SAFETY DATA SHEET

Ertugliflozin Formulation

Version	Revision Date:	SDS Number:	Date of last issue: 04.04.2023
4.1	30.09.2023	2338800-00016	Date of first issue: 13.12.2017

SECTION 1. IDENTIFICATION

Product name : Ertugliflozin Formulation

Manufacturer or supplier's details

Company : MSD

Address : 855 Leandro N. Alem St., 8 Floor
Buenos Aires, Argentina C1001AFB

Telephone : 908-740-4000

Emergency telephone : 1-908-423-6000

E-mail address : EHSDATASTEWARD@msd.com

Recommended use of the chemical and restrictions on use

Recommended use : Pharmaceutical
Restrictions on use : Not applicable

SECTION 2. HAZARDS IDENTIFICATION

GHS Classification

Serious eye damage/eye irritation : Category 1

GHS label elements

Hazard pictograms :

Signal Word : Danger

Hazard Statements : H318 Causes serious eye damage.

Precautionary Statements :

Prevention:

P280 Wear eye protection/ face protection.

Response:

P305 + P351 + P338 + P310 IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. Immediately call a POISON CENTER/ doctor.

Other hazards which do not result in classification

Contact with dust can cause mechanical irritation or drying of the skin.

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

SECTION 3. COMPOSITION/INFORMATION ON INGREDIENTS

Substance / Mixture : Mixture

Components

Chemical name	CAS-No.	Concentration (% w/w)
Cellulose	9004-34-6	>= 50 -< 70
Ertugliflozin	1210344-83-4	>= 5 -< 10
Titanium dioxide	13463-67-7	>= 0,1 -< 1

SECTION 4. FIRST AID MEASURES

General advice : In the case of accident or if you feel unwell, seek medical advice immediately.
When symptoms persist or in all cases of doubt seek medical advice.

If inhaled : If inhaled, remove to fresh air.
Get medical attention if symptoms occur.

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

In case of eye contact : In case of contact, immediately flush eyes with plenty of water for at least 15 minutes.
If easy to do, remove contact lens, if worn.
Get medical attention immediately.

If swallowed : If swallowed, DO NOT induce vomiting.
Get medical attention if symptoms occur.
Rinse mouth thoroughly with water.

Most important symptoms and effects, both acute and delayed : Causes serious eye damage.
Contact with dust can cause mechanical irritation or drying of the skin.

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

Notes to physician : Treat symptomatically and supportively.

SECTION 5. FIRE-FIGHTING MEASURES

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

Unsuitable extinguishing media : None known.

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

Hazardous combustion products : Carbon oxides
Metal oxides

Specific extinguishing methods	:	Use extinguishing measures that are appropriate to local circumstances and the surrounding environment. Use water spray to cool unopened containers. Remove undamaged containers from fire area if it is safe to do so. Evacuate area.
Special protective equipment for fire-fighters	:	In the event of fire, wear self-contained breathing apparatus. Use personal protective equipment.

SECTION 6. ACCIDENTAL RELEASE MEASURES

Personal precautions, protective equipment and emergency procedures	:	Use personal protective equipment. Follow safe handling advice (see section 7) and personal protective equipment recommendations (see section 8).
Environmental precautions	:	Avoid release to the environment. Prevent further leakage or spillage if safe to do so. Retain and dispose of contaminated wash water. Local authorities should be advised if significant spillages cannot be contained.
Methods and materials for containment and cleaning up	:	Sweep up or vacuum up spillage and collect in suitable container for disposal. Avoid dispersal of dust in the air (i.e., clearing dust surfaces with compressed air). Dust deposits should not be allowed to accumulate on surfaces, as these may form an explosive mixture if they are released into the atmosphere in sufficient concentration. Local or national regulations may apply to releases and disposal of this material, as well as those materials and items employed in the cleanup of releases. You will need to determine which regulations are applicable. Sections 13 and 15 of this SDS provide information regarding certain local or national requirements.

SECTION 7. HANDLING AND STORAGE

Technical measures	:	Static electricity may accumulate and ignite suspended dust causing an explosion. Provide adequate precautions, such as electrical grounding and bonding, or inert atmospheres.
Local/Total ventilation	:	Use only with adequate ventilation.
Advice on safe handling	:	Do not breathe dust. Do not swallow. Do not get in eyes. Avoid prolonged or repeated contact with skin. Handle in accordance with good industrial hygiene and safety practice, based on the results of the workplace exposure assessment Keep container tightly closed. Minimize dust generation and accumulation. Keep container closed when not in use. Keep away from heat and sources of ignition. Take precautionary measures against static discharges.

Take care to prevent spills, waste and minimize release to the environment.

Conditions for safe storage : Keep in properly labeled containers.
Keep tightly closed.
Store in accordance with the particular national regulations.

Materials to avoid : Do not store with the following product types:
Strong oxidizing agents

SECTION 8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Ingredients with workplace control parameters

Components	CAS-No.	Value type (Form of exposure)	Control parame-ters / Permissible concentration	Basis
Cellulose	9004-34-6	CMP	10 mg/m³	AR OEL
		TWA	10 mg/m³	ACGIH
Ertugliflozin	1210344-83-4	TWA	10 µg/m3 (OEB 3)	Internal
		Wipe limit	100 µg/100 cm²	Internal
Titanium dioxide	13463-67-7	CMP	10 mg/m³	AR OEL
	Further information: A4 - Not classifiable as a human carcinogen			
		TWA (Respirable particulate matter)	2,5 mg/m³ (Titanium dioxide)	ACGIH

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

Titanium dioxide

Engineering measures : All engineering controls should be implemented by facility design and operated in accordance with GMP principles to protect products, workers, and the environment.
Containment technologies suitable for controlling compounds are required to control at source and to prevent migration of the compound to uncontrolled areas (e.g., open-face containment devices).
Minimize open handling.

Personal protective equipment

Respiratory protection : If adequate local exhaust ventilation is not available or exposure assessment demonstrates exposures outside the recommended guidelines, use respiratory protection.

Filter type : Particulates type

Hand protection

Material : Chemical-resistant gloves

Remarks : Consider double gloving.

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

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

SECTION 9. PHYSICAL AND CHEMICAL PROPERTIES

Appearance	:	powder
Color	:	No data available
Odor	:	No data available
Odor Threshold	:	No data available
pH	:	No data available
Melting point/freezing point	:	No data available
Initial boiling point and boiling range	:	No data available
Flash point	:	Not applicable
Evaporation rate	:	Not applicable
Flammability (solid, gas)	:	May form explosive dust-air mixture during processing, handling or other means.
Flammability (liquids)	:	No data available
Upper explosion limit / Upper flammability limit	:	No data available
Lower explosion limit / Lower flammability limit	:	No data available
Vapor pressure	:	Not applicable
Relative vapor density	:	Not applicable

Relative density	:	No data available
Density	:	No data available
Solubility(ies)		
Water solubility	:	No data available
Partition coefficient: n-octanol/water	:	Not applicable
Autoignition temperature	:	No data available
Decomposition temperature	:	No data available
Viscosity		
Viscosity, kinematic	:	Not applicable
Explosive properties	:	Not explosive
Oxidizing properties	:	The substance or mixture is not classified as oxidizing.
Particle size	:	No data available

SECTION 10. STABILITY AND REACTIVITY

Reactivity	:	Not classified as a reactivity hazard.
Chemical stability	:	Stable under normal conditions.
Possibility of hazardous reactions	:	May form explosive dust-air mixture during processing, handling or other means. Can react with strong oxidizing agents.
Conditions to avoid	:	Heat, flames and sparks. Avoid dust formation.
Incompatible materials	:	Oxidizing agents
Hazardous decomposition products	:	No hazardous decomposition products are known.

SECTION 11. TOXICOLOGICAL INFORMATION

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

Acute toxicity

Not classified based on available information.

Product:

Acute oral toxicity : Acute toxicity estimate: > 5.000 mg/kg
Method: Calculation method

Components:

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

Ertugliflozin:

Acute oral toxicity	:	LD50 (Rat): 500 mg/kg
Acute inhalation toxicity	:	Remarks: No data available
Acute dermal toxicity	:	Remarks: No data available

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.

Product:

Assessment	:	No skin irritation
Method	:	EpiDerm
Result	:	Not corrosive

Components:

Ertugliflozin:

Result	:	Corrosive

Titanium dioxide:

Species	:	Rabbit
Result	:	No skin irritation

Serious eye damage/eye irritation

Causes serious eye damage.

Components:

Ertugliflozin:

Result	:	Severe irritation

Titanium dioxide:

Species	:	Rabbit

Result : No eye irritation

Respiratory or skin sensitization

Skin sensitization

Not classified based on available information.

Respiratory sensitization

Not classified based on available information.

Components:

Ertugliflozin:

Test Type : Local lymph node assay (LLNA)
Result : Not a skin sensitizer.

Titanium dioxide:

Test Type : Local lymph node assay (LLNA)
Routes of exposure : Skin contact
Species : Mouse
Result : negative

Germ cell mutagenicity

Not classified based on available information.

Components:

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

Ertugliflozin:

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

Test Type: Chromosome aberration test in vitro
Result: negative

Genotoxicity in vivo : Test Type: Mammalian erythrocyte micronucleus test (in vivo cytogenetic assay)
Species: Rat
Result: negative

Titanium dioxide:

Genotoxicity in vitro	:	Test Type: Bacterial reverse mutation assay (AMES) Result: negative
Genotoxicity in vivo	:	Test Type: In vivo micronucleus test Species: Mouse Result: negative

Carcinogenicity

Not classified based on available information.

Components:

Cellulose:

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

Ertugliflozin:

Species	:	Mouse
Application Route	:	Oral
Exposure time	:	2 Years
Result	:	negative

Species	:	Rat
Application Route	:	Oral
Exposure time	:	2 Years
Result	:	negative
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. 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:

Cellulose:

Effects on fertility	:	Test Type: One-generation reproduction toxicity study

Species: Rat
Application Route: Ingestion
Result: negative

Effects on fetal development : Test Type: Fertility/early embryonic development
Species: Rat
Application Route: Ingestion
Result: negative

Ertugliflozin:

Effects on fertility : Test Type: Fertility/early embryonic development
Species: Rat
Application Route: Oral
Fertility: NOAEL: 250 mg/kg body weight
Remarks: Maternal toxicity observed.
No significant adverse effects were reported

Test Type: Fertility/early embryonic development
Species: Rabbit
Application Route: Oral
Fertility: NOAEL: 200 mg/kg body weight
Remarks: No significant adverse effects were reported

Effects on fetal development : Test Type: Embryo-fetal development
Species: Rat
Application Route: Oral
Developmental Toxicity: NOAEL: 50 mg/kg body weight
Remarks: Adverse developmental effects were observed

Test Type: Embryo-fetal development
Species: Rabbit
Application Route: Oral
Developmental Toxicity: NOAEL: 250 mg/kg body weight
Remarks: No significant adverse effects were reported

STOT-single exposure

Not classified based on available information.

STOT-repeated exposure

Not classified based on available information.

Components:

Ertugliflozin:

Routes of exposure : Oral
Target Organs : Kidney, Stomach, Prostate
Assessment : May cause damage to organs through prolonged or repeated exposure.

Repeated dose toxicity

Components:

Cellulose:

Species	:	Rat
NOAEL	:	>= 9.000 mg/kg
Application Route	:	Ingestion
Exposure time	:	90 Days

Ertugliflozin:

Species	:	Rat
LOAEL	:	500 mg/kg
Application Route	:	Oral
Exposure time	:	30 d

Species	:	Rat
LOAEL	:	250 mg/kg
Application Route	:	Oral
Exposure time	:	30 d
Target Organs	:	Kidney

Species	:	Rat
LOAEL	:	25 mg/kg
Application Route	:	Oral
Exposure time	:	180 d
Target Organs	:	Kidney, Bone, Stomach

Species	:	Rat
LOAEL	:	25 mg/kg
Exposure time	:	90 d
Target Organs	:	Kidney, Gastrointestinal tract, Prostate

Species	:	Dog
NOAEL	:	150 mg/kg
Application Route	:	Oral
Exposure time	:	270 d
Remarks	:	No significant adverse effects were reported

Species	:	Mouse
NOAEL	:	100 mg/kg
Application Route	:	Oral
Exposure time	:	90 d
Remarks	:	No significant adverse effects were reported

Species	:	Mouse
NOAEL	:	100 mg/kg
Application Route	:	Oral
Exposure time	:	28 d
Target Organs	:	Bone
Remarks	:	No significant adverse effects were reported

Titanium dioxide:

Species	:	Rat
NOAEL	:	24.000 mg/kg
Application Route	:	Ingestion
Exposure time	:	28 Days

Species	:	Rat

NOAEL : 10 mg/m³
Application Route : inhalation (dust/mist/fume)
Exposure time : 2 y

Aspiration toxicity

Not classified based on available information.

Experience with human exposure

Components:

Ertugliflozin:

Ingestion : Symptoms: The most common side effects are:, Headache, constipation, Diarrhea, Nausea, urinary tract infection, muscle pain, upper respiratory tract infection

SECTION 12. ECOLOGICAL INFORMATION

Ecotoxicity

Components:

Cellulose:

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

Ertugliflozin:

Toxicity to algae/aquatic plants : EC50 (Pseudokirchneriella subcapitata (green algae)): 77 mg/l
Exposure time: 72 h
Method: OECD Test Guideline 201

NOEC (Pseudokirchneriella subcapitata (green algae)): 50 mg/l
Exposure time: 72 h
Method: OECD Test Guideline 201

Toxicity to fish (Chronic toxicity) : NOEC (Pimephales promelas (fathead minnow)): 1 mg/l
Exposure time: 32 d
Method: OECD Test Guideline 210
Remarks: No toxicity at the limit of solubility.

Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity) : NOEC (Daphnia magna (Water flea)): 2,14 mg/l
Exposure time: 21 d
Method: OECD Test Guideline 211
Remarks: No toxicity at the limit of solubility.

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

NOEC: 1.000 mg/l
Exposure time: 3 h

Test Type: Respiration inhibition
Method: OECD Test Guideline 209

Titanium dioxide:

Toxicity to fish : LC50 (Oncorhynchus mykiss (rainbow trout)): > 100 mg/l
Exposure time: 96 h
Method: OECD Test Guideline 203

Toxicity to daphnia and other aquatic invertebrates : EC50 (Daphnia magna (Water flea)): > 100 mg/l
Exposure time: 48 h

Toxicity to algae/aquatic plants : EC50 (Skeletonema costatum (marine diatom)): > 10.000 mg/l
Exposure time: 72 h

Toxicity to microorganisms : EC50: > 1.000 mg/l
Exposure time: 3 h
Method: OECD Test Guideline 209

Persistence and degradability

Components:

Cellulose:

Biodegradability : Result: Readily biodegradable.

Ertugliflozin:

Biodegradability : Result: Not readily biodegradable.
Biodegradation: 40,8 %
Exposure time: 28 d

Bioaccumulative potential

Components:

Ertugliflozin:

Partition coefficient: n-octanol/water : log Pow: 2,47

Mobility in soil

Components:

Ertugliflozin:

Distribution among environmental compartments : log Koc: 2,88

Other adverse effects

No data available

SECTION 13. DISPOSAL CONSIDERATIONS

Disposal methods

Waste from residues : Do not dispose of waste into sewer.

Contaminated packaging	:	Dispose of in accordance with local regulations. Empty containers should be taken to an approved waste handling site for recycling or disposal. If not otherwise specified: Dispose of as unused product.

SECTION 14. TRANSPORT INFORMATION

International Regulations

UNRTDG
Not regulated as a dangerous good

IATA-DGR
Not regulated as a dangerous good

IMDG-Code
Not regulated as a dangerous good

Transport in bulk according to Annex II of MARPOL 73/78 and the IBC Code
Not applicable for product as supplied.

Special precautions for user
Not applicable

SECTION 15. REGULATORY INFORMATION

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

Argentina. Carcinogenic Substances and Agents Registry.	:	Not applicable
Control of precursors and essential chemicals for the preparation of drugs.	:	Not applicable

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

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

SECTION 16. OTHER INFORMATION

Revision Date	:	30.09.2023
Date format	:	dd.mm.yyyy

Further information

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

Full text of other abbreviations

ACGIH	:	USA. ACGIH Threshold Limit Values (TLV)
AR OEL	:	Argentina. Occupational Exposure Limits
ACGIH / TWA	:	8-hour, time-weighted average
AR OEL / CMP	:	TLV (Threshold Limit Value)

AIIC - 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 Concentration to 50 % of a test population; LD50 - Lethal Dose to 50% of a test population (Median Lethal Dose); MARPOL - International Convention for the Prevention of Pollution from Ships; n.o.s. - Not Otherwise Specified; Nch - Chilean Norm; NO(A)EC - No Observed (Adverse) Effect Concentration; NO(A)EL - No Observed (Adverse) Effect Level; NOELR - No Observable Effect Loading Rate; NOM - Official Mexican Norm; NTP - National Toxicology Program; NZIoC - New Zealand Inventory of Chemicals; OECD - Organization for Economic Co-operation and Development; OPPTS - Office of Chemical Safety and Pollution Prevention; PBT - Persistent, Bioaccumulative and Toxic substance; PICCS - Philippines Inventory of Chemicals and Chemical Substances; (Q)SAR - (Quantitative) Structure Activity Relationship; REACH - Regulation (EC) No 1907/2006 of the European Parliament and of the Council concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals; SADT - Self-Accelerating Decomposition Temperature; SDS - Safety Data Sheet; TCSI - Taiwan Chemical Substance Inventory; TDG - Transportation of Dangerous Goods; 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.

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