SAFETY DATA SHEET

Doxycycline Formulation

SECTION 1. PRODUCT AND COMPANY IDENTIFICATION

Product name : Doxycycline Formulation

Manufacturer or supplier’s details

Company : MSD
Address : Rua Coronel Bento Soares, 530
Cruzeiro - Sao Paulo - Brazil  CEP 12730-340
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 : Veterinary product

SECTION 2. HAZARDS IDENTIFICATION

GHS Classification in accordance with ABNT NBR 14725 Standard

Acute toxicity (Oral) : Category 5
Skin corrosion : Category 1
Serious eye damage : Category 1
Short-term (acute) aquatic hazard : Category 1
Long-term (chronic) aquatic hazard : Category 2

GHS label elements in accordance with ABNT NBR 14725 Standard

Signal Word : Danger
Hazard Statements : H303 May be harmful if swallowed. 
H314 Causes severe skin burns and eye damage. 
H400 Very toxic to aquatic life. 
H411 Toxic to aquatic life with long lasting effects.

Precautionary Statements : Prevention:
P260 Do not breathe dust. 
P273 Avoid release to the environment.
P280 Wear protective gloves/ protective clothing/ eye protection/ face protection.

Response:
P303 + P361 + P353 + P310 IF ON SKIN (or hair): Take off immediately all contaminated clothing. Rinse skin with water/ shower. Immediately call a POISON CENTER/ doctor.
P305 + P351 + P338 + P310 IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. Immediately call a POISON CENTER/ doctor.
P391 Collect spillage.

Other hazards which do not result in classification
May form explosive dust-air mixture during processing, handling or other means.

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>Doxycycline Hyclate</td>
<td>24390-14-5</td>
<td>Acute toxicity (Oral), Short-term (acute) aquatic hazard, Long-term (chronic) aquatic hazard,</td>
<td>&gt;= 50 &lt; 70</td>
</tr>
</tbody>
</table>

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. If not breathing, give artificial respiration. If breathing is difficult, give oxygen. Get medical attention immediately.

In case of skin contact : In case of contact, immediately flush skin with plenty of water for at least 15 minutes while removing contaminated clothing and shoes. Get medical attention immediately. Wash clothing before reuse. Thoroughly clean shoes before reuse.

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

If swallowed : If swallowed, DO NOT induce vomiting.
If vomiting occurs have person lean forward. Call a physician or poison control center immediately. Rinse mouth thoroughly with water. Never give anything by mouth to an unconscious person.

Most important symptoms and effects, both acute and delayed:
- May be harmful if swallowed.
- Causes serious eye damage.
- Causes severe burns.
- Causes digestive tract burns.

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

Notes to physician:
Treat symptomatically and supportively.

SECTION 5. FIRE-FIGHTING MEASURES

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

Unsuitable extinguishing media:
None known.

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

Hazardous combustion products:
Carbon oxides

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

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

SECTION 6. ACCIDENTAL RELEASE MEASURES

Personal precautions, protective equipment and emergency procedures:
Use personal protective equipment. Follow safe handling advice (see section 7) and personal protective equipment recommendations (see section 8).

Environmental precautions:
- Avoid release to the environment.
- Prevent further leakage or spillage if safe to do so.
- Retain and dispose of contaminated wash water. Local authorities should be advised if significant spillages cannot be contained.

Methods and materials for containment and cleaning up:
- Sweep up or vacuum up spillage and collect in suitable container for disposal.
- Avoid dispersal of dust in the air (i.e., clearing dust surfaces with compressed air).
- Dust deposits should not be allowed to accumulate on
surfaces, as these may form an explosive mixture if they are released into the atmosphere in sufficient concentration. Local or national regulations may apply to releases and disposal of this material, as well as those materials and items employed in the cleanup of releases. You will need to determine which regulations are applicable. Sections 13 and 15 of this SDS provide information regarding certain local or national requirements.

SECTION 7. HANDLING AND STORAGE

Technical measures: Static electricity may accumulate and ignite suspended dust causing an explosion. Provide adequate precautions, such as electrical grounding and bonding, or inert atmospheres.

Local/Total ventilation: If sufficient ventilation is unavailable, use with local exhaust ventilation.

Advice on safe handling: Do not get on skin or clothing. Do not breathe dust. Do not swallow. Do not get in 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. Keep container tightly closed. Minimize dust generation and accumulation. Keep container closed when not in use. Keep away from heat and sources of ignition. Take precautionary measures against static discharges. Take care to prevent spills, waste and minimize release to the environment.

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. Keep tightly closed. Store in accordance with the particular national regulations.

Materials to avoid: Do not store with the following product types: Strong oxidizing agents Organic peroxides Explosives
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>Doxycycline Hyclate</td>
<td>24390-14-5</td>
<td>TWA</td>
<td>OEL = 100 µg/m³ (OEB 2)</td>
<td>Internal</td>
</tr>
</tbody>
</table>

**Engineering measures**: Use feasible engineering controls to minimize exposure to compound. All engineering controls should be implemented by facility design and operated in accordance with GMP principles to protect products, workers, and the environment.

**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

- **Eye protection**: Wear safety glasses with side shields or 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**: powder
- **Color**: light yellow
- **Odor**: No data available
- **Odor Threshold**: No data available
- **pH**: 1.5 - 3.5
- **Melting point/freezing point**: No data available
- **Initial boiling point and boiling range**: No data available
- **Flash point**: Not applicable
- **Evaporation rate**: Not applicable
- **Flammability (solid, gas)**: May form explosive dust-air mixture during processing, handling or other means.
Flammability (liquids): Not applicable
Upper explosion limit / Upper flammability limit: No data available
Lower explosion limit / Lower flammability limit: No data available
Vapor pressure: Not applicable
Relative vapor density: Not applicable
Relative density: No data available
Density: No data available
Solubility(ies)
  Water solubility: No data available
Partition coefficient: n-octanol/water: Not applicable
Autoignition temperature: No data available
Decomposition temperature: No data available
Viscosity
  Viscosity, kinematic: Not applicable
Explosive properties: Not explosive
Oxidizing properties: The substance or mixture is not classified as oxidizing.
Molecular weight: No data available
Particle size: No data available

SECTION 10. STABILITY AND REACTIVITY

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

SECTION 11. TOXICOLOGICAL INFORMATION
Information on likely routes of exposure:
- Inhalation
- Skin contact
- Ingestion
- Eye contact

**Acute toxicity**
May be harmful if swallowed.

**Product:**
Acute oral toxicity : Acute toxicity estimate: 4.000 mg/kg
Method: Calculation method

**Components:**
**Doxycycline Hyclate:**
Acute oral toxicity : LD50 (Rat): 2.000 mg/kg
LD50 (Mouse): 1.870 mg/kg
LD50 (Dog): 500 mg/kg

Acute toxicity (other routes of administration) : LD50 (Rat): 222 mg/kg
Application Route: Intravenous

**Skin corrosion/irritation**
Causes severe burns.

**Components:**
**Doxycycline Hyclate:**
Remarks : No data available
May irritate skin.

**Serious eye damage/eye irritation**
Causes serious eye damage.

**Components:**
**Doxycycline Hyclate:**
Remarks : No data available
May irritate eyes.

**Respiratory or skin sensitization**

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

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

**Components:**
**Doxycycline Hyclate:**
Remarks : No data available
May cause sensitization by skin contact.
May cause sensitization of susceptible persons by skin contact or by inhalation of dust.

**Germ cell mutagenicity**
Not classified based on available information.

**Components:**

**Doxycycline Hyclate:**

*Genotoxicity in vitro:*
- Test Type: Chromosome aberration test in vitro
  - Test system: Chinese hamster cells
  - Result: Weakly positive
  - Remarks: Based on data from similar materials
- Test Type: In vitro mammalian cell gene mutation test
  - Test system: Chinese hamster cells
  - Result: negative
  - Remarks: Based on data from similar materials

*Genotoxicity in vivo:*
- Test Type: In vivo micronucleus test
  - Species: Mouse
  - Application Route: Oral
  - Result: negative
  - Remarks: Based on data from similar materials

**Carcinogenicity**
Not classified based on available information.

**Components:**

**Doxycycline Hyclate:**

*Species:*
  - Rat

*Application Route:*
  - Oral

*Exposure time:*
  - 2 Years
  - 200 mg/kg body weight

*Symptoms:*
  - females

*Target Organs:*
  - Uterus (including cervix)

*Remarks:*
  - Benign tumor(s)

**Reproductive toxicity**
Not classified based on available information.

**Components:**

**Doxycycline Hyclate:**

*Effects on fetal development:*
- Test Type: Fertility/early embryonic development
  - Species: Rat, females
  - Application Route: Oral
  - General Toxicity Maternal: NOAEL: 250 mg/kg body weight
  - Result: No adverse effects.
- Test Type: Fertility/early embryonic development
  - Species: Rat, male
Application Route: Oral  
General Toxicity Maternal: NOAEL: 50 mg/kg body weight  
Symptoms: male reproductive effects  
Remarks: Fertility and developmental toxicity tests did not reveal any effect on reproduction.

**STOT-single exposure**  
Not classified based on available information.

**STOT-repeated exposure**  
Not classified based on available information.

**Repeated dose toxicity**

**Components:**

**Doxycycline Hyclate:**

Species: Rat  
NOAEL: 25 mg/kg  
Application Route: Oral  
Exposure time: 28 d  
Symptoms: Thyroid effects

**Aspiration toxicity**

Not classified based on available information.

**Experience with human exposure**

**Components:**

**Doxycycline Hyclate:**

General Information: May cause  
Target Organs: Teeth  
Symptoms: Gastrointestinal disturbance  
Skin contact: Remarks: May cause photosensitization.

**Further information**

**Components:**

**Doxycycline Hyclate:**

Remarks: Well tolerated in clinical use

**SECTION 12. ECOLOGICAL INFORMATION**

**Ecotoxicity**

**Components:**

**Doxycycline Hyclate:**

Toxicity to algae/aquatic plants: EC10 (Anabaena flos-aquae): 0.251 mg/l  
End point: Growth rate  
Exposure time: 72 h
Ecotoxicology Assessment
Acute aquatic toxicity: Very toxic to aquatic life.
Chronic aquatic toxicity: Toxic to aquatic life with long lasting effects.

Persistence and degradability
No data available

Bioaccumulative potential

Components:
Doxycycline Hyclate:
Partition coefficient: n-octanol/water: log Pow: 0.02

Mobility in soil
No data available

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
UN number: UN 3077
Proper shipping name: ENVIRONMENTALLY HAZARDOUS SUBSTANCE, SOLID, N.O.S. (Doxycycline Hyclate)
Class: 9
Packing group: III
Labels: 9

IATA-DGR
UN/ID No.: UN 3077
Proper shipping name: Environmentally hazardous substance, solid, n.o.s. (Doxycycline Hyclate)
Class: 9
Packing group: III
Labels: Miscellaneous
Packing instruction (cargo aircraft): 956
Packing instruction (passenger aircraft): 956
Environmentally hazardous: yes
IMDG-Code
UN number : UN 3077
Proper shipping name : ENVIRONMENTALLY HAZARDOUS SUBSTANCE, SOLID, N.O.S. (Doxycycline Hyclate)

Class : 9
Packing group : III
Labels : 9
EmS Code : F-A, S-F
Marine pollutant : yes

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

Domestic regulation

ANTT
UN number : UN 3077
Proper shipping name : ENVIRONMENTALLY HAZARDOUS SUBSTANCE, SOLID, N.O.S. (Doxycycline Hyclate)

Class : 9
Packing group : III
Labels : 9
Hazard Identification Number : 90

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.

SECTION 15. REGULATORY INFORMATION

Safety, health and environmental regulations/legislation specific for the substance or mixture
National List of Carcinogenic Agents for Humans - (LINACH) : Not applicable
Brazil. List of chemicals controlled by the Federal Police : Not applicable

The ingredients of this product are reported in the following inventories:
AICS : not determined
DSL : not determined
IECSC : not determined

SECTION 16. OTHER INFORMATION

Further information
SAFETY DATA SHEET

Doxycycline Formulation

<table>
<thead>
<tr>
<th>Version</th>
<th>Revision Date:</th>
<th>SDS Number:</th>
<th>Date of last issue:</th>
<th>Date of first issue:</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.2</td>
<td>27.08.2021</td>
<td>6105684-00003</td>
<td>09.04.2021</td>
<td>06.07.2020</td>
</tr>
</tbody>
</table>

Sources of key data used to compile the Material Safety Data Sheet:

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 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; SDAT - 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.

BR / Z8