SAFETY DATA SHEET

Sitagliptin / Simvastatin Formulation

SECTION 1. PRODUCT AND COMPANY IDENTIFICATION

Product name : Sitagliptin / Simvastatin Formulation

Manufacturer or supplier's details
Company name of supplier : MSD
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@msd.com

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

SECTION 2. HAZARDS IDENTIFICATION

GHS Classification
Skin irritation : Category 3
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 : ![Danger Symbol]

Signal Word : Danger

Hazard Statements : H316 Causes mild skin irritation.
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 should 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 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.
P362 + P364 Take off contaminated clothing and wash it before reuse.

Storage:
P405 Store locked up.

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

Other hazards
May form explosive dust-air mixture during processing, handling or other means.

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>

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:
- Causes mild skin irritation.
- 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.

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.

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>
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<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>VLE-PPT</td>
<td>10 mg/m³</td>
<td>NOM-010-STPS-2014</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>VLE-PPT</td>
<td>10 mg/m³</td>
<td>NOM-010-STPS-2014</td>
</tr>
<tr>
<td>Titanium dioxide</td>
<td>13463-67-7</td>
<td>TWA</td>
<td>10 mg/m³</td>
<td>ACGIH</td>
</tr>
</tbody>
</table>

Further information: DSEN

<p>| | | | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Wipe limit</td>
<td>250 µg/100 cm²</td>
<td>Internal</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Starch</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TWA</td>
<td>10 mg/m³</td>
<td>ACGIH</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Titanium dioxide</td>
<td></td>
<td></td>
<td>10 mg/m³</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: If adequate local exhaust ventilation is not available or exposure assessment demonstrates exposures outside the recommended guidelines, use respiratory protection.

Filter type: Particulates type

Hand protection

Material: Chemical-resistant gloves

Remarks: Consider double gloving.

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

Skin and body protection: Work uniform or laboratory coat. Additional body garments should be used based upon the task being performed (e.g., sleevelets, apron, gauntlets,
disposable suits) to avoid exposed skin surfaces. Use appropriate degowning techniques to remove potentially contaminated clothing.

SECTION 9. PHYSICAL AND CHEMICAL PROPERTIES

<table>
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<tr>
<th>Property</th>
<th>Value</th>
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<td>Appearance</td>
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<td>Color</td>
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<td>Odor</td>
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<tr>
<td>Odor Threshold</td>
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<tr>
<td>pH</td>
<td>No data available</td>
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<tr>
<td>Melting point/freezing point</td>
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</tr>
<tr>
<td>Initial boiling point and boiling range</td>
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</tr>
<tr>
<td>Flash point</td>
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<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>
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<tr>
<td>Flammability (liquids)</td>
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</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>
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</tr>
<tr>
<td>Vapor pressure</td>
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</tr>
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<td>Relative vapor density</td>
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</tr>
<tr>
<td>Relative density</td>
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</tr>
<tr>
<td>Density</td>
<td>No data available</td>
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<tr>
<td>Solubility(ies)</td>
<td>Water solubility</td>
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<tr>
<td>Partition coefficient: n-octanol/water</td>
<td>Not applicable</td>
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<tr>
<td>Autoignition temperature</td>
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</tr>
<tr>
<td>Decomposition temperature</td>
<td>No data available</td>
</tr>
<tr>
<td>Viscosity</td>
<td>Viscosity, kinematic</td>
</tr>
<tr>
<td></td>
<td>Not applicable</td>
</tr>
</tbody>
</table>
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
Causes mild skin irritation.

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
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: 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 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
## 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>
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</table>

**Sitagliptin**

<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>27 Weeks</td>
</tr>
<tr>
<td>Target Organs</td>
<td>Skeletal muscle, Central nervous system</td>
</tr>
<tr>
<td>Symptoms</td>
<td>Loss of balance</td>
</tr>
<tr>
<td>Remarks</td>
<td>The mechanism or mode of action may not be relevant in humans.</td>
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</table>

**Species**

<table>
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<tr>
<th>Species</th>
<th>Monkey</th>
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**NOAEL**

<table>
<thead>
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<th>100 mg/kg</th>
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**Application Route**

<table>
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<tr>
<th>Application Route</th>
<th>Oral</th>
<th>Exposure time</th>
<th>14 Weeks</th>
</tr>
</thead>
</table>

**Remarks**

No significant adverse effects were reported

---

**Cellulose**

**Species**

<table>
<thead>
<tr>
<th>Species</th>
<th>Rat</th>
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**NOAEL**

<table>
<thead>
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<th>&gt;= 9,000 mg/kg</th>
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**Application Route**

<table>
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<tr>
<th>Application Route</th>
<th>Ingestion</th>
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**Simvastatin**

**Species**

<table>
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<tr>
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<th>Rat</th>
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**NOAEL**

<table>
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<tr>
<th>NOAEL</th>
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</table>

**LOAEL**

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</table>

**Application Route**

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<th>Exposure time</th>
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**Target Organs**

<table>
<thead>
<tr>
<th>Target Organs</th>
<th>Liver, Testis, Musculo-skeletal system, Eye</th>
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</table>

**Species**

<table>
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<tr>
<th>Species</th>
<th>Dog</th>
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**NOAEL**

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**LOAEL**

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**Application Route**

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**Target Organs**

<table>
<thead>
<tr>
<th>Target Organs</th>
<th>Liver, Testis, Eye</th>
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</table>

**Species**

<table>
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<tr>
<th>Species</th>
<th>Rabbit</th>
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</table>

**NOAEL**

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<thead>
<tr>
<th>NOAEL</th>
<th>30 mg/kg</th>
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</table>

**LOAEL**

<table>
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<th>50 mg/kg</th>
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**Application Route**

<table>
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<tr>
<th>Application Route</th>
<th>Oral</th>
<th>Exposure time</th>
<th>14 - 104 Weeks</th>
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</table>

**Target Organs**

<table>
<thead>
<tr>
<th>Target Organs</th>
<th>Liver, Kidney</th>
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</table>

**Starch**

**Species**

<table>
<thead>
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<th>Species</th>
<th>Rat</th>
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</table>

**NOAEL**

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

**Application Route**

<table>
<thead>
<tr>
<th>Application Route</th>
<th>Ingestion</th>
<th>Exposure time</th>
<th>28 Days</th>
</tr>
</thead>
</table>

**Method**

<table>
<thead>
<tr>
<th>Method</th>
<th>OECD Test Guideline 410</th>
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</thead>
</table>

**Titanium dioxide**

**Species**

<table>
<thead>
<tr>
<th>Species</th>
<th>Rat</th>
</tr>
</thead>
</table>

**NOAEL**

<table>
<thead>
<tr>
<th>NOAEL</th>
<th>24,000 mg/kg</th>
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</thead>
</table>

**Application Route**

<table>
<thead>
<tr>
<th>Application Route</th>
<th>Ingestion</th>
<th>Exposure time</th>
<th>28 Days</th>
</tr>
</thead>
</table>

---
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)** | NOEC (Daphnia magna (Water flea)): 9.8 mg/l  
Exposure time: 21 d  
Method: OECD Test Guideline 211 |
|------------------|--------------------------------------------------------------------------------------------------------------------------------|
| **Toxicity to microorganisms** | EC50: > 150 mg/l  
Exposure time: 3 h  
Test Type: Respiration inhibition  
Method: OECD Test Guideline 209  
NOEC: 150 mg/l  
Exposure time: 3 h  
Test Type: Respiration inhibition |

**Cellulose:**

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

**Simvastatin:**

| Toxicity to fish | LC50 (Pimephales promelas (fathead minnow)): 2.91 mg/l  
Exposure time: 96 h  
Method: OECD Test Guideline 203 |
| Toxicity to daphnia and other aquatic invertebrates | EC50 (Daphnia magna (Water flea)): 3.5 mg/l  
Exposure time: 48 h  
Method: OECD Test Guideline 202 |
| Toxicity to algae/aquatic plants | EC50 (Pseudokirchneriella subcapitata (green algae)): > 25 mg/l  
Exposure time: 96 h  
NOEC (Pseudokirchneriella subcapitata (green algae)): 25 mg/l  
Exposure time: 96 h |
| Toxicity to microorganisms | EC50: > 30 mg/l  
Exposure time: 3 h  
Test Type: Respiration inhibition  
Method: OECD Test Guideline 209  
NOEC: 21 mg/l  
Exposure time: 3 h  
Test Type: Respiration inhibition  
Method: OECD Test Guideline 209 |

**Titanium dioxide:**

| Toxicity to fish | LC50 (Oncorhynchus mykiss (rainbow trout)): > 100 mg/l  
Exposure time: 96 h  
Method: OECD Test Guideline 203 |
| Toxicity to daphnia and other aquatic invertebrates | EC50 (Daphnia magna (Water flea)): > 100 mg/l  
Exposure time: 48 h |
Toxicity to algae/aquatic plants:
EC50 (Skeletonema costatum (marine diatom)): > 10,000 mg/l
Exposure time: 72 h

Toxicity to microorganisms:
EC50: > 1,000 mg/l
Exposure time: 3 h
Method: OECD Test Guideline 209

Persistence and degradability

Components:

Sitagliptin:
Biodegradability: Result: not rapidly degradable
Biodegradation: 39.7 %
Exposure time: 28 d
Method: OECD Test Guideline 314

Stability in water: Hydrolysis: 50 % (401 d)
Method: OECD Test Guideline 111

Cellulose:
Biodegradability: Result: Readily biodegradable.

Simvastatin:
Biodegradability: Result: rapidly degradable
Stability in water: Hydrolysis: 50 % (3.2 d)

Bioaccumulative potential

Components:

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

Simvastatin:
Partition coefficient: n-octanol/water: 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

NOM-002-SCT
Not regulated as a dangerous good

Special precautions for user
Not applicable

SECTION 15. REGULATORY INFORMATION

Safety, health and environmental regulations/legislation specific for the substance or mixture

Federal Law for the control of chemical precursors, essential chemical products and machinery for producing capsules, tablets and pills. : Not applicable

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

SECTION 16. OTHER INFORMATION

Full text of other abbreviations
ACGIH : USA. ACGIH Threshold Limit Values (TLV)
NOM-010-STPS-2014 : Mexico. Norm NOM-010-STPS-2014 on Chemicals Polluting
SAFETY DATA SHEET

Sitagliptin / Simvastatin Formulation

Version 6.4 Revision Date: 16.10.2020 SDS Number: 24506-00015 Date of last issue: 23.03.2020


Revision Date: 16.10.2020

The information is considered as correct, but not exhaustive, and will be used only as a guide, which is based in the current knowledge of the substance or mixture, and is applicable to proper safety precautions for the product.

MX / Z8