SAFETY DATA SHEET
Sitagliptin / Simvastatin Formulation

SECTION 1. IDENTIFICATION

Product name : Sitagliptin / Simvastatin Formulation

Manufacturer or supplier’s details
Company name of supplier : Merck & Co., Inc
Address : 2000 Galloping Hill Road
           Kenilworth - New Jersey - U.S.A. 07033
Telephone : 908-740-4000
Telefax : 908-735-1496
Emergency telephone : 1-908-423-6000
E-mail address : EHSDATASTEWARD@merck.com

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

SECTION 2. HAZARDS IDENTIFICATION

GHS classification in accordance with 29 CFR 1910.1200
Combustible dust

Eye irritation : Category 2A
Skin sensitization : Category 1
Carcinogenicity (Inhalation) : Category 2
Specific target organ toxicity - repeated exposure : Category 1 (Liver, muscle, optic nerve, Eye)

GHS label elements
Hazard pictograms :

Signal Word : Danger

Hazard Statements : If small particles are generated during further processing, handling or by other means, may form combustible dust concentrations in air.
H317 May cause an allergic skin reaction.
H319 Causes serious eye irritation.
H351 Suspected of causing cancer if inhaled.
H372 Causes damage to organs (Liver, muscle, optic nerve, Eye) through prolonged or repeated exposure.

Precautionary Statements : Prevention:
P201 Obtain special instructions before use.
P202 Do not handle until all safety precautions have been read and understood.
P260 Do not breathe dust.
P264 Wash skin thoroughly after handling.
P270 Do not eat, drink or smoke when using this product.
P272 Contaminated work clothing must not be allowed out of the workplace.
P280 Wear protective gloves/ protective clothing/ eye protection/ face protection.

**Response:**
P302 + P352 IF ON SKIN: Wash with plenty of soap and 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.
P308 + P313 IF exposed or concerned: Get medical advice/ attention.
P333 + P313 If skin irritation or rash occurs: Get medical advice/ attention.
P337 + P313 If eye irritation persists: Get medical advice/ attention.
P363 Wash contaminated clothing before reuse.

**Storage:**
P405 Store locked up.

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

**Other hazards**
None known.

### SECTION 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>
</tr>
</thead>
<tbody>
<tr>
<td>Sitagliptin</td>
<td>654671-77-9</td>
<td>&gt;= 10 - &lt; 20</td>
</tr>
<tr>
<td>Cellulose</td>
<td>9004-34-6</td>
<td>&gt;= 5 - &lt; 10</td>
</tr>
<tr>
<td>Simvastatin</td>
<td>79902-63-9</td>
<td>&gt;= 1 - &lt; 5</td>
</tr>
<tr>
<td>Starch</td>
<td>9005-25-8</td>
<td>&gt;= 1 - &lt; 5</td>
</tr>
<tr>
<td>Titanium dioxide</td>
<td>13463-67-7</td>
<td>&gt;= 0.1 - &lt; 1</td>
</tr>
</tbody>
</table>

Actual concentration is withheld as a trade secret

### SECTION 4. FIRST AID MEASURES

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

**If inhaled** : If inhaled, remove to fresh air. Get medical attention.

**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. Suspected of causing cancer if inhaled. Causes 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.

SECTION 5. FIRE-FIGHTING MEASURES

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

 Unsuitable extinguishing media: None known.

Specific hazards during fire fighting: 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 fire-fighters: In the event of fire, wear self-contained breathing apparatus. Use personal protective equipment.

SECTION 6. ACCIDENTAL RELEASE MEASURES

Personal precautions, protective equipment and emergency procedures: Use personal protective equipment. Follow safe handling advice 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
Methods and materials for containment and cleaning up:
Sweep up or vacuum up spillage and collect in suitable container for disposal.
Avoid dispersal of dust in the air (i.e., clearing dust surfaces with compressed air).
Dust deposits should not be allowed to accumulate on surfaces, as these may form an explosive mixture if they are released into the atmosphere in sufficient concentration.
Local or national regulations may apply to releases and disposal of this material, as well as those materials and items employed in the cleanup of releases. You will need to determine which regulations are applicable.
Sections 13 and 15 of this SDS provide information regarding certain local or national requirements.

SECTION 7. HANDLING AND STORAGE

Technical measures:
Static electricity may accumulate and ignite suspended dust causing an explosion.
Provide adequate precautions, such as electrical grounding and bonding, or inert atmospheres.

Local/Total ventilation:
Use only with adequate ventilation.

Advice on safe handling:
Do not 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.

Conditions for safe storage:
Keep in properly labeled containers.
Store in accordance with the particular national regulations.

Materials to avoid:
Do not store with the following product types:
Strong oxidizing agents
Organic peroxides
Explosives
Gases

SECTION 8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Ingredients with workplace control parameters

<table>
<thead>
<tr>
<th>Components</th>
<th>CAS-No.</th>
<th>Value type (Form of exposure)</th>
<th>Control parameters / Permissible concentration</th>
<th>Basis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sitagliptin</td>
<td>654671-77-9</td>
<td>TWA</td>
<td>0.5 mg/m³ (OEB 2)</td>
<td>Internal</td>
</tr>
</tbody>
</table>

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SAFETY DATA SHEET

Sitagliptin / Simvastatin Formulation

<table>
<thead>
<tr>
<th>Component</th>
<th>CAS Number</th>
<th>TWA Exposure</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cellulose</td>
<td>9004-34-6</td>
<td>TWA 10 mg/m³</td>
<td>ACGIH</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA (Respirable) 5 mg/m³</td>
<td>NIOSH REL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA (total) 10 mg/m³</td>
<td>NIOSH REL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA (total dust) 15 mg/m³</td>
<td>OSHA Z-1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA (respirable fraction) 5 mg/m³</td>
<td>OSHA Z-1</td>
</tr>
<tr>
<td>Simvastatin</td>
<td>79902-63-9</td>
<td>TWA 25 µg/m³ (OEB 3)</td>
<td>Internal</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Further information: DSEN</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Wipe limit 250 µg/100 cm²</td>
<td>Internal</td>
</tr>
<tr>
<td>Starch</td>
<td>9005-25-8</td>
<td>TWA 10 mg/m³</td>
<td>ACGIH</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA (Respirable) 5 mg/m³</td>
<td>NIOSH REL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA (total) 10 mg/m³</td>
<td>NIOSH REL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA (total dust) 15 mg/m³</td>
<td>OSHA Z-1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA (respirable fraction) 5 mg/m³</td>
<td>OSHA Z-1</td>
</tr>
<tr>
<td>Titanium dioxide</td>
<td>13463-67-7</td>
<td>TWA (total dust) 15 mg/m³</td>
<td>OSHA Z-1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA 10 mg/m³ (Titanium dioxide)</td>
<td>ACGIH</td>
</tr>
</tbody>
</table>

**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**

- General and local exhaust ventilation is recommended to maintain vapor exposures below recommended limits. Where concentrations are above recommended limits or are unknown, appropriate respiratory protection should be worn.
- Follow OSHA respirator regulations (29 CFR 1910.134) and use NIOSH/MSHA approved respirators. Protection provided by air purifying respirators against exposure to any hazardous chemical is limited. Use a positive pressure air supplied respirator if there is any potential for uncontrolled release, exposure levels are unknown, or any other circumstance where air purifying respirators may not provide adequate protection.

**Hand protection**

- Chemical-resistant gloves

**Eye protection**

- Wear safety glasses with side shields or goggles.
- If the work environment or activity involves dusty conditions,
mists or aerosols, wear the appropriate goggles. Wear a faceshield or other full face protection if there is a potential for direct contact to the face with dusts, mists, or aerosols.

**Skin and body protection**: Work uniform or laboratory coat. 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.

**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.

### SECTION 9. PHYSICAL AND CHEMICAL PROPERTIES

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Appearance</strong></td>
<td>powder</td>
</tr>
<tr>
<td><strong>Color</strong></td>
<td>pink</td>
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<tr>
<td><strong>Odor</strong></td>
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</tr>
<tr>
<td><strong>Odor Threshold</strong></td>
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</tr>
<tr>
<td><strong>pH</strong></td>
<td>No data available</td>
</tr>
<tr>
<td><strong>Melting point/freezing point</strong></td>
<td>No data available</td>
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<tr>
<td><strong>Initial boiling point and boiling range</strong></td>
<td>No data available</td>
</tr>
<tr>
<td><strong>Flash point</strong></td>
<td>Not applicable</td>
</tr>
<tr>
<td><strong>Evaporation rate</strong></td>
<td>Not applicable</td>
</tr>
<tr>
<td><strong>Flammability (solid, gas)</strong></td>
<td>May form explosive dust-air mixture during processing, handling or other means.</td>
</tr>
<tr>
<td><strong>Flammability (liquids)</strong></td>
<td>No data available</td>
</tr>
<tr>
<td><strong>Upper explosion limit / Upper flammability limit</strong></td>
<td>No data available</td>
</tr>
<tr>
<td><strong>Lower explosion limit / Lower flammability limit</strong></td>
<td>No data available</td>
</tr>
<tr>
<td><strong>Vapor pressure</strong></td>
<td>Not applicable</td>
</tr>
<tr>
<td><strong>Relative vapor density</strong></td>
<td>Not applicable</td>
</tr>
</tbody>
</table>
Relative density : No data available
Density : No data available
Solubility(ies)
   Water solubility : No data available
Partition coefficient: n-octanol/water : Not applicable
Autoignition temperature : No data available
Decomposition temperature : No data available
Viscosity
   Viscosity, kinematic : Not applicable
Explosive properties : Not explosive
Oxidizing properties : The substance or mixture is not classified as oxidizing.
Particle size : No data available

SECTION 10. STABILITY AND REACTIVITY
Reactivity : Not classified as a reactivity hazard.
Chemical stability : Stable under normal conditions.
Possibility of hazardous reactions
   May form explosive dust-air mixture during processing, handling or other means.
   Can react with strong oxidizing agents.
Conditions to avoid : Heat, flames and sparks.
   Avoid dust formation.
Incompatible materials : Oxidizing agents
Hazardous decomposition products : No hazardous decomposition products are known.

SECTION 11. TOXICOLOGICAL INFORMATION
Information on likely routes of exposure
   Inhalation
   Skin contact
   Ingestion
   Eye contact

Acute toxicity
   Not classified based on available information.

Components:
Sitagliptin:
   Acute oral toxicity : LD50 (Rat): > 3,000 mg/kg
SAFETY DATA SHEET

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Version 8.1  Revision Date: 09/13/2019  SDS Number: 24515-00013  Date of last issue: 04/24/2019  Date of first issue: 10/21/2014

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

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

**Starch:**
Acute oral toxicity: LD50 (Mouse): > 5,000 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:**

**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 sensitization

Skin sensitization
May cause an allergic skin reaction.

Respiratory sensitization
Not classified based on available information.

Components:

Sitagliptin:
Test Type : Local lymph node assay (LLNA)  
Species : Mouse  
Method : OECD Test Guideline 429  
Result : Not a skin sensitizer.

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

Titanium dioxide:
Test Type : Local lymph node assay (LLNA)  
Routes of exposure : Skin contact  
Species : Mouse  
Result : negative

Germ cell mutagenicity
Not classified based on available information.

Components:

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

Test Type: Chromosome aberration test in vitro  
Test system: Chinese hamster ovary cells
Result: negative

Test Type: DNA damage and repair, unscheduled DNA synthesis in mammalian cells (in vitro)
Test system: rat hepatocytes
Result: negative

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

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

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

Genotoxicity in vivo
: Test Type: Mammalian erythrocyte micronucleus test (in vivo cytogenetic assay)
Species: Mouse
Application Route: Ingestion
Result: negative

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

Test Type: Alkaline elution assay
Result: negative

Test Type: Chromosomal aberration
Result: negative

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
Suspected of causing cancer if inhaled.

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
IARC Group 2B: Possibly carcinogenic to humans
Titanium dioxide 13463-67-7

OSHA No component of this product present at levels greater than or equal to 0.1% is on OSHA’s list of regulated carcinogens.

NTP No ingredient of this product present at levels greater than or equal to 0.1% is identified as a known or anticipated carcinogen by NTP.

Reproductive toxicity
Not classified based on available information.

Components:

Sitagliptin:
Effects on fertility: Test Type: Fertility/early embryonic development
Species: Rat
Application Route: Oral
Fertility: NOAEL Parent: 1,000 mg/kg body weight
Result: Animal testing did not show any effects on fertility.

Effects on fetal development: Test Type: Embryo-fetal development
Species: Rat
Application Route: Oral
Teratogenicity: LOAEL: 250 mg/kg body weight
Result: Embryotoxic effects and adverse effects on the offspring were detected. No teratogenic effects.

Test Type: Embryo-fetal development
Species: Rabbit
Teratogenicity: NOAEL: 125 mg/kg body weight
Result: No teratogenic effects.

Cellulose:
Effects on fertility: Test Type: One-generation reproduction toxicity study
Species: Rat
Application Route: Ingestion
Result: negative

Effects on fetal development: Test Type: Fertility/early embryonic development
Species: Rat
Application Route: Ingestion
Result: negative

Simvastatin:
Effects on fertility: Test Type: Fertility
Species: Rat, male
Application Route: Oral
Fertility: LOAEL: 25 mg/kg body weight
Effects on fetal development: Test Type: Embryo-fetal development
### Species: Rat
- **Species:** Rat
- **Application Route:** Oral
- **Embryo-fetal toxicity:** NOAEL: 25 mg/kg body weight
- **Result:** No teratogenic effects, No adverse effects.

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

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

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### STOT-single exposure
Not classified based on available information.

### STOT-repeated exposure
Causes 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 y
- **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
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
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 y

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, Diarrhea

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

SECTION 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)

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

### Toxicity to microorganisms

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

<table>
<thead>
<tr>
<th>Compound</th>
<th>NOEC: 150 mg/l</th>
<th>Exposure time</th>
<th>Test Type</th>
<th>Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sitagliptin / Simvastatin</td>
<td></td>
<td>3 h</td>
<td>Respiration inhibition</td>
<td>OECD Test Guideline 209</td>
</tr>
</tbody>
</table>

### Cellulose:

<table>
<thead>
<tr>
<th>Compound</th>
<th>LC50 (Oryzias latipes (Japanese medaka)): &gt; 100 mg/l</th>
<th>Exposure time</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Simvastatin</td>
<td></td>
<td>48 h</td>
<td>Based on data from similar materials</td>
</tr>
</tbody>
</table>

### Simvastatin:

<table>
<thead>
<tr>
<th>Compound</th>
<th>LC50 (Pimephales promelas (fathead minnow)): 2.91 mg/l</th>
<th>Exposure time</th>
<th>Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>Simvastatin</td>
<td></td>
<td>96 h</td>
<td>OECD Test Guideline 203</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Compound</th>
<th>EC50 (Daphnia magna (Water flea)): 3.5 mg/l</th>
<th>Exposure time</th>
<th>Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>Simvastatin</td>
<td></td>
<td>48 h</td>
<td>OECD Test Guideline 202</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Compound</th>
<th>EC50 (Pseudokirchneriella subcapitata (green algae)): &gt; 25 mg/l</th>
<th>Exposure time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Simvastatin</td>
<td></td>
<td>96 h</td>
</tr>
</tbody>
</table>

| Compound                  | NOEC (Pseudokirchneriella subcapitata (green algae)): 25 mg/l | Exposure time | Method                                      |
|---------------------------|                                                               | 96 h          | OECD Test Guideline 209                     |

### Toxicity to microorganisms

<table>
<thead>
<tr>
<th>Compound</th>
<th>EC50: &gt; 30 mg/l</th>
<th>Exposure time</th>
<th>Test Type</th>
<th>Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>Simvastatin</td>
<td></td>
<td>3 h</td>
<td>Respiration inhibition</td>
<td>OECD Test Guideline 209</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Compound</th>
<th>NOEC: 21 mg/l</th>
<th>Exposure time</th>
<th>Test Type</th>
<th>Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>Simvastatin</td>
<td></td>
<td>3 h</td>
<td>Respiration inhibition</td>
<td>OECD Test Guideline 209</td>
</tr>
</tbody>
</table>

### Titanium dioxide:

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

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

---
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: log Pow: > 4.07

Mobility in soil

Components:

Sitagliptin:
Distribution among environmental compartments: log Koc: 4.37

Other adverse effects
No data available
SECTION 13. DISPOSAL CONSIDERATIONS

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

SECTION 14. TRANSPORT INFORMATION

International Regulations

UNRTDG
Not regulated as a dangerous good

IATA-DGR
Not regulated as a dangerous good

IMDG-Code
Not regulated as a dangerous good

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

Domestic regulation

49 CFR
Not regulated as a dangerous good

SECTION 15. REGULATORY INFORMATION

EPCRA - Emergency Planning and Community Right-to-Know

CERCLA Reportable Quantity
This material does not contain any components with a CERCLA RQ.

SARA 304 Extremely Hazardous Substances Reportable Quantity
This material does not contain any components with a section 304 EHS RQ.

SARA 302 Extremely Hazardous Substances Threshold Planning Quantity
This material does not contain any components with a section 302 EHS TPQ.

SARA 311/312 Hazards: Combustible dust
Serious eye damage or eye irritation
Respiratory or skin sensitization
Carcinogenicity
Specific target organ toxicity (single or repeated exposure)

SARA 313: This material does not contain any chemical components with known CAS numbers that exceed the threshold (De Minimis) reporting levels established by SARA Title III, Section 313.

US State Regulations

Pennsylvania Right To Know
D-Glucose, 4-O-beta-D-galactopyranosyl-, monohydrate 64044-51-5
Calcium hydrogenorthophosphate 7757-93-9
Sitagliptin 654671-77-9
Cellulose 9004-34-6
Starch 9005-25-8
Simvastatin 79902-63-9

California Prop. 65
WARNING: This product can expose you to chemicals including Titanium dioxide, which is/are known to the State of California to cause cancer. For more information go to www.P65Warnings.ca.gov.

California Permissible Exposure Limits for Chemical Contaminants
Cellulose 9004-34-6
Starch 9005-25-8

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

SECTION 16. OTHER INFORMATION

Further information

<table>
<thead>
<tr>
<th>NFPA 704:</th>
<th>HMIS® IV:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flammability</td>
<td>HEALTH</td>
</tr>
<tr>
<td>Health</td>
<td>FLAMMABILITY</td>
</tr>
<tr>
<td>Special hazard</td>
<td>PHYSICAL HAZARD</td>
</tr>
</tbody>
</table>

HMIS® ratings are based on a 0-4 rating scale, with 0 representing minimal hazards or risks, and 4 representing significant hazards or risks. The "*" represents a chronic hazard, while the "/'" represents the absence of a chronic hazard.

Full text of other abbreviations
ACGIH : USA. ACGIH Threshold Limit Values (TLV)
NIOSH REL : USA. NIOSH Recommended Exposure Limits
OSHA Z-1 : USA. Occupational Exposure Limits (OSHA) - Table Z-1 Limits for Air Contaminants
ACGIH / TWA : 8-hour, time-weighted average
NIOSH REL / TWA : Time-weighted average concentration for up to a 10-hour workday during a 40-hour workweek
OSHA Z-1 / TWA : 8-hour time weighted average
SAFETY DATA SHEET

Sitagliptin / Simvastatin 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>8.1</td>
<td>09/13/2019</td>
<td>24515-00013</td>
<td>04/24/2019</td>
<td>10/21/2014</td>
</tr>
</tbody>
</table>

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

Revision Date: 09/13/2019

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.

US / Z8