SAFETY DATA SHEET

Ertugliflozin / Metformin Formulation

SECTION 1. IDENTIFICATION

Product name : Ertugliflozin / Metformin Formulation

Manufacturer or supplier's details
Company name of supplier : Merck & Co., Inc
Address : 126 E. Lincoln Avenue
Rahway, New Jersey U.S.A. 07065
Telephone : 908-740-4000
Emergency telephone : 1-908-423-6000
E-mail address : EHSDATASTEWARD@merck.com

Recommended use of the chemical and restrictions on use
Recommended use : Pharmaceutical
Restrictions on use : Not applicable

SECTION 2. HAZARDS IDENTIFICATION

GHS classification in accordance with the OSHA Hazard Communication Standard (29 CFR 1910.1200)
Combustible dust
Acute toxicity (Oral) : Category 4

GHS label elements
Signal Word : Warning
Hazard pictograms : 

Hazard Statements : If small particles are generated during further processing, handling or by other means, may form combustible dust concentrations in air.
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 doctor if you feel unwell. Rinse mouth.
Disposal:
P501 Dispose of contents and container to an approved waste disposal plant.
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Other hazards
Dust contact with the eyes can lead to mechanical irritation.
Contact with dust can cause mechanical irritation or drying of the skin.

SECTION 3. COMPOSITION/INFORMATION ON INGREDIENTS

Substance / Mixture : Mixture

Components

<table>
<thead>
<tr>
<th>Chemical name</th>
<th>CAS-No.</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metformin hydrochloride</td>
<td>1115-70-4</td>
<td>&gt;= 70 - &lt; 90</td>
</tr>
<tr>
<td>Cellulose</td>
<td>9004-34-6</td>
<td>&gt;= 10 - &lt; 20</td>
</tr>
<tr>
<td>Magnesium stearate</td>
<td>557-04-0</td>
<td>&gt;= 1 - &lt; 5</td>
</tr>
<tr>
<td>Ertugliflozin</td>
<td>1210344-83-4</td>
<td>&gt;= 0.1 - &lt; 1</td>
</tr>
</tbody>
</table>

Actual concentration is withheld as a trade secret

SECTION 4. FIRST AID MEASURES

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

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

In case of skin contact : 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 : Contact with dust can cause mechanical irritation or drying of the skin.
Dust contact with the eyes can lead to mechanical irritation.
Harmful if swallowed.

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 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 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 (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.

SECTION 7. HANDLING AND STORAGE

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

Local/Total ventilation: Use only with adequate ventilation.

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

Conditions for safe storage:
- Keep in properly labeled containers.
- Store in accordance with the particular national regulations.

Materials to avoid:
- Do not store with the following product types:
  - Strong oxidizing agents

### SECTION 8. EXPOSURE CONTROLS/PERSONAL PROTECTION

#### Ingredients with workplace control parameters

- **Inert or nuisance dust**
  - Value type (Form of exposure): TWA (total dust)
  - Basis: OSHA Z-3
  - 15 mg/m³
  - Value type (Form of exposure): TWA (total dust)
  - Basis: OSHA Z-3
  - 5 mg/m³
  - Value type (Form of exposure): TWA (respirable fraction)
  - Basis: OSHA Z-3
  - 15 Million particles per cubic foot
  - Value type (Form of exposure): TWA (respirable fraction)
  - Basis: OSHA Z-3

- **Dust, nuisance dust and particulates**
  - Value type (Form of exposure): PEL (Total dust)
  - Basis: CAL PEL
  - 10 mg/m³
  - Value type (Form of exposure): PEL (respirable dust fraction)
  - Basis: CAL PEL
  - 5 mg/m³

<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>1 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></td>
<td></td>
<td>TWA (Respirable)</td>
<td>5 mg/m³</td>
<td>NIOSH REL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA (total)</td>
<td>10 mg/m³</td>
<td>NIOSH REL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA (total dust)</td>
<td>15 mg/m³</td>
<td>OSHA Z-1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA (respirable fraction)</td>
<td>5 mg/m³</td>
<td>OSHA Z-1</td>
</tr>
</tbody>
</table>
Magnesium stearate  557-04-0  TWA (Inhalable particulate matter)  10 mg/m³  ACGIH

Ertugliflozin  1210344-83-4  TWA  10 µg/m³ (OEB 3)  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: General and local exhaust ventilation is recommended to maintain vapor exposures below recommended limits. Where concentrations are above recommended limits or are unknown, appropriate respiratory protection should be worn. Follow OSHA respirator regulations (29 CFR 1910.134) and use NIOSH/MSHA approved respirators. Protection provided by air purifying respirators against exposure to any hazardous chemical is limited. Use a positive pressure air supplied respirator if there is any potential for uncontrolled release, exposure levels are unknown, or any other circumstance where air purifying respirators may not provide adequate protection.

Hand protection

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.
### SECTION 9. PHYSICAL AND CHEMICAL PROPERTIES

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appearance</td>
<td>powder</td>
</tr>
<tr>
<td>Color</td>
<td>No data available</td>
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<tr>
<td>Odor</td>
<td>No data available</td>
</tr>
<tr>
<td>Odor Threshold</td>
<td>No data available</td>
</tr>
<tr>
<td>pH</td>
<td>No data available</td>
</tr>
<tr>
<td>Melting point/freezing point</td>
<td>No data available</td>
</tr>
<tr>
<td>Initial boiling point and boiling range</td>
<td>No data available</td>
</tr>
<tr>
<td>Flash point</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Evaporation rate</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Flammability (solid, gas)</td>
<td>May form explosive dust-air mixture during processing, handling or other means.</td>
</tr>
<tr>
<td>Flammability (liquids)</td>
<td>No data available</td>
</tr>
<tr>
<td>Upper explosion limit / Upper flammability limit</td>
<td>No data available</td>
</tr>
<tr>
<td>Lower explosion limit / Lower flammability limit</td>
<td>No data available</td>
</tr>
<tr>
<td>Vapor pressure</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Relative vapor density</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Relative density</td>
<td>No data available</td>
</tr>
<tr>
<td>Density</td>
<td>No data available</td>
</tr>
<tr>
<td>Solubility (ies)</td>
<td>Water solubility</td>
</tr>
<tr>
<td>Partition coefficient: n-octanol/water</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Autoignition temperature</td>
<td>No data available</td>
</tr>
<tr>
<td>Decomposition temperature</td>
<td>No data available</td>
</tr>
</tbody>
</table>
Viscosity
  Viscosity, kinematic : Not applicable

Explosive properties : Not explosive

Oxidizing properties : The substance or mixture is not classified as oxidizing.

Particle size : No data available

SECTION 10. STABILITY AND REACTIVITY

Reactivity : Not classified as a reactivity hazard.

Chemical stability : Stable under normal conditions.

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

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

Incompatible materials : Oxidizing agents

Hazardous decomposition products : No hazardous decomposition products are known.

SECTION 11. TOXICOLOGICAL INFORMATION

Information on likely routes of exposure

Inhalation
Skin contact
Ingestion
Eye contact

Acute toxicity
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:
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Acute oral toxicity: LD50 (Rat): > 5,000 mg/kg

Acute inhalation toxicity:
Exposure time: 4 h
Test atmosphere: dust/mist
LC50 (Rat): > 5.8 mg/l

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

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:

<table>
<thead>
<tr>
<th>Species</th>
<th>Rabbit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Result</td>
<td>No eye irritation</td>
</tr>
<tr>
<td>Remarks</td>
<td>Based on data from similar materials</td>
</tr>
</tbody>
</table>

Ertugliflozin:

| Result     | Severe irritation |

Respiratory or skin sensitization

Skin sensitization
Not classified based on available information.

Respiratory sensitization
Not classified based on available information.

Components:

Magnesium stearate:

<table>
<thead>
<tr>
<th>Test Type</th>
<th>Maximization Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Routes of exposure</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></td>
<td>Result: negative</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Genotoxicity in vivo</th>
<th>Test Type: in vitro test</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Test system: mouse lymphoma cells</td>
</tr>
<tr>
<td></td>
<td>Result: negative</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Genotoxicity in vivo</th>
<th>Test Type: Chromosomal aberration</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Test system: Human lymphocytes</td>
</tr>
<tr>
<td></td>
<td>Result: negative</td>
</tr>
</tbody>
</table>

Cellulose:
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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

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:
- **Species**: Mouse
- **Exposure time**: 91 weeks
- **Dose**: 1500 mg/kg body weight
- **Result**: negative

**Species**: Rat, male
- **Application Route**: Oral
- **Exposure time**: 104 weeks
- **Dose**: 900 mg/kg body weight
Result: negative

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

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

IARC: No ingredient of this product present at levels greater than or equal to 0.1% is identified as probable, possible or confirmed human carcinogen by IARC.

OSHA: No component of this product present at levels greater than or equal to 0.1% is on OSHA’s list of regulated carcinogens.

NTP: No ingredient of this product present at levels greater than or equal to 0.1% is identified as a known or anticipated carcinogen by NTP.

Reproductive toxicity
Not classified based on available information.

Components:

metformin hydrochloride:

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

Effects on fetal development: Test Type: Development
Species: Rat
Application Route: Oral
Developmental Toxicity: NOAEL: 600 mg/kg body weight
Result: No teratogenic effects.

Test Type: Embryo-fetal development
Species: Rabbit
Application Route: Oral
Embryo-fetal toxicity.: NOAEL: 140 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 fetal development**
- Test Type: Fertility/early embryonic development
- Species: Rat
- Application Route: Ingestion
- Result: negative

**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

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

Test Type: Embryo-fetal 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:

<table>
<thead>
<tr>
<th>Routes of exposure</th>
<th>Oral</th>
</tr>
</thead>
<tbody>
<tr>
<td>Target Organs</td>
<td>Kidney, Stomach, Prostate</td>
</tr>
<tr>
<td>Assessment</td>
<td>May cause damage to organs through prolonged or repeated exposure.</td>
</tr>
</tbody>
</table>

Repeated dose toxicity

Components:

metformin hydrochloride:

<table>
<thead>
<tr>
<th>Species</th>
<th>Rat</th>
</tr>
</thead>
<tbody>
<tr>
<td>NOAEL</td>
<td>125 mg/kg</td>
</tr>
<tr>
<td>Application Route</td>
<td>Oral</td>
</tr>
<tr>
<td>Exposure time</td>
<td>1 year</td>
</tr>
<tr>
<td>Remarks</td>
<td>No significant adverse effects were reported</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Species</th>
<th>Rabbit</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>1 Year</td>
</tr>
<tr>
<td>Remarks</td>
<td>No significant adverse effects were reported</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Species</th>
<th>Dog</th>
</tr>
</thead>
<tbody>
<tr>
<td>NOAEL</td>
<td>50 mg/kg</td>
</tr>
<tr>
<td>Application Route</td>
<td>Subcutaneous</td>
</tr>
<tr>
<td>Exposure time</td>
<td>2 year</td>
</tr>
<tr>
<td>Remarks</td>
<td>No significant adverse effects were reported</td>
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</table>

Cellulose:

<table>
<thead>
<tr>
<th>Species</th>
<th>Rat</th>
</tr>
</thead>
<tbody>
<tr>
<td>NOAEL</td>
<td>&gt;= 9,000 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:
- **Species**: Rat
- **NOAEL**: > 100 mg/kg
- **Application Route**: Ingestion
- **Exposure time**: 90 Days
- **Remarks**: Based on data from similar materials

Ertugliflozin:
- **Species**: Rat
- **LOAEL**: 500 mg/kg
- **Application Route**: Oral
- **Exposure time**: 30 d

- **Species**: Rat
- **LOAEL**: 250 mg/kg
- **Application Route**: Oral
- **Exposure time**: 30 d
- **Target Organs**: Kidney

- **Species**: Rat
- **LOAEL**: 25 mg/kg
- **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

**Aspiration toxicity**
Not classified based on available information.
Experience with human exposure

Components:

metformin hydrochloride:

| Skin contact | Remarks: May irritate skin. |
| Eye contact  | Remarks: May irritate eyes. |
| Ingestion    | Symptoms: Diarrhea, Nausea, Vomiting, Gastrointestinal discomfort, flatulence, asthenia, Fatigue, Headache |

Ertugliflozin:

| Ingestion     | Symptoms: The most common side effects are:, Headache, constipation, Diarrhea, Nausea, urinary tract infection, muscle pain, upper respiratory tract infection |

SECTION 12. ECOLOGICAL INFORMATION

Ecotoxicity

Components:

metformin hydrochloride:

Toxicity to algae/aquatic plants: EC50 (Pseudokirchneriella subcapitata (green algae)): > 100 mg/l
            Exposure time: 72 h
            Method: OECD Test Guideline 201

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

Toxicity to fish (Chronic toxicity): NOEC (Pimephales promelas (fathead minnow)): 10 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)): 40 mg/l
            Exposure time: 21 d
            Method: OECD Test Guideline 211

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

Cellulose:

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

Magnesium stearate:

Toxicity to fish: LC50 (Leuciscus idus (Golden orfe)): > 100 mg/l
            Exposure time: 48 h
            Method: DIN 38412
<table>
<thead>
<tr>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Toxicity to daphnia and other aquatic invertebrates:</td>
</tr>
<tr>
<td>EL50 (Daphnia magna (Water flea)): &gt; 1 mg/l</td>
</tr>
<tr>
<td>Exposure time: 47 h</td>
</tr>
<tr>
<td>No toxicity at the limit of solubility.</td>
</tr>
<tr>
<td>Toxicity to algae/aquatic plants:</td>
</tr>
<tr>
<td>EL50 (Pseudokirchneriella subcapitata (green algae)): &gt; 1 mg/l</td>
</tr>
<tr>
<td>Exposure time: 72 h</td>
</tr>
<tr>
<td>Test substance: Water Accommodated Fraction Method: OECD Test Guideline 201Remarks: Based on data from similar materials</td>
</tr>
<tr>
<td>No toxicity at the limit of solubility.</td>
</tr>
<tr>
<td>NOELR (Pseudokirchneriella subcapitata (green algae)): &gt; 1 mg/l</td>
</tr>
<tr>
<td>Exposure time: 72 h</td>
</tr>
<tr>
<td>Test substance: Water Accommodated Fraction Method: OECD Test Guideline 201Remarks: Based on data from similar materials</td>
</tr>
<tr>
<td>Toxicity to microorganisms:</td>
</tr>
<tr>
<td>EC10 (Pseudomonas putida): &gt; 100 mg/l</td>
</tr>
<tr>
<td>Exposure time: 16 h</td>
</tr>
<tr>
<td>Test substance: Water Accommodated Fraction Method: OECD Test Guideline 201Remarks: Based on data from similar materials</td>
</tr>
<tr>
<td>Ertugliflozin:</td>
</tr>
<tr>
<td>Toxicity to algae/aquatic plants:</td>
</tr>
<tr>
<td>EC50 (Pseudokirchneriella subcapitata (green algae)): 77 mg/l</td>
</tr>
<tr>
<td>Exposure time: 72 h</td>
</tr>
<tr>
<td>Method: OECD Test Guideline 201Remarks:</td>
</tr>
<tr>
<td>NOEC (Pseudokirchneriella subcapitata (green algae)): 50 mg/l</td>
</tr>
<tr>
<td>Exposure time: 72 h</td>
</tr>
<tr>
<td>Method: OECD Test Guideline 201Remarks:</td>
</tr>
<tr>
<td>Toxicity to fish (Chronic toxicity):</td>
</tr>
<tr>
<td>NOEC (Pimephales promelas (fathead minnow)): 1 mg/l</td>
</tr>
<tr>
<td>Exposure time: 32 d</td>
</tr>
<tr>
<td>Method: OECD Test Guideline 210Remarks: No toxicity at the limit of solubility.</td>
</tr>
<tr>
<td>Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity):</td>
</tr>
<tr>
<td>NOEC (Daphnia magna (Water flea)): 2.14 mg/l</td>
</tr>
<tr>
<td>Exposure time: 21 d</td>
</tr>
<tr>
<td>Method: OECD Test Guideline 211Remarks: No toxicity at the limit of solubility.</td>
</tr>
<tr>
<td>Toxicity to microorganisms:</td>
</tr>
<tr>
<td>EC50: &gt; 1,000 mg/l</td>
</tr>
<tr>
<td>Exposure time: 3 h</td>
</tr>
<tr>
<td>Test Type: Respiration inhibition Method: OECD Test Guideline 209Remarks:</td>
</tr>
</tbody>
</table>
NOEC: 1,000 mg/l  
Exposure time: 3 h  
Test Type: Respiration inhibition  
Method: OECD Test Guideline 209

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

Ertugliflozin:
- Distribution among environmental compartments: log Koc: 2.88
mental compartments

Other adverse effects
No data available

SECTION 13. DISPOSAL CONSIDERATIONS

Disposal methods

<table>
<thead>
<tr>
<th>Waste from residues</th>
<th>Contaminated packaging</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dispose of in accordance with local regulations.</td>
<td>Empty containers should be taken to an approved waste handling site for recycling or disposal. Do not dispose of waste into sewer.</td>
</tr>
</tbody>
</table>

If not otherwise specified: Dispose of as unused product.

SECTION 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.

Domestic regulation

49 CFR
Not regulated as a dangerous good

Special precautions for user
Not applicable

SECTION 15. REGULATORY INFORMATION

CERCLA Reportable Quantity
This material does not contain any components with a CERCLA RQ.

SARA 304 Extremely Hazardous Substances Reportable Quantity
This material does not contain any components with a section 304 EHS RQ.

SARA 302 Extremely Hazardous Substances Threshold Planning Quantity
This material does not contain any components with a section 302 EHS TPQ.

SARA 311/312 Hazards
- Combustible dust
- Acute toxicity (any route of exposure)

SARA 313
This material does not contain any chemical components with known CAS numbers that exceed the threshold (De Minimis) reporting levels established by SARA Title III, Section 313.
SAFETY DATA SHEET

Ertugliflozin / Metformin Formulation

Version 7.0  Revision Date: 04/04/2023  SDS Number: 590562-00017  Date of last issue: 10/01/2022
Date of first issue: 04/01/2016

US State Regulations

Pennsylvania Right To Know
- metformin hydrochloride 1115-70-4
- Cellulose 9004-34-6
- Polyvinyl pyrrolidone 9003-39-8

California List of Hazardous Substances
- Polyvinyl pyrrolidone 9003-39-8

California Permissible Exposure Limits for Chemical Contaminants
- Cellulose 9004-34-6
- Magnesium stearate 557-04-0

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

NFPA 704:
- Flammability: 1
- Health: 1
- Special hazard: 0
- Instability: 0

HMIS® IV:
- HEALTH: / 1
- FLAMMABILITY: 3
- PHYSICAL HAZARD: 0

HMIS® ratings are based on a 0-4 rating scale, with 0 representing minimal hazards or risks, and 4 representing significant hazards or risks. The "*" represents a chronic hazard, while the "/" represents the absence of a chronic hazard.

Full text of other abbreviations
- ACGIH: USA. ACGIH Threshold Limit Values (TLV)
- CAL PEL: California permissible exposure limits for chemical contaminants (Title 8, Article 107)
- NIOSH REL: USA. NIOSH Recommended Exposure Limits
- OSHA Z-1: USA. Occupational Exposure Limits (OSHA) - Table Z-1 Limits for Air Contaminants
- OSHA Z-3: USA. Occupational Exposure Limits (OSHA) - Table Z-3 Min-
SAFETY DATA SHEET

Ertugliflozin / Metformin Formulation

<table>
<thead>
<tr>
<th>Version</th>
<th>Revision Date</th>
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<th>Date of last issue: 10/01/2022</th>
<th>Date of first issue: 04/01/2016</th>
</tr>
</thead>
<tbody>
<tr>
<td>7.0</td>
<td>04/04/2023</td>
<td>590562-00017</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

General Dusts

ACGIH / TWA: 8-hour, time-weighted average
CAL PEL / PEL: Permissible exposure limit
NIOSH REL / TWA: Time-weighted average concentration for up to a 10-hour workday during a 40-hour workweek

OSHA Z-1 / TWA: 8-hour time weighted average
OSHA Z-3 / TWA: 8-hour time weighted average

AIIc - Australian Inventory of Industrial Chemicals; ASTM - American Society for the Testing of Materials; bw - Body weight; CERCLA - Comprehensive Environmental Response, Compensation, and Liability Act; CMR - Carcinogen, Mutagen or Reproductive Toxicant; DIN - Standard of the German Institute for Standardisation; DOT - Department of Transportation; DSL - Domestic Substances List (Canada); ECx - Concentration associated with x% response; EHS - Extremely Hazardous Substance; 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; HMIS - Hazardous Materials Identification System; 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; IECS - Inventory of Existing Chemical Substances; 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; MSHA - Mine Safety and Health Administration; n.o.s. - Not Otherwise Specified; NFPA - National Fire Protection Association; NO(A)EC - No Observed (Adverse) Effect Concentration; NO(A)EL - No Observed (Adverse) Effect Level; NOELR - No Observable Effect Loading Rate; 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; RCRA - Resource Conservation and Recovery Act; REACH - Regulation (EC) No 1907/2006 of the European Parliament and of the Council concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals; RQ - Reportable Quantity; SADT - Self-Accelerating Decomposition Temperature; SARA - Superfund Amendments and Reauthorization Act; SDS - Safety Data Sheet; TCSI - Taiwan Chemical Substance Inventory; TCEC - Thailand Existing Chemicals Inventory; TSCA - Toxic Substances Control Act (United States); UN - United Nations; UNRTDG - United Nations Recommendations on the Transport of Dangerous Goods; vPvB - Very Persistent and Very Bioaccumulative


Revision Date: 04/04/2023

Items where changes have been made to the previous version are highlighted in the body of this document by two vertical lines.

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
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