1. PRODUCT AND COMPANY IDENTIFICATION

Chemical product name : Sitagliptin / Simvastatin Formulation

Supplier’s company name, address and phone number

Company name of supplier : MSD
Address : Kumagaya, Saitama Prefecture, Xicheng 810 MSD Co., Ltd. Menuma factory
Telephone : 048-588-8411
E-mail address : EHSDATASTEWARD@msd.com
Emergency telephone number : 1-908-423-6000

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

2. HAZARDS IDENTIFICATION

GHS classification of chemical product

Serious eye damage/eye irritation : Category 2
Skin sensitisation : Category 1
Specific target organ toxicity - repeated exposure : Category 2 (Liver, muscle, optic nerve, Eye)
Short-term (acute) aquatic hazard : Category 3
Long-term (chronic) aquatic hazard : Category 3

GHS label elements

Hazard pictograms :

Signal word : Warning

Hazard statements :
H317 May cause an allergic skin reaction.
H319 Causes serious eye irritation.
H373 May cause damage to organs (Liver, muscle, optic nerve, Eye) through prolonged or repeated exposure.
H412 Harmful to aquatic life with long lasting effects.

Precautionary statements :

Prevention:
P260 Do not breathe dust.
P264 Wash skin thoroughly after handling.
P272 Contaminated work clothing should not be allowed out of the workplace.
P273 Avoid release to the environment.
P280 Wear protective gloves/ eye protection/ face protection.

Response:
P302 + P352 IF ON SKIN: Wash with plenty of water.
P305 + P351 + P338 IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
P314 Get medical advice/ attention if you feel unwell.
P333 + P313 If skin irritation or rash occurs: Get medical advice/ attention.
P337 + P313 If eye irritation persists: Get medical advice/ attention.
P362 + P364 Take off contaminated clothing and wash it before reuse.

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

Other hazards which do not result in classification
Important symptoms and outlines of the emergency assumed:
May form explosive dust-air mixture during processing, handling or other means.

3. COMPOSITION/INFORMATION ON INGREDIENTS

Substance / Mixture : Mixture

Components

<table>
<thead>
<tr>
<th>Chemical name</th>
<th>CAS-No.</th>
<th>Concentration (% w/w)</th>
<th>ENCS No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sitagliptin</td>
<td>654671-77-9</td>
<td>&gt;= 10 - &lt; 20</td>
<td></td>
</tr>
<tr>
<td>Cellulose</td>
<td>9004-34-6</td>
<td>&gt;= 1 - &lt; 10</td>
<td></td>
</tr>
<tr>
<td>Starch</td>
<td>9005-25-8</td>
<td>&gt;= 1 - &lt; 10</td>
<td></td>
</tr>
<tr>
<td>Simvastatin</td>
<td>79902-63-9</td>
<td>&gt;= 2.5 - &lt; 10</td>
<td></td>
</tr>
<tr>
<td>Titanium dioxide</td>
<td>13463-67-7</td>
<td>&gt;= 0.1 - &lt; 1</td>
<td>1-558, 5-5225</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.

In case of skin contact : In case of contact, immediately flush skin with plenty of water.
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
Metal oxides
Oxides of phosphorus

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

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 get on skin or clothing. Do not breathe dust. Do not swallow. Do not get in eyes. 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
- Hygiene measures: Oxidizing agents
- 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. Contaminated work clothing should not be allowed out of the workplace. 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.
**SAFETY DATA SHEET**

**Sitagliptin / Simvastatin Formulation**

**Version** 6.1  
**Revision Date:** 2020/10/16  
**SDS Number:** 24504-00015  
**Date of last issue:** 2020/03/23  
**Date of first issue:** 2014/10/21

---

**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**

**Threshold limit value and permissible exposure limits for each component in the work environment**

<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>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>Simvastatin</td>
<td>79902-63-9</td>
<td>TWA</td>
<td>25 µg/m³ (OEB 3)</td>
<td>Internal</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Starch</td>
<td>9005-25-8</td>
<td>TWA</td>
<td>10 mg/m³</td>
<td>ACGIH</td>
</tr>
<tr>
<td>Titanium dioxide</td>
<td>13463-67-7</td>
<td>OEL-M (Respirable dust)</td>
<td>1 mg/m³ (Titanium)</td>
<td>JP OEL JSOH</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

**Further information:** DSEN  
Wipe limit 250 µg/100 cm² Internal

<table>
<thead>
<tr>
<th>Components</th>
<th>Value type (Form of exposure)</th>
<th>Control parameters / Permissible concentration</th>
<th>Basis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OEL-M (Total dust)</td>
<td>4 mg/m³ (Titanium)</td>
<td>JP OEL JSOH</td>
</tr>
</tbody>
</table>

**Further information:** Class 2 Dust  
TWA 10 mg/m³ (Titanium dioxide) ACGIH

---

**Engineering measures:**  
All engineering controls should be implemented by facility design and operated in accordance with GMP principles to protect products, workers, and the environment. Containment technologies suitable for controlling compounds are required to control at source and to prevent migration of the compound to uncontrolled areas (e.g., open-face containment devices). Minimize open handling.

**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

**Remarks:** Consider double gloving.

**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.
- Additional body garments should be used based upon the task being performed (e.g., sleevelets, apron, gauntlets, disposable suits) to avoid exposed skin surfaces.
- Use appropriate degowning techniques to remove potentially contaminated clothing.

9. PHYSICAL AND CHEMICAL PROPERTIES

Physical state: powder
Colour: pink
Odour: No data available
Odour Threshold: No data available
Melting point/freezing point: No data available
Boiling point, initial boiling point and boiling range: No data available
Flammability (solid, gas):
- May form explosive dust-air mixture during processing, handling or other means.
Flammability (liquids): No data available
Lower explosion limit and upper explosion limit / flammability limit
Upper explosion limit / Upper flammability limit: No data available
Lower explosion limit / Lower flammability limit: No data available
Flash point: Not applicable
Decomposition temperature: No data available
pH: No data available
Evaporation rate: Not applicable
Auto-ignition temperature: No data available
Viscosity
- Viscosity, kinematic: Not applicable
Solubility(ies)
- Water solubility: No data available
Partition coefficient: n-
octanol/water
Vapour pressure : Not applicable
Density and / or relative density
  Relative density : No data available
  Density : No data available
Relative vapour density : Not applicable
Explosive properties : Not explosive
Oxidizing properties : The substance or mixture is not classified as oxidizing.
Particle characteristics
  Particle size : No data available

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
Not classified based on available information.
Components:
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

Starch:
Acute oral toxicity: LD50 (Rabbit): > 5,000 mg/kg
Acute dermal toxicity: LD50 (Rabbit): > 2,000 mg/kg

Simvastatin:
Acute oral toxicity: LD50 (Rat): 5,000 mg/kg
    LD50 (Mouse): 3,800 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:

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

Simvastatin:
Species: Rabbit
Remarks: Moderate skin irritation

Titanium dioxide:
Species: Rabbit
Result: No skin irritation

Serious eye damage/eye irritation
Causes serious eye irritation.

Components:

Sitagliptin:
Species: Rabbit
Result: Irritating to eyes.
SAFETY DATA SHEET

Sitagliptin / Simvastatin Formulation

Method : Draize Test

Starch:
Species : Rabbit
Result : No eye irritation

Simvastatin:
Species : Rabbit
Remarks : slight irritation

Titanium dioxide:
Species : Rabbit
Result : No eye irritation

Respiratory or skin sensitisation

Skin sensitisation
May cause an allergic skin reaction.

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.

Starch:
Test Type : Maximisation Test
Exposure routes : Skin contact
Species : Guinea pig
Result : negative

Simvastatin:
Assessment : Probability or evidence of skin sensitisation in humans
Result : positive

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:

#### Sitagliptin:

<table>
<thead>
<tr>
<th>Genotoxicity in vitro</th>
<th>Test Type: Ames test</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Result: negative</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Genotoxicity in vitro</th>
<th>Test Type: Chromosome aberration test in vitro</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Test system: Chinese hamster ovary cells</td>
</tr>
<tr>
<td></td>
<td>Result: negative</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Genotoxicity in vitro</th>
<th>Test Type: DNA damage and repair, unscheduled DNA synthesis in mammalian cells (in vitro)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Test system: rat hepatocytes</td>
</tr>
<tr>
<td></td>
<td>Result: negative</td>
</tr>
</tbody>
</table>

#### Cellulose:

<table>
<thead>
<tr>
<th>Genotoxicity in vitro</th>
<th>Test Type: Bacterial reverse mutation assay (AMES)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Result: negative</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Genotoxicity in vivo</th>
<th>Test Type: In vitro mammalian cell gene mutation test</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Result: negative</td>
</tr>
</tbody>
</table>

#### Starch:

<table>
<thead>
<tr>
<th>Genotoxicity in vitro</th>
<th>Test Type: Bacterial reverse mutation assay (AMES)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Result: negative</td>
</tr>
</tbody>
</table>

#### Simvastatin:

<table>
<thead>
<tr>
<th>Genotoxicity in vitro</th>
<th>Test Type: Bacterial reverse mutation assay (AMES)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Result: negative</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Genotoxicity in vitro</th>
<th>Test Type: Alkaline elution assay</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Result: negative</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Genotoxicity in vitro</th>
<th>Test Type: Chromosomal aberration</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Result: negative</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Genotoxicity in vivo</th>
<th>Test Type: In vitro mammalian cell gene mutation test</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Result: negative</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Genotoxicity in vivo</th>
<th>Test Type: Micronucleus test</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Species: Mouse</td>
</tr>
<tr>
<td></td>
<td>Application Route: Oral</td>
</tr>
<tr>
<td></td>
<td>Result: negative</td>
</tr>
</tbody>
</table>
result: negative

Germ cell mutagenicity - Assessment: Weight of evidence does not support classification as a germ cell mutagen.

**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:**

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

Species: Rat
- Application Route: oral (drinking water)
- Exposure time: 2 Years
- Result: positive
- Target Organs: Liver
- Remarks: Significant toxicity observed in testing

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

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

**Simvastatin:**
- Species: Mouse
- Application Route: Oral
- Exposure time: < 92 weeks
- Target Organs: Harderian gland
- Tumor Type: Liver, Lungs
- Remarks: The significance of these findings for humans is not certain.

Species: Rat
- Application Route: Oral
- Exposure time: 2 Years
- Tumor Type: Liver, Thyroid
Remarks: The significance of these findings for humans is not certain.

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:

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

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

Simvastatin:
Effects on fertility: Test Type: Fertility
Species: Rat, male
Application Route: Oral
Fertility: LOAEL: 25 mg/kg body weight

Effects on foetal development:
Test Type: Embryo-foetal development
Species: Rat
Application Route: Oral
Embryo-foetal toxicity: NOAEL: 25 mg/kg body weight
Result: No teratogenic effects, No adverse effects

Test Type: Embryo-foetal development
Species: Rabbit
Application Route: Oral
Embryo-foetal toxicity: NOAEL: 10 mg/kg body weight
Result: No teratogenic effects, No adverse effects

Test Type: Embryo-foetal development
Species: Rat
Application Route: Oral
Embryo-foetal toxicity: LOAEL: 60 mg/kg body weight
Result: Teratogenic potential
Remarks: Based on data from similar materials

STOT - single exposure
Not classified based on available information.

STOT - repeated exposure
May cause damage to organs (Liver, muscle, optic nerve, Eye) through prolonged or repeated exposure.

Components:

Simvastatin:
Target Organs: Liver, muscle, optic nerve, Eye
Assessment: Causes damage to organs through prolonged or repeated exposure.

Repeated dose toxicity

Components:

Sitagliptin:
Species: Mouse
NOAEL: 500 mg/kg
LOAEL: 1,000 mg/kg
Application Route: Oral
Exposure time: > 2 yr
Target Organs: Kidney

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

### Sitagliptin / Simvastatin Formulation

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

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

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

### Cellulose:

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

### Starch:

<table>
<thead>
<tr>
<th>Species</th>
<th>Rat</th>
</tr>
</thead>
<tbody>
<tr>
<td>NOAEL</td>
<td>&gt;= 2,000 mg/kg</td>
</tr>
<tr>
<td>Application Route</td>
<td>Skin contact</td>
</tr>
<tr>
<td>Exposure time</td>
<td>28 Days</td>
</tr>
<tr>
<td>Method</td>
<td>OECD Test Guideline 410</td>
</tr>
</tbody>
</table>

### Simvastatin:

<table>
<thead>
<tr>
<th>Species</th>
<th>Rat</th>
</tr>
</thead>
<tbody>
<tr>
<td>NOAEL</td>
<td>5 mg/kg</td>
</tr>
<tr>
<td>LOAEL</td>
<td>30 mg/kg</td>
</tr>
<tr>
<td>Application Route</td>
<td>Oral</td>
</tr>
<tr>
<td>Exposure time</td>
<td>14 - 104 Weeks</td>
</tr>
<tr>
<td>Target Organs</td>
<td>Liver, Testis, Musculo-skeletal system, Eye</td>
</tr>
</tbody>
</table>

Species: Dog  
NOAEL: 10 mg/kg  
Application Route: Oral  
Exposure time: 14 - 104 Weeks  
Target Organs: Liver, Testis, Eye
Species: Rabbit
NOAEL: 30 mg/kg
LOAEL: 50 mg/kg
Application Route: Oral
Target Organs: Liver, Kidney

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:

Sitagliptin:
Inhalation:
Symptoms: upper respiratory tract infection, pharyngitis, Headache

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

Simvastatin:
Skin contact:
Remarks: May produce an allergic reaction.

Ingestion:
Target Organs: Liver
Symptoms: upper respiratory tract infection, Headache, Abdominal pain, constipation, Nausea

Target Organs: Musculo-skeletal system

12. ECOLOGICAL INFORMATION

Ecotoxicity

Components:

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: EC50 (Daphnia magna (Water flea)): 60 mg/l
aquatic invertebrates
Exposure time: 48 h
Method: OECD Test Guideline 202

Toxicity to algae/aquatic plants
EC50 (Pseudokirchneriella subcapitata (green algae)): > 39 mg/l
Exposure time: 96 h
Method: OECD Test Guideline 201

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

Toxicity to fish (Chronic toxicity)
NOEC (Pimephales promelas (fathead minnow)): 9.2 mg/l
Exposure time: 33 d
Method: OECD Test Guideline 210

Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity)
NOEC (Daphnia magna (Water flea)): 9.8 mg/l
Exposure time: 21 d
Method: OECD Test Guideline 211

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

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

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

Simvastatin:
Toxicity to fish
LC50 (Pimephales promelas (fathead minnow)): 2.91 mg/l
Exposure time: 96 h
Method: OECD Test Guideline 203

Toxicity to daphnia and other aquatic invertebrates
EC50 (Daphnia magna (Water flea)): 3.5 mg/l
Exposure time: 48 h
Method: OECD Test Guideline 202

Toxicity to algae/aquatic plants
EC50 (Pseudokirchneriella subcapitata (green algae)): > 25 mg/l
Exposure time: 96 h

NOEC (Pseudokirchneriella subcapitata (green algae)): 25 mg/l
Exposure time: 96 h

Toxicity to microorganisms
EC50: > 30 mg/l
Exposure time: 3 h
Test Type: Respiration inhibition
Method: OECD Test Guideline 209

NOEC: 21 mg/l
Exposure time: 3 h
Test Type: Respiration inhibition
Method: OECD Test Guideline 209

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:

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.

Simvastatin:
Biodegradability : Result: rapidly degradable

Stability in water : Hydrolysis: 50 %(3.2 d)

Bioaccumulative potential

Components:

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

Simvastatin:
Partition coefficient: n-octanol/water

Mobility in soil

Components:

Sitagliptin:
Distribution among environmental compartments

Hazardous to the ozone layer

Not applicable

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

Refer to section 15 for specific national regulation.

15. REGULATORY INFORMATION

Related Regulations

Fire Service Law
Not applicable to dangerous materials / designated flammables.

Chemical Substance Control Law
Not applicable for Specified Chemical Substance, Monitoring Chemical Substance and Priority Assessment Chemical Substance.
Industrial Safety and Health Law
Harmful Substances Prohibited from Manufacture
Not applicable
Harmful Substances Required Permission for Manufacture
Not applicable
Substances Prevented From Impairment of Health
Not applicable
Circular concerning Information on Chemicals having Mutagenicity - Annex 2: Information on Existing Chemicals having Mutagenicity
Not applicable
Circular concerning Information on Chemicals having Mutagenicity - Annex 1: Information on Notified Substances having Mutagenicity
Not applicable
Substances Subject to be Notified Names
Article 57-2 (Enforcement Order Table 9)
<table>
<thead>
<tr>
<th>Chemical name</th>
<th>Number</th>
<th>Concentration (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Titanium(IV) oxide</td>
<td>191</td>
<td>&gt;=0.1 - &lt;1</td>
</tr>
</tbody>
</table>
Substances Subject to be Indicated Names
Not applicable
Ordinance on Prevention of Hazards Due to Specified Chemical Substances
Not applicable
Ordinance on Prevention of Lead Poisoning
Not applicable
Ordinance on Prevention of Tetraalkyl Lead Poisoning
Not applicable
Ordinance on Prevention of Organic Solvent Poisoning
Not applicable
Enforcement Order of the Industrial Safety and Health Law - Attached table 1 (Dangerous Substances)
Not applicable
Poisonous and Deleterious Substances Control Law
Not applicable
Act on Confirmation, etc. of Release Amounts of Specific Chemical Substances in the Environment and Promotion of Improvements to the Management Thereof
Not applicable
High Pressure Gas Safety Act
Not applicable
Explosive Control Law
Not applicable
Vessel Safety Law
Not regulated as a dangerous good
Aviation Law
Not regulated as a dangerous good

Marine Pollution and Sea Disaster Prevention etc Law
Bulk transportation: Not classified as noxious liquid substance
Pack transportation: Not classified as marine pollutant

Narcotics and Psychotropics Control Act
Narcotic or Psychotropic Raw Material (Export / Import Permission)
Not applicable
Specific Narcotic or Psychotropic Raw Material (Export / Import permission)
Not applicable

Waste Disposal and Public Cleansing Law
Industrial waste

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)
- ACGIH / TWA: 8-hour, time-weighted average
- JP OEL JSOH / OEL-M: Occupational Exposure Limit-Mean
- AIIC - 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; IBC - 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
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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