

Belzutifan Formulation

Version 3.2 Revision Date: 30.09.2023 SDS Number: 5276386-00011 Date of last issue: 27.04.2023
Date of first issue: 14.11.2019

SECTION 1. PRODUCT AND COMPANY IDENTIFICATION

Product name : Belzutifan Formulation

Manufacturer or supplier's details

Company name of supplier : MSD
Address : Avenida 16 de Septiembre No. 301
Xaltocan - Xochimilco Mexico 16090
Telephone : +52 55 57284444
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**

Reproductive toxicity : Category 2
Specific target organ toxicity : Category 2 (Blood, epididymis, Testis)
- repeated exposure (Oral)

GHS label elements

Hazard pictograms :



Signal Word : Warning

Hazard Statements : H361fd Suspected of damaging fertility. Suspected of damaging the unborn child.
H373 May cause damage to organs (Blood, epididymis, Testis) through prolonged or repeated exposure if swallowed.

Precautionary Statements : **Prevention:**
P201 Obtain special instructions before use.
P202 Do not handle until all safety precautions have been read and understood.
P260 Do not breathe dust.
P280 Wear protective gloves/ protective clothing/ eye protection/ face protection.
Response:
P308 + P313 IF exposed or concerned: Get medical advice/ attention.
Storage:
P405 Store locked up.

Belzutifan Formulation

Version 3.2 Revision Date: 30.09.2023 SDS Number: 5276386-00011 Date of last issue: 27.04.2023
 Date of first issue: 14.11.2019

Disposal:

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

Other hazards

Dust contact with the eyes can lead to mechanical irritation.
 Contact with dust can cause mechanical irritation or drying of the skin.
 May form combustible dust concentrations in air 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	>= 30 -< 50
Belzutifan	1672668-24-4	>= 5 -< 10

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.

In case of skin contact : In case of contact, immediately flush skin with soap and plenty of water.
 Remove contaminated clothing and shoes.
 Get medical attention.
 Wash clothing before reuse.
 Thoroughly clean shoes before reuse.

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.
 Get medical attention.
 Rinse mouth thoroughly with water.

Most important symptoms and effects, both acute and delayed : Suspected of damaging fertility. Suspected of damaging the unborn child.
 May cause damage to organs through prolonged or repeated exposure if swallowed.
 Contact with dust can cause mechanical irritation or drying of the skin.
 Dust contact with the eyes can lead to mechanical irritation.

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

Notes to physician : Treat symptomatically and supportively.

SECTION 5. FIRE-FIGHTING MEASURES

Suitable extinguishing media : Water spray

Belzutifan Formulation

Version	Revision Date:	SDS Number:	Date of last issue: 27.04.2023
3.2	30.09.2023	5276386-00011	Date of first issue: 14.11.2019

		Alcohol-resistant foam Carbon dioxide (CO ₂) 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.
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Belzutifan Formulation

Version 3.2 Revision Date: 30.09.2023 SDS Number: 5276386-00011 Date of last issue: 27.04.2023
 Date of first issue: 14.11.2019

- Local/Total ventilation : Use only with adequate ventilation.
- Advice on safe handling : Do not breathe dust.
 Do not swallow.
 Avoid contact with eyes.
 Avoid prolonged or repeated contact with skin.
 Handle in accordance with good industrial hygiene and safety practice, based on the results of the workplace exposure assessment
 Minimize dust generation and accumulation.
 Keep container closed when not in use.
 Keep away from heat and sources of ignition.
 Take precautionary measures against static discharges.
 Take care to prevent spills, waste and minimize release to the environment.
- Hygiene measures : If exposure to chemical is likely during typical use, provide eye flushing systems and safety showers close to the working place.
 When using do not eat, drink or smoke.
 Wash contaminated clothing before re-use.
 The effective operation of a facility should include review of engineering controls, proper personal protective equipment, appropriate degowning and decontamination procedures, industrial hygiene monitoring, medical surveillance and the use of administrative controls.
- Conditions for safe storage : Keep in properly labeled containers.
 Store locked up.
 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 parameters / Permissible concentration	Basis
Cellulose	9004-34-6	VLE-PPT	10 mg/m ³	NOM-010-STPS-2014
		TWA	10 mg/m ³	ACGIH
Belzutifan	1672668-24-4	TWA	70 µg/m ³ (OEB 3)	Internal
		Wipe limit	70 µg/100 cm ²	Internal

- 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.

Belzutifan Formulation

Version	Revision Date:	SDS Number:	Date of last issue: 27.04.2023
3.2	30.09.2023	5276386-00011	Date of first issue: 14.11.2019

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.

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 combustible dust concentrations in air during processing, handling or other means.
Flammability (liquids)	:	Not applicable
Burning number	:	5
Upper explosion limit / Upper flammability limit	:	No data available
Lower explosion limit / Lower	:	No data available

Belzutifan Formulation

Version	Revision Date:	SDS Number:	Date of last issue: 27.04.2023
3.2	30.09.2023	5276386-00011	Date of first issue: 14.11.2019

flammability limit

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.

Molecular weight : No data available

Minimum ignition energy : 3 - 10 mJ
Method: With inductance
10 - 30 mJ
Method: Without inductance

Particle size : 26.13 µm

SECTION 10. STABILITY AND REACTIVITY

Reactivity : Not classified as a reactivity hazard.

Chemical stability : Stable under normal conditions.

Possibility of hazardous reactions : May form combustible dust concentrations in air 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.

Belzutifan Formulation

Version 3.2 Revision Date: 30.09.2023 SDS Number: 5276386-00011 Date of last issue: 27.04.2023
Date of first issue: 14.11.2019

SECTION 11. TOXICOLOGICAL INFORMATION**Information on likely routes of exposure**

Inhalation
Skin contact
Ingestion
Eye contact

Acute toxicity

Not classified based on available information.

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

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Acute oral toxicity : LD0 (Rat): 200 mg/kg
LD0 (Dog): 30 mg/kg

Skin corrosion/irritation

Not classified based on available information.

Components:**Belzutifan:**

Species : human skin
Method : EpiDerm
Result : No skin irritation
Remarks : Not classified due to lack of data.

Serious eye damage/eye irritation

Not classified based on available information.

Components:**Belzutifan:**

Result : No eye irritation
Method : Bovine cornea (BCOP)
Remarks : Not classified due to lack of data.

Respiratory or skin sensitization**Skin sensitization**

Not classified based on available information.

Belzutifan Formulation

Version 3.2 Revision Date: 30.09.2023 SDS Number: 5276386-00011 Date of last issue: 27.04.2023
Date of first issue: 14.11.2019

Respiratory sensitization

Not classified based on available information.

Components:**Belzutifan:**

Test Type : Local lymph node assay (LLNA)
Routes of exposure : Dermal
Species : Mouse
Result : Not a skin sensitizer.
Remarks : Not classified due to lack of data.

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

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Genotoxicity in vitro : Test Type: Ames test
Result: negative

Test Type: Micronucleus test
Test system: mammalian cells
Result: negative

Genotoxicity in vivo : Remarks: Not classified due to lack of data.

Carcinogenicity

Not classified based on available information.

Components:**Cellulose:**

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

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Remarks : Not classified due to lack of data.

Belzutifan Formulation

Version 3.2 Revision Date: 30.09.2023 SDS Number: 5276386-00011 Date of last issue: 27.04.2023
Date of first issue: 14.11.2019

Reproductive toxicity

Suspected of damaging fertility. Suspected of damaging the unborn child.

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

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Effects on fertility : Remarks: Information taken from reference works and the literature.

Effects on fetal development : Remarks: Information taken from reference works and the literature.

Reproductive toxicity - Assessment : Suspected of damaging fertility. Suspected of damaging the unborn child.

STOT-single exposure

Not classified based on available information.

STOT-repeated exposure

May cause damage to organs (Blood, epididymis, Testis) through prolonged or repeated exposure if swallowed.

Components:**Belzutifan:**

Routes of exposure : Ingestion
Target Organs : Blood, epididymis, Testis
Assessment : Shown to produce significant health effects in animals at concentrations of >10 to 100 mg/kg bw.

Routes of exposure : Oral
Target Organs : Blood, epididymis, Testis
Assessment : May cause damage to organs through prolonged or repeated exposure.

Repeated dose toxicity**Components:****Cellulose:**

Species : Rat

Belzutifan Formulation

Version 3.2 Revision Date: 30.09.2023 SDS Number: 5276386-00011 Date of last issue: 27.04.2023
 Date of first issue: 14.11.2019

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

Belzutifan:

Species : Rat
 LOAEL : 6 mg/kg
 Application Route : Oral
 Exposure time : 28 d
 Target Organs : Blood, Testis, epididymis

Species : Rat, male
 NOAEL : 2 mg/kg
 LOAEL : 6 mg/kg
 Application Route : Oral
 Exposure time : 13 Weeks
 Target Organs : Blood, Central nervous system, epididymis, Liver, Testis

Species : Rat, female
 LOAEL : 200 mg/kg
 Application Route : Oral
 Exposure time : 13 Weeks
 Target Organs : Blood, Central nervous system, Liver

Species : Dog
 LOAEL : 1 mg/kg
 Application Route : Oral
 Exposure time : 28 d
 Target Organs : Blood

Species : Dog
 LOAEL : 1 mg/kg
 Application Route : Oral
 Exposure time : 13 Weeks
 Target Organs : Blood

Aspiration toxicity

Not classified based on available information.

Components:**Belzutifan:**

Not applicable

Experience with human exposure**Components:****Belzutifan:**

General Information : Symptoms: Fatigue, flu-like symptoms, fluid retention, Head-ache, musculoskeletal pain, Nausea
 Ingestion : Target Organs: Blood
 Symptoms: anemia, Changes in the blood count

Belzutifan Formulation

Version 3.2 Revision Date: 30.09.2023 SDS Number: 5276386-00011 Date of last issue: 27.04.2023
Date of first issue: 14.11.2019

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

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Toxicity to algae/aquatic plants : EC50 (*Raphidocelis subcapitata* (freshwater green alga)): > 10 mg/l
End point: Growth rate
Exposure time: 72 h
Method: OECD Test Guideline 201

EC10 (*Raphidocelis subcapitata* (freshwater green alga)): > 10 mg/l
End point: Growth rate
Exposure time: 72 h
Method: OECD Test Guideline 201

Toxicity to fish (Chronic toxicity) : NOEC (*Pimephales promelas* (fathead minnow)): 0.52 mg/l
Exposure time: 32 d
Method: OECD Test Guideline 210

Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity) : EC10 (*Daphnia magna* (Water flea)): 3.9 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 of activated sludge
Method: OECD Test Guideline 209

NOEC: 1,000 mg/l
Exposure time: 3 h
Test Type: Respiration inhibition of activated sludge
Method: OECD Test Guideline 209

Persistence and degradability**Components:****Cellulose:**

Biodegradability : Result: Readily biodegradable.

Belzutifan:

Biodegradability : Result: Not readily biodegradable.
Biodegradation: 50 %

Belzutifan Formulation

Version	Revision Date:	SDS Number:	Date of last issue: 27.04.2023
3.2	30.09.2023	5276386-00011	Date of first issue: 14.11.2019

Exposure time: 18.1 d
Method: OECD Test Guideline 314

Bioaccumulative potential

Components:

Belzutifan:

Partition coefficient: n-octanol/water : log Pow: 1.11
pH: 7

Mobility in soil

Components:

Belzutifan:

Distribution among environmental compartments : log Koc: 2.52
Method: OECD Test Guideline 106

Other adverse effects

No data available

SECTION 13. DISPOSAL CONSIDERATIONS

Disposal methods

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

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

SECTION 14. TRANSPORT INFORMATION

International Regulations

UNRTDG

Not regulated as a dangerous good

IATA-DGR

Not regulated as a dangerous good

IMDG-Code

Not regulated as a dangerous good

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

Not applicable for product as supplied.

Domestic regulation

NOM-002-SCT

Not regulated as a dangerous good

Special precautions for user

Not applicable

Belzutifan Formulation

Version	Revision Date:	SDS Number:	Date of last issue: 27.04.2023
3.2	30.09.2023	5276386-00011	Date of first issue: 14.11.2019

SECTION 15. REGULATORY INFORMATION**Safety, health and environmental regulations/legislation specific for the substance or mixture**

Federal Law for the control of chemical precursors, essential chemical products and machinery for producing capsules, tablets and pills. : Not applicable

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

CEPA : not determined

AICS : not determined

IECSC : not determined

SECTION 16. OTHER INFORMATION

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

Full text of other abbreviations

ACGIH : USA. ACGIH Threshold Limit Values (TLV)
NOM-010-STPS-2014 : Mexico. Norm NOM-010-STPS-2014 on Chemicals Polluting the Work Environment - Identification, Assessment and Control - Appendix 1 Occupational Exposure Limits
ACGIH / TWA : 8-hour, time-weighted average
NOM-010-STPS-2014 / VLE- : Time weighted average limit value
PPT

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

SAFETY DATA SHEET



Belzutifan Formulation

Version	Revision Date:	SDS Number:	Date of last issue: 27.04.2023
3.2	30.09.2023	5276386-00011	Date of first issue: 14.11.2019

es; (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

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/>

The information is considered as correct, but not exhaustive, and will be used only as a guide, which is based in the current knowledge of the substance or mixture, and is applicable to proper safety precautions for the product.

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