

# Sitagliptin / Metformin Extended Release Formulation

Version 12.0      Revision Date: 2023/09/30      SDS Number: 29107-00024      Date of last issue: 2023/04/04  
Date of first issue: 2014/11/07

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## 1. PRODUCT AND COMPANY IDENTIFICATION

Chemical product name : Sitagliptin / Metformin Extended Release Formulation

### Supplier's company name, address and phone number

Company name of supplier : MSD

Address : Kumagaya, Saitama Prefecture , Xicheng 810 MSD Co., Ltd.  
Menuma factory

Telephone : 048-588-8411

E-mail address : EHSDATASTEWARD@msd.com

Emergency telephone number : +1-908-423-6000

### Recommended use of the chemical and restrictions on use

Recommended use : Pharmaceutical

Restrictions on use : Not applicable

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## 2. HAZARDS IDENTIFICATION

### GHS classification of chemical product

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/ doctor if you feel unwell. Rinse mouth.

#### Disposal:

P501 Dispose of contents/ container to an approved waste

## Sitagliptin / Metformin Extended Release Formulation

Version 12.0      Revision Date: 2023/09/30      SDS Number: 29107-00024      Date of last issue: 2023/04/04  
Date of first issue: 2014/11/07

disposal plant.

### Other hazards which do not result in classification

Important symptoms and out- : Dust contact with the eyes can lead to mechanical irritation.  
lines of the emergency as- : Contact with dust can cause mechanical irritation or drying of  
sumed : the skin.  
May form explosive dust-air mixture during processing, handling or other means.

### 3. COMPOSITION/INFORMATION ON INGREDIENTS

Substance / Mixture : Mixture

#### Components

Chemical name	CAS-No.	Concentration (% w/w)	ENCS No.
metformin hydrochloride	1115-70-4	>= 60 - < 70	2-2883
Cellulose	9004-34-6	>= 10 - < 20	
Sitagliptin	654671-77-9	>= 2.5 - < 10	
Kaolin	1332-58-7	>= 1 - < 10	1-26
Titanium dioxide	13463-67-7	>= 0.1 - < 1	1-558, 5-5225

### 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

## Sitagliptin / Metformin Extended Release Formulation

Version	Revision Date:	SDS Number:	Date of last issue: 2023/04/04
12.0	2023/09/30	29107-00024	Date of first issue: 2014/11/07

---

Notes to physician : when the potential for exposure exists (see section 8).  
: Treat symptomatically and supportively.

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### 5. FIREFIGHTING MEASURES

Suitable extinguishing media : Water spray  
Alcohol-resistant foam  
Carbon dioxide (CO<sub>2</sub>)  
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 (NO<sub>x</sub>)  
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 firefighters : In the event of fire, wear self-contained breathing apparatus.  
Use personal protective equipment.

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### 6. ACCIDENTAL RELEASE MEASURES

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

Environmental precautions : Avoid release to the environment.  
Prevent further leakage or spillage if safe to do so.  
Retain and dispose of contaminated wash water.  
Local authorities should be advised if significant spillages cannot be contained.

Methods and materials for containment and cleaning up : Sweep up or vacuum up spillage and collect in suitable container for disposal.  
Avoid dispersal of dust in the air (i.e., clearing dust surfaces with compressed air).  
Dust deposits should not be allowed to accumulate on surfaces, as these may form an explosive mixture if they are released into the atmosphere in sufficient concentration.  
Local or national regulations may apply to releases and disposal of this material, as well as those materials and items

## Sitagliptin / Metformin Extended Release Formulation

Version	Revision Date:	SDS Number:	Date of last issue: 2023/04/04
12.0	2023/09/30	29107-00024	Date of first issue: 2014/11/07

---

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.

### 7. HANDLING AND STORAGE

#### Handling

- |                         |   |   |
|-------------------------|---|---|
| Technical measures      | : | Static electricity may accumulate and ignite suspended dust causing an explosion.<br>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.<br>Do not swallow.<br>Avoid contact with eyes.<br>Avoid prolonged or repeated contact with skin.<br>Wash skin thoroughly after handling.<br>Handle in accordance with good industrial hygiene and safety practice, based on the results of the workplace exposure assessment<br>Minimize dust generation and accumulation.<br>Keep container closed when not in use.<br>Keep away from heat and sources of ignition.<br>Take precautionary measures against static discharges.<br>Do not eat, drink or smoke when using this product.<br>Take care to prevent spills, waste and minimize release to the environment. |
| Avoidance of contact    | : | Oxidizing agents  |
| Hygiene measures        | : | If exposure to chemical is likely during typical use, provide eye flushing systems and safety showers close to the working place.<br>When using do not eat, drink or smoke.<br>Wash contaminated clothing before re-use.<br>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.  |

#### Storage

- |                             |   |  |
|-----------------------------|---|--|
| Conditions for safe storage | : | Keep in properly labelled containers.<br>Store in accordance with the particular national regulations. |
| Materials to avoid          | : | Do not store with the following product types:<br>Strong oxidizing agents                              |
| Packaging material          | : | Unsuitable material: None known.   |

## Sitagliptin / Metformin Extended Release Formulation

Version 12.0      Revision Date: 2023/09/30      SDS Number: 29107-00024      Date of last issue: 2023/04/04  
 Date of first issue: 2014/11/07

### 8. EXPOSURE CONTROLS/PERSONAL PROTECTION

**Threshold limit value and permissible exposure limits for each component in the work environment**

Components	CAS-No.	Value type (Form of exposure)	Control parameters / Reference concentration / Permissible concentration	Basis
metformin hydrochloride	1115-70-4	TWA	1 mg/m <sup>3</sup> (OEB 1)	Internal
Cellulose	9004-34-6	TWA	10 mg/m <sup>3</sup>	ACGIH
Sitagliptin	654671-77-9	TWA	0.5 mg/m <sup>3</sup> (OEB 2)	Internal
Kaolin	1332-58-7	OEL-M (Respirable dust)	0.5 mg/m <sup>3</sup>	JP OEL JSOH
		OEL-M (Total dust)	2 mg/m <sup>3</sup>	JP OEL JSOH
		TWA (Respirable particulate matter)	2 mg/m <sup>3</sup>	ACGIH
Titanium dioxide	13463-67-7	OEL-M (Respirable particulate matter)	1.5 mg/m <sup>3</sup> (Titanium)	JP OEL JSOH
		Further information: Group 2B: possibly carcinogenic to humans		
		OEL-M (Total particulate matter)	2 mg/m <sup>3</sup> (Titanium)	JP OEL JSOH
		Further information: Group 2B: possibly carcinogenic to humans		
		TWA (Respirable particulate matter)	2.5 mg/m <sup>3</sup> (Titanium dioxide)	ACGIH

**This substance(s) is not bioavailable and therefore does 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 rec-

## Sitagliptin / Metformin Extended Release Formulation

Version	Revision Date:	SDS Number:	Date of last issue: 2023/04/04
12.0	2023/09/30	29107-00024	Date of first issue: 2014/11/07

---

Filter type	:	Recommended guidelines, use respiratory protection.
Hand protection	:	Particulates type
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.

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### 9. PHYSICAL AND CHEMICAL PROPERTIES

Physical state	:	powder
Colour	:	blue green
Odour	:	No data available
Odour Threshold	:	No data available
Melting point/freezing point	:	No data available
Boiling point, initial boiling point and boiling range	:	No data available
Flammability (solid, gas)	:	May form explosive dust-air mixture during processing, handling or other means.
Flammability (liquids)	:	No data available
Lower explosion limit and upper explosion limit / flammability limit	:	
Upper explosion limit / Upper per flammability limit	:	No data available
Lower explosion limit / Lower flammability limit	:	No data available
Flash point	:	Not applicable
Decomposition temperature	:	No data available
pH	:	No data available
Evaporation rate	:	Not applicable
Auto-ignition temperature	:	No data available
Viscosity	:	

**Sitagliptin / Metformin Extended Release Formulation**

Version 12.0      Revision Date: 2023/09/30      SDS Number: 29107-00024      Date of last issue: 2023/04/04  
Date of first issue: 2014/11/07

---

Viscosity, kinematic : Not applicable

Solubility(ies)  
Water solubility : No data available

Partition coefficient: n-octanol/water : Not applicable

Vapour pressure : Not applicable

Density and / or relative density  
Relative density : No data available

Density : No data available

Relative vapour density : Not applicable

Explosive properties : Not explosive

Oxidizing properties : The substance or mixture is not classified as oxidizing.

Molecular weight : No data available

Particle characteristics  
Particle size : No data available

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**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.

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**11. TOXICOLOGICAL INFORMATION**

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

## Sitagliptin / Metformin Extended Release Formulation

Version	Revision Date:	SDS Number:	Date of last issue: 2023/04/04
12.0	2023/09/30	29107-00024	Date of first issue: 2014/11/07

---

### 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



**Sitagliptin / Metformin Extended Release Formulation**

Version 12.0      Revision Date: 2023/09/30      SDS Number: 29107-00024      Date of last issue: 2023/04/04  
Date of first issue: 2014/11/07

---

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

## Sitagliptin / Metformin Extended Release Formulation

Version	Revision Date:	SDS Number:	Date of last issue: 2023/04/04
12.0	2023/09/30	29107-00024	Date of first issue: 2014/11/07

---

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 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

## Sitagliptin / Metformin Extended Release Formulation

Version 12.0      Revision Date: 2023/09/30      SDS Number: 29107-00024      Date of last issue: 2023/04/04  
 Date of first issue: 2014/11/07

Genotoxicity in vivo : Test system: Human lymphocytes  
 Result: negative  
 : Test Type: Micronucleus test  
 Species: Mouse  
 Application Route: Oral  
 Result: negative

### Cellulose:

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

Test Type: In vitro mammalian cell gene mutation test  
 Result: negative

Genotoxicity in vivo : Test Type: Mammalian erythrocyte micronucleus test (in vivo cytogenetic assay)  
 Species: Mouse  
 Application Route: Ingestion  
 Result: negative

### 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

## Sitagliptin / Metformin Extended Release Formulation

Version 12.0      Revision Date: 2023/09/30      SDS Number: 29107-00024      Date of last issue: 2023/04/04  
 Date of first issue: 2014/11/07

---

### 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
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

## Sitagliptin / Metformin Extended Release Formulation

Version 12.0      Revision Date: 2023/09/30      SDS Number: 29107-00024      Date of last issue: 2023/04/04  
 Date of first issue: 2014/11/07

### 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.  
 This substance(s) is not bioavailable and therefore does not contribute to a dust inhalation hazard.

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

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

#### 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

## Sitagliptin / Metformin Extended Release Formulation

Version 12.0      Revision Date: 2023/09/30      SDS Number: 29107-00024      Date of last issue: 2023/04/04  
 Date of first issue: 2014/11/07

### 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

### 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

#### Cellulose:

Species	:	Rat
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## Sitagliptin / Metformin Extended Release Formulation

Version 12.0      Revision Date: 2023/09/30      SDS Number: 29107-00024      Date of last issue: 2023/04/04  
 Date of first issue: 2014/11/07

---

NOAEL :  $\geq 9,000$  mg/kg  
 Application Route : Ingestion  
 Exposure time : 90 Days

### 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  
 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

## Sitagliptin / Metformin Extended Release Formulation

Version	Revision Date:	SDS Number:	Date of last issue: 2023/04/04
12.0	2023/09/30	29107-00024	Date of first issue: 2014/11/07

---

Exposure time	:	28 Days
Species	:	Rat
NOAEL	:	10 mg/m <sup>3</sup>
Application Route	:	inhalation (dust/mist/fume)
Exposure time	:	2 yr

### 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

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## 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



## Sitagliptin / Metformin Extended Release Formulation

Version 12.0      Revision Date: 2023/09/30      SDS Number: 29107-00024      Date of last issue: 2023/04/04  
 Date of first issue: 2014/11/07

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

## Sitagliptin / Metformin Extended Release Formulation

Version 12.0      Revision Date: 2023/09/30      SDS Number: 29107-00024      Date of last issue: 2023/04/04  
 Date of first issue: 2014/11/07

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:**

## Sitagliptin / Metformin Extended Release Formulation

Version	Revision Date:	SDS Number:	Date of last issue: 2023/04/04
12.0	2023/09/30	29107-00024	Date of first issue: 2014/11/07

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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

### Hazardous to the ozone layer

Not applicable

### Other adverse effects

No data available

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## 13. DISPOSAL CONSIDERATIONS

### Disposal methods

Waste from residues : Dispose of in accordance with local regulations.  
Do not dispose of waste into sewer.

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.

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## 14. TRANSPORT INFORMATION

### International Regulations

#### UNRTDG

UN number : Not applicable  
Proper shipping name : Not applicable  
Class : Not applicable  
Subsidiary risk : Not applicable  
Packing group : Not applicable  
Labels : Not applicable

#### IATA-DGR

UN/ID No. : Not applicable  
Proper shipping name : Not applicable  
Class : Not applicable  
Subsidiary risk : Not applicable

**Sitagliptin / Metformin Extended Release Formulation**

Version 12.0      Revision Date: 2023/09/30      SDS Number: 29107-00024      Date of last issue: 2023/04/04  
Date of first issue: 2014/11/07

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Packing group : Not applicable  
Labels : Not applicable  
Packing instruction (cargo aircraft) : Not applicable  
Packing instruction (passenger aircraft) : Not applicable

**IMDG-Code**

UN number : Not applicable  
Proper shipping name : Not applicable  
Class : Not applicable  
Subsidiary risk : Not applicable  
Packing group : Not applicable  
Labels : Not applicable  
EmS Code : Not applicable  
Marine pollutant : Not applicable

**Transport in bulk according to Annex II of MARPOL 73/78 and the IBC Code**

Not applicable for product as supplied.

**National Regulations**

Refer to section 15 for specific national regulation.

**Special precautions for user**

Not applicable

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**15. REGULATORY INFORMATION****Related Regulations****Fire Service Law**

Not applicable to dangerous materials / designated flammables.

**Chemical Substance Control Law**

Not applicable for Specified Chemical Substance, Monitoring Chemical Substance and Priority Assessment Chemical Substance.

**Industrial Safety and Health Law****Harmful Substances Prohibited from Manufacture**

Not applicable

**Harmful Substances Required Permission for Manufacture**

Not applicable

**Substances Prevented From Impairment of Health**

Not applicable

**Circular concerning Information on Chemicals having Mutagenicity - Annex 2: Information on Existing Chemicals having Mutagenicity**

Not applicable

# Sitagliptin / Metformin Extended Release Formulation

Version 12.0      Revision Date: 2023/09/30      SDS Number: 29107-00024      Date of last issue: 2023/04/04  
Date of first issue: 2014/11/07

## Circular concerning Information on Chemicals having Mutagenicity - Annex 1: Information on Notified Substances having Mutagenicity

Not applicable

### Substances Subject to be Notified Names

Article 57-2 (Enforcement Order Table 9)

Chemical name	Concentration (%)	Remarks
Titanium(IV) oxide	$\geq 0.1 - < 1$	-

### Substances Subject to be Indicated Names

Not applicable

### Ordinance on Prevention of Hazards Due to Specified Chemical Substances

Not applicable

### Ordinance on Prevention of Lead Poisoning

Not applicable

### Ordinance on Prevention of Tetraalkyl Lead Poisoning

Not applicable

### Ordinance on Prevention of Organic Solvent Poisoning

Not applicable

### Enforcement Order of the Industrial Safety and Health Law - Attached table 1 (Dangerous Substances)

Not applicable

### Poisonous and Deleterious Substances Control Law

Not applicable

### Act on Confirmation, etc. of Release Amounts of Specific Chemical Substances in the Environment and Promotion of Improvements to the Management Thereof

|| Not applicable

### High Pressure Gas Safety Act

Not applicable

### Explosive Control Law

Not applicable

### Vessel Safety Law

Not regulated as a dangerous good

### Aviation Law

Not regulated as a dangerous good

### Marine Pollution and Sea Disaster Prevention etc Law

Bulk transportation : Not classified as noxious liquid substance

Pack transportation : Not classified as marine pollutant

## Sitagliptin / Metformin Extended Release Formulation

Version	Revision Date:	SDS Number:	Date of last issue: 2023/04/04
12.0	2023/09/30	29107-00024	Date of first issue: 2014/11/07

---

### Narcotics and Psychotropics Control Act

Narcotic or Psychotropic Raw Material (Export / Import Permission)

Not applicable

Specific Narcotic or Psychotropic Raw Material (Export / Import permission)

Not applicable

### Waste Disposal and Public Cleansing Law

Industrial waste

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

AICS : not determined

DSL : not determined

IECSC : not determined

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## 16. OTHER INFORMATION

### Further information

Sources of key data used to compile the Safety Data Sheet : Internal technical data, data from raw material SDSs, OECD eChem Portal search results and European Chemicals Agency, <http://echa.europa.eu/>

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

Date format : yyyy/mm/dd

### Full text of other abbreviations

ACGIH : USA. ACGIH Threshold Limit Values (TLV)

JP OEL JSOH : Japan. The Japan Society for Occupational Health. Recommendation of Occupational Exposure Limits

ACGIH / TWA : 8-hour, time-weighted average

JP OEL JSOH / OEL-M : Occupational Exposure Limit-Mean

All - Australian Inventory of Industrial Chemicals; 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 Maritime Organization; ISHL - Industrial Safety and Health Law (Japan); ISO - International Organisation for Standardization; KECI - Korea Existing Chemicals Inventory; LC50 - Lethal Con-

## Sitagliptin / Metformin Extended Release Formulation

Version	Revision Date:	SDS Number:	Date of last issue: 2023/04/04
12.0	2023/09/30	29107-00024	Date of first issue: 2014/11/07

---

centration 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; TECI - Thailand Existing Chemicals 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; WHMIS - Workplace Hazardous Materials Information System

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.

JP / EN