table>
<thead>
<tr>
<th>Genotoxicity in vitro</th>
<th>Test Type: Bacterial reverse mutation assay (AMES)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Result</td>
<td>negative</td>
</tr>
</tbody>
</table>
## Genotoxicity in vitro

- **Test Type:** In vitro assay  
  **Test system:** mouse lymphoma cells  
  **Result:** negative

- **Test Type:** Chromosomal aberration  
  **Test system:** Human lymphocytes  
  **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

### 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

### 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
Carcinogenicity
Not classified based on available information.

### Components:

**metformin hydrochloride:**

<table>
<thead>
<tr>
<th>Species</th>
<th>Mouse</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exposure time</td>
<td>91 weeks</td>
</tr>
<tr>
<td>Dose</td>
<td>1500 mg/kg body weight</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</td>
</tr>
<tr>
<td>Exposure time</td>
<td>104 weeks</td>
</tr>
<tr>
<td>Dose</td>
<td>900 mg/kg body weight</td>
</tr>
<tr>
<td>Result</td>
<td>negative</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Species</th>
<th>Rat, female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Application Route</td>
<td>Oral</td>
</tr>
<tr>
<td>Exposure time</td>
<td>104 weeks</td>
</tr>
<tr>
<td>LOAEL</td>
<td>900 mg/kg body weight</td>
</tr>
<tr>
<td>Result</td>
<td>negative</td>
</tr>
<tr>
<td>Target Organs</td>
<td>Uterus (including cervix)</td>
</tr>
<tr>
<td>Remarks</td>
<td>The mechanism or mode of action may not be relevant in humans.</td>
</tr>
</tbody>
</table>

**Cellulose:**

<table>
<thead>
<tr>
<th>Species</th>
<th>Rat</th>
</tr>
</thead>
<tbody>
<tr>
<td>Application Route</td>
<td>Ingestion</td>
</tr>
<tr>
<td>Exposure time</td>
<td>72 weeks</td>
</tr>
<tr>
<td>Result</td>
<td>negative</td>
</tr>
</tbody>
</table>

**Ertugliflozin:**

<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>2 Years</td>
</tr>
<tr>
<td>Result</td>
<td>negative</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>Result</td>
<td>negative</td>
</tr>
</tbody>
</table>

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

Reproductive toxicity
Not classified based on available information.

### Components:

**metformin hydrochloride:**

<table>
<thead>
<tr>
<th>Effects on fertility</th>
<th>Test Type: Fertility</th>
</tr>
</thead>
</table>

Species: Rat  
Application Route: Oral  
Fertility: NOAEL: 600 mg/kg body weight  
Result: No effects on fertility

**Effects on foetal development**  
Species: Rat  
Application Route: Oral  
Developmental Toxicity: NOAEL: 600 mg/kg body weight  
Result: No teratogenic effects

Test Type: Embryo-foetal development  
Species: Rabbit  
Application Route: Oral  
Embryo-foetal toxicity: NOAEL: 140 mg/kg body weight  
Result: No teratogenic effects

**Cellulose:**  
Effects on fertility  
Species: Rat  
Application Route: Ingestion  
Result: negative

Effects on foetal development  
Species: Rat  
Application Route: Ingestion  
Result: negative

**Magnesium stearate:**  
Effects on fertility  
Species: Rat  
Application Route: Ingestion  
Result: negative  
Remarks: Based on data from similar materials

Effects on foetal development  
Species: Rat  
Application Route: Ingestion  
Result: negative  
Remarks: Based on data from similar materials

**Ertugliflozin:**  
Effects on fertility  
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

### STOT - single exposure
Not classified based on available information.

### STOT - repeated exposure
Not classified based on available information.

#### Components:

**Ertugliflozin:**
- Exposure routes: Oral
- Target Organs: Kidney, Stomach, Prostate
- Assessment: May cause damage to organs through prolonged or repeated exposure.

#### Repeated dose toxicity

**Components:**

**metformin hydrochloride:**
- Species: Rat
- NOAEL: 125 mg/kg
- Application Route: Oral
- Exposure time: 1 year
- Remarks: No significant adverse effects were reported

- Species: Rabbit
- NOAEL: 100 mg/kg
- Application Route: Oral
- Exposure time: 1 Year
- Remarks: No significant adverse effects were reported

- Species: Dog
- NOAEL: 50 mg/kg
- Application Route: Subcutaneous
- Exposure time: 2 year
- Remarks: No significant adverse effects were reported

**Cellulose:**
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<table>
<thead>
<tr>
<th>Species</th>
<th>Rat</th>
</tr>
</thead>
<tbody>
<tr>
<td>NOAEL</td>
<td>( \geq 9,000 \text{ mg/kg} )</td>
</tr>
<tr>
<td>Application Route</td>
<td>Ingestion</td>
</tr>
<tr>
<td>Exposure time</td>
<td>90 Days</td>
</tr>
</tbody>
</table>

**Magnesium stearate:**

<table>
<thead>
<tr>
<th>Species</th>
<th>Rat</th>
</tr>
</thead>
<tbody>
<tr>
<td>NOAEL</td>
<td>( &gt; 100 \text{ mg/kg} )</td>
</tr>
<tr>
<td>Application Route</td>
<td>Ingestion</td>
</tr>
<tr>
<td>Exposure time</td>
<td>90 Days</td>
</tr>
<tr>
<td>Remarks</td>
<td>Based on data from similar materials</td>
</tr>
</tbody>
</table>

**Ertugliflozin:**

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

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

<table>
<thead>
<tr>
<th>Species</th>
<th>Rat</th>
</tr>
</thead>
<tbody>
<tr>
<td>LOAEL</td>
<td>25 mg/kg</td>
</tr>
<tr>
<td>Application Route</td>
<td>Oral</td>
</tr>
<tr>
<td>Exposure time</td>
<td>180 d</td>
</tr>
<tr>
<td>Target Organs</td>
<td>Kidney, Bone, Stomach</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Species</th>
<th>Rat</th>
</tr>
</thead>
<tbody>
<tr>
<td>LOAEL</td>
<td>25 mg/kg</td>
</tr>
<tr>
<td>Application Route</td>
<td>Oral</td>
</tr>
<tr>
<td>Exposure time</td>
<td>90 d</td>
</tr>
<tr>
<td>Target Organs</td>
<td>Kidney, Gastrointestinal tract, Prostate</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Species</th>
<th>Dog</th>
</tr>
</thead>
<tbody>
<tr>
<td>NOAEL</td>
<td>150 mg/kg</td>
</tr>
<tr>
<td>Application Route</td>
<td>Oral</td>
</tr>
<tr>
<td>Exposure time</td>
<td>270 d</td>
</tr>
<tr>
<td>Remarks</td>
<td>No significant adverse effects were reported</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Species</th>
<th>Mouse</th>
</tr>
</thead>
<tbody>
<tr>
<td>NOAEL</td>
<td>100 mg/kg</td>
</tr>
<tr>
<td>Application Route</td>
<td>Oral</td>
</tr>
<tr>
<td>Exposure time</td>
<td>90 d</td>
</tr>
<tr>
<td>Remarks</td>
<td>No significant adverse effects were reported</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Species</th>
<th>Mouse</th>
</tr>
</thead>
<tbody>
<tr>
<td>NOAEL</td>
<td>100 mg/kg</td>
</tr>
<tr>
<td>Application Route</td>
<td>Oral</td>
</tr>
<tr>
<td>Exposure time</td>
<td>28 d</td>
</tr>
<tr>
<td>Target Organs</td>
<td>Bone</td>
</tr>
<tr>
<td>Remarks</td>
<td>No significant adverse effects were reported</td>
</tr>
</tbody>
</table>
Aspiration toxicity
Not classified based on available information.

Experience with human exposure

Components:

metformin hydrochloride:

<table>
<thead>
<tr>
<th>Component</th>
<th>Skin contact</th>
<th>Remarks</th>
<th>Eye contact</th>
<th>Remarks</th>
<th>Ingestion</th>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>May irritate skin.</td>
<td></td>
<td>May irritate eyes.</td>
<td>Diarrhoea, Nausea, Vomiting, Gastrointestinal discomfort, flatulence, asthenia, Fatigue, Headache</td>
<td></td>
</tr>
</tbody>
</table>

Ertugliflozin:

<table>
<thead>
<tr>
<th>Component</th>
<th>Ingestion</th>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>The most common side effects are: Headache, constipation, Diarrhoea, Nausea, urinary tract infection, muscle pain, upper respiratory tract infection</td>
</tr>
</tbody>
</table>

12. ECOLOGICAL INFORMATION

Ecotoxicity

Components:

metformin hydrochloride:

<table>
<thead>
<tr>
<th>Component</th>
<th>Toxicity to algae/aquatic plants</th>
<th>Method</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>EC50 (Pseudokirchneriella subcapitata (green algae)): &gt; 100 mg/l</td>
<td>OECD Test Guideline 201</td>
</tr>
<tr>
<td></td>
<td>Exposure time: 72 h</td>
<td></td>
</tr>
</tbody>
</table>

NOEC (Pseudokirchneriella subcapitata (green algae)): 100 mg/l
Exposure time: 72 h
Method: OECD Test Guideline 201

Toxicity to fish (Chronic toxicity):

<table>
<thead>
<tr>
<th>Component</th>
<th>NOEC (Pimephales promelas (fathead minnow)): 10 mg/l</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Exposure time: 33 d</td>
</tr>
<tr>
<td></td>
<td>Method: OECD Test Guideline 210</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Component</th>
<th>NOEC (Daphnia magna (Water flea)): 40 mg/l</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Exposure time: 21 d</td>
</tr>
<tr>
<td></td>
<td>Method: OECD Test Guideline 211</td>
</tr>
</tbody>
</table>

Toxicity to microorganisms:

<table>
<thead>
<tr>
<th>Component</th>
<th>EC50: &gt; 1,000 mg/l</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Exposure time: 3 h</td>
</tr>
<tr>
<td></td>
<td>Test Type: Respiration inhibition</td>
</tr>
<tr>
<td></td>
<td>Method: OECD Test Guideline 209</td>
</tr>
</tbody>
</table>

Cellulose:

Toxicity to fish:

<table>
<thead>
<tr>
<th>Component</th>
<th>LC50 (Oryzias latipes (Japanese medaka)): &gt; 100 mg/l</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Exposure time: 48 h</td>
</tr>
<tr>
<td></td>
<td>Remarks: Based on data from similar materials</td>
</tr>
</tbody>
</table>

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

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 mg/l
                                      Exposure time: 72 h
                                      Method: OECD Test Guideline 201

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
Persistence and degradability

Components:

- **metformin hydrochloride**
  - Biodegradability: Result: rapidly degradable
  - Biodegradation: 50%
  - Exposure time: 2 hrs

- **Cellulose**
  - Biodegradability: Result: Readily biodegradable.

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

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

Bioaccumulative potential

Components:

- **metformin hydrochloride**
  - Partition coefficient: n-octanol/water: log Pow: -2

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

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

Mobility in soil

Components:

- **metformin hydrochloride**
  - Distribution among environmental compartments: log Koc: 4.3
  - Method: OECD Test Guideline 106
SAFETY DATA SHEET

Ertugliflozin / Metformin Formulation

Version: 2.7
Revision Date: 09/13/2019
SDS Number: 590553-00009
Date of last issue: 2019/04/24
Date of first issue: 2016/04/01

Ertugliflozin:
- Distribution among environmental compartments: log Koc: 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
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

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