SAFETY DATA SHEET

Sitagliptin / Metformin Formulation

SECTION 1. IDENTIFICATION

Product name : Sitagliptin / 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
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.
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

<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>Sitagliptin</td>
<td>654671-77-9</td>
<td>&gt;= 5 - &lt; 10</td>
</tr>
<tr>
<td>Cellulose</td>
<td>9004-34-6</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 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
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>inert or nuisance dust</th>
<th>50 Million particles per cubic foot</th>
</tr>
</thead>
<tbody>
<tr>
<td>Value type (Form of exposure): TWA (total dust)</td>
<td></td>
</tr>
<tr>
<td>Basis: OSHA Z-3</td>
<td></td>
</tr>
<tr>
<td>15 mg/m³</td>
<td></td>
</tr>
<tr>
<td>Value type (Form of exposure): TWA (total dust)</td>
<td></td>
</tr>
<tr>
<td>Basis: OSHA Z-3</td>
<td></td>
</tr>
<tr>
<td>5 mg/m³</td>
<td></td>
</tr>
<tr>
<td>Value type (Form of exposure): TWA (respirable fraction)</td>
<td></td>
</tr>
<tr>
<td>Basis: OSHA Z-3</td>
<td></td>
</tr>
<tr>
<td>15 Million particles per cubic foot</td>
<td></td>
</tr>
<tr>
<td>Value type (Form of exposure): TWA (respirable fraction)</td>
<td></td>
</tr>
<tr>
<td>Basis: OSHA Z-3</td>
<td></td>
</tr>
<tr>
<td>Dust, nuisance dust and particulates</td>
<td></td>
</tr>
<tr>
<td>10 mg/m³</td>
<td></td>
</tr>
<tr>
<td>Value type (Form of exposure): PEL (Total dust)</td>
<td></td>
</tr>
<tr>
<td>Basis: CAL PEL</td>
<td></td>
</tr>
<tr>
<td>5 mg/m³</td>
<td></td>
</tr>
<tr>
<td>Value type (Form of exposure): PEL (respirable dust fraction)</td>
<td></td>
</tr>
<tr>
<td>Basis: CAL PEL</td>
<td></td>
</tr>
</tbody>
</table>

<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>Sitagliptin</td>
<td>654671-77-9</td>
<td>TWA</td>
<td>0.5 mg/m³ (OEB 2)</td>
<td>Internal</td>
</tr>
<tr>
<td>Cellulose</td>
<td>9004-34-6</td>
<td>TWA</td>
<td>10 mg/m³</td>
<td>ACGIH</td>
</tr>
<tr>
<td></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>
</tbody>
</table>
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.

**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

**Eye protection**
- **Material**: 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**
- **Hygiene measures**: Work uniform or laboratory coat. 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.

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**Titanium dioxide**

<table>
<thead>
<tr>
<th>Substance</th>
<th>TWA (respirable fraction)</th>
<th>TWA (total dust)</th>
<th>TWA (Respirable particulate matter)</th>
</tr>
</thead>
<tbody>
<tr>
<td>13463-67-7</td>
<td>5 mg/m³</td>
<td>15 mg/m³</td>
<td>2.5 mg/m³ (Titanium dioxide)</td>
</tr>
</tbody>
</table>

_This substance(s) is not bioavailable and therefore does not contribute to a dust inhalation hazard._
### Appearance
- Powder

### Color
- No data available

### 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.
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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: 1,380 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

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

Cellulose:
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Sitagliptin / Metformin Formulation

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

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

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

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

**Sitagliptin:**
- **Genotoxicity in vitro:**
  - **Test Type:** Ames test
    - **Result:** negative
  - **Test Type:** Chromosome aberration test in vitro
    - **Test system:** Chinese hamster ovary cells
    - **Result:** negative
Test Type: DNA damage and repair, unscheduled DNA synthesis in mammalian cells (in vitro)
Test system: rat hepatocytes
Result: negative

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

**Cellulose:**
  Genotoxicity in vitro : Test Type: Bacterial reverse mutation assay (AMES)
    Result: negative
  Test Type: In vitro mammalian cell gene mutation test
    Result: negative
  Genotoxicity in vivo : Test Type: Mammalian erythrocyte micronucleus test (in vivo cytogenetic assay)
    Species: Mouse
    Application Route: Ingestion
    Result: negative

**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:**

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

<table>
<thead>
<tr>
<th>Species</th>
<th>Rat, male</th>
</tr>
</thead>
<tbody>
<tr>
<td>Application Route</td>
<td>Oral</td>
</tr>
<tr>
<td>Exposure time</td>
<td>104 weeks</td>
</tr>
<tr>
<td>Dose</td>
<td>900 mg/kg body weight</td>
</tr>
<tr>
<td>Result</td>
<td>negative</td>
</tr>
</tbody>
</table>

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

#### 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:

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

- **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**:
  - **Titanium dioxide**: 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:**

- **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.

**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.

**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

**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>Oral</td>
<td>2 year</td>
<td>No significant adverse effects were reported</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>
<th>Remarks</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>
<td>The mechanism or mode of action may not be relevant in humans.</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>
<th>Symptoms</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>
<td>Central nervous system</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>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dog</td>
<td>10 mg/kg</td>
<td>50 mg/kg</td>
<td>Oral</td>
<td>53 Weeks</td>
<td>Central nervous system</td>
<td>Loss of balance</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Species</th>
<th>NOAEL</th>
<th>LOAEL</th>
<th>Application Route</th>
<th>Symptoms</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dog</td>
<td>2 mg/kg</td>
<td>10 mg/kg</td>
<td>Oral</td>
<td>Central nervous system</td>
<td>The mechanism or mode of action may not be relevant in humans.</td>
</tr>
</tbody>
</table>
## Exposure time
- **Target Organs:** Skeletal muscle, Central nervous system
- **Symptoms:** Loss of balance
- **Remarks:** The mechanism or mode of action may not be relevant in humans.

### Cellulose:
- **Species:** Rat
- **NOAEL:** >= 9,000 mg/kg
- **Application Route:** Ingestion
- **Exposure time:** 90 Days

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

### Experience with human exposure

### Aspiration toxicity
Not classified based on available information.

### 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

**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 
  - 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:** 
  - NOEC (Daphnia magna (Water flea)): 9.8 mg/l
aquatic invertebrates (Chronic toxicity) Exposure time: 21 d
Method: OECD Test Guideline 211

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

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

**Cellulose:**

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

**Titanium dioxide:**

Toxicity to fish LC50 (Onchorhynchus 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

**Sitagliptin:**

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

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

**Cellulose:**

Biodegradability Result: Readily biodegradable.
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**

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
- Sitagliptin 654671-77-9
- Polyvinyl pyrrolidone 9003-39-8
- Cellulose 9004-34-6

#### 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

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
SAFETY DATA SHEET

Sitagliptin / Metformin Formulation

NFPA 704:

HMIS® IV:

Full text of other abbreviations

ACGIH: USA. ACGIH Threshold Limit Values (TLV)
CAL PEL: California permissible exposure limits for chemical contami-
nants (Title 8, Article 107)
NIOSH REL: USA. NIOSH Recommended Exposure Limits
OSHA Z-1: USA. Occupational Exposure Limits (OSHA) - Table Z-1 Lim-
its for Air Contaminants
OSHA Z-3: USA. Occupational Exposure Limits (OSHA) - Table Z-3 Min-
eral 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 Sub-
stances List (Canada); ECx - Concentration associated with x% response; EHS - Extremely Haz-
ardous 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 Sys-
tem; 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 Organiza-
tion; IECSC - Inventory of Existing Chemical Substances in China; IMDG - International Maritime
Dangerous Goods; IMO - International Maritime Organization; ISHL - Industrial Safety and Health
Law (Japan); ISO - International Organisation for Standardization; KECI - Korea Existing Chemi-
cals 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 Pre-
vention of Pollution from Ships; MSHA - Mine Safety and Health Administration; n.o.s. - Not Oth-

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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.

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