SECTION 1: Identification of the substance/mixture and of the company/undertaking

1.1 Product identifier
Trade name: Sitagliptin / Metformin Extended Release Formulation

1.2 Relevant identified uses of the substance or mixture and uses advised against
Use of the Substance/Mixture: Pharmaceutical

1.3 Details of the supplier of the safety data sheet
Company: MSD Kilsheelan Clonmel Tipperary, IE
Telephone: 353-51-601000
E-mail address of person responsible for the SDS: EHSDATASTEWARD@msd.com

1.4 Emergency telephone number
National Poison Control Center (UZEM): 114
Emergency: 1-908-423-6000

SECTION 2: Hazards identification

2.1 Classification of the substance or mixture
Classification T.R. SEA No 28848
Acute toxicity, Category 4 H302: Harmful if swallowed.

2.2 Label elements
Labelling T.R. SEA No 28848
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.
SAFETY DATA SHEET
According to 13 December 2014, No:29204, “Ministry of Environment and Urbanization; Regulation on Safety data sheets regarding hazardous substances and mixtures; Part I”.

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<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
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<td>27.08.2021</td>
<td>2805575-00009</td>
<td>09.04.2021</td>
<td>18.05.2018</td>
</tr>
</tbody>
</table>

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

Hazardous components which must be listed on the label:
metformin hydrochloride

2.3 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

3.2 Mixtures

<table>
<thead>
<tr>
<th>Chemical name</th>
<th>CAS-No.</th>
<th>EC-No.</th>
<th>Index-No.</th>
<th>Registration number</th>
<th>Classification</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td>metformin hydrochloride</td>
<td>1115-70-4</td>
<td>214-230-6</td>
<td></td>
<td></td>
<td>Acute Tox. 4;</td>
<td>&gt;= 50 - &lt; 70</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>H302</td>
<td></td>
</tr>
<tr>
<td>Sitagliptin</td>
<td>654671-77-9</td>
<td></td>
<td></td>
<td></td>
<td>Eye Irrit. 2;</td>
<td>&gt;= 1 - &lt; 10</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>H319</td>
<td></td>
</tr>
<tr>
<td>Titanium dioxide</td>
<td>13463-67-7 236-675-5 022-006-00-2</td>
<td></td>
<td></td>
<td></td>
<td>Carc. 2; H351</td>
<td>&gt;= 0,1 - &lt; 1</td>
</tr>
</tbody>
</table>

Substances with a workplace exposure limit:

<table>
<thead>
<tr>
<th>Chemical name</th>
<th>CAS-No.</th>
<th>EC-No.</th>
<th>Index-No.</th>
<th>Registration number</th>
<th>Classification</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cellulose</td>
<td>9004-34-6 232-674-9</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>&gt;= 10 - &lt; 20</td>
</tr>
<tr>
<td>Kaolin</td>
<td>1332-58-7 310-194-1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>&gt;= 1 - &lt; 10</td>
</tr>
</tbody>
</table>

For explanation of abbreviations see section 16.

SECTION 4: First aid measures

4.1 Description of 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.

Protection of first-aiders: First Aid responders should pay attention to self-protection, and use the recommended personal protective equipment.
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when the potential for exposure exists (see section 8).

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.

4.2 Most important symptoms and effects, both acute and delayed

Risks
- 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.

4.3 Indication of any immediate medical attention and special treatment needed

Treatment
- Treat symptomatically and supportively.

SECTION 5: Firefighting measures

5.1 Extinguishing media

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

Unsuitable extinguishing media
- None known.

5.2 Special hazards arising from the substance or mixture

Specific hazards during firefighting
- Avoid generating dust; fine dust dispersed in air in sufficient concentrations, and in the presence of an ignition source is a potential dust explosion hazard.
- Exposure to combustion products may be a hazard to health.

Hazardous combustion products
- Carbon oxides
- Metal oxides
- Nitrogen oxides (NOx)
silicon oxides

5.3 Advice for firefighters

Special protective equipment for firefighters: In the event of fire, wear self-contained breathing apparatus. Use personal protective equipment.

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.

SECTION 6: Accidental release measures

6.1 Personal precautions, protective equipment and emergency procedures

Personal precautions: Use personal protective equipment. Follow safe handling advice (see section 7) and personal protective equipment recommendations (see section 8).

6.2 Environmental precautions

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.

6.3 Methods and material for containment and cleaning up

Methods for 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.

6.4 Reference to other sections

See sections: 7, 8, 11, 12 and 13.
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SECTION 7: Handling and storage

7.1 Precautions for safe handling

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

Local/Total ventilation:
- Use only with adequate ventilation.

Advice on safe handling:
- Do not breathe dust.
- Do not swallow.
- Avoid contact with eyes.
- Avoid prolonged or repeated contact with skin.
- 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. 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.

7.2 Conditions for safe storage, including any incompatibilities

Requirements for storage areas and containers:
- Keep in properly labelled containers. Store in accordance with the particular national regulations.

Advice on common storage:
- Do not store with the following product types:
  - Strong oxidizing agents

7.3 Specific end use(s)

Specific use(s):
- No data available

SECTION 8: Exposure controls/personal protection

8.1 Control parameters

Occupational Exposure Limits
### Components

<table>
<thead>
<tr>
<th>CAS-No.</th>
<th>Value type (Form of exposure)</th>
<th>Control parameters</th>
<th>Basis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1115-70-4</td>
<td>TWA</td>
<td>1 mg/m3 (OEB 1)</td>
<td>Internal</td>
</tr>
<tr>
<td>9004-34-6</td>
<td>ZOAD/TWA (Total dust)</td>
<td>15 mg/m3</td>
<td>TR OEL DU</td>
</tr>
<tr>
<td>654671-77-9</td>
<td>TWA</td>
<td>0.5 mg/m3 (OEB 2)</td>
<td>Internal</td>
</tr>
<tr>
<td>1332-58-7</td>
<td>ZOAD/TWA (Total dust)</td>
<td>15 mg/m3</td>
<td>TR OEL DU</td>
</tr>
<tr>
<td>13463-67-7</td>
<td>ZOAD/TWA (Respirable dust)</td>
<td>5 mg/m3</td>
<td>TR OEL DU</td>
</tr>
</tbody>
</table>

Further information: Allowable occupational exposure limit values of chemicals in dust form

Titanium dioxide

### 8.2 Exposure controls

#### 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

| 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. |
| Hand protection | : Chemical-resistant gloves |
| Skin and body protection | : Work uniform or laboratory coat. |
| Respiratory protection | : If adequate local exhaust ventilation is not available or exp-
SAFETY DATA SHEET
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</thead>
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</tr>
</tbody>
</table>

Sure assessment demonstrates exposures outside the recommended guidelines, use respiratory protection. Equipment should conform to TS EN 143 Filter type: Particulates type (P)

SECTION 9: Physical and chemical properties

9.1 Information on basic physical and chemical properties
- **Appearance**: powder
- **Colour**: blue green
- **Odour**: No data available
- **Odour Threshold**: No data available
- **pH**: No data available
- **Melting point/freezing point**: No data available
- **Initial boiling point and boiling range**: No data available
- **Flash point**: Not applicable
- **Evaporation rate**: Not applicable
- **Flammability (solid, gas)**: May form explosive dust-air mixture during processing, handling or other means.
- **Upper explosion limit / Upper flammability limit**: No data available
- **Lower explosion limit / Lower flammability limit**: No data available
- **Vapour pressure**: Not applicable
- **Relative vapour density**: Not applicable
- **Relative density**: No data available
- **Density**: No data available
- **Solubility(ies)**
  - **Water solubility**: No data available
  - **Partition coefficient: n-octanol/water**: Not applicable
  - **Auto-ignition temperature**: No data available
- **Decomposition temperature**: No data available
- **Viscosity**
  - **Viscosity, kinematic**: Not applicable
SAFETY DATA SHEET
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Explosive properties  : Not explosive
Oxidizing properties : The substance or mixture is not classified as oxidizing.

9.2 Other information
Flammability (liquids) : No data available
Molecular weight : No data available
Particle size : No data available

SECTION 10: Stability and reactivity

10.1 Reactivity
Not classified as a reactivity hazard.

10.2 Chemical stability
Stable under normal conditions.

10.3 Possibility of hazardous reactions
Hazardous reactions : May form explosive dust-air mixture during processing, handling or other means. Can react with strong oxidizing agents.

10.4 Conditions to avoid
Conditions to avoid : Heat, flames and sparks. Avoid dust formation.

10.5 Incompatible materials
Materials to avoid : Oxidizing agents

10.6 Hazardous decomposition products
No hazardous decomposition products are known.

SECTION 11: Toxicological information

11.1 Information on toxicological effects
Information on likely routes of exposure : Inhalation
Ingestion
Skin contact
Eye contact

Acute toxicity
Harmful if swallowed.

Product:
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<table>
<thead>
<tr>
<th>Component</th>
<th>Acute oral toxicity</th>
<th>Acute inhalation toxicity</th>
<th>Acute dermal toxicity</th>
</tr>
</thead>
<tbody>
<tr>
<td>metformin hydrochloride</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute oral toxicity</td>
<td>LD50 (Rat): 1.000 mg/kg</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>LD50 (Mouse): 1.450 - 3.500 mg/kg</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>LD50 (Monkey): 463 mg/kg</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>LD50 (Rabbit): 350 mg/kg</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>LD50 (Guinea pig): 500 mg/kg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sitagliptin</td>
<td>LD50 (Rat): &gt; 3.000 mg/kg</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>LD50 (Mouse): 3.000 mg/kg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Titanium dioxide</td>
<td>LD50 (Rat): &gt; 5.000 mg/kg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute oral toxicity</td>
<td></td>
<td>LC50 (Rat): &gt; 6.82 mg/l</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Exposure time: 4 h</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Test atmosphere: dust/mist</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Assessment: The substance or mixture has no acute inhalation toxicity</td>
<td></td>
</tr>
<tr>
<td>Cellulose</td>
<td>LD50 (Rat): &gt; 5.000 mg/kg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute oral toxicity</td>
<td></td>
<td>LC50 (Rat): &gt; 5.8 mg/l</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Exposure time: 4 h</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Test atmosphere: dust/mist</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Assessment: The substance or mixture has no acute inhalation toxicity</td>
<td></td>
</tr>
<tr>
<td>Kaolin</td>
<td>LD50 (Rat): &gt; 5.000 mg/kg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute oral toxicity</td>
<td></td>
<td>LC50 (Rat): &gt; 2.07 mg/l</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Exposure time: 4 h</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Test atmosphere: dust/mist</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Assessment: The substance or mixture has no acute inhalation toxicity</td>
<td></td>
</tr>
</tbody>
</table>

**Components:**

**Acute oral toxicity:** Acute toxicity estimate: 1.588 mg/kg

Method: Calculation method

**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
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Acute dermal toxicity:
Remarks: Based on data from similar materials

Assessment: The substance or mixture has no acute dermal toxicity
Remarks: Based on data from similar materials

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

Titanium dioxide:
- Species: Rabbit
- Result: No skin irritation

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

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

Components:

metformin hydrochloride:
- Species: Rabbit
- Result: Mild eye irritation

Sitagliptin:
- Species: Rabbit
- Method: Draize Test
- Result: Irritating to eyes.
SAFETY DATA SHEET
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Titanium dioxide:
Species: Rabbit  Result: No eye irritation

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

Respiratory or skin sensitisation
Skin sensitisation
Not classified based on available information.
Respiratory sensitisation
Not classified based on available information.

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

Titanium dioxide:
Test Type: Local lymph node assay (LLNA)  Exposure routes: Skin contact  Species: Mouse  Result: negative

Germ cell mutagenicity
Not classified based on available information.

Components:
metformin hydrochloride:
Genotoxicity in vitro: Test Type: Bacterial reverse mutation assay (AMES)  Result: negative
Test Type: in vitro assay  Test system: mouse lymphoma cells  Result: negative
Test Type: Chromosomal aberration  Test system: Human lymphocytes  Result: negative
Genotoxicity in vivo: Test Type: Micronucleus test
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Species: Mouse
Application Route: Oral
Result: negative

**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

**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

**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

**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>LOAEL</td>
<td>900 mg/kg body weight</td>
</tr>
<tr>
<td>Result</td>
<td>negative</td>
</tr>
<tr>
<td>Target Organs</td>
<td>Uterus (including cervix)</td>
</tr>
<tr>
<td>Remarks</td>
<td>The mechanism or mode of action may not be relevant in humans.</td>
</tr>
</tbody>
</table>

**Sitagliptin:**

<table>
<thead>
<tr>
<th>Species</th>
<th>Mouse</th>
</tr>
</thead>
<tbody>
<tr>
<td>Application Route</td>
<td>Oral</td>
</tr>
<tr>
<td>Exposure time</td>
<td>2 Years</td>
</tr>
<tr>
<td>Result</td>
<td>negative</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Species</th>
<th>Rat</th>
</tr>
</thead>
<tbody>
<tr>
<td>Application Route</td>
<td>oral (drinking water)</td>
</tr>
<tr>
<td>Exposure time</td>
<td>2 Years</td>
</tr>
<tr>
<td>Result</td>
<td>positive</td>
</tr>
<tr>
<td>Target Organs</td>
<td>Liver</td>
</tr>
<tr>
<td>Remarks</td>
<td>Significant toxicity observed in testing</td>
</tr>
</tbody>
</table>

**Carcinogenicity - Assessment:**

Weight of evidence does not support classification as a carcinogen

**Titanium dioxide:**

<table>
<thead>
<tr>
<th>Species</th>
<th>Rat</th>
</tr>
</thead>
<tbody>
<tr>
<td>Application Route</td>
<td>inhalation (dust/mist/fume)</td>
</tr>
<tr>
<td>Exposure time</td>
<td>2 Years</td>
</tr>
<tr>
<td>Method</td>
<td>OECD Test Guideline 453</td>
</tr>
<tr>
<td>Result</td>
<td>positive</td>
</tr>
</tbody>
</table>
| Remarks     | The mechanism or mode of action may not be relevant in humans. These substance(s) are inextricably bound in the product and therefore do not contribute to a dust inhalation hazard.
Carcinogenicity - Assessment:

Limited evidence of carcinogenicity in inhalation studies with animals.

**Cellulose:**

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

**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

- **Effects on foetal development**
  - **Test Type:** Development
  - **Species:** Rat
  - **Application Route:** Oral
  - **Developmental Toxicity:** NOAEL: 600 mg/kg body weight
  - **Result:** No teratogenic effects

  - **Test Type:** Embryo-foetal development
    - **Species:** Rabbit
    - **Application Route:** Oral
    - **Embryo-foetal toxicity:** NOAEL: 140 mg/kg body weight
    - **Result:** No teratogenic effects

**Sitagliptin:**

- **Effects on fertility**
  - **Test Type:** Fertility/early embryonic development
    - **Species:** Rat
    - **Application Route:** Oral
    - **Fertility:** NOAEL Parent: 1.000 mg/kg body weight
    - **Result:** Animal testing did not show any effects on fertility.

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

    **Test Type:** Embryo-foetal development
Sitagliptin / Metformin Extended Release Formulation

Species: Rabbit
Teratogenicity: NOAEL: 125 mg/kg body weight
Result: No teratogenic effects

Cellulose:

<table>
<thead>
<tr>
<th>Effects on fertility</th>
<th>Test Type: One-generation reproduction toxicity study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Species: Rat</td>
<td>Application Route: Ingestion</td>
</tr>
<tr>
<td>Application Route: Ingestion</td>
<td>Result: negative</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Effects on foetal development</th>
<th>Test Type: Fertility/early embryonic development</th>
</tr>
</thead>
<tbody>
<tr>
<td>Species: Rat</td>
<td>Application Route: Ingestion</td>
</tr>
<tr>
<td>Application Route: Ingestion</td>
<td>Result: negative</td>
</tr>
</tbody>
</table>

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>
</tbody>
</table>

<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>Rabbit</td>
<td>100 mg/kg</td>
<td>Oral</td>
<td>1 Year</td>
<td>No significant adverse effects were reported</td>
</tr>
</tbody>
</table>

<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>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>

Sitagliptin:

<table>
<thead>
<tr>
<th>Species</th>
<th>NOAEL</th>
<th>LOAEL</th>
<th>Application Route</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mouse</td>
<td>500 mg/kg</td>
<td>1,000 mg/kg</td>
<td>Oral</td>
</tr>
</tbody>
</table>
SAFETY DATA SHEET
According to 13 December 2014, No:29204, “Ministry of Environment and Urbanization; Regulation on Safety data sheets regarding hazardous substances and mixtures; Part I”.

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<td>18.05.2018</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Exposure time</th>
<th>Target Organs</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 2 yr</td>
<td>Kidney</td>
</tr>
</tbody>
</table>

**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

**Titanium dioxide**

<table>
<thead>
<tr>
<th>Species</th>
<th>NOAEL</th>
<th>Application Route</th>
<th>Exposure time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rat</td>
<td>24.000 mg/kg</td>
<td>Ingestion</td>
<td>28 Days</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Species</th>
<th>NOAEL</th>
<th>Application Route</th>
<th>Exposure time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rat</td>
<td>10 mg/m3</td>
<td>Inhalation (dust/mist/fume)</td>
<td>2 yr</td>
</tr>
</tbody>
</table>

**Cellulose**

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

: >= 9.000 mg/kg

**Application Route**

: Ingestion

**Exposure time**

: 90 Days

**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: Diarrhoea, 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, Diarrhoea |

**SECTION 12: Ecological information**

**12.1 Toxicity**

**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 microorganisms | EC50 : > 1.000 mg/l |
| Exposure time: 3 h Test Type: Respiration inhibition Method: OECD Test Guideline 209 |

| Toxicity to fish (Chronic toxicity) | NOEC: 10 mg/l |
| Exposure time: 33 d Species: Pimephales promelas (fathead minnow) Method: OECD Test Guideline 210 |

| Toxicity to daphnia and other | NOEC: 40 mg/l |
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<table>
<thead>
<tr>
<th>aquatic invertebrates (Chronic toxicity)</th>
<th>Exposure time: 21 d</th>
</tr>
</thead>
<tbody>
<tr>
<td>Species: Daphnia magna (Water flea)</td>
<td>Method: OECD Test Guideline 211</td>
</tr>
</tbody>
</table>

### Sitagliptin:

<table>
<thead>
<tr>
<th>Toxicity to fish</th>
<th>LC50 (Pimephales promelas (fathead minnow)): &gt; 100 mg/l</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exposure time: 96 h</td>
<td></td>
</tr>
<tr>
<td>Method: OECD Test Guideline 203</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Toxicity to daphnia and other aquatic invertebrates</th>
<th>EC50 (Daphnia magna (Water flea)): 60 mg/l</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exposure time: 48 h</td>
<td></td>
</tr>
<tr>
<td>Method: OECD Test Guideline 202</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Toxicity to algae/aquatic plants</th>
<th>EC50 (Pseudokirchneriella subcapitata (green algae)): &gt; 39 mg/l</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exposure time: 96 h</td>
<td></td>
</tr>
<tr>
<td>Method: OECD Test Guideline 201</td>
<td></td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Toxicity to fish (Chronic toxicity)</th>
<th>NOEC: 9.2 mg/l</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exposure time: 33 d</td>
<td></td>
</tr>
<tr>
<td>Species: Pimephales promelas (fathead minnow)</td>
<td></td>
</tr>
<tr>
<td>Method: OECD Test Guideline 210</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity)</th>
<th>NOEC: 9.8 mg/l</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exposure time: 21 d</td>
<td></td>
</tr>
<tr>
<td>Species: Daphnia magna (Water flea)</td>
<td></td>
</tr>
<tr>
<td>Method: OECD Test Guideline 211</td>
<td></td>
</tr>
</tbody>
</table>

### Titanium dioxide:

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

<table>
<thead>
<tr>
<th>Toxicity to daphnia and other aquatic invertebrates</th>
<th>EC50 (Daphnia magna (Water flea)): &gt; 100 mg/l</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exposure time: 48 h</td>
<td></td>
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</tbody>
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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

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

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

### 12.2 Persistence and degradability

**Components:**

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

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

- **Stability in water**
  - pH: 7
  - Hydrolysis: 50 %/(401 d)
  - Method: OECD Test Guideline 111

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

### 12.3 Bioaccumulative potential

**Components:**

**metformin hydrochloride:**
- **Partition coefficient: n-octanol/water**
  - log Pow: -2
SAFETY DATA SHEET

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</tr>
</tbody>
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12.4 Mobility in soil

Components:

**Sitagliptin:**
- Partition coefficient: n-octanol/water
  - log Pow: -0,03

**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

12.5 Results of PBT and vPvB assessment

Not relevant

12.6 Other adverse effects

No data available

SECTION 13: Disposal considerations

13.1 Waste treatment methods

- **Product**
  - 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

14.1 UN number

- Not regulated as a dangerous good

14.2 UN proper shipping name

- Not regulated as a dangerous good

14.3 Transport hazard class(es)

- Not regulated as a dangerous good

14.4 Packing group

- Not regulated as a dangerous good
SAFETY DATA SHEET

According to 13 December 2014, No:29204, “Ministry of Environment and Urbanization; Regulation on Safety data sheets regarding hazardous substances and mixtures; Part I”.

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14.5 Environmental hazards
Not regulated as a dangerous good

14.6 Special precautions for user
Not applicable

14.7 Transport in bulk according to Annex II of Marpol and the IBC Code
Remarks : Not applicable for product as supplied.

SECTION 15: Regulatory information

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

- KKDIK (30105 (Bis)) - Restrictions on the manufacture, placing on the market and use of certain dangerous substances, mixtures and articles (Annex 17):
  Remarks : Not applicable

- Regulation on Persistent Organic Pollutants (Number 30595):
  Remarks : Not applicable

- Regulation on prevention of major industrial accidents. Reg number 30702:
  Remarks : Not applicable

Other regulations:
According to 13 December 2014, No:29204, “Ministry of Environment and Urbanization; Regulation on Safety data sheets regarding hazardous substances and mixtures; Part I”.
Regulation on Classification, Labelling and Packaging of Substances and Mixtures. Dated 11 December 2013, Numbered 28848 (Bis) Ministry of Environment and Forestry.
Regulation on Dust Control (No: 28812, 2013). Occupational Dust Exposure Limit Values (Annex 1)

The components of this product are reported in the following inventories:

- AICS : not determined
- DSL : not determined
- IECSC : not determined

SECTION 16: Other information

Other information : The SDS has been prepared by: Name: Gökhan Ardıç; Contact email: stds@chemleg.com; Telephone number: +90 216 706 1307; Certificate Number: Lonca KDU 34 / 2020.08; Certificate Date: 22 September 2020; Valid Until: 22 September 2025

Items where changes have been made to the previous version are highlighted in the body of this document by two vertical lines.
SAFETY DATA SHEET
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Full text of H-Statements
H302 : Harmful if swallowed.
H319 : Causes serious eye irritation.
H351 : Suspected of causing cancer if inhaled.

The Turkish SDS has been prepared according to the Regulation on Safety Data Sheets for Hazardous Substances and Mixtures No. 29204.

Full text of other abbreviations
Acute Tox. : Acute toxicity
Carc. : Carcinogenicity
Eye Irrit. : Eye irritation
TR OEL DU : Turkey. Regulation on Dust Control. Occupational Dust Exposure Limit Values (Annex 1)
TR OEL DU / ZOAD/TWA : Time Weighted Average Value

ADN - European Agreement concerning the International Carriage of Dangerous Goods by Inland Waterways; ADR - European Agreement concerning the International Carriage of Dangerous Goods by Road; AIIC - Australian Inventory of Industrial Chemicals; ASTM - American Society for the Testing of Materials; bw - Body weight; CLP - Classification Labelling Packaging Regulation; Regulation (EC) No 1272/2008; CMR - Carcinogen, Mutagen or Reproductive Toxicant; DIN - Standard of the German Institute for Standardisation; DSL - Domestic Substances List (Canada); ECHA - European Chemicals Agency; EC-Number - European Community number; 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; 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; IMOI - 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; n.o.s. - Not Otherwise Specified; NO(A)EC - No Observed (Adverse) Effect Concentration; NO(A)EL - No Observed (Adverse) Effect Level; NOELR - No Observable Effect Loading Rate; 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; RID - Regulations concerning the International Carriage of Dangerous Goods by Rail; SADT - Self-Accelerating Decomposition Temperature; SDS - Safety Data Sheet; SVHC - Substance of very high concern; TCSI - Taiwan Chemical Substance Inventory; 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

Further information
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Date of first issue: 18.05.2018

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

Classification of the mixture:
Acute Tox. 4 H302

Classification procedure:
Calculation method

Items where changes have been made to the previous version are highlighted in the body of this document by two vertical lines.
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.

TR / EN