according to the Globally Harmonized System



# **Belzutifan Formulation**

 Version
 Revision Date:
 SDS Number:
 Date of last issue: 27.04.2023

 4.2
 30.09.2023
 5276384-00011
 Date of first issue: 14.11.2019

#### 1. PRODUCT AND COMPANY IDENTIFICATION

Product name : Belzutifan Formulation

Manufacturer or supplier's details

Company : MSD

Address : Briahnager - Off Pune Nagar Road

Wagholi - Pune - India 412 207

Telephone : +1-908-740-4000

Emergency telephone number : +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

### 2. HAZARDS IDENTIFICATION

### Manufacture, Storage and Import of Hazardous Chemicals Rules 1989

#### Classification

Not classified as hazardous according to criteria laid down in Part I of Schedule-1.

**GHS Classification** 

Reproductive toxicity : Category 2

Long-term (chronic) aquatic

hazard

Category 3

**GHS** label elements

Hazard pictograms :

Signal word : Warning

Hazard statements : H361fd Suspected of damaging fertility. Suspected of damag-

ing the unborn child.

H412 Harmful to aquatic life with long lasting effects.

Precautionary statements : **Prevention:** 

P203 Obtain, read and follow all safety instructions before use.

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P273 Avoid release to the environment.

P280 Wear protective gloves/ protective clothing/ eye protec-

tion/ face protection.

Response:

P318 IF exposed or concerned, get medical advice.

Storage:

P405 Store locked up.

Disposal:

P501 Dispose of contents/ container to an approved waste

disposal plant.

#### Other hazards which do not result in classification

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.

### 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

#### 4. FIRST AID MEASURES

General advice In the case of accident or if you feel unwell, seek medical ad-

vice 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 eves, 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.

Contact with dust can cause mechanical irritation or drying of

Dust contact with the eyes can lead to mechanical irritation.

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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.

5. FIREFIGHTING 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 prod-

ucts

Carbon oxides

Metal oxides

Specific extinguishing meth-

ods

Use extinguishing measures that are appropriate to local cir-

cumstances 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.

#### 6. ACCIDENTAL RELEASE MEASURES

Personal precautions, protec: :

tive equipment and emer-

gency procedures

Use personal protective equipment.

Follow safe handling advice (see section 7) and personal pro-

tective 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 con-

tainer 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 deter-

mine which regulations are applicable.

Sections 13 and 15 of this SDS provide information regarding

certain local or national requirements.

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#### 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 Advice on safe handling Use only with adequate ventilation.

Do not breathe dust. Do not swallow.

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 as-

sessment

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 labelled 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

#### 8. EXPOSURE CONTROLS/PERSONAL PROTECTION

### Components with workplace control parameters

Components	CAS-No.	Value type (Form of exposure)	Control parameters / Permissible concentration	Basis
Cellulose	9004-34-6	TWA	10 mg/m3	ACGIH
Belzutifan	1672668-24- 4	TWA	70 μg/m3 (OEB 3)	Internal
		Wipe limit	70 μg/100 cm2	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 contain-

ment devices).

Minimize open handling.

Personal protective equipment

Respiratory protection : If adequate local exhaust ventilation is not available or expo-

sure assessment demonstrates exposures outside the rec-

ommended guidelines, use respiratory protection.

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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.

#### 9. 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 combustible dust concentrations in air during pro-

cessing, handling or other means.

Flammability (liquids) : Not applicable

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Burning number : 5

Upper explosion limit / Upper

flammability limit

No data available

Lower explosion limit / Lower :

flammability limit

No data available

Vapour pressure : Not applicable

Relative vapour density : Not applicable

Relative density : No data available

Density : No data available

Solubility(ies)

Water solubility : No data available

Partition coefficient: n-

octanol/water

Not applicable

Auto-ignition temperature : No

: 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

### 10. STABILITY AND REACTIVITY

Reactivity : Not classified as a reactivity hazard. Chemical stability : Stable under normal conditions.

Possibility of hazardous reac-

tions

May form combustible dust concentrations in air during pro-

cessing, handling or other means. Can react with strong oxidizing agents.

Conditions to avoid : Heat, flames and sparks.

Avoid dust formation.

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Incompatible materials Oxidizing agents

Hazardous decomposition

products

No hazardous decomposition products are known.

#### 11. TOXICOLOGICAL INFORMATION

Information on likely routes of: Inhalation

Skin contact exposure

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

Belzutifan:

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** 

No skin irritation Result

Remarks Not classified due to lack of data.

### Serious eye damage/eye irritation

Not classified based on available information.

**Components:** 

Belzutifan:

Method Bovine cornea (BCOP)

Result No eye irritation

Remarks Not classified due to lack of data.

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### Respiratory or skin sensitisation

#### Skin sensitisation

Not classified based on available information.

### Respiratory sensitisation

Not classified based on available information.

### **Components:**

#### Belzutifan:

Test Type : Local lymph node assay (LLNA)

Exposure routes : 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

Belzutifan:

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

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Result : negative

Belzutifan:

Remarks : Not classified due to lack of data.

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 foetal develop-

ment

Test Type: Fertility/early embryonic development

Species: Rat

Application Route: Ingestion

Result: negative

Belzutifan:

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

literature.

Effects on foetal develop-

ment

Remarks: Information taken from reference works and the

literature.

Reproductive toxicity - As-

sessment

Suspected of damaging fertility. Suspected of damaging the

unborn child.

STOT - single exposure

Not classified based on available information.

STOT - repeated exposure

Not classified based on available information.

**Components:** 

Belzutifan:

Exposure routes : Ingestion

Target Organs : Blood, epididymis, Testis

Assessment : Shown to produce significant health effects in animals at con-

centrations of >10 to 100 mg/kg bw.

Exposure routes : Oral

Target Organs : Blood, epididymis, Testis

Assessment : May cause damage to organs through prolonged or repeated

exposure.

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### Repeated dose toxicity

### **Components:**

#### Cellulose:

Species : Rat

 $\dot{NOAEL}$  : >= 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

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## 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

#### 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

Belzutifan:

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 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

Toxicity to fish (Chronic tox-

icity)

NOEC: 0.52 mg/l Exposure time: 32 d

Species: Pimephales promelas (fathead minnow)

Method: OECD Test Guideline 210

Toxicity to daphnia and other : aquatic invertebrates (Chron-

ic toxicity)

EC10: 3.9 mg/l Exposure time: 21 d

Species: Daphnia magna (Water flea) Method: OECD Test Guideline 211

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### Persistence and degradability

**Components:** 

Cellulose:

Biodegradability : Result: Readily biodegradable.

Belzutifan:

Biodegradability : Result: Not readily biodegradable.

Biodegradation: 50 % Exposure time: 18.1 d

Method: OECD Test Guideline 314

**Bioaccumulative potential** 

**Components:** 

Belzutifan:

Partition coefficient: n- : log Pow: 1.11

octanol/water pH: 7

Mobility in soil

**Components:** 

Belzutifan:

Distribution among environ- : log Koc: 2.52

mental compartments Method: OECD Test Guideline 106

Other adverse effects

No data available

#### 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 han-

dling site for recycling or disposal.

If not otherwise specified: Dispose of as unused product.

### 14. TRANSPORT INFORMATION

### **International Regulations**

**UNRTDG** 

Not regulated as a dangerous good

**IATA-DGR** 

Not regulated as a dangerous good

**IMDG-Code** 

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Not regulated as a dangerous good

Transport in bulk according to IMO instruments

Not applicable for product as supplied.

Special precautions for user

Not applicable

### 15. REGULATORY INFORMATION

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

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

CEPA : not determined

AICS : not determined

IECSC : not determined

#### 16. OTHER INFORMATION

Revision Date : 30.09.2023

**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 Agen-

cy, http://echa.europa.eu/

Date format : dd.mm.yyyy

Full text of other abbreviations

ACGIH : USA. ACGIH Threshold Limit Values (TLV)

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

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

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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.

IN / EN