1. PRODUCT AND COMPANY IDENTIFICATION

Product name : Sitagliptin / Metformin Formulation

Manufacturer or supplier’s details
Company : MSD
Address : 199 Wenhai North Road
           HEDA, Hangzhou - Zhejiang Province - CHINA 310018
Telephone : 908-740-4000
Emergency telephone number : 86-571-87268110
E-mail address : EHSDATASEWARD@msd.com

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

2. HAZARDS IDENTIFICATION

Emergency Overview

<table>
<thead>
<tr>
<th>Appearance</th>
<th>Colour</th>
<th>Odour</th>
</tr>
</thead>
<tbody>
<tr>
<td>: powder</td>
<td>: No data available</td>
<td>: No data available</td>
</tr>
</tbody>
</table>

Harmful if swallowed.

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.

Physical and chemical hazards
Not classified based on available information.

Health hazards
Harmful if swallowed.

Environmental hazards
Not classified based on available information.

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>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>metformin hydrochloride</td>
</tr>
<tr>
<td></td>
<td>Sitagliptin</td>
</tr>
<tr>
<td></td>
<td>Cellulose</td>
</tr>
<tr>
<td></td>
<td>Titanium dioxide</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
Harmful if swallowed.
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).
5. FIREFIGHTING 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 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 spills 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

Handling
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.
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.

Avoidance of contact: Oxidizing agents

Storage
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

Packaging material: Unsuitable material: None known.

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Components with workplace control parameters

<table>
<thead>
<tr>
<th>Components</th>
<th>CAS-No.</th>
<th>Value type</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>PC-TWA</td>
<td>10 mg/m3</td>
<td>CN 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>PC-TWA</td>
<td>8 mg/m3</td>
<td>CN OEL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(Total dust)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Further information: G2B - Possibly carcinogenic to humans</td>
<td></td>
<td>TWA</td>
<td>10 mg/m3 (Titanium dioxide)</td>
<td>ACGIH</td>
</tr>
</tbody>
</table>

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
Eye/face 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

Appearance: powder
Colour: No data available
Odour: No data available
Odour 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
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
No hazardous decomposition products are known.
11. TOXICOLOGICAL INFORMATION

Exposure routes:
- 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:
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 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
  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
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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

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.

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

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

Result: positive
Target Organs: Liver
Remarks: Significant toxicity observed in testing

Carcinogenicity - Assessment: Weight of evidence does not support classification as a carcinogen

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.

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.

STOT - repeated exposure
Not classified based on available information.

Repeated dose toxicity

Components:

metformin hydrochloride:
Species: Rat
NOAEL: 125 mg/kg
Application Route: Oral
Exposure time: 1 year
Remarks: No significant adverse effects were reported

Species: Rabbit
NOAEL: 100 mg/kg
Application Route: Oral
Exposure time: 1 Year
Remarks: No significant adverse effects were reported

Species: Dog
NOAEL: 50 mg/kg
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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>1.16</td>
<td>2020/10/02</td>
<td>27101-00017</td>
<td>2020/05/20</td>
<td>2014/10/31</td>
</tr>
</tbody>
</table>

- **Application Route**: Subcutaneous
- **Exposure time**: 2 year
- **Remarks**: No significant adverse effects were reported

### 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>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Symptoms: Loss of balance</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Remarks: 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>
</tr>
</thead>
<tbody>
<tr>
<td>Dog</td>
<td>2 mg/kg</td>
<td>10 mg/kg</td>
<td>Oral</td>
<td>27 Weeks</td>
<td>Skeletal muscle, Central nervous system</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Symptoms: Loss of balance</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Remarks: 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>Application Route</th>
<th>Exposure time</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monkey</td>
<td>100 mg/kg</td>
<td>Oral</td>
<td>14 Weeks</td>
<td>No significant adverse effects were reported</td>
</tr>
</tbody>
</table>

### Cellulose:

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

### Titanium dioxide:

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Date of first issue: 2014/10/31

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
## Sitagliptin / Metformin Formulation

<table>
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<tr>
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<th>Revision Date:</th>
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</tr>
</tbody>
</table>

### Toxicity to microorganisms

| Test Type       | EC50: > 1,000 mg/l | Exposure time: 3 h | Method: OECD Test Guideline 209 |

### Sitagliptin:

#### Toxicity to fish

<table>
<thead>
<tr>
<th>Method: OECD Test Guideline 203</th>
</tr>
</thead>
<tbody>
<tr>
<td>LC50 (Pimephales promelas (fathead minnow)): &gt; 100 mg/l</td>
</tr>
<tr>
<td>Exposure time: 96 h</td>
</tr>
</tbody>
</table>

#### Toxicity to daphnia and other aquatic invertebrates

<table>
<thead>
<tr>
<th>Method: OECD Test Guideline 202</th>
</tr>
</thead>
<tbody>
<tr>
<td>EC50 (Daphnia magna (Water flea)): 60 mg/l</td>
</tr>
<tr>
<td>Exposure time: 48 h</td>
</tr>
</tbody>
</table>

#### Toxicity to algae/aquatic plants

<table>
<thead>
<tr>
<th>Method: OECD Test Guideline 201</th>
</tr>
</thead>
<tbody>
<tr>
<td>EC50 (Pseudokirchneriella subcapitata (green algae)): &gt; 39 mg/l</td>
</tr>
<tr>
<td>Exposure time: 96 h</td>
</tr>
</tbody>
</table>

| NOEC (Pseudokirchneriella subcapitata (green algae)): 2.2 mg/l |
| Exposure time: 96 h |
| Method: OECD Test Guideline 201 |

#### Toxicity to fish (Chronic toxicity)

<table>
<thead>
<tr>
<th>Method: OECD Test Guideline 210</th>
</tr>
</thead>
<tbody>
<tr>
<td>NOEC (Pimephales promelas (fathead minnow)): 9.2 mg/l</td>
</tr>
<tr>
<td>Exposure time: 33 d</td>
</tr>
</tbody>
</table>

#### Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity)

<table>
<thead>
<tr>
<th>Method: OECD Test Guideline 211</th>
</tr>
</thead>
<tbody>
<tr>
<td>NOEC (Daphnia magna (Water flea)): 9.8 mg/l</td>
</tr>
<tr>
<td>Exposure time: 21 d</td>
</tr>
</tbody>
</table>

### Toxicity to microorganisms

<table>
<thead>
<tr>
<th>Method: OECD Test Guideline 209</th>
</tr>
</thead>
<tbody>
<tr>
<td>EC50: &gt; 150 mg/l</td>
</tr>
<tr>
<td>Exposure time: 3 h</td>
</tr>
</tbody>
</table>

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

### Cellulose:

#### Toxicity to fish

<table>
<thead>
<tr>
<th>Method: OECD Test Guideline 203</th>
</tr>
</thead>
<tbody>
<tr>
<td>LC50 (Oryzias latipes (Japanese medaka)): &gt; 100 mg/l</td>
</tr>
<tr>
<td>Exposure time: 48 h</td>
</tr>
</tbody>
</table>

Remarks: Based on data from similar materials

### Titanium dioxide:

#### Toxicity to fish

<table>
<thead>
<tr>
<th>Method: OECD Test Guideline 203</th>
</tr>
</thead>
<tbody>
<tr>
<td>LC50 (Oncorhynchus mykiss (rainbow trout)): &gt; 100 mg/l</td>
</tr>
<tr>
<td>Exposure time: 96 h</td>
</tr>
</tbody>
</table>

#### Toxicity to daphnia and other aquatic invertebrates

<table>
<thead>
<tr>
<th>Method: OECD Test Guideline 203</th>
</tr>
</thead>
<tbody>
<tr>
<td>EC50 (Daphnia magna (Water flea)): &gt; 100 mg/l</td>
</tr>
</tbody>
</table>
**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>1.16</td>
<td>2020/10/02</td>
<td>27101-00017</td>
<td>2020/05/20</td>
<td>2014/10/31</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Aquatic invertebrates</th>
<th>Exposure time: 48 h</th>
</tr>
</thead>
<tbody>
<tr>
<td>Toxicity to algae/aquatic plants</td>
<td>EC50 (Skeletonema costatum (marine diatom)): &gt; 10,000 mg/l Exposure time: 72 h</td>
</tr>
<tr>
<td>Toxicity to microorganisms</td>
<td>EC50: &gt; 1,000 mg/l Exposure time: 3 h Method: OECD Test Guideline 209</td>
</tr>
</tbody>
</table>

**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
mental compartments

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.

National Regulations
GB 6944/12268
Not regulated as a dangerous good
Special precautions for user
Not applicable

15. REGULATORY INFORMATION

National regulatory information
Law on the Prevention and Control of Occupational Diseases

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
SAFETY DATA SHEET
according to GB/T 16483 and GB/T 17519

Sitagliptin / Metformin Formulation

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

Date format: yyyy(mm-dd)

Full text of other abbreviations:
- ACGIH: USA. ACGIH Threshold Limit Values (TLV)
- CN OEL: Occupational exposure limits for hazardous agents in the workplace - Chemical hazardous agents.
- ACGIH / TWA: 8-hour, time-weighted average
- CN OEL / PC-TWA: Permissible concentration - time weighted average

AIIIC - Australian Inventory of Industrial Chemicals; ANTT - National Agency for Transport by Land of Brazil; ASTM - American Society for the Testing of Materials; bw - Body weight; CMR - Carcinogen, Mutagen or Reproductive Toxicant; DIN - Standard of the German Institute for Standardisation; DSL - Domestic Substances List (Canada); ECx - Concentration associated with x% response; ELx - Loading rate associated with x% response; EmS - Emergency Schedule; ENCS - Existing and New Chemical Substances (Japan); ErCx - Concentration associated with x% growth rate response; ERG - Emergency Response Guide; GHS - Globally Harmonized System; GLP - Good Laboratory Practice; IARC - International Agency for Research on Cancer; IATA - International Air Transport Association; IECSC - International Code for the Construction and Equipment of Ships carrying Dangerous Chemicals in Bulk; IC50 - Half maximal inhibitory concentration; ICAO - International Civil Aviation Organization; 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 Chemicals Inventory; LC50 - Lethal Concentration to 50% of a test population; LD50 - Lethal Dose to 50% of a test population (Median Lethal Dose); MARPOL - International Convention for the Prevention of Pollution from Ships; n.o.s. - Not Otherwise Specified; Nch - Chilean Norm; NO(A)EC - No Observed (Adverse) Effect Concentration; NO(A)EL - No Observed (Adverse) Effect Level; NOELR - No Observable Effect Loading Rate; NOM - Official Mexican Norm; NTP - National Toxicology Program; NZIoC - New Zealand Inventory of Chemicals; OECD - Organization for Economic Co-operation and Development; OPPTS - Office of Chemical Safety and Pollution Prevention; PBT - Persistent, Bioaccumulative and Toxic substance; PICCS - Philippines Inventory of Chemicals and Chemical Substances; (Q)SAR - (Quantitative) Structure Activity Relationship; REACH - Regulation (EC) No 1907/2006 of the European Parliament and of the Council concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals; SADT - Self-Accelerating Decomposition Temperature; SDS - Safety Data Sheet; TCSI - Taiwan Chemical Substance Inventory; TDG - Transportation of Dangerous Goods; TSCA - Toxic Substances Control Act (United States); UN - United Nations; UNRTDG - United Nations Recommendations on the Transport of Dangerous Goods; vPvB - Very Persistent and Very Bioaccumulative; WHMIS - Workplace Hazardous Materials Information System

Disclaimer:
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.