SAFETY DATA SHEET

Sitagliptin / Metformin Formulation

1. PRODUCT AND COMPANY IDENTIFICATION

Product name: Sitagliptin / Metformin Formulation

Manufacturer or supplier's details
Company: Merck & Co., Inc
Address: 2000 Galloping Hill Road
Kenilworth - New Jersey - U.S.A. 07033
Telephone: 908-740-4000
Emergency telephone number: 1-908-423-6000
E-mail address: EHSDATASTEWARD@msd.com

Recommended use of the chemical and restrictions on use
Recommended use: Pharmaceutical

2. HAZARDS IDENTIFICATION

GHS Classification
Acute toxicity (Oral): Category 4

GHS label elements
Hazard pictograms: ❄️

Signal word: Warning
Hazard statements: H302 Harmful if swallowed.
Precautionary statements:
Prevention: P264 Wash skin thoroughly after handling.
P270 Do not eat, drink or smoke when using this product.
Response: P301 + P312 + P330 IF SWALLOWED: Call a POISON CENTER/ doctor if you feel unwell. Rinse mouth.
Disposal: P501 Dispose of contents/ container to an approved waste disposal plant.

Other hazards which do not result in classification
Dust contact with the eyes can lead to mechanical irritation.
Contact with dust can cause mechanical irritation or drying of the skin.
May form explosive dust-air mixture during processing, handling or other means.
3. COMPOSITION/INFORMATION ON INGREDIENTS

<table>
<thead>
<tr>
<th>Substance / Mixture</th>
<th>Components</th>
<th>Chemical name</th>
<th>CAS-No.</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>metformin hydrochloride</td>
<td>1115-70-4</td>
<td>&gt;= 60 -&lt;= 100</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Sitagliptin</td>
<td>654671-77-9</td>
<td>&lt; 10</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cellulose</td>
<td>9004-34-6</td>
<td>&lt; 10</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Titanium dioxide</td>
<td>13463-67-7</td>
<td>&lt; 1</td>
</tr>
</tbody>
</table>

4. FIRST AID MEASURES

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

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

In case of skin contact: Wash with water and soap. Get medical attention if symptoms occur.

In case of eye contact: If in eyes, rinse well with water. Get medical attention if irritation develops and persists.

If swallowed: If swallowed, DO NOT induce vomiting unless directed to do so by medical personnel. Get medical attention. Rinse mouth thoroughly with water. Never give anything by mouth to an unconscious person.

Most important symptoms and effects, both acute and delayed: Contact with dust can cause mechanical irritation or drying of the skin. Dust contact with the eyes can lead to mechanical irritation.

Protection of first-aiders: First Aid responders should pay attention to self-protection, and use the recommended personal protective equipment when the potential for exposure exists (see section 8).

Notes to physician: Treat symptomatically and supportively.

5. FIREFIGHTING MEASURES

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

Unsuitable extinguishing media: None known.

Specific hazards during firefighting: Avoid generating dust; fine dust dispersed in air in sufficient concentrations, and in the presence of an ignition source is a potential dust explosion hazard. Exposure to combustion products may be a hazard to health.

Hazardous combustion products: Carbon oxides
Nitrogen oxides (NOx)
Metal oxides
Specific extinguishing methods: Use extinguishing measures that are appropriate to local circumstances and the surrounding environment. Use water spray to cool unopened containers. Remove undamaged containers from fire area if it is safe to do so. Evacuate area.

Special protective equipment for firefighters: In the event of fire, wear self-contained breathing apparatus. Use personal protective equipment.

6. ACCIDENTAL RELEASE MEASURES

Personal precautions, protective equipment and emergency procedures: Use personal protective equipment. Follow safe handling advice (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.

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 labelled containers.
- Store in accordance with the particular national regulations.

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

## 8. EXPOSURE CONTROLS/PERSONAL PROTECTION

### Components with workplace control parameters

<table>
<thead>
<tr>
<th>Components</th>
<th>CAS-No.</th>
<th>Value type (Form of exposure)</th>
<th>Control parameters / Permissible concentration</th>
<th>Basis</th>
</tr>
</thead>
<tbody>
<tr>
<td>metformin hydrochloride</td>
<td>1115-70-4</td>
<td>TWA</td>
<td>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>NAB</td>
<td>10 mg/m³</td>
<td>ID OEL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA</td>
<td>10 mg/m³</td>
<td>ACGIH</td>
</tr>
<tr>
<td>Titanium dioxide</td>
<td>13463-67-7</td>
<td>NAB</td>
<td>10 mg/m³</td>
<td>ID OEL</td>
</tr>
</tbody>
</table>

Further information:
- Not classified as carcinogenic to humans. Not enough data to classify these materials as carcinogenic to humans or animals
- TWA 10 mg/m³ (Titanium dioxide) ACGIH

**These substance(s) are inextricably bound in the product and therefore do 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.
  - 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.

9. PHYSICAL AND CHEMICAL PROPERTIES

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

Reactivity : Not classified as a reactivity hazard.
Chemical stability : Stable under normal conditions.
Possibility of hazardous reactions :
- May form explosive dust-air mixture during processing, handling or other means.
- Can react with strong oxidizing agents.

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

Incompatible materials : Oxidizing agents

Hazardous decomposition products : No hazardous decomposition products are known.

11. TOXICOLOGICAL INFORMATION

Information on likely routes of exposure : Inhalation
Skin contact
Ingestion
Eye contact

Acute toxicity
Harmful if swallowed.

Product:
Acute oral toxicity : Acute toxicity estimate: 1,380 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
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LD50 (Guinea pig): 500 mg/kg

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

**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
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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 sensitisation

Skin sensitisation
Not classified based on available information.

Respiratory sensitisation
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)
Exposure routes : 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 assay
Test system: mouse lymphoma cells
Result: negative

Test Type: Chromosomal aberration
Test system: Human lymphocytes
Result: negative

Genotoxicity in vivo : Test Type: Micronucleus test
Species: Mouse
Application Route: Oral
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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:**
- Species: Mouse
- Exposure time: 91 weeks
- Dose: 1500 mg/kg body weight
- Result: negative
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<table>
<thead>
<tr>
<th>Species</th>
<th>Rat, male</th>
</tr>
</thead>
<tbody>
<tr>
<td>Application Route</td>
<td>Oral</td>
</tr>
<tr>
<td>Exposure time</td>
<td>104 weeks</td>
</tr>
<tr>
<td>Dose</td>
<td>900 mg/kg body weight</td>
</tr>
<tr>
<td>Result</td>
<td>negative</td>
</tr>
</tbody>
</table>

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

#### Sitagliptin:

<table>
<thead>
<tr>
<th>Species</th>
<th>Mouse</th>
</tr>
</thead>
<tbody>
<tr>
<td>Application Route</td>
<td>Oral</td>
</tr>
<tr>
<td>Exposure time</td>
<td>2 Years</td>
</tr>
<tr>
<td>Result</td>
<td>negative</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Species</th>
<th>Rat</th>
</tr>
</thead>
<tbody>
<tr>
<td>Application Route</td>
<td>oral (drinking water)</td>
</tr>
<tr>
<td>Exposure time</td>
<td>2 Years</td>
</tr>
<tr>
<td>Result</td>
<td>positive</td>
</tr>
<tr>
<td>Target Organs</td>
<td>Liver</td>
</tr>
<tr>
<td>Remarks</td>
<td>Significant toxicity observed in testing</td>
</tr>
</tbody>
</table>

#### Carcinogenicity - Assessment

Weight of evidence does not support classification as a carcinogen.

#### 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>

#### Titanium dioxide:

<table>
<thead>
<tr>
<th>Species</th>
<th>Rat</th>
</tr>
</thead>
<tbody>
<tr>
<td>Application Route</td>
<td>inhalation (dust/mist/fume)</td>
</tr>
<tr>
<td>Exposure time</td>
<td>2 Years</td>
</tr>
<tr>
<td>Method</td>
<td>OECD Test Guideline 453</td>
</tr>
<tr>
<td>Result</td>
<td>positive</td>
</tr>
<tr>
<td>Remarks</td>
<td>The mechanism or mode of action may not be relevant in humans.</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:**

**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 foetal development**
- Test Type: Development
  - Species: Rat
  - Application Route: Oral
  - Developmental Toxicity: NOAEL: 600 mg/kg body weight
  - Result: No teratogenic effects

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

**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 foetal development**
- Test Type: Embryo-foetal 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-foetal 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 foetal development**
- Test Type: Fertility/early embryonic development
  - Species: Rat
  - Application Route: Ingestion
  - Result: negative

**STOT - single exposure**

Not classified based on available information.
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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>2.16</td>
<td>2021/04/09</td>
<td>27106-00018</td>
<td>2020/10/02</td>
<td>2014/10/31</td>
</tr>
</tbody>
</table>

**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>

**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 yr</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>

<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>Dog</td>
<td>10 mg/kg</td>
<td>50 mg/kg</td>
<td>Oral</td>
<td>53 Weeks</td>
<td>Central nervous system</td>
</tr>
</tbody>
</table>

**Symptoms:**
Loss of balance

**Remarks:**
The mechanism or mode of action may not be relevant in humans.

<table>
<thead>
<tr>
<th>Species</th>
<th>NOAEL</th>
<th>LOAEL</th>
<th>Application Route</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dog</td>
<td>2 mg/kg</td>
<td>10 mg/kg</td>
<td>Oral</td>
</tr>
</tbody>
</table>
**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

**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

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

**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: Diarrhoea, 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, Diarrhoea
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
  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:
- NOEC (Daphnia magna (Water flea)): 9.8 mg/l
**SAFETY DATA SHEET**

**Sitagliptin / Metformin 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>2.16</td>
<td>2021/04/09</td>
<td>27106-00018</td>
<td>2020/10/02</td>
<td>2014/10/31</td>
</tr>
</tbody>
</table>

**aquatic invertebrates (Chronic toxicity)**

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** (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

**Sitagliptin**:

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

**Cellulose**:

- Biodegradability: Result: Readily biodegradable.

**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

### 13. DISPOSAL CONSIDERATIONS

**Disposal methods**

Waste from residues : Dispose of in accordance with local regulations.
Contaminated packaging : Empty containers should be taken to an approved waste handling site for recycling or disposal.
If not otherwise specified: Dispose of as unused product.

### 14. TRANSPORT INFORMATION

**International Regulations**

**UNRTDG**
Not regulated as a dangerous good

**IATA-DGR**
Not regulated as a dangerous good

**IMDG-Code**
Not regulated as a dangerous good

**Transport in bulk according to Annex II of MARPOL 73/78 and the IBC Code**
Not applicable for product as supplied.
SAFETY DATA SHEET

Sitagliptin / Metformin Formulation

Version  2.16  Revision Date:  2021/04/09  SDS Number:  27106-00018  Date of last issue:  2020/10/02  Date of first issue:  2014/10/31

15. REGULATORY INFORMATION

Safety, health and environmental regulations/legislation specific for the substance or mixture

Minister of Industry Regulation No. 23/M-IND/PER/4/2013 concerning the Revision of Minister of Industry Regulation No. 87/M-IND/PER/9/2009 concerning Globally Harmonized System of Classification and Labelling of Chemicals.

Regulation of the Minister of Health No. 472 of 1996 on the Safeguarding of Substances Hazardous to Health
Hazardous substances that must be registered : Not applicable

Government Regulation No. 74 of 2001 on the Management of Hazardous and Toxic Substances
Hazardous substances approved for use : Not applicable
Prohibited substances : Not applicable
Restricted substances : Not applicable

Regulation of the Minister of Trade No. 44 of 2009 on Procurement, Distribution and Supervision of Hazardous Materials
Type of Hazardous Materials Restricted to Import, Distribution and Supervision : Not applicable

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

16. OTHER INFORMATION

Further information

Date format : yyyy/mm/dd

Full text of other abbreviations
ACGIH : USA. ACGIH Threshold Limit Values (TLV)
ID OEL : Indonesia. Occupational Exposure Limits
ACGIH / TWA : 8-hour, time-weighted average
ID OEL / NAB : Long term exposure limit
<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>AIIC</td>
<td>Australian Inventory of Industrial Chemicals</td>
</tr>
<tr>
<td>ANTT</td>
<td>National Agency for Transport by Land of Brazil</td>
</tr>
<tr>
<td>ASTM</td>
<td>American Society for the Testing of Materials</td>
</tr>
<tr>
<td>bw</td>
<td>Body weight</td>
</tr>
<tr>
<td>CMR</td>
<td>Carcinogen, Mutagen or Reproductive Toxicant</td>
</tr>
<tr>
<td>DIN</td>
<td>Standard of the German Institute for Standardisation</td>
</tr>
<tr>
<td>DSL</td>
<td>Domestic Substances List (Canada)</td>
</tr>
<tr>
<td>ECx</td>
<td>Concentration associated with x% response</td>
</tr>
<tr>
<td>ELx</td>
<td>Loading rate associated with x% response</td>
</tr>
<tr>
<td>EmS</td>
<td>Emergency Schedule</td>
</tr>
<tr>
<td>ENCS</td>
<td>Existing and New Chemical Substances (Japan)</td>
</tr>
<tr>
<td>ErCx</td>
<td>Concentration associated with x% growth rate response</td>
</tr>
<tr>
<td>ERG</td>
<td>Emergency Response Guide</td>
</tr>
<tr>
<td>GHS</td>
<td>Globally Harmonized System</td>
</tr>
<tr>
<td>GLP</td>
<td>Good Laboratory Practice</td>
</tr>
<tr>
<td>IARC</td>
<td>International Agency for Research on Cancer</td>
</tr>
<tr>
<td>IATA</td>
<td>International Air Transport Association</td>
</tr>
<tr>
<td>IBC</td>
<td>International Code for the Construction and Equipment of Ships carrying Dangerous Chemicals in Bulk</td>
</tr>
<tr>
<td>ICAO</td>
<td>International Civil Aviation Organization</td>
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<tr>
<td>IECSC</td>
<td>Inventory of Existing Chemicals in China</td>
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<tr>
<td>IMDG</td>
<td>International Marine Dangerous Goods</td>
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<tr>
<td>IMO</td>
<td>International Maritime Organization</td>
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<tr>
<td>IISU</td>
<td>Industrial Safety and Health Law (Japan)</td>
</tr>
<tr>
<td>ISO</td>
<td>International Organisation for Standardization</td>
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<tr>
<td>KECI</td>
<td>Korea Existing Chemicals Inventory</td>
</tr>
<tr>
<td>LC50</td>
<td>Lethal Concentration to 50% of a test population</td>
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<tr>
<td>LD50</td>
<td>Lethal Dose to 50% of a test population</td>
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<tr>
<td>MARPOL</td>
<td>International Convention for the Prevention of Pollution from Ships</td>
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<tr>
<td>n.o.s.</td>
<td>Not Otherwise Specified</td>
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<td>Nch</td>
<td>Chilean Norm</td>
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<td>NO(A)EC</td>
<td>No Observed (Adverse) Effect Concentration</td>
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<td>NO(A)EL</td>
<td>No Observed (Adverse) Effect Level</td>
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<td>NOELR</td>
<td>No Observable Effect Loading Rate</td>
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<tr>
<td>NTP</td>
<td>National Toxicology Program</td>
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<tr>
<td>NZIoC</td>
<td>New Zealand Inventory of Chemicals</td>
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<td>OECD</td>
<td>Organization for Economic Co-operation and Development</td>
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<td>OPPTS</td>
<td>Office of Chemical Safety and Pollution Prevention</td>
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<td>PBT</td>
<td>Persistent, Bioaccumulative and Toxic substance</td>
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<td>PICCS</td>
<td>Philippines Inventory of Chemicals and Chemical Substances</td>
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<td>(Q)SAR</td>
<td>(Quantitative) Structure Activity Relationship</td>
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<tr>
<td>SADT</td>
<td>Self-Accelerating Decomposition Temperature</td>
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<td>SDS</td>
<td>Safety Data Sheet</td>
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<td>TCSI</td>
<td>Taiwan Chemical Substance Inventory</td>
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<td>TDG</td>
<td>Transport of Dangerous Goods</td>
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<td>TSCA</td>
<td>Toxic Substances Control Act (United States)</td>
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<tr>
<td>UN</td>
<td>United Nations</td>
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<tr>
<td>UNRTDG</td>
<td>United Nations Recommendations on the Transport of Dangerous Goods</td>
</tr>
<tr>
<td>vPvB</td>
<td>Very Persistent and Very Bioaccumulative</td>
</tr>
<tr>
<td>WHMIS</td>
<td>Workplace Hazardous Materials Information System</td>
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</tbody>
</table>

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