SAFETY DATA SHEET

Sitagliptin / Metformin Extended Release Formulation

SECTION 1. PRODUCT AND COMPANY IDENTIFICATION

Product name : Sitagliptin / Metformin Extended Release Formulation

Manufacturer or supplier’s details
Company name of supplier : MSD
Address : Avenida 16 de Septiembre No. 301
Xaltocan - Xochimilco Mexico 16090
Telephone : 52 55 57284444
Telefax : 908-735-1496
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
Acute toxicity (Oral) : Category 4

GHS label elements
Hazard pictograms :

Signal Word : Warning
Hazard Statements : H302 Harmful if swallowed.

Precautionary Statements :
Prevention:
P264 Wash skin thoroughly after handling.
P270 Do not eat, drink or smoke when using this product.

Response:
P301 + P312 + P330 IF SWALLOWED: Call a POISON CENTER or doctor/ physician if you feel unwell. Rinse mouth.

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

Other hazards
Dust contact with the eyes can lead to mechanical irritation.
Contact with dust can cause mechanical irritation or drying of the skin.
May form explosive dust-air mixture during processing, handling or other means.

SECTION 3. COMPOSITION/INFORMATION ON INGREDIENTS

Substance / Mixture : Mixture
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 if symptoms occur.

In case of skin contact: Wash with water and soap. Get medical attention if symptoms occur.

In case of eye contact: If in eyes, rinse well with water. Get medical attention if irritation develops and persists.

If swallowed: If swallowed, DO NOT induce vomiting unless directed to do so by medical personnel. Get medical attention. Rinse mouth thoroughly with water. Never give anything by mouth to an unconscious person.

Most important symptoms and effects, both acute and delayed: Harmful if swallowed. Contact with dust can cause mechanical irritation or drying of the skin. Dust contact with the eyes can lead to mechanical irritation.

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
Nitrogen oxides (NOx)
Silicon oxides
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 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 breathe dust. Do not swallow. Avoid contact with eyes. Avoid prolonged or repeated contact with skin. 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.

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.

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.

SECTION 8. EXPOSURE CONTROLS/PERSOINAL 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>metformin hydrochloride</td>
<td>1115-70-4</td>
<td>TWA</td>
<td>2 mg/m³ (OEB 1)</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></td>
<td></td>
<td>TWA</td>
<td>10 mg/m³</td>
<td>ACGIH</td>
</tr>
<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>Kaolin</td>
<td>1332-58-7</td>
<td>VLE-PPT (Respirable fraction)</td>
<td>2 mg/m³</td>
<td>NOM-010-STPS-2014</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA (Respirable fraction)</td>
<td>2 mg/m³</td>
<td>ACGIH</td>
</tr>
<tr>
<td>Titanium dioxide</td>
<td>13463-67-7</td>
<td>VLE-PPT</td>
<td>10 mg/m³</td>
<td>NOM-010- STPS-2014</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA</td>
<td>10 mg/m³ (Titanium dioxide)</td>
<td>ACGIH</td>
</tr>
</tbody>
</table>

These substance(s) are inextricably bound in the product and therefore do not contribute to a dust inhalation hazard.

Titanium dioxide

Engineering measures: Use feasible engineering controls to minimize exposure to compound. All engineering controls should be implemented by facility design and operated in accordance with GMP principles to protect products, workers, and the environment.
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

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.

SECTION 9. PHYSICAL AND CHEMICAL PROPERTIES

Appearance: powder

Color: blue green

Odor: No data available

Odor Threshold: No data available

pH: No data available

Melting point/freezing point: No data available

Initial boiling point and boiling range: No data available

Flash point: Not applicable

Evaporation rate: Not applicable

Flammability (solid, gas): May form explosive dust-air mixture during processing, handling or other means.

Flammability (liquids): No data available

Upper explosion limit / Upper flammability limit: No data available

Lower explosion limit / Lower flammability limit: No data available

Vapor pressure: Not applicable

Relative vapor density: Not applicable

Relative density: 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
Harmful if swallowed.

Product:
Acute oral toxicity: Acute toxicity estimate: 1,588 mg/kg
Method: Calculation method
Components:

metformin hydrochloride:
Acute oral toxicity: LD50 (Rat): 1,000 mg/kg
LD50 (Mouse): 1,450 - 3,500 mg/kg
LD50 (Monkey): 463 mg/kg
LD50 (Rabbit): 350 mg/kg
LD50 (Guinea pig): 500 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

Sitagliptin:
Acute oral toxicity: LD50 (Rat): > 3,000 mg/kg
LD50 (Mouse): 3,000 mg/kg

Kaolin:
Acute oral toxicity: LD50 (Rat): > 5,000 mg/kg
Remarks: Based on data from similar materials

Acute inhalation toxicity:
LC50 (Rat): > 2.07 mg/l
Exposure time: 4 h
Test atmosphere: dust/mist
Assessment: The substance or mixture has no acute inhalation toxicity
Remarks: Based on data from similar materials

Acute dermal toxicity: LD50 (Rat): > 5,000 mg/kg
Assessment: The substance or mixture has no acute dermal toxicity
Remarks: Based on data from similar materials

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:

metformin hydrochloride:
Species : Rabbit
Result : Mild skin irritation

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

Kaolin:
Species : Rabbit
Method : OECD Test Guideline 404
Result : No skin irritation
Remarks : Based on data from similar materials

Titanium dioxide:
Species : Rabbit
Result : No skin irritation

Serious eye damage/eye irritation
Not classified based on available information.

Components:

metformin hydrochloride:
Species : Rabbit
Result : Mild eye irritation

Sitagliptin:
Species : Rabbit
Result : Irritating to eyes.
Method : Draize Test

Kaolin:
Species : Rabbit
Result : No eye irritation
Remarks : Based on data from similar materials

Titanium dioxide:
Species : Rabbit
Result : No eye irritation
Respiratory or skin sensitization

Skin sensitization
Not classified based on available information.

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.

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:

Metformin hydrochloride:
- Genotoxicity in vitro: Test Type: Bacterial reverse mutation assay (AMES)
  Result: negative
  Test Type: in vitro test
  Test system: mouse lymphoma cells
  Result: negative
  Test Type: Chromosomal aberration
  Test system: Human lymphocytes
  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
### Cytoxicity

<table>
<thead>
<tr>
<th>Test System</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Test Type: Chromosome aberration test in vitro</td>
<td>negative</td>
</tr>
<tr>
<td>Test Type: DNA damage and repair, unscheduled DNA synthesis in mammalian cells (in vitro)</td>
<td>negative</td>
</tr>
</tbody>
</table>

### Genotoxicity in vivo

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

### Carcinogenicity

Not classified based on available information.

### Components

#### Metformin hydrochloride:

<table>
<thead>
<tr>
<th>Species</th>
<th>Mouse</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exposure time</td>
<td>91 weeks</td>
</tr>
<tr>
<td>Dose</td>
<td>1500 mg/kg body weight</td>
</tr>
<tr>
<td>Result</td>
<td>negative</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Species</th>
<th>Rat, male</th>
</tr>
</thead>
<tbody>
<tr>
<td>Application Route</td>
<td>Oral</td>
</tr>
<tr>
<td>Exposure time</td>
<td>104 weeks</td>
</tr>
<tr>
<td>Dose</td>
<td>900 mg/kg body weight</td>
</tr>
<tr>
<td>Result</td>
<td>negative</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Species</th>
<th>Rat, female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Application Route</td>
<td>Oral</td>
</tr>
<tr>
<td>Exposure time</td>
<td>104 weeks</td>
</tr>
<tr>
<td>Dose</td>
<td>900 mg/kg body weight</td>
</tr>
<tr>
<td>Result</td>
<td>negative</td>
</tr>
</tbody>
</table>
Result: negative
Target Organs: Uterus (including cervix)
Remarks: The mechanism or mode of action may not be relevant in humans.

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

**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

**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:**

**metformin hydrochloride:**
Effects on fertility: Test Type: Fertility
Species: Rat
Application Route: Oral
Fertility: NOAEL: 600 mg/kg body weight
Result: No effects on fertility.
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Effects on fetal development:
- **Test Type:** Development
  - **Species:** Rat
  - **Application Route:** Oral
  - **Developmental Toxicity:** NOAEL: 600 mg/kg body weight
  - **Result:** No teratogenic effects.

- **Test Type:** Embryo-fetal development
  - **Species:** Rabbit
  - **Application Route:** Oral
  - **Embryo-fetal Toxicity:** NOAEL: 140 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

**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.

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

**STOT-repeated exposure**
Not classified based on available information.
Repeated dose toxicity

**Components:**

**metformin hydrochloride:**

<table>
<thead>
<tr>
<th>Species</th>
<th>NOAEL</th>
<th>Application Route</th>
<th>Exposure time</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rat</td>
<td>125 mg/kg</td>
<td>Oral</td>
<td>1 year</td>
<td>No significant adverse effects were reported</td>
</tr>
<tr>
<td>Rabbit</td>
<td>100 mg/kg</td>
<td>Oral</td>
<td>1 Year</td>
<td>No significant adverse effects were reported</td>
</tr>
<tr>
<td>Dog</td>
<td>50 mg/kg</td>
<td>Subcutaneous</td>
<td>2 year</td>
<td>No significant adverse effects were reported</td>
</tr>
</tbody>
</table>

**Cellulose:**

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

**Sitagliptin:**

<table>
<thead>
<tr>
<th>Species</th>
<th>NOAEL</th>
<th>LOAEL</th>
<th>Application Route</th>
<th>Exposure time</th>
<th>Target Organs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mouse</td>
<td>500 mg/kg</td>
<td>1,000 mg/kg</td>
<td>Oral</td>
<td>&gt; 2 y</td>
<td>Kidney</td>
</tr>
<tr>
<td>Rat</td>
<td>500 mg/kg</td>
<td>1,000 mg/kg</td>
<td>Oral</td>
<td>14 Weeks</td>
<td>Liver, Kidney, Heart, Teeth</td>
</tr>
<tr>
<td>Dog</td>
<td>10 mg/kg</td>
<td>50 mg/kg</td>
<td>Oral</td>
<td>53 Weeks</td>
<td>Central nervous system</td>
</tr>
</tbody>
</table>

**Symptoms:** Loss of balance

**Remarks:** The mechanism or mode of action may not be relevant in
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Version: 3.2  Revision Date: 09/13/2019  SDS Number: 29109-00014  Date of last issue: 24.04.2019
Date of first issue: 07.11.2014

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

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:

metformin hydrochloride:
Skin contact: Remarks: May irritate skin.
Eye contact: Remarks: May irritate eyes.
Ingestion: Symptoms: Diarrhea, Nausea, Vomiting, Gastrointestinal discomfort, flatulence, asthenia, Fatigue, Headache

Sitagliptin:
Inhalation: Symptoms: upper respiratory tract infection, pharyngitis, Headache
Ingestion: Symptoms: upper respiratory tract infection, nasopharyngitis, Headache, Nausea, Abdominal pain, Diarrhea
SECTION 12. ECOLOGICAL INFORMATION

Ecotoxicity

Components:

**metformin hydrochloride:**

Toxicity to algae/aquatic plants: EC50 (Pseudokirchneriella subcapitata (green algae)): > 100 mg/l
Exposure time: 72 h
Method: OECD Test Guideline 201

NOEC (Pseudokirchneriella subcapitata (green algae)): 100 mg/l
Exposure time: 72 h
Method: OECD Test Guideline 201

Toxicity to fish (Chronic toxicity): NOEC (Pimephales promelas (fathead minnow)): 10 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)): 40 mg/l
Exposure time: 21 d
Method: OECD Test Guideline 211

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

**Cellulose:**

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

**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

Kaolin:
Toxicity to fish (Chronic toxicity):
- NOELR (Oncorhynchus mykiss (rainbow trout)): > 100 mg/l
  Exposure time: 30 d

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:**

**metformin hydrochloride:**
Biodegradability:
- Result: rapidly degradable
- Biodegradation: 50 %
- Exposure time: 2 hrs

**Cellulose:**
Biodegradability:
- Result: Readily biodegradable.

**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

Bioaccumulative potential

Components:

metformin hydrochloride:
Partition coefficient: n-octanol/water
  log Pow: -2

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

Mobility in soil

Components:

metformin hydrochloride:
Distribution among environmental compartments
  log Koc: 4.3
  Method: OECD Test Guideline 106

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.

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 the Work Environment - Identification, Assessment and Control - Appendix 1 Occupational Exposure Limits
- **ACGIH / TWA**: 8-hour, time-weighted average
- **NOM-010-STPS-2014 / VLE-PPT**: Time weighted average limit value

AICS - Australian Inventory of Chemical Substances; ANTT - National Agency for Transport by Land of Brazil; ASTM - American Society for the Testing of Materials; bw - Body weight; CMR - Carcinogen, Mutagen or Reproductive Toxicant; DIN - Standard of the German Institute for Standardisation; DSL - Domestic Substances List (Canada); ECx - Concentration associated with x% response; ELx - Loading rate associated with x% response; EmS - Emergency Schedule; ENCS - Existing and New Chemical Substances (Japan); ErCx - Concentration associated with x% growth rate response; ERG - Emergency Response Guide; GHS - Globally Harmonized System; GLP - Good Laboratory Practice; IARC - International Agency for Research on Cancer; IATA - International Air Transport Association; IBC - International Code for the Construction and Equipment of Ships carrying Dangerous Chemicals in Bulk; IC50 - Half maximal inhibitory concentration; ICAO - International Civil Aviation Organization; IECSC - Inventory of Existing Chemical Substances in China; IMDG - International Maritime Dangerous Goods; IMO - International
SAFETY DATA SHEET

Sitagliptin / Metformin Extended Release Formulation

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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; n.o.s. - Not Otherwise Specified; Nch - Chilean Norm; NO(A)EC - No Observed (Adverse) Effect Concentration; NO(A)EL - No Observed (Adverse) Effect Level; NOELR - No Observable Effect Loading Rate; NOM - Official Mexican Norm; 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; REACH - Regulation (EC) No 1907/2006 of the European Parliament and of the Council concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals; SADT - Self-Accelerating Decomposition Temperature; SDS - Safety Data Sheet; TCSI - Taiwan Chemical Substance Inventory; TDG - Transportation of Dangerous Goods; TSCA - Toxic Substances Control Act (United States); UN - United Nations; UNRTDG - United Nations Recommendations on the Transport of Dangerous Goods; vPvB - Very Persistent and Very Bioaccumulative; WHMIS - Workplace Hazardous Materials Information System

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

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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.

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