SAFETY DATA SHEET

Dorzolamide Formulation

SECTION 1: Identification of the substance/mixture and of the company/undertaking

1.1 Product identifier
   Trade name: Dorzolamide Formulation

1.2 Relevant identified uses of the substance or mixture and uses advised against
   Use of the Substance/Mixture: Pharmaceutical

1.3 Details of the supplier of the safety data sheet
   Company: MSD
   117 16th Road
   1685 Halfway house, Midrand, South Africa
   Telephone: +27 11 655 3000
   E-mail address of person responsible for the SDS: EHSDATASTEWARD@msd.com

1.4 Emergency telephone number
   +1-908-423-6000

SECTION 2: Hazards identification

2.1 Classification of the substance or mixture
   Classification (REGULATION (EC) No 1272/2008)
   Not a hazardous substance or mixture.

2.2 Label elements
   Labelling (REGULATION (EC) No 1272/2008)
   Not a hazardous substance or mixture.

   Additional Labelling
   EUH210 Safety data sheet available on request.

2.3 Other hazards
   This substance/mixture contains no components considered to be either persistent, bioaccumulative and toxic (PBT), or very persistent and very bioaccumulative (vPvB) at levels of 0.1% or higher.

SECTION 3: Composition/information on ingredients

3.2 Mixtures

<table>
<thead>
<tr>
<th>Components</th>
<th>Chemical name</th>
<th>CAS-No.</th>
<th>Classification</th>
<th>Concentration</th>
</tr>
</thead>
</table>
SECTION 4: First aid measures

4.1 Description of 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.

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).

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. Get medical attention if irritation develops and persists.

If swallowed: If swallowed, DO NOT induce vomiting. Get medical attention if symptoms occur. Rinse mouth thoroughly with water.

4.2 Most important symptoms and effects, both acute and delayed

None known.

4.3 Indication of any immediate medical attention and special treatment needed

Treatment: Treat symptomatically and supportively.

SECTION 5: Firefighting measures

5.1 Extinguishing media

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

Dorzolamide Formulation

Unsuitable extinguishing media : None known.

5.2 Special hazards arising from the substance or mixture
Specific hazards during firefighting : Exposure to combustion products may be a hazard to health.
Hazardous combustion products : Carbon oxides
Nitrogen oxides (NOx)
Sulphur oxides
Hydrogen chloride

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

SECTION 6: Accidental release measures

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

6.2 Environmental precautions
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.

6.3 Methods and material for containment and cleaning up
Methods for 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
6.4 Reference to other sections
See sections: 7, 8, 11, 12 and 13.

SECTION 7: Handling and storage

7.1 Precautions for safe handling
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.
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.
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.

7.2 Conditions for safe storage, including any incompatibilities
Requirements for storage areas and containers: Keep in properly labelled containers. Store in accordance with the particular national regulations.
Advice on common storage: Do not store with the following product types: Strong oxidizing agents

7.3 Specific end use(s)
Specific use(s): No data available

SECTION 8: Exposure controls/personal protection

8.1 Control parameters

<table>
<thead>
<tr>
<th>Occupational Exposure Limits</th>
<th>Components</th>
<th>CAS-No.</th>
<th>Value type (Form of exposure)</th>
<th>Control parameters</th>
<th>Basis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<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></td>
<td></td>
<td>Wipe limit</td>
<td>100 µg/100 cm²</td>
</tr>
</tbody>
</table>

Further information: Eye
8.2 Exposure controls

**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.
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**

**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.

**Hand protection**
- Material: Chemical-resistant gloves
- Remarks: Consider double gloving.

**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.

**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 (P)

**SECTION 9: Physical and chemical properties**

**9.1 Information on basic physical and chemical properties**

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appearance</td>
<td>Aqueous solution</td>
</tr>
<tr>
<td>Colour</td>
<td>No data available</td>
</tr>
<tr>
<td>Odour</td>
<td>No data available</td>
</tr>
<tr>
<td>Odour Threshold</td>
<td>No data available</td>
</tr>
<tr>
<td>pH</td>
<td>5.6</td>
</tr>
<tr>
<td>Melting point/freezing point</td>
<td>No data available</td>
</tr>
<tr>
<td>Initial boiling point and boiling range</td>
<td>No data available</td>
</tr>
<tr>
<td>Flash point</td>
<td>No data available</td>
</tr>
<tr>
<td>Evaporation rate</td>
<td>No data available</td>
</tr>
</tbody>
</table>
SAFETY DATA SHEET
Dorzolamide Formulation

Flammability (solid, gas) : Not applicable
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 : No data available
Solubility(ies)
   Water solubility : soluble
Partition coefficient: n-octanol/water : No data available
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.

9.2 Other information
   Flammability (liquids) : No data available
   Molecular weight : Not applicable
   Particle size : Not applicable

SECTION 10: Stability and reactivity

10.1 Reactivity
   Not classified as a reactivity hazard.

10.2 Chemical stability
   Stable under normal conditions.

10.3 Possibility of hazardous reactions
   Hazardous reactions : Can react with strong oxidizing agents.

10.4 Conditions to avoid
   Conditions to avoid : None known.
10.5 Incompatible materials

Materials to avoid: Oxidizing agents

10.6 Hazardous decomposition products

No hazardous decomposition products are known.

SECTION 11: Toxicological information

11.1 Information on toxicological effects

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: > 2.000 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 sensitisation

Skin sensitisation

Not classified based on available information.

Respiratory sensitisation

Not classified based on available information.
Components:

Dorzolamide:

Test Type: Maximisation Test
Exposure routes: 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
20 mg/kg body weight
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 foetal 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 yr

Target Organs:
- Gastrointestinal tract, Bone, Blood

Species:
- Monkey
NOAEL: 0,05 mg/kg
Exposure time: 1 yr
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

12.1 Toxicity

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

12.2 Persistence and degradability

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

12.3 Bioaccumulative potential

Components:
Dorzolamide:
Partition coefficient: n-octanol/water: log Pow: 0,292

12.4 Mobility in soil
No data available
12.5 Results of PBT and vPvB assessment

**Product:**
Assessment: This substance/mixture contains no components considered to be either persistent, bioaccumulative and toxic (PBT), or very persistent and very bioaccumulative (vPvB) at levels of 0.1% or higher.

12.6 Other adverse effects

**Product:**
Endocrine disrupting potential: The substance/mixture does not contain components considered to have endocrine disrupting properties according to REACH Article 57(f) or Commission Delegated regulation (EU) 2017/2100 or Commission Regulation (EU) 2018/605 at levels of 0.1% or higher.

SECTION 13: Disposal considerations

13.1 Waste treatment methods

**Product:**
Dispose of in accordance with local regulations. According to the European Waste Catalogue, Waste Codes are not product specific, but application specific. Waste codes should be assigned by the user, preferably in discussion with the waste disposal authorities.

**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

14.1 UN number
Not regulated as a dangerous good

14.2 UN proper shipping name
Not regulated as a dangerous good

14.3 Transport hazard class(es)
Not regulated as a dangerous good

14.4 Packing group
Not regulated as a dangerous good

14.5 Environmental hazards
Not regulated as a dangerous good

14.6 Special precautions for user
Not applicable

14.7 Transport in bulk according to Annex II of Marpol and the IBC Code
Remarks: Not applicable for product as supplied.
SAFETY DATA SHEET

Dorzolamide Formulation

SECTION 15: Regulatory information

15.1 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

15.2 Chemical safety assessment

A Chemical Safety Assessment has not been carried out.

SECTION 16: Other information

Other information: Items where changes have been made to the previous version are highlighted in the body of this document by two vertical lines.

Full text of H-Statements

H302: Harmful if swallowed.
H373: May cause damage to organs through prolonged or repeated exposure.

Full text of other abbreviations

Acute Tox.: Acute toxicity
STOT RE: Specific target organ toxicity - repeated exposure

ADN - European Agreement concerning the International Carriage of Dangerous Goods by Inland Waterways; ADR - European Agreement concerning the International Carriage of Dangerous Goods by Road; AIIC - Australian Inventory of Industrial Chemicals; ASTM - American Society for the Testing of Materials; bw - Body weight; CLP - Classification Labelling Packaging Regulation; Regulation (EC) No 1272/2008; CMR - Carcinogen, Mutagen or Reproductive Toxicant; DIN - Standard of the German Institute for Standardisation; DSL - Domestic Substances List (Canada); ECHA - European Chemicals Agency; EC-Number - European Community number; 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; 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; NO(A)EC - No Observed (Adverse) Effect Concentration; NO(A)EL - No Observed (Adverse) Effect Level; NOELR - No Observable Effect Loading Rate; 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 sub-
Further information

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

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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