SAFETY DATA SHEET

Sitagliptin / Metformin Extended Release Formulation

Version 5.0  Revision Date: 04/04/2023  SDS Number: 29090-00022  Date of last issue: 10/01/2022
Date of first issue: 11/07/2014

SECTION 1. IDENTIFICATION

Product name: Sitagliptin / Metformin Extended Release Formulation
Other means of identification: No data available

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 Hazardous Products Regulations
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 doctor if you feel unwell. Rinse mouth.

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

Other hazards
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.
SECTION 3. COMPOSITION/INFORMATION ON INGREDIENTS

Substance / Mixture : Mixture

<table>
<thead>
<tr>
<th>Components</th>
<th>Chemical name</th>
<th>Common Name/Synonym</th>
<th>CAS-No.</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td>metformin hydrochloride</td>
<td>No data available</td>
<td>1115-70-4</td>
<td>&gt;= 60 - &lt; 80 *</td>
<td></td>
</tr>
<tr>
<td>Cellulose</td>
<td>No data available</td>
<td>9004-34-6</td>
<td>&gt;= 10 - &lt; 30 *</td>
<td></td>
</tr>
<tr>
<td>Sitagliptin</td>
<td>No data available</td>
<td>654671-77-9</td>
<td>&gt;= 5 - &lt; 10 *</td>
<td></td>
</tr>
<tr>
<td>Kaolin</td>
<td>Hydrated aluminum silicate</td>
<td>1332-58-7</td>
<td>&gt;= 1 - &lt; 5 *</td>
<td></td>
</tr>
<tr>
<td>Titanium dioxide</td>
<td>Titanium anhydride</td>
<td>13463-67-7</td>
<td>&gt;= 0.1 - &lt; 1 *</td>
<td></td>
</tr>
</tbody>
</table>

* Actual concentration or concentration range 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
SECTION 6. ACCIDENTAL RELEASE MEASURES

Unsuitable extinguishing media : None known.
Specific hazards during firefighting : Avoid generating dust; fine dust dispersed in air in sufficient concentrations, and in the presence of an ignition source is a potential dust explosion hazard. Exposure to combustion products may be a hazard to health.

Hazardous combustion products : Carbon oxides
Metal oxides
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 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.
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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.
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>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>CA AB OEL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA (Total dust)</td>
<td>10 mg/m³</td>
<td>CA BC OEL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA (respirable dust fraction)</td>
<td>3 mg/m³</td>
<td>CA BC OEL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA (total dust)</td>
<td>10 mg/m³</td>
<td>CA QC OEL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWAEV (respirable dust)</td>
<td>2 mg/m³</td>
<td>ACGIH</td>
</tr>
<tr>
<td>Sitagliptin</td>
<td>654671-77-9</td>
<td>TWA</td>
<td>0.5 mg/m³ (OEB 2)</td>
<td>Internal</td>
</tr>
<tr>
<td>Kaolin</td>
<td>1332-58-7</td>
<td>TWA (Respirable)</td>
<td>2 mg/m³</td>
<td>CA AB OEL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA (Respirable)</td>
<td>2 mg/m³</td>
<td>CA BC OEL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWAEV (respirable dust)</td>
<td>2 mg/m³</td>
<td>CA QC OEL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA (Respirable particulate matter)</td>
<td>2 mg/m³</td>
<td>ACGIH</td>
</tr>
<tr>
<td>Titanium dioxide</td>
<td>13463-67-7</td>
<td>TWA</td>
<td>10 mg/m³</td>
<td>CA AB OEL</td>
</tr>
</tbody>
</table>
TWA (Total dust) | 10 mg/m³ | CA BC OEL
--- | --- | ---
TWA (respirable dust fraction) | 3 mg/m³ | CA BC OEL
TWAEV (total dust) | 10 mg/m³ | CA QC OEL
TWA (Respirable particulate matter) | 2.5 mg/m³ (Titanium dioxide) | ACGIH

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**

If adequate local exhaust ventilation is not available or exposure assessment demonstrates exposures outside the recommended guidelines, use respiratory protection.

- **Filter type**: Particulates type

**Hand protection**

- **Material**: Chemical-resistant gloves

**Eye protection**

- Wear safety glasses with side shields or 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**

- **Hygiene measures**: Work uniform or laboratory coat.
- 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)

<table>
<thead>
<tr>
<th>Water solubility</th>
<th>No data available</th>
</tr>
</thead>
</table>

### Partition coefficient: n-octanol/water
Not applicable

### Autoignition temperature
No data available

### Decomposition temperature
No data available

### Viscosity

<table>
<thead>
<tr>
<th>Viscosity, kinematic</th>
<th>Not applicable</th>
</tr>
</thead>
</table>

### Explosive properties
Not explosive

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

### Molecular weight
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
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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
- **Result:** Irritating to eyes.
- **Method:** Draize Test

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

**Titanium dioxide:**
- **Test Type:** Local lymph node assay (LLNA)
- **Routes of exposure:** Skin contact
- **Species:** Mouse
- **Result:** negative
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 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
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
  - **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

**Sitagliptin**:

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

- **Species**: Rat
  - **Application Route**: oral (drinking water)
  - **Exposure time**: 2 Years
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**Sitagliptin / Metformin Extended Release Formulation**

<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>5.0</td>
<td>04/04/2023</td>
<td>29090-00022</td>
<td>10/01/2022</td>
<td>11/07/2014</td>
</tr>
</tbody>
</table>

### Result

<table>
<thead>
<tr>
<th>Target Organs</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver</td>
<td>Significant toxicity observed in testing</td>
</tr>
</tbody>
</table>

### Carcinogenicity - Assessment

<table>
<thead>
<tr>
<th>Species: Titanium dioxide</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight of evidence does not support classification as a carcinogen</td>
</tr>
</tbody>
</table>

**Titanium dioxide**:

<table>
<thead>
<tr>
<th>Species: Rat</th>
</tr>
</thead>
<tbody>
<tr>
<td>Application Route: inhalation (dust/mist/fume)</td>
</tr>
<tr>
<td>Exposure time: 2 Years</td>
</tr>
<tr>
<td>Method: OECD Test Guideline 453</td>
</tr>
<tr>
<td>Result: positive</td>
</tr>
<tr>
<td>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.</td>
</tr>
</tbody>
</table>

### Carcinogenicity - Assessment

| Limited evidence of carcinogenicity in inhalation studies with animals. |

### Reproductive toxicity

Not classified based on available information.

### Components:

**metformin hydrochloride**:

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

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

<table>
<thead>
<tr>
<th>Test Type: Embryo-fetal development</th>
</tr>
</thead>
<tbody>
<tr>
<td>Species: Rabbit</td>
</tr>
<tr>
<td>Application Route: Oral</td>
</tr>
<tr>
<td>Embryo-fetal toxicity: NOAEL: 140 mg/kg body weight</td>
</tr>
<tr>
<td>Result: No teratogenic effects.</td>
</tr>
</tbody>
</table>

### Cellulose:

<table>
<thead>
<tr>
<th>Effects on fertility: Test Type: One-generation reproduction toxicity study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Species: Rat</td>
</tr>
<tr>
<td>Application Route: Ingestion</td>
</tr>
<tr>
<td>Result: negative</td>
</tr>
</tbody>
</table>

| Effects on fetal development: Test Type: Fertility/early embryonic development |
Species: Rat  
Application Route: Ingestion  
Result: negative

**Sitagliptin:**

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

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

Test Type: Embryo-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>
<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>
<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>
<tr>
<td>Cellulose:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>----------------------------------------</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Species: Rat</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NOAEL: &gt;= 9,000 mg/kg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Application Route: Ingestion</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Exposure time: 90 Days</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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

| Species: Rat                          |
| NOAEL: 500 mg/kg                      |
| LOAEL: 1,000 mg/kg                    |
| Application Route: Oral               |
| Exposure time: 14 Weeks               |
| Target Organs: Liver, Kidney, Heart, Teeth |

| 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 |

<table>
<thead>
<tr>
<th>Titanium dioxide:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Species: Rat</td>
</tr>
<tr>
<td>NOAEL: 24,000 mg/kg</td>
</tr>
<tr>
<td>Application Route: Ingestion</td>
</tr>
<tr>
<td>Exposure time: 28 Days</td>
</tr>
</tbody>
</table>
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
- **Ingestion**
  - Symptoms: upper respiratory tract infection, nasopharyngitis, Headache, Nausea, Abdominal pain, Diarrhea

**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
SAFETY DATA SHEET

Sitagliptin / Metformin Extended Release Formulation

<p>| |
||</p>
<table>
<thead>
<tr>
<th>Cellulose:</th>
</tr>
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</table>
| **Toxicity to fish** | LC50 (Oryzias latipes (Japanese medaka)): > 100 mg/l  
Exposure time: 48 h  
Remarks: Based on data from similar materials |

<table>
<thead>
<tr>
<th>Sitagliptin:</th>
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</thead>
</table>
| **Toxicity to fish** | LC50 (Pimephales promelas (fathead minnow)): > 100 mg/l  
Exposure time: 96 h  
Method: OECD Test Guideline 203 |
| **Toxicity to daphnia and other aquatic invertebrates** | EC50 (Daphnia magna (Water flea)): 60 mg/l  
Exposure time: 48 h  
Method: OECD Test Guideline 202 |
| **Toxicity to algae/aquatic plants** | EC50 (Pseudokirchneriella subcapitata (green algae)): > 39 mg/l  
Exposure time: 96 h  
Method: OECD Test Guideline 201  
NOEC (Pseudokirchneriella subcapitata (green algae)): 2.2 mg/l  
Exposure time: 96 h  
Method: OECD Test Guideline 201 |
| **Toxicity to fish (Chronic toxicity)** | NOEC (Pimephales promelas (fathead minnow)): 9.2 mg/l  
Exposure time: 33 d  
Method: OECD Test Guideline 210 |
| **Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity)** | NOEC (Daphnia magna (Water flea)): 9.8 mg/l  
Exposure time: 21 d  
Method: OECD Test Guideline 211 |
| **Toxicity to microorganisms** | EC50: > 150 mg/l  
Exposure time: 3 h  
Test Type: Respiration inhibition  
Method: OECD Test Guideline 209  
NOEC: 150 mg/l  
Exposure time: 3 h  
Test Type: Respiration inhibition |

<table>
<thead>
<tr>
<th>Kaolin:</th>
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</table>
| **Toxicity to fish (Chronic toxicity)** | NOELR (Oncorhynchus mykiss (rainbow trout)): > 100 mg/l  
Exposure time: 30 d |

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<tr>
<th>Titanium dioxide:</th>
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</table>
| **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

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.

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:
- TDG: Not regulated as a dangerous good

Special precautions for user:
Not applicable

SECTION 15. REGULATORY INFORMATION

The ingredients of this product are reported in the following inventories:
- AICS: not determined
- DSL: not determined
- IECSC: not determined

SECTION 16. OTHER INFORMATION

Full text of other abbreviations:
- ACGIH: USA. ACGIH Threshold Limit Values (TLV)
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Version: 5.0
Revision Date: 04/04/2023
SDS Number: 29090-00022
Date of last issue: 10/01/2022
Date of first issue: 11/07/2014

CA BC OEL: Canada. British Columbia OEL
CA QC OEL: Québec. Regulation respecting occupational health and safety, Schedule 1, Part 1: Permissible exposure values for airborne contaminants
ACGIH / TWA: 8-hour, time-weighted average
CA AB OEL / TWA: 8-hour Occupational exposure limit
CA BC OEL / TWA: 8-hour time weighted average
CA QC OEL / TWA: Time-weighted average exposure value

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

Revision Date: 04/04/2023
Date format: mm/dd/yyyy

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.

CA / Z8