1. PRODUCT AND COMPANY IDENTIFICATION

Product name: Sitagliptin / Simvastatin Formulation

Manufacturer or supplier's details

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

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 ad-
dvice/ attention.
P337 + P313 If eye irritation persists: Get medical advice/ at-
tention.
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 out-
lines of the emergency as-
sumed
May form explosive dust-air mixture during processing, han-
dling 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>8-98</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 ad-
dvice 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.
Remove contaminated clothing and shoes.
Get medical attention.
Wash clothing before reuse.
Thoroughly clean shoes before reuse.

In case of eye contact:
In case of contact, immediately flush eyes with plenty of water for at least 15 minutes.
If easy to do, remove contact lens, if worn.
Get medical attention.

If swallowed:
If swallowed, DO NOT induce vomiting.
Get medical attention if symptoms occur.
Rinse mouth thoroughly with water.

Most important symptoms and effects, both acute and delayed:
May cause an allergic skin reaction.
Causes serious eye irritation.
May cause damage to organs through prolonged or repeated exposure.

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)
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 and personal protective equipment recommendations.

Environmental precautions:
Discharge into the environment must be avoided.
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.
- 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.
- Take care to prevent spills, waste and minimize release to the environment.

Avoidance of contact:
- Oxidizing agents

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 decontamination and decontamination procedures, industrial hygiene monitoring, medical surveillance and the use of administrative controls.

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:
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>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>OEL-M (Total dust)</td>
<td>4 mg/m³ (Titanium)</td>
<td>JP OEL JSOH</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA</td>
<td>10 mg/m³ (Titanium dioxide)</td>
<td>ACGIH</td>
</tr>
</tbody>
</table>

Further information:
- Wipe limit 250 µg/100 cm² Internal
- Class 2 Dust

**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

- **Material**
  - Chemical-resistant gloves

- **Remarks**
  - Consider double gloving.
  - 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
**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

- **Appearance:** powder
- **Colour:** pink
- **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
- **Flammability (solid, gas):** May form explosive dust-air mixture during processing, handling or other means.
- **Flammability (liquids):** No data available
- **Upper explosion limit / Upper flammability limit:** No data available
- **Lower explosion limit / Lower flammability limit:** No data available
- **Vapour pressure:** Not applicable
- **Relative vapour density:** Not applicable
- **Relative density:** No data available
- **Density:** No data available
- **Solubility(ies):**
  - **Water solubility:** No data available
- **Partition coefficient: n-octanol/water:** Not applicable
- **Auto-ignition temperature:** No data available
- **Decomposition temperature:** No data available
Viscosity
Viscosity, kinematic : Not applicable

Explosive properties : Not explosive

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

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

Starch:
Acute oral toxicity : LD50 (Mouse): > 5,000 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.
Method : Draize Test

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.

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:
Genotoxicity in vitro:
Test Type: Ames test
Result: negative

Genotoxicity in vivo:
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

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

**Simvastatin:**

Genotoxicity in vitro : Test Type: Bacterial reverse mutation assay (AMES)  
Result: negative

Genotoxicity in vivo : Test Type: Alkaline elution assay  
Result: negative

Genotoxicity in vivo : Test Type: Chromosomal aberration  
Result: negative

Genotoxicity in vitro : Test Type: In vitro mammalian cell gene mutation test  
Result: negative

Genotoxicity in vivo : Test Type: Micronucleus test  
Species: Mouse  
Application Route: Oral  
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
SAFETY DATA SHEET

Sitagliptin / Simvastatin Formulation

Version 5.2
Revision Date: 09/13/2019
SDS Number: 24504-00013
Date of last issue: 2019/04/24
Date of first issue: 2014/10/21

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

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

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

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

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

Cellulose:
Species: Rat
SAFETY DATA SHEET

Sitagliptin / Simvastatin Formulation

Version 5.2 Revision Date: 09/13/2019 SDS Number: 24504-00013 Date of last issue: 2019/04/24 Date of first issue: 2014/10/21

NOAEL: >= 9,000 mg/kg
Application Route: Ingestion
Exposure time: 90 Days

Simvastatin:
Species: Rat
NOAEL: 5 mg/kg
LOAEL: 30 mg/kg
Application Route: Oral
Exposure time: 14 - 104 Weeks
Target Organs: Liver, Testis, Musculo-skeletal system, Eye

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

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

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

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

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

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

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

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 : EC50 (Daphnia magna (Water flea)): 3.5 mg/l
### aquatic invertebrates

Exposure time: 48 h  
Method: OECD Test Guideline 202

### Toxicity to algae/aquatic plants

<table>
<thead>
<tr>
<th>Compound</th>
<th>EC50</th>
<th>NOEC</th>
<th>Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pseudokirchneriella subcapitata (green algae)</td>
<td>&gt; 25 mg/l</td>
<td>25 mg/l</td>
<td>OECD Test Guideline</td>
</tr>
<tr>
<td>Exposure time</td>
<td>96 h</td>
<td>96 h</td>
<td></td>
</tr>
</tbody>
</table>

### Toxicity to microorganisms

<table>
<thead>
<tr>
<th>Compound</th>
<th>EC50</th>
<th>NOEC</th>
<th>Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pseudokirchneriella subcapitata (green algae)</td>
<td>&gt; 25 mg/l</td>
<td>21 mg/l</td>
<td>OECD Test Guideline</td>
</tr>
<tr>
<td>Exposure time</td>
<td>96 h</td>
<td>96 h</td>
<td></td>
</tr>
</tbody>
</table>

### Titanium dioxide:

#### Toxicity to fish

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

#### Toxicity to daphnia and other aquatic invertebrates

<table>
<thead>
<tr>
<th>Compound</th>
<th>EC50</th>
<th>Exposure time</th>
<th>Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daphnia magna (Water flea)</td>
<td>&gt; 100 mg/l</td>
<td>48 h</td>
<td>OECD Test Guideline</td>
</tr>
</tbody>
</table>

#### Toxicity to algae/aquatic plants

<table>
<thead>
<tr>
<th>Compound</th>
<th>EC50</th>
<th>Exposure time</th>
<th>Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skeletonema costatum (marine diatom)</td>
<td>&gt; 10,000 mg/l</td>
<td>72 h</td>
<td>OECD Test Guideline</td>
</tr>
</tbody>
</table>

#### Toxicity to microorganisms

<table>
<thead>
<tr>
<th>Compound</th>
<th>EC50</th>
<th>Exposure time</th>
<th>Method</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&gt; 1,000 mg/l</td>
<td>3 h</td>
<td>OECD Test Guideline</td>
</tr>
</tbody>
</table>

### 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
: log Pow: > 4.07

Mobility in soil

Components:

**Sitagliptin:**
Distribution among environmental compartments
: log Koc: 4.37

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

<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
SAFETY DATA SHEET

Sitagliptin / Simvastatin Formulation

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
<table>
<thead>
<tr>
<th>Term</th>
<th>Full Form</th>
</tr>
</thead>
<tbody>
<tr>
<td>AICS</td>
<td>Australian Inventory of Chemical Substances</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>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>IC50</td>
<td>Half maximal inhibitory concentration</td>
</tr>
<tr>
<td>ICAO</td>
<td>International Civil Aviation Organization</td>
</tr>
<tr>
<td>IECSC</td>
<td>Inventory of Existing Chemical Substances in China</td>
</tr>
<tr>
<td>IMDG</td>
<td>International Maritime Dangerous Goods</td>
</tr>
<tr>
<td>IMO</td>
<td>International Maritime Organization</td>
</tr>
<tr>
<td>ISHL</td>
<td>Industrial Safety and Health Law (Japan)</td>
</tr>
<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>
</tr>
<tr>
<td>LD50</td>
<td>Lethal Dose to 50% of a test population (Median Lethal Dose)</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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<tr>
<td>Nch</td>
<td>Chilean Norm</td>
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<tr>
<td>NO(A)EC</td>
<td>No Observed (Adverse) Effect Concentration</td>
</tr>
<tr>
<td>NO(A)EL</td>
<td>No Observed (Adverse) Effect Level</td>
</tr>
<tr>
<td>NOELR</td>
<td>No Observable Effect Loading Rate</td>
</tr>
<tr>
<td>NOM</td>
<td>Official Mexican Norm</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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<tr>
<td>OECD</td>
<td>Organization for Economic Co-operation and Development</td>
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<tr>
<td>OPPTS</td>
<td>Office of Chemical Safety and Pollution Prevention</td>
</tr>
<tr>
<td>PBT</td>
<td>Persistent, Bioaccumulative and Toxic substance</td>
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<tr>
<td>PICCS</td>
<td>Philippines Inventory of Chemicals and Chemical Substances</td>
</tr>
<tr>
<td>(Q)SAR</td>
<td>(Quantitative) Structure Activity Relationship</td>
</tr>
<tr>
<td>SADT</td>
<td>Self-Accelerating Decomposition Temperature</td>
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<tr>
<td>SDS</td>
<td>Safety Data Sheet</td>
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<tr>
<td>TCSI</td>
<td>Taiwan Chemical Substance Inventory</td>
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<tr>
<td>TDG</td>
<td>Transport of Dangerous Goods</td>
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<tr>
<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>
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<tr>
<td>WHMIS</td>
<td>Workplace Hazardous Materials Information System</td>
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</tbody>
</table>

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JP / EN