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”.

Sitagliptin / Metformin Formulation

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

1.1 Product identifier
   Trade name : Sitagliptin / Metformin 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.
   Response:
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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

Components

<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; H302</td>
<td>&gt;= 70 - &lt; 90</td>
</tr>
<tr>
<td></td>
<td>654671-77-9</td>
<td></td>
<td></td>
<td></td>
<td>Eye Irrit. 2; H319</td>
<td>&gt;= 1 - &lt; 10</td>
</tr>
<tr>
<td>Sitagliptin</td>
<td>13463-67-7</td>
<td>236-675-5</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>
</tr>
</thead>
<tbody>
<tr>
<td>Cellulose</td>
<td>9004-34-6</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>232-674-9</td>
<td></td>
<td></td>
<td></td>
<td></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 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
                                    Nitrogen oxides (NOx)
                                    Metal 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.
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</tbody>
</table>

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.

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.
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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

<table>
<thead>
<tr>
<th>Components</th>
<th>CAS-No.</th>
<th>Value type (Form of exposure)</th>
<th>Control parameters</th>
<th>Basis</th>
</tr>
</thead>
<tbody>
<tr>
<td>metformin hydrochloride</td>
<td>1115-70-4</td>
<td>TWA</td>
<td>1 mg/m3 (OEB 1)</td>
<td>Internal</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>Cellulose</td>
<td>9004-34-6</td>
<td>ZOAD/TWA (Total dust)</td>
<td>15 mg/m3</td>
<td>TR OEL DU</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Components</th>
<th>Value type (Form of exposure)</th>
<th>Control parameters</th>
<th>Basis</th>
</tr>
</thead>
<tbody>
<tr>
<td>ZOAD/TWA (Respirable dust)</td>
<td></td>
<td>5 mg/m3</td>
<td>TR OEL DU</td>
</tr>
</tbody>
</table>

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

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

Material : Chemical-resistant gloves

Skin and body protection : Work uniform or laboratory coat.

Respiratory protection : If adequate local exhaust ventilation is not available or exposure 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 : No data available
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
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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
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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
- Skin contact
- Ingestion
- Eye contact

Acute toxicity
Harmful if swallowed.

Product:
Acute oral toxicity : Acute toxicity estimate: 1.380 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

Sitagliptin:
- Acute oral toxicity : LD50 (Rat): > 3.000 mg/kg
  LD50 (Mouse): 3.000 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

Cellulose:
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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

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

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.

Titanium dioxide:

Species: Rabbit
Result: No eye irritation

Respiratory or skin sensitisation

Skin sensitisation
Not classified based on available information.
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</table>

#### Respiratory sensitisation
Not classified based on available information.

#### Components:

**Sitagliptin:**

<table>
<thead>
<tr>
<th>Test Type</th>
<th>Local lymph node assay (LLNA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Species</td>
<td>Mouse</td>
</tr>
<tr>
<td>Method</td>
<td>OECD Test Guideline 429</td>
</tr>
<tr>
<td>Result</td>
<td>Not a skin sensitizer.</td>
</tr>
</tbody>
</table>

**Titanium dioxide:**

<table>
<thead>
<tr>
<th>Test Type</th>
<th>Local lymph node assay (LLNA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exposure routes</td>
<td>Skin contact</td>
</tr>
<tr>
<td>Species</td>
<td>Mouse</td>
</tr>
<tr>
<td>Result</td>
<td>negative</td>
</tr>
</tbody>
</table>

**Germ cell mutagenicity**

Not classified based on available information.

#### Components:

**metformin hydrochloride:**

<table>
<thead>
<tr>
<th>Genotoxicity in vitro</th>
<th>Test Type: Bacterial reverse mutation assay (AMES)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Result: negative</td>
</tr>
</tbody>
</table>

- Test Type: in vitro assay
  - Test system: mouse lymphoma cells
  - Result: negative

- Test Type: Chromosomal aberration
  - Test system: Human lymphocytes
  - Result: negative

<table>
<thead>
<tr>
<th>Genotoxicity in vivo</th>
<th>Test Type: Micronucleus test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Species</td>
<td>Mouse</td>
</tr>
<tr>
<td>Application Route</td>
<td>Oral</td>
</tr>
<tr>
<td>Result</td>
<td>negative</td>
</tr>
</tbody>
</table>

**Sitagliptin:**

<table>
<thead>
<tr>
<th>Genotoxicity in vitro</th>
<th>Test Type: Ames test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Result</td>
<td>negative</td>
</tr>
</tbody>
</table>

- 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
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</tbody>
</table>

### 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
- **Species**: Mouse  
  **Exposure time**: 91 weeks  
  **Dose**: 1500 mg/kg body weight  
  **Result**: negative
- **Species**: Rat, male  
  **Application Route**: Oral  
  **Exposure time**: 104 weeks  
  **Dose**: 900 mg/kg body weight  
  **Result**: negative
- **Species**: Rat, female  
  **Application Route**: Oral  
  **Exposure time**: 104 weeks  
  **LOAEL**: 900 mg/kg body weight  
  **Result**: negative
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| Target Organs | Uterus (including cervix) |
| Remarks | The mechanism or mode of action may not be relevant in humans. |

**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. |

**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 |
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**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
    - **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 foetal development**
  - **Test Type:** Fertility/early embryonic development
    - **Species:** Rat
    - **Application Route:** Ingestion
    - **Result:** negative

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

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

**Components:**

- **metformin hydrochloride:**
  - **Species**: Rat
  - **NOAEL**: 125 mg/kg
  - **Application Route**: Oral
  - **Exposure time**: 1 year
  - **Remarks**: No significant adverse effects were reported
  - **Species**: Rabbit
  - **NOAEL**: 100 mg/kg
  - **Application Route**: Oral
  - **Exposure time**: 1 Year
  - **Remarks**: No significant adverse effects were reported
  - **Species**: Dog
  - **NOAEL**: 50 mg/kg
  - **Application Route**: Subcutaneous
  - **Exposure time**: 2 year
  - **Remarks**: No significant adverse effects were reported

- **Sitagliptin:**
  - **Species**: Mouse
  - **NOAEL**: 500 mg/kg
  - **LOAEL**: 1,000 mg/kg
  - **Application Route**: Oral
  - **Exposure time**: > 2 yr
  - **Target Organs**: Kidney
  - **Species**: Rat
  - **NOAEL**: 500 mg/kg
  - **LOAEL**: 1,000 mg/kg
  - **Application Route**: Oral
  - **Exposure time**: 14 Weeks
  - **Target Organs**: Liver, Kidney, Heart, Teeth
  - **Species**: Dog
  - **NOAEL**: 10 mg/kg
  - **LOAEL**: 50 mg/kg
  - **Application Route**: Oral
  - **Exposure time**: 53 Weeks
  - **Target Organs**: Central nervous system
  - **Symptoms**: Loss of balance
  - **Remarks**: The mechanism or mode of action may not be relevant in humans.
  - **Species**: Dog
  - **NOAEL**: 2 mg/kg
  - **LOAEL**: 10 mg/kg
  - **Application Route**: Oral
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- **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 yr

**Cellulose**:

- **Species**: Rat
- **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
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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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 aquatic invertebrates (Chronic toxicity)

- NOEC: 40 mg/l
  Exposure time: 21 d
  Species: Daphnia magna (Water flea)
  Method: OECD Test Guideline 211

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
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**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

**Toxicity to fish (Chronic toxicity)**

- NOEC: 9.2 mg/l
- Exposure time: 33 d
- Species: Pimephales promelas (fathead minnow)
- Method: OECD Test Guideline 210

**Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity)**

- NOEC: 9.8 mg/l
- Exposure time: 21 d
- Species: Daphnia magna (Water flea)
- Method: OECD Test Guideline 211

**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

**Cellulose**

**Toxicity to fish**

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

### 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

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

### 12.4 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

### 12.5 Results of PBT and vPvB assessment

Not relevant

### 12.6 Other adverse effects

No data available

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## SECTION 13: Disposal considerations

### 13.1 Waste treatment methods

**Product:** Dispose of in accordance with local regulations.

According to the European Waste Catalogue, Waste Codes are not product specific, but application specific. Waste codes should be assigned by the user, preferably in discussion with the waste disposal authorities.
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

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): Not applicable
Regulation on Persistent Organic Pollutants (Number 30595): Not applicable
Regulation on prevention of major industrial accidents. Reg number 30702 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
SECTION 16: Other information

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

The SDS has been prepared by: Name: Gökhan Ardıç; Contact email: sds@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

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; IMO - International Maritime Organization; ISHL - Industrial Safety and Health Law (Japan); ISO - International Organisation for Standardization; KECI - Korea Existing Chemicals Inventory; LC50 - Lethal Concentration to 50 % of a test population; LD50 - Lethal Dose to 50% of a test population (Median Lethal Dose); MARPOL - International Convention for the Prevention of Pollution from Ships; 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
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Further information


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