SAFETY DATA SHEET

Sitagliptin / Simvastatin Formulation

Version 8.3  Revision Date: 10/16/2020  SDS Number: 24515-00015  Date of last issue: 03/23/2020
Date of first issue: 10/21/2014

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
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 the OSHA Hazard Communication Standard (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  
and 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 attention.  
P333 + P313 If skin irritation or rash occurs: Get medical atten-  
tion.  
P337 + P313 If eye irritation persists: Get medical attention.  
P363 Wash contaminated clothing before reuse.  

**Storage:**  
P405 Store locked up.  

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

**Other hazards**  
None known.  

**SECTION 3. COMPOSITION/INFORMATION ON INGREDIENTS**  

**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  
advise immediately.  
When symptoms persist or in all cases of doubt seek medical  
advise.  

**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 (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.

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.
- Wash skin thoroughly after handling.
- Handle in accordance with good industrial hygiene and safety practice, based on the results of the workplace exposure assessment
- Minimize dust generation and accumulation.
- Keep container closed when not in use.
- Keep away from heat and sources of ignition.
- Take precautionary measures against static discharges.
- Do not eat, drink or smoke when using this product.
- Take care to prevent spills, waste and minimize release to the environment.

Conditions for safe storage:
- Keep in properly 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>
### 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

- Material: Chemical-resistant gloves

#### Eye protection

- 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.

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<table>
<thead>
<tr>
<th>Material</th>
<th>Concentration</th>
<th>Standard</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cellulose</strong></td>
<td>9004-34-6</td>
<td>TWA</td>
</tr>
<tr>
<td></td>
<td>10 mg/m³</td>
<td>ACGIH</td>
</tr>
<tr>
<td></td>
<td>TWA (Respirable)</td>
<td>5 mg/m³</td>
</tr>
<tr>
<td></td>
<td>TWA (total)</td>
<td>10 mg/m³</td>
</tr>
<tr>
<td></td>
<td>TWA (total dust)</td>
<td>15 mg/m³</td>
</tr>
<tr>
<td></td>
<td>TWA (respirable fraction)</td>
<td>5 mg/m³</td>
</tr>
<tr>
<td><strong>Simvastatin</strong></td>
<td>79902-63-9</td>
<td>TWA</td>
</tr>
<tr>
<td></td>
<td>25 µg/m³ (OEB 3)</td>
<td>Internal</td>
</tr>
<tr>
<td></td>
<td>Wipe limit</td>
<td>250 µg/100 cm²</td>
</tr>
<tr>
<td><strong>Starch</strong></td>
<td>9005-25-8</td>
<td>TWA</td>
</tr>
<tr>
<td></td>
<td>10 mg/m³</td>
<td>ACGIH</td>
</tr>
<tr>
<td></td>
<td>TWA (Respirable)</td>
<td>5 mg/m³</td>
</tr>
<tr>
<td></td>
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<tr>
<td></td>
<td>TWA (total dust)</td>
<td>15 mg/m³</td>
</tr>
<tr>
<td></td>
<td>TWA (respirable fraction)</td>
<td>5 mg/m³</td>
</tr>
<tr>
<td><strong>Titanium dioxide</strong></td>
<td>13463-67-7</td>
<td>TWA (total dust)</td>
</tr>
<tr>
<td></td>
<td>TWA</td>
<td>10 mg/m³</td>
</tr>
<tr>
<td></td>
<td>(Titanium dioxide)</td>
<td></td>
</tr>
</tbody>
</table>
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. 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.

**SECTION 9. PHYSICAL AND CHEMICAL PROPERTIES**

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
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</thead>
<tbody>
<tr>
<td>Appearance</td>
<td>powder</td>
</tr>
<tr>
<td>Color</td>
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</tr>
<tr>
<td>Odor</td>
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</tr>
<tr>
<td>Odor Threshold</td>
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</tr>
<tr>
<td>pH</td>
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</tr>
<tr>
<td>Melting point/freezing point</td>
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<tr>
<td>Initial boiling point and boiling range</td>
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</tr>
<tr>
<td>Flash point</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Evaporation rate</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Flammability (solid, gas)</td>
<td>May form explosive dust-air mixture during processing, handling or other means.</td>
</tr>
<tr>
<td>Flammability (liquids)</td>
<td>No data available</td>
</tr>
<tr>
<td>Upper explosion limit / Upper flammability limit</td>
<td>No data available</td>
</tr>
<tr>
<td>Lower explosion limit / Lower flammability limit</td>
<td>No data available</td>
</tr>
<tr>
<td>Vapor pressure</td>
<td>Not applicable</td>
</tr>
</tbody>
</table>
Relative vapor 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
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
  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 (Rat): > 5,000 mg/kg
  Acute dermal toxicity:
    LD50 (Rabbit): > 2,000 mg/kg

Titanium dioxide:
  Acute oral toxicity:
    LD50 (Rat): > 5,000 mg/kg
  Acute inhalation toxicity:
    LC50 (Rat): > 6.82 mg/l
      Exposure time: 4 h
      Test atmosphere: dust/mist
    Assessment: The substance or mixture has no acute inhalation toxicity

Skin corrosion/irritation
Not classified based on available information.

Components:

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

**Starch:**
- **Species:** Rabbit
- **Result:** No eye 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

**Starch:**
- **Test Type:** Maximization Test
- **Routes of exposure:** Skin contact
- **Species:** Guinea pig
- **Result:** negative

**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
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Species: Mouse
Application Route: Oral
Result: negative

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

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

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

Genotoxicity in vivo : Test Type: In vivo micronucleus test
Species: Mouse
Result: negative

Carcinogenicity
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
- **Titanium dioxide:** 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.
- **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
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

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
<table>
<thead>
<tr>
<th>LOAEL</th>
<th>30 mg/kg</th>
</tr>
</thead>
<tbody>
<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

<table>
<thead>
<tr>
<th>LOAEL</th>
<th>10 mg/kg</th>
</tr>
</thead>
<tbody>
<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, Eye</td>
</tr>
</tbody>
</table>

**Species:** Rabbit

<table>
<thead>
<tr>
<th>NOAEL</th>
<th>30 mg/kg</th>
</tr>
</thead>
<tbody>
<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, Kidney</td>
</tr>
</tbody>
</table>

**Starch:**

<table>
<thead>
<tr>
<th>NOAEL</th>
<th>&gt;= 2,000 mg/kg</th>
</tr>
</thead>
<tbody>
<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>

**Titanium dioxide:**

<table>
<thead>
<tr>
<th>NOAEL</th>
<th>24,000 mg/kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Application Route</td>
<td>Ingestion</td>
</tr>
<tr>
<td>Exposure time</td>
<td>28 Days</td>
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</table>

<table>
<thead>
<tr>
<th>NOAEL</th>
<th>10 mg/m³</th>
</tr>
</thead>
<tbody>
<tr>
<td>Application Route</td>
<td>inhalation (dust/mist/fume)</td>
</tr>
<tr>
<td>Exposure time</td>
<td>2 y</td>
</tr>
</tbody>
</table>

**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): 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
aquatic invertebrates

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 : 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
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
- Respiratory or skin sensitization
- Carcinogenicity
- Specific target organ toxicity (single or repeated exposure)
- Serious eye damage or eye irritation

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
SAFETY DATA SHEET
Sitagliptin / Simvastatin Formulation

Version 8.3 Revision Date: 10/16/2020 SDS Number: 24515-00015 Date of last issue: 03/23/2020
Date of first issue: 10/21/2014

NFPA 704:

HMIS® IV:

HEALTH * 3
FLAMMABILITY 3
PHYSICAL HAZARD 0

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

AIIC - Australian Inventory of Industrial Chemicals; ASTM - American Society for the Testing of Materials; bw - Body weight; CERCLA - Comprehensive Environmental Response, Compensation, and Liability Act; CMR - Carcinogen, Mutagen or Reproductive Toxicant; DIN - Standard of the German Institute for Standardisation; DOT - Department of Transportation; DSL - Domestic Substances List (Canada); ECx - Concentration associated with x% response; EHS - Extremely Hazardous Substance; 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; HMIS - Hazardous Materials Identification System; 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 Maritime Organization; ISHL - Industrial Safety and Health Law (Japan); ISO - International Organisation for Standardization; KECI - Korea Existing Chemicals Inventory; LC50 - Lethal Concentration to 50% of a test population; LD50 - Lethal Dose to 50% of a test population (Median Lethal Dose); MARPOL - International Convention for the Prevention of Pollution from Ships; MSHA - Mine Safety and Health Administration; n.o.s. - Not Otherwise Specified; NFPA - National Fire Protection Association; NO(A)EC - No Observed (Adverse) Effect Concentration; NO(A)EL - No Observed (Adverse) Effect Level; NOELR - No Observable Effect Loading Rate; NTP - National Toxicology Program; NZIoC - New Zealand Inventory of Chemicals; OECD - Organization for Economic Co-operation and Development; OPPTS - Office of Chemical Safety and Pollution Prevention; PBT - Persistent, Bioaccumulative and Toxic substance; PICCS - Philippines Inventory of Chemicals and Chemical Substances; (Q)SAR - (Quantitative) Structure Activity Relationship. 

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Revision Date: 10/16/2020

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