SAFETY DATA SHEET

Sitagliptin / Metformin Extended Release Formulation

Version 11.0 Revision Date: 04/04/2023 SDS Number: 29118-00023 Date of last issue: 10/01/2022
Date of first issue: 11/07/2014

SECTION 1. IDENTIFICATION

Product name: Sitagliptin / Metformin Extended Release 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: EHSDATASTEWAR@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
Hazard pictograms:

Signal Word: Warning

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;= 50 - &lt; 70</td>
</tr>
<tr>
<td>Cellulose</td>
<td>9004-34-6</td>
<td>&gt;= 10 - &lt; 20</td>
</tr>
<tr>
<td>Sitagliptin</td>
<td>654671-77-9</td>
<td>&gt;= 5 - &lt; 10</td>
</tr>
<tr>
<td>Kaolin</td>
<td>1332-58-7</td>
<td>&gt;= 1 - &lt; 5</td>
</tr>
<tr>
<td>Titanium dioxide</td>
<td>13463-67-7</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 fire : Avoid generating dust; fine dust dispersed in air in sufficient

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fighting 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
- Nitrogen oxides (NOx)
- Silicon 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 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

<table>
<thead>
<tr>
<th></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>inert or nuisance dust</td>
<td>1115-70-4</td>
<td>TWA (total dust)</td>
<td>1 mg/m³ (OEB 1)</td>
<td>Internal</td>
</tr>
<tr>
<td></td>
<td>9004-34-6</td>
<td>TWA (respirable)</td>
<td>10 mg/m³</td>
<td>ACGIH</td>
</tr>
<tr>
<td>Dust, nuisance dust and particulates</td>
<td>1115-70-4</td>
<td>TWA (total dust)</td>
<td>10 mg/m³</td>
<td>CAL PEL</td>
</tr>
<tr>
<td></td>
<td>9004-34-6</td>
<td>TWA (respirable)</td>
<td>5 mg/m³</td>
<td>NIOSH REL</td>
</tr>
</tbody>
</table>
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<table>
<thead>
<tr>
<th></th>
<th>TWA (total)</th>
<th>TWA (total dust)</th>
<th>TWA (respirable fraction)</th>
<th>Sitagliptin</th>
<th>654671-77-9</th>
<th>TWA</th>
<th>0.5 mg/m³ (OEB 2)</th>
<th>Internal</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th></th>
<th>TWA (Respirable)</th>
<th>TWA (total)</th>
<th>TWA (total dust)</th>
<th>TWA (respirable fraction)</th>
<th>Kaolin</th>
<th>1332-58-7</th>
<th>2 mg/m³</th>
<th>ACGIH</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th></th>
<th>TWA (Respirable)</th>
<th>TWA (total)</th>
<th>TWA (total dust)</th>
<th>TWA (respirable fraction)</th>
<th>Titanium dioxide</th>
<th>13463-67-7</th>
<th>2.5 mg/m³ (Titanium dioxide)</th>
<th>ACGIH</th>
</tr>
</thead>
</table>

**This substance(s) is not bioavailable and therefore does not contribute to a dust inhalation hazard.**

Titanium dioxide

**Engineering measures**: Use feasible engineering controls to minimize exposure to compound. All engineering controls should be implemented by facility design and operated in accordance with GMP principles to protect products, workers, and the environment.

**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: Chemical-resistant gloves

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.

Hygiene measures:
- If exposure to chemical is likely during typical use, provide eye flushing systems and safety showers close to the working place.
- When using do not eat, drink or smoke.
- Wash contaminated clothing before re-use.

The effective operation of a facility should include review of engineering controls, proper personal protective equipment, appropriate degowning and decontamination procedures, industrial hygiene monitoring, medical surveillance and the use of administrative controls.

### SECTION 9. PHYSICAL AND CHEMICAL PROPERTIES

- **Appearance**: powder
- **Color**: blue green
- **Odor**: No data available
- **Odor Threshold**: No data available
- **pH**: No data available
- **Melting point/freezing point**: No data available
- **Initial boiling point and boiling range**: No data available
- **Flash point**: Not applicable
- **Evaporation rate**: Not applicable
- **Flammability (solid, gas)**: May form explosive dust-air mixture during processing, handling or other means.
- **Flammability (liquids)**: No data available
- **Upper explosion limit / Upper flammability limit**: No data available
- **Lower explosion limit / Lower flammability limit**: No data available
- **Vapor pressure**: Not applicable
- **Relative vapor density**: Not applicable
- **Relative density**: No data available
Density : No data available
Solubility(ies)
Water solubility : No data available
Partition coefficient: n-octanol/water : Not applicable
Autoignition temperature : No data available
Decomposition temperature : No data available
Viscosity
Viscosity, kinematic : Not applicable
Explosive properties : Not explosive
Oxidizing properties : The substance or mixture is not classified as oxidizing.
Molecular weight : No data available
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: 1,588 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

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

**Kaolin:**
- Acute oral toxicity: LD50 (Rat): > 5,000 mg/kg
- Remarks: Based on data from similar materials
- Acute inhalation toxicity:
  - LC50 (Rat): > 2.07 mg/l
  - Exposure time: 4 h
  - Test atmosphere: dust/mist
  - Assessment: The substance or mixture has no acute inhalation toxicity
  - Remarks: Based on data from similar materials
- Acute dermal toxicity: LD50 (Rat): > 5,000 mg/kg
  - Assessment: The substance or mixture has no acute dermal toxicity
  - Remarks: Based on data from similar materials

**Titanium dioxide:**
- Acute oral toxicity: LD50 (Rat): > 5,000 mg/kg
- Acute inhalation toxicity:
  - LC50 (Rat): > 6.82 mg/l
  - Exposure time: 4 h
  - Test atmosphere: dust/mist
  - Assessment: The substance or mixture has no acute inhalation toxicity
Skin corrosion/irritation
Not classified based on available information.

**Components:**

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

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

**Kaolin:**
- **Species**: Rabbit
- **Method**: OECD Test Guideline 404
- **Result**: No skin irritation
- **Remarks**: Based on data from similar materials

**Titanium dioxide:**
- **Species**: Rabbit
- **Result**: No skin irritation

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

**Components:**

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

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

**Kaolin:**
- **Species**: Rabbit
- **Result**: No eye irritation
- **Remarks**: Based on data from similar materials

**Titanium dioxide:**
- **Species**: Rabbit
- **Result**: No eye irritation
Respiratory or skin sensitization

Skin sensitization
Not classified based on available information.

Respiratory sensitization
Not classified based on available information.

Components:

Sitagliptin:

<table>
<thead>
<tr>
<th>Test Type</th>
<th>Local lymph node assay (LLNA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Species</td>
<td>Mouse</td>
</tr>
<tr>
<td>Method</td>
<td>OECD Test Guideline 429</td>
</tr>
<tr>
<td>Result</td>
<td>Not a skin sensitizer.</td>
</tr>
</tbody>
</table>

Titanium dioxide:

<table>
<thead>
<tr>
<th>Test Type</th>
<th>Local lymph node assay (LLNA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Routes of exposure</td>
<td>Skin contact</td>
</tr>
<tr>
<td>Species</td>
<td>Mouse</td>
</tr>
<tr>
<td>Result</td>
<td>negative</td>
</tr>
</tbody>
</table>

Germ cell mutagenicity
Not classified based on available information.

Components:

metformin hydrochloride:

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

Test Type: in vitro test
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

Genotoxicity in vivo
Test Type: Mammalian erythrocyte micronucleus test (in vivo
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<table>
<thead>
<tr>
<th>Version</th>
<th>Revision Date:</th>
<th>SDS Number:</th>
<th>Date of last issue:</th>
<th>Date of first issue:</th>
</tr>
</thead>
<tbody>
<tr>
<td>11.0</td>
<td>04/04/2023</td>
<td>29118-00023</td>
<td>10/01/2022</td>
<td>11/07/2014</td>
</tr>
</tbody>
</table>

### Cytogenetic Assay

- **Species**: Mouse
- **Application Route**: Ingestion
- **Result**: negative

### 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

### Titanium Dioxide:

#### Genotoxicity in vitro

- **Test Type**: Bacterial reverse mutation assay (AMES)
  - **Result**: negative

#### Genotoxicity in vivo

- **Test Type**: In vivo micronucleus test
  - **Species**: Mouse
  - **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
  - **Dose**: 900 mg/kg body weight
  - **LOAEL**: 900 mg/kg body weight
### 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>

### 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**

### Titanium dioxide:

- **Species**: Rat
- **Application Route**: inhalation (dust/mist/fume)
- **Exposure time**: 2 Years
- **Method**: OECD Test Guideline 453
- **Result**: positive
- **Remarks**: The mechanism or mode of action may not be relevant in humans. This substance(s) is not bioavailable and therefore does not contribute to a dust inhalation hazard.

### Carcinogenicity - Assessment:

- **Limited evidence of carcinogenicity in inhalation studies with animals.**

### IARC

- **Group 2B: Possibly carcinogenic to humans**
  - Titanium dioxide: 13463-67-7

### 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:

<table>
<thead>
<tr>
<th>Test Type</th>
<th>Species</th>
<th>Application Route</th>
<th>NOAEL</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Effects on fertility</td>
<td>Fertility</td>
<td>Oral</td>
<td>600 mg/kg body weight</td>
<td>No effects on fertility.</td>
</tr>
<tr>
<td>Effects on fetal development</td>
<td>Development</td>
<td>Oral</td>
<td>600 mg/kg body weight</td>
<td>No teratogenic effects.</td>
</tr>
</tbody>
</table>

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

#### Cellulose:

<table>
<thead>
<tr>
<th>Test Type</th>
<th>Species</th>
<th>Application Route</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Effects on fertility</td>
<td>One-generation reproduction toxicity study</td>
<td>Rat</td>
<td>negative</td>
</tr>
<tr>
<td>Effects on fetal development</td>
<td>Fertility/early embryonic development</td>
<td>Rat</td>
<td>negative</td>
</tr>
</tbody>
</table>

#### Sitagliptin:

<table>
<thead>
<tr>
<th>Test Type</th>
<th>Species</th>
<th>Application Route</th>
<th>NOAEL</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Effects on fertility</td>
<td>Fertility/early embryonic development</td>
<td>Rat</td>
<td>1,000 mg/kg body weight</td>
<td>Animal testing did not show any effects on fertility.</td>
</tr>
<tr>
<td>Effects on fetal development</td>
<td>Embryo-fetal development</td>
<td>Rat</td>
<td>LOAEL: 250 mg/kg body weight</td>
<td>Embryotoxic effects and adverse effects on the offspring were detected., No teratogenic effects.</td>
</tr>
</tbody>
</table>

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

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

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

**Repeated dose toxicity**

**Components:**

**metformin hydrochloride:**

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

<table>
<thead>
<tr>
<th>Species</th>
<th>NOAEL</th>
<th>Application Route</th>
<th>Exposure time</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rabbit</td>
<td>100 mg/kg</td>
<td>Oral</td>
<td>1 Year</td>
<td>No significant adverse effects were reported</td>
</tr>
</tbody>
</table>

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

**Cellulose:**

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

**Sitagliptin:**

<table>
<thead>
<tr>
<th>Species</th>
<th>NOAEL</th>
<th>LOAEL</th>
<th>Application Route</th>
<th>Exposure time</th>
<th>Target Organs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mouse</td>
<td>500 mg/kg</td>
<td>1,000 mg/kg</td>
<td>Oral</td>
<td>&gt; 2 y</td>
<td>Kidney</td>
</tr>
</tbody>
</table>

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

Species: Dog
NOAEL: 2 mg/kg
LOAEL: 10 mg/kg
Application Route: Oral
Exposure time: 27 Weeks
Target Organs: Skeletal muscle, Central nervous system
Symptoms: Loss of balance
Remarks: The mechanism or mode of action may not be relevant in humans.

Species: Monkey
NOAEL: 100 mg/kg
Application Route: Oral
Exposure time: 14 Weeks
Remarks: No significant adverse effects were reported

Titanium dioxide:
Species: Rat
NOAEL: 24,000 mg/kg
Application Route: Ingestion
Exposure time: 28 Days

Species: Rat
NOAEL: 10 mg/m³
Application Route: inhalation (dust/mist/fume)
Exposure time: 2 y

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

Sitagliptin:
Inhalation: Symptoms: upper respiratory tract infection, pharyngitis, Headache
**Safety Data Sheet**

**Sitagliptin / Metformin Extended Release Formulation**

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**Ingestion**

Symptoms: upper respiratory tract infection, nasopharyngitis, Headache, Nausea, Abdominal pain, Diarrhea

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**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

**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

Kaolin:

Toxicity to fish (Chronic toxicity)

NOELR (Oncorhynchus mykiss (rainbow trout)): > 100 mg/l
Exposure time: 30 d

Titanium dioxide:

Toxicity to fish

LC50 (Oncorhynchus mykiss (rainbow trout)): > 100 mg/l
Exposure time: 96 h
Method: OECD Test Guideline 203

Toxicity to daphnia and other aquatic invertebrates

EC50 (Daphnia magna (Water flea)): > 100 mg/l
Exposure time: 48 h

Toxicity to algae/aquatic plants

EC50 (Skeletonema costatum (marine diatom)): > 10,000 mg/l
Exposure time: 72 h

Toxicity to microorganisms

EC50: > 1,000 mg/l
Exposure time: 3 h
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.

**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

**Bioaccumulative potential**

**Components:**

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

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

**Mobility in soil**

**Components:**

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

**Sitagliptin:**
Distribution among environmental compartments: log Koc: 4.37

**Other adverse effects**
No data available

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**SECTION 13. DISPOSAL CONSIDERATIONS**

**Disposal methods**

**Waste from residues:** Dispose of in accordance with local regulations.
Do not dispose of waste into sewer.

**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.

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**SECTION 14. TRANSPORT INFORMATION**

**International Regulations**

**UNRTDG**
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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.

US State Regulations

Pennsylvania Right To Know
- metformin hydrochloride 1115-70-4
- Hydroxypropyl methylcellulose 9004-65-3
- Cellulose 9004-34-6
- Sitagliptin 654671-77-9
- Polyvinyl pyrrolidone 9003-39-8
- Kaolin 1332-58-7

California Prop. 65
WARNING: This product can expose you to chemicals including Titanium dioxide, which is/are known to the State of California to cause cancer. For more information go to www.P65Warnings.ca.gov.

California List of Hazardous Substances
- Polyvinyl pyrrolidone 9003-39-8
California Permissible Exposure Limits for Chemical Contaminants

- Cellulose: 9004-34-6
- Kaolin: 1332-58-7

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
- Instability: 0
- Special hazard: 

**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 Mineral 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
SAFETY DATA SHEET

Sitagliptin / Metformin Extended Release Formulation

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Sources of key data used to compile the Material Safety Data Sheet:

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 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.