SAFETY DATA SHEET

Dorzolamide Formulation

SECTION 1. PRODUCT AND COMPANY IDENTIFICATION

Product name : Dorzolamide Formulation

Manufacturer or supplier's details
Company : MSD
Address : 855 Leandro N. Alem St., 8 Floor
Buenos Aires, Argentina C1001AFB
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
Not a hazardous substance or mixture.

GHS label elements
Not a hazardous substance or mixture.

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>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dorzolamide</td>
<td>130693-82-2</td>
<td>&gt;= 1 - &lt; 5</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. Get medical attention if symptoms occur.

In case of skin contact : In case of contact, immediately flush skin with soap and plenty of water. Get medical attention if symptoms occur.

In case of eye contact : Flush eyes with water as a precaution.
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If swallowed: Get medical attention if irritation develops and persists. If swallowed, DO NOT induce vomiting. Get medical attention if symptoms occur. Rinse mouth thoroughly with water.

Most important symptoms and effects, both acute and delayed: None known.

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

Hazardous combustion products: Carbon oxides
Nitrogen oxides (NOx)
Sulfur oxides
Hydrogen chloride

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). Retain and dispose of contaminated wash water. Local authorities should be advised if significant spills 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 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 vapors.
               : 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
               : Take care to prevent spills, waste and minimize release to the environment.
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

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>Dorzolamide</td>
<td>130693-82-2</td>
<td>TWA</td>
<td>10 µg/m3 (OEB 3)</td>
<td>Internal</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Further information: Eye</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Wipe limit</td>
<td>100 µg/100 cm²</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.
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.

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

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.

SECTION 9. PHYSICAL AND CHEMICAL PROPERTIES

Appearance: Aqueous solution
Color: No data available
Odor: No data available
Odor Threshold: No data available
pH: 5.6
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
Flammability (solid, gas): Not applicable
Flammability (liquids): No data available
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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: No data available
Solubility(ies)
   Water solubility: soluble
Partition coefficient: n-octanol/water: No data available
Autoignition 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: Not applicable
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.

**Product:**
Acute oral toxicity : Acute toxicity estimate: > 5.000 mg/kg
Method: Calculation method

**Components:**

**Dorzolamide:**
Acute oral toxicity : LD50 (Rat): 1.927 mg/kg
LD50 (Mouse): 1.320 mg/kg

Acute inhalation toxicity : Remarks: No data available

Acute dermal toxicity : Remarks: No data available

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

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

**Components:**

**Dorzolamide:**
Species : Monkey
Result : Mild eye irritation

**Respiratory or skin sensitization**

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

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

**Components:**

**Dorzolamide:**
Test Type : Maximization Test
Routes of exposure : Skin contact
Species : Guinea pig
Result : Weak sensitizer

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

**Components:**

**Dorzolamide:**
Genotoxicity in vitro : Test Type: Chromosomal aberration
Result: negative
Test Type: Alkaline elution assay  
Test system: rat hepatocytes  
Result: negative

Test Type: In vitro mammalian cell gene mutation test  
Test system: Chinese hamster fibroblasts  
Result: negative

Test Type: Bacterial reverse mutation assay (AMES)  
Result: negative

Genotoxicity in vivo:  
Test Type: Cytogenetic assay  
Species: Mouse  
Result: negative

Carcinogenicity  
Not classified based on available information.

Components:

Dorzolamide:  
Species: Rat, male
Application Route: Oral
Exposure time: 2 Years
Result: negative
Remarks: The mechanism or mode of action may not be relevant in humans.

Species: Mouse
Application Route: Oral
Exposure time: 21 month(s)
Result: negative

Reproductive toxicity  
Not classified based on available information.

Components:

Dorzolamide:  
Effects on fertility:  
Test Type: Fertility  
Species: Rat, male and female  
Application Route: Oral  
Fertility: NOAEL: 7.5 mg/kg body weight  
Result: Animal testing did not show any effects on fertility.

Effects on fetal development:  
Test Type: Development  
Species: Rabbit  
Application Route: Oral  
Developmental Toxicity: NOAEL: 1 mg/kg body weight  
Result: Embryotoxic effects and adverse effects on the offspring were detected only at high maternally toxic doses
STOT-single exposure
Not classified based on available information.

STOT-repeated exposure
Not classified based on available information.

Components:

Dorzolamide:
Target Organs: Central nervous system, Gastrointestinal tract, Bone, Blood, Bladder
Assessment: May cause damage to organs through prolonged or repeated exposure.

Repeated dose toxicity

Components:

Dorzolamide:
Species: Rat
NOAEL: 0,05 mg/kg
Application Route: Oral
Target Organs: Bladder, Kidney

Species: Dog
NOAEL: 0,05 mg/kg
LOAEL: 2 mg/kg
Application Route: Oral
Exposure time: 1 y
Target Organs: Gastrointestinal tract, Bone, Blood

Species: Monkey
NOAEL: 0,05 mg/kg
Exposure time: 1 y
Target Organs: Gastrointestinal tract, Bone, Blood

Aspiration toxicity
Not classified based on available information.

Experience with human exposure

Components:

Dorzolamide:
Eye contact: Symptoms: burning or stinging of the eye, Blurred vision, tearing, asthenia, bitter taste, Nausea, dry mouth, Headache
SECTION 12. ECOLOGICAL INFORMATION

Ecotoxicity

Components:

Dorzolamide:
Toxicity to fish : LC50 (Pimephales promelas (fathead minnow)): > 1.000 mg/l
Exposure time: 96 h

Toxicity to daphnia and other aquatic invertebrates : EC50 (Daphnia magna (Water flea)): 699 mg/l
Exposure time: 48 h

Toxicity to microorganisms : EC50 (Natural microorganism): > 800 mg/l
Exposure time: 3 h
Test Type: Respiration inhibition
Method: OECD Test Guideline 209

Persistence and degradability

Components:

Dorzolamide:
Biodegradability : Result: not rapidly degradable
Biodegradation: 5 %
Exposure time: 28 d
Method: OECD Test Guideline 314

Bioaccumulative potential

Components:

Dorzolamide:
Partition coefficient: n-octanol/water : log Pow: 0.292

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
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.

SECTION 15. REGULATORY INFORMATION

Safety, health and environmental regulations/legislation specific for the substance or mixture
Argentina. Carcinogenic Substances and Agents Registry: Not applicable

Control of precursors and essential chemicals for the preparation of drugs: 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; ICS0 - Half maximal inhibitory con-
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