SAFETY DATA SHEET

Posaconazole Suspension Formulation

Version 5.3  Revision Date: 02.10.2020  SDS Number: 28763-00013  Date of last issue: 13.09.2019
Date of first issue: 06.11.2014

1. PRODUCT AND COMPANY IDENTIFICATION

Product name: Posaconazole Suspension 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

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
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 2
Long-term (chronic) aquatic hazard: Category 2

GHS label elements
Hazard pictograms:

Signal word: Warning
Hazard statements:
H361d Suspected of damaging the unborn child.
H373 May cause damage to organs (Adrenal gland, Bone marrow, Kidney, Liver, Nervous system, Reproductive organs) through prolonged or repeated exposure if swallowed.
H411 Toxic to aquatic life with long lasting effects.
Precautionary statements:

Prevention:
P203 Obtain, read and follow all safety instructions before use.
P260 Do not breathe mist or vapours.
P273 Avoid release to the environment.
P280 Wear protective gloves/ protective clothing/ eye protection/ face protection.

Response:
P318 IF exposed or concerned, get medical advice.
P391 Collect spillage.

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
None known.

3. COMPOSITION/INFORMATION ON INGREDIENTS

Substance / Mixture : Mixture

Components

<table>
<thead>
<tr>
<th>Chemical name</th>
<th>CAS-No.</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Posaconazole</td>
<td>171228-49-2</td>
<td>&gt;= 3 - &lt; 5</td>
</tr>
<tr>
<td>Titanium dioxide</td>
<td>13463-67-7</td>
<td>&gt;= 0.1 - &lt; 1</td>
</tr>
</tbody>
</table>

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 : Diarrhoea
Fever
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delayed
Nausea
Headache
Vomiting
Suspected of damaging the unborn child.
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.

5. FIREFIGHTING MEASURES

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

Unsuitable extinguishing media:
None known.

Specific hazards during firefighting:
Exposure to combustion products may be a hazard to health.

Hazardous combustion products:
Carbon oxides

Specific extinguishing methods:
Use extinguishing measures that are appropriate to local circumstances and the surrounding environment.
Use water spray to cool unopened containers.
Remove undamaged containers from fire area if it is safe to do so.
Evacuate area.

Special protective equipment for firefighters:
In the event of fire, wear self-contained breathing apparatus.
Use personal protective equipment.

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).
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 dyking or other appropriate containment to keep material from spreading. If dyked 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.

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 breathe mist or vapours.
Avoid contact with eyes.
Avoid prolonged or repeated contact with skin.
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.

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

<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>
<tr>
<td>Titanium dioxide</td>
<td>13463-67-7</td>
<td>TWA</td>
<td>10 mg/m3 (Titanium dioxide)</td>
<td>ACGIH</td>
</tr>
</tbody>
</table>

Engineering measures : Use appropriate engineering controls and manufacturing technologies to control airborne concentrations (e.g., drip-less 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
Hand protection : Combined particulates and organic vapour type
Material : Chemical-resistant gloves
Eye protection : Wear safety glasses with side shields or goggles. If the work environment or activity involves dusty conditions, mists or aerosols, wear the appropriate goggles. Wear a faceshield or other full face protection if there is a potential for direct contact to the face with dusts, mists, or aerosols.
Skin and body protection : Work uniform or laboratory coat.
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 : suspension
Colour : white
Odour : No data available
Odour Threshold : No data available
pH : 4.2 - 4.8
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
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
Vapour pressure : No data available
Relative vapour density : No data available
Relative density: No data available
Density: 1 g/cm³
Solubility(ies):
  Water solubility: soluble
Partition coefficient: n-octanol/water: Not applicable
Auto-ignition temperature: No data available
Decomposition temperature: No data available
Viscosity:
  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

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.

11. TOXICOLOGICAL INFORMATION

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

Acute toxicity:
Not classified based on available information.

Components:

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
Titanium dioxide:
Acute oral toxicity: LD50 (Rat): > 5,000 mg/kg
Acute inhalation toxicity: LC50 (Rat): > 6.82 mg/l
Exposure time: 4 h
Test atmosphere: dust/mist
Assessment: The substance or mixture has no acute inhalation toxicity

Skin corrosion/irritation
Not classified based on available information.

Components:

Posaconazole:
Species: Rabbit
Result: No skin irritation

Titanium dioxide:
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

Titanium dioxide:
Species: Rabbit
Result: No eye irritation

Respiratory or skin sensitisation

Skin sensitisation
Not classified based on available information.

Respiratory sensitisation
Not classified based on available information.

Components:

Posaconazole:
Test Type: Magnusson-Kligman-Test
Exposure routes: Skin contact
Species: Guinea pig
Result: negative

Titanium dioxide:
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<tr>
<td>5.3</td>
<td>02.10.2020</td>
<td>28763-00013</td>
<td>13.09.2019</td>
<td>06.11.2014</td>
</tr>
</tbody>
</table>

Test Type: Local lymph node assay (LLNA)
Exposure routes: Skin contact
Species: Mouse
Result: negative

Germ cell mutagenicity
Not classified based on available information.

Components:

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

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:

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.

Titanium dioxide:
Species: Rat
Carcinogenicity - Assessment: Limited evidence of carcinogenicity in inhalation studies with animals.

Reproductive toxicity
Suspected of damaging the unborn child.

Components:

**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

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 foetal development:
- Test Type: Embryo-foetal development
Species: Rat, female
Application Route: Oral
Frequency of Treatment: 6 - 15 days
Developmental Toxicity: LOAEL: 29 mg/kg body weight
Result: Fetotoxicity, Malformations were observed.

Test Type: Embryo-foetal development
Species: Rabbit, female
Frequency of Treatment: 7 - 19 days
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:

Exposure routes: Ingestion
Target Organs: 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 Organs: Adrenal gland, Lungs, Heart, Liver, spleen, Kidney, Ovary

Species: Dog
LOAEL: 3 mg/kg
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

Titanium dioxide:

Species: Rat
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**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 yr

**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, Diarrhoea, hypertension, neutropenia, electrolyte imbalance

**12. ECOLOGICAL INFORMATION**

**Ecotoxicity**

**Components**:

**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 microorganisms**: EC50 (Natural microorganism): > 1,000 mg/l
  - Exposure time: 3 h
  - Test Type: Respiration inhibition
  - Method: OECD Test Guideline 209
Toxicity to fish (Chronic toxicity): NOEC: 0.206 mg/l
Exposure time: 33 d
Species: Pimephales promelas (fathead minnow)
Method: OECD Test Guideline 210

Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity): NOEC: 0.244 mg/l
Exposure time: 21 d
Species: Daphnia magna (Water flea)
Method: OECD Test Guideline 211
Remarks: No toxicity at the limit of solubility

M-Factor (Chronic aquatic toxicity): 1

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:

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

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.

14. TRANSPORT INFORMATION

**International Regulations**

**UNRTDG**
UN number : UN 3082
Proper shipping name : ENVIRONMENTALLY HAZARDOUS SUBSTANCE, LIQUID, N.O.S. (Posaconazole)
Class : 9
Packing group : III
Labels : 9

**IATA-DGR**
UN/ID No. : UN 3082
Proper shipping name : Environmentally hazardous substance, liquid, n.o.s. (Posaconazole)
Class : 9
Packing group : III
Labels : Miscellaneous
Packing instruction (cargo aircraft) : 964
Packing instruction (passenger aircraft) : 964
Environmentally hazardous : yes

**IMDG-Code**
UN number : UN 3082
Proper shipping name : ENVIRONMENTALLY HAZARDOUS SUBSTANCE, LIQUID, N.O.S. (Posaconazole)
Class : 9
Packing group : III
Labels : 9
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EmS Code: F-A, S-F
Marine pollutant: yes

Transport in bulk according to IMO instruments
Not applicable for product as supplied.

Special precautions for user
The transport classification(s) provided herein are for informational purposes only, and solely based upon the properties of the unpackaged material as it is described within this Safety Data Sheet. Transportation classifications may vary by mode of transportation, package sizes, and variations in regional or country regulations.

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

16. OTHER INFORMATION

Further information
Date format: dd.mm.yyyy
Full text of other abbreviations
ACGIH: USA. ACGIH Threshold Limit Values (TLV)
ACGIH / TWA: 8-hour, time-weighted average

AICIC - 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 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