SAFETY DATA SHEET
Posaconazole Injection Formulation

SECTION 1. PRODUCT AND COMPANY IDENTIFICATION

Product name : Posaconazole Injection Formulation

Manufacturer or supplier's details
Company : MSD
Address : Avenida Tanner de Melo, Quadra 10 Lote 4A, Galpão A Parque Industrial Vice Presidente José Alencar Aparecida de Goias – GO, Brazil
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

SECTION 2. HAZARDS IDENTIFICATION

GHS Classification in accordance with ABNT NBR 14725 Standard
Skin sensitization : Category 1
Specific target organ toxicity - repeated exposure (Oral) : Category 2 (Adrenal gland, Bone marrow, Kidney, Liver, Nervous system, Reproductive organs)
Short-term (acute) aquatic hazard : Category 3
Long-term (chronic) aquatic hazard : Category 3

GHS label elements in accordance with ABNT NBR 14725 Standard
Hazard pictograms :

Signal Word : Warning
Hazard Statements : H317 May cause an allergic skin reaction. H373 May cause damage to organs (Adrenal gland, Bone marrow, Kidney, Liver, Nervous system, Reproductive organs) through prolonged or repeated exposure if swallowed. H412 Harmful to aquatic life with long lasting effects.

Precautionary Statements : Prevention:
P272 Contaminated work clothing should not be allowed out of
the workplace.
P273 Avoid release to the environment.
P280 Wear protective gloves.

Response:
P314 Get medical advice/attention if you feel unwell.
P333 + P313 If skin irritation or rash occurs: Get medical advice/attention.
P362 + P364 Take off contaminated clothing and wash it before reuse.

Other hazards which do not result in classification
None known.

SECTION 3. COMPOSITION/INFORMATION ON INGREDIENTS

Substance / Mixture : Mixture

Components

<table>
<thead>
<tr>
<th>Chemical name</th>
<th>CAS-No.</th>
<th>Classification</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td>beta.-Cyclodextrin, sulfobutyl ethers, sodium salts</td>
<td>182410-00-0</td>
<td>Skin sensitization, Category 1</td>
<td>&gt;= 30 -&lt; 50</td>
</tr>
<tr>
<td>Posaconazole</td>
<td>171228-49-2</td>
<td>Eye irritation, Category 2B</td>
<td>&gt;= 1 -&lt; 2,5</td>
</tr>
</tbody>
</table>

|                                                                 |                                                                 |                                                                 |                                                                 |
| Specific target organ toxicity - repeated exposure (Oral) (Adrenal gland, Bone marrow, Kidney, Liver, Nervous system, Reproductive organs), Category 1 | Short-term (acute) aquatic hazard, Category 1                                      |
| Long-term (chronic) aquatic hazard, Category 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.

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: Flush eyes with water as a precaution. 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: Diarrhea Fever Headache Nausea Vomiting

May cause an allergic skin reaction.

May cause damage to organs through prolonged or repeated exposure if swallowed.

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: Exposure to combustion products may be a hazard to health.

Hazardous combustion products: Carbon oxides Sulfur 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. Prevent spreading over a wide area (e.g., by containment or oil barriers).
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Section 7. Handling and Storage

Technical measures:
See Engineering measures under EXPOSURE CONTROLS/PERSONAL PROTECTION section.

Local/Total ventilation:
Use only with adequate ventilation.

Advice on safe handling:
Do not get on skin or clothing.
Do not breathe mist or vapors.
Do not swallow.
Avoid contact with eyes.
Wash skin thoroughly after handling.
Handle in accordance with good industrial hygiene and safety practice, based on the results of the workplace exposure assessment.
Do not eat, drink or smoke when using this product.
Take care to prevent spills, waste and minimize release to the environment.

Hygiene measures:
If exposure to chemical is likely during typical use, provide eye flushing systems and safety showers close to the working place.
When using do not eat, drink or smoke.
Contaminated work clothing should not be allowed out of the workplace.
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 in accordance with the particular national regulations.

Materials to avoid:
Do not store with the following product types:
Strong oxidizing agents
Organic peroxides
Explosives
Gases

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:
Soak up with inert absorbent material.
For large spills, provide diking or other appropriate containment to keep material from spreading. If diked material can be pumped, store recovered material in appropriate container.
Clean up remaining materials from spill with suitable absorbent.
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 8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Ingredients with workplace control parameters

<table>
<thead>
<tr>
<th>Components</th>
<th>CAS-No.</th>
<th>Value type (Form of exposure)</th>
<th>Control parameters / Permissible concentration</th>
<th>Basis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Posaconazole</td>
<td>171228-49-2</td>
<td>TWA</td>
<td>300 µg/m3 (OEB 2)</td>
<td>Internal</td>
</tr>
</tbody>
</table>

Engineering measures:
Use appropriate engineering controls and manufacturing technologies to control airborne concentrations (e.g., dripless quick connections).
All engineering controls should be implemented by facility design and operated in accordance with GMP principles to protect products, workers, and the environment.
Laboratory operations do not require special containment.

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:
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.

SECTION 9. PHYSICAL AND CHEMICAL PROPERTIES

Appearance:
Aqueous solution

Color:
Colorless to pale yellow

Odor:
odorless

Odor Threshold:
No data available

pH:
2.6

Melting point/freezing point:
No data available

Initial boiling point and boiling range:
No data available

Flash point:
No data available

Evaporation rate:
No data available
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| Flammability (solid, gas)                     | Not applicable |
| 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                               | No data available |
| Relative vapor density                       | No data available |
| Relative density                              | No data available |
| Density                                       | 1.15 g/cm³ |
| Solubility(ies)                               | No data available |
| Water solubility                              | No data available |
| Partition coefficient: n-octanol/water        | Not applicable |
| Autoignition temperature                      | No data available |
| Decomposition temperature                     | No data available |
| Viscosity                                     | No data available |
| Viscosity, kinematic                          | No data available |
| Explosive properties                          | Not explosive |
| Oxidizing properties                          | The substance or mixture is not classified as oxidizing. |
| Molecular weight                              | No data available |
| Particle size                                 | Not applicable |

SECTION 10. STABILITY AND REACTIVITY

| Reactivity                                    | Not classified as a reactivity hazard. |
| Chemical stability                            | Stable under normal conditions. |
| Possibility of hazardous reactions            | Can react with strong oxidizing agents. |
| Conditions to avoid                           | None known. |
| 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.

**Components:**

**.beta.-Cyclodextrin, sulfobutyl ethers, sodium salts:**
Acute oral toxicity : LD50 (Rat): > 8.800 mg/kg

**Posaconazole:**
Acute oral toxicity : LD50 (Rat): > 5.000 mg/kg
LD50 (Mouse): > 3.000 mg/kg
Acute dermal toxicity : LD50 (Rat): > 2.000 mg/kg

**Skin corrosion/irritation**
Not classified based on available information.

**Components:**

**Posaconazole:**
Species : Rabbit
Result : No skin irritation

**Serious eye damage/eye irritation**
Not classified based on available information.

**Components:**

**Posaconazole:**
Species : Rabbit
Result : Mild eye irritation

**Respiratory or skin sensitization**

**Skin sensitization**
May cause an allergic skin reaction.

**Respiratory sensitization**
Not classified based on available information.

**Components:**

**.beta.-Cyclodextrin, sulfobutyl ethers, sodium salts:**
Assessment : Probability or evidence of skin sensitization in humans

**Posaconazole:**
Test Type : Magnusson-Kligman-Test
Routes of exposure : Skin contact
Species : Guinea pig
Result : negative
Germ cell mutagenicity
Not classified based on available information.

**Components:**

**Posaconazole:**
- Genotoxicity in vitro:
  - Test Type: Bacterial reverse mutation assay (AMES)
    - Result: negative
  - Test Type: Chromosomal aberration
    - Result: negative
- Genotoxicity in vivo:
  - Test Type: Micronucleus test
    - Species: Mouse
    - Cell type: Bone marrow
    - Application Route: Intravenous
    - Result: negative

Carcinogenicity
Not classified based on available information.

**Components:**

**Posaconazole:**
- Species: Rat
- Application Route: oral (feed)
- Exposure time: 2 Years
- Result: positive
- Remarks: The mechanism or mode of action is not relevant in humans.
- Species: Mouse
- Application Route: Oral
- Exposure time: 2 Years
- Result: positive
- Remarks: The mechanism or mode of action is not relevant in humans.

Reproductive toxicity
Not classified based on available information.

**Components:**

**.beta.-Cyclodextrin, sulfobutyl ethers, sodium salts:**
- Effects on fertility:
  - Test Type: Fertility
    - Species: Rat
    - Application Route: Intravenous injection
    - Result: negative
- Effects on fetal development:
  - Test Type: Embryo-fetal development
    - Species: Rat
    - Application Route: Intravenous injection
    - Result: negative

Posaconazole:
Effects on fertility: Test Type: Fertility/early embryonic development
Species: Rat, male
General Toxicity Parent: NOAEL: 180 mg/kg body weight
Symptoms: No effects on mating performance.
Result: negative

Effects on fetal development: Test Type: Fertility/early embryonic development
Species: Rat, female
General Toxicity Parent: NOAEL: 45 mg/kg body weight
Symptoms: No effects on mating performance.
Result: negative

Effects on fetal development: Test Type: Embryo-fetal development
Species: Rat, female
Application Route: Oral
Developmental Toxicity: LOAEL: 29 mg/kg body weight
Result: Fetotoxicity, Malformations were observed.

Effects on fetal development: Test Type: Embryo-fetal development
Species: Rabbit, female
Developmental Toxicity: LOAEL: 40 mg/kg body weight
Result: Fetotoxicity.

Reproductive toxicity - Assessment: Some evidence of adverse effects on development, based on animal experiments.

STOT-single exposure
Not classified based on available information.

STOT-repeated exposure
May cause damage to organs (Adrenal gland, Bone marrow, Kidney, Liver, Nervous system, Reproductive organs) through prolonged or repeated exposure if swallowed.

Components:

**Posaconazole:**
Routes of exposure: Ingestion
Target Organ: Adrenal gland, Bone marrow, Kidney, Liver, Reproductive organs, Nervous system
Assessment: Causes damage to organs through prolonged or repeated exposure.

Repeated dose toxicity

Components:

**Posaconazole:**
Species: Rat, female
LOAEL: 5 mg/kg
Application Route: Oral
Exposure time: 6 Months
Target Organ: Adrenal gland, Lungs, Heart, Liver, spleen, Kidney, Ovary

Species: Dog
LOAEL: 3 mg/kg
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Application Route: Oral
Exposure time: 392 Days
Target Organs: Lungs, Liver, Brain, small intestine, Adrenal gland, Spinal cord, lymphoid tissue

Species: Monkey
LOAEL: 15 mg/kg
Application Route: Oral
Exposure time: 1 Months
Target Organs: Bone marrow, Adrenal gland, Lymph nodes, Blood

Species: Dog
LOAEL: 3 mg/kg
Application Route: Oral
Exposure time: 56 Weeks
Target Organs: Adrenal gland, Bone marrow, Kidney, Nervous system, spleen, thymus gland, Testis, lymphoid tissue

Species: Monkey
LOAEL: 180 mg/kg
Application Route: Oral
Exposure time: 12 Months
Target Organs: Blood, Gastrointestinal tract, spleen

Species: Monkey
LOAEL: 8 mg/kg
Application Route: Intravenous
Exposure time: 1 Months
Target Organs: Cardio-vascular system, Lungs, Adrenal gland, Blood

Aspiration toxicity
Not classified based on available information.

Experience with human exposure

Components:

Posaconazole:
Ingestion: Symptoms: Cough, Headache, Nausea, Vomiting, Fever, Liver effects, Rash, pruritis, Diarrhea, hypertension, neutropenia, electrolyte imbalance

SECTION 12. ECOLOGICAL INFORMATION

Ecotoxicity

Components:

.beta.-Cyclodextrin, sulfobutyl ethers, sodium salts:
Toxicity to fish: LC50 (Oncorhynchus mykiss (rainbow trout)): > 220 mg/l
Exposure time: 96 h

Toxicity to daphnia and other aquatic invertebrates: EC50 (Daphnia magna (Water flea)): > 96 mg/l
Exposure time: 48 h
Toxicity to algae/aquatic plants: EC50 (Selenastrum capricornutum (green algae)): > 100 mg/l
Exposure time: 72 h

**Posaconazole:**

**Toxicity to fish:**
LC50 (Oncorhynchus mykiss (rainbow trout)): > 0.95 mg/l
Exposure time: 96 h
Method: OECD Test Guideline 203
Remarks: No toxicity at the limit of solubility.

**Toxicity to daphnia and other aquatic invertebrates:**
EC50 (Daphnia magna (Water flea)): 0.276 mg/l
Exposure time: 48 h
Method: OECD Test Guideline 202

**Toxicity to algae/aquatic plants:**
EC50 (Pseudokirchneriella subcapitata (green algae)): > 0.509 mg/l
Exposure time: 72 h
Method: OECD Test Guideline 201
NOEC (Pseudokirchneriella subcapitata (green algae)): 0.041 mg/l
Exposure time: 72 h
Method: OECD Test Guideline 201

**M-Factor (Acute aquatic toxicity):**
1

**Toxicity to fish (Chronic toxicity):**
NOEC (Pimephales promelas (fathead minnow)): 0.206 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)): 0.244 mg/l
Exposure time: 21 d
Method: OECD Test Guideline 211
Remarks: No toxicity at the limit of solubility.

**M-Factor (Chronic aquatic toxicity):**
1

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

**Persistence and degradability**

**Components:**

**Posaconazole:**

**Biodegradability:**
Result: Not readily biodegradable.
Biodegradation: 50 %
Exposure time: 28 h
Method: OECD Test Guideline 314

**Stability in water:**
Degradation half life (DT50): > 30 d
Method: OECD Test Guideline 111
Bioaccumulative potential

Components:

Posaconazole:
Bioaccumulation:
Species: Lepomis macrochirus (Bluegill sunfish)
Bioconcentration factor (BCF): 20
Method: OECD Test Guideline 305

Partition coefficient: n-octanol/water
log Pow: 4.15

Mobility in soil

Components:

Posaconazole:
Distribution among environmental compartments
log Koc: 5.52

Other adverse effects
No data available

SECTION 13. DISPOSAL CONSIDERATIONS

Disposal methods
Waste from residues: 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

ANTT
Not regulated as a dangerous good

SECTION 15. REGULATORY INFORMATION

Safety, health and environmental regulations/legislation specific for the substance or mixture
National List of Carcinogenic Agents for Humans:
Not applicable
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Version 9.2  Revision Date: 04.01.2021  SDS Number: 22490-00018  Date of last issue: 01.10.2020
Date of first issue: 16.10.2014

(LINACH)

Brazil. List of chemicals controlled by the Federal Police : Not applicable

International Regulations

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

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

SECTION 16. OTHER INFORMATION

Further information


Full text of other abbreviations

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; TSCA - Toxic Substances Control Act (United States); UN - United Na-
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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