SECTION 1. IDENTIFICATION

Product name : Dorzolamide Formulation

Manufacturer or supplier’s details
Company name of supplier : Merck & Co., Inc
Address : 2000 Galloping Hill Road
          Kenilworth - New Jersey - U.S.A. 07033
Telephone : 908-740-4000
Telefax : 908-735-1496
Emergency telephone : 1-908-423-6000
E-mail address : EHSDATASTEWARD@merck.com

Recommended use of the chemical and restrictions on use
Recommended use : Pharmaceutical

SECTION 2. HAZARDS IDENTIFICATION

GHS classification in accordance with 29 CFR 1910.1200
Specific target organ toxicity - repeated exposure : Category 2 (Central nervous system, Gastrointestinal tract, Bone, Blood, Bladder)

GHS label elements
Hazard pictograms : 

Signal Word : Warning
Hazard Statements : H373 May cause damage to organs (Central nervous system, Gastrointestinal tract, Bone, Blood, Bladder) through prolonged or repeated exposure.

Precautionary Statements : Prevention:
P260 Do not breathe mist or vapors.
Response:
P314 Get medical advice/ attention if you feel unwell.
Disposal:
P501 Dispose of contents/ container to an approved waste disposal plant.

Other hazards
None known.

SECTION 3. COMPOSITION/INFORMATION ON INGREDIENTS

Substance / Mixture : Mixture

Components
SAFETY DATA SHEET

Dorzolamide Formulation

Version 6.3  Revision Date: 03/23/2020  SDS Number: 29001-00015  Date of last issue: 09/13/2019
Date of first issue: 11/07/2014

<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>

Actual concentration is withheld as a trade secret

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. 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.

Most important symptoms and effects, both acute and delayed: May cause damage to organs through prolonged or repeated exposure.

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 and personal protective equipment recommendations.

**Environmental precautions**

Discharge into the environment must be avoided. 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 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.

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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**

Avoid inhalation of vapor or mist. 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.

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**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>
</tbody>
</table>
Further information: Eye

Internal

| Wipe limit | 100 µg/100 cm² |

**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**
General and local exhaust ventilation is recommended to maintain vapor exposures below recommended limits. Where concentrations are above recommended limits or are unknown, appropriate respiratory protection should be worn.
Follow OSHA respirator regulations (29 CFR 1910.134) and use NIOSH/MSHA approved respirators. Protection provided by air purifying respirators against exposure to any hazardous chemical is limited. Use a positive pressure air supplied respirator if there is any potential for uncontrolled release, exposure levels are unknown, or any other circumstance where air purifying respirators may not provide adequate protection.

**Hand protection**

**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

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
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</thead>
<tbody>
<tr>
<td>Appearance</td>
<td>Aqueous solution</td>
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<td>Color</td>
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<tr>
<td>Odor</td>
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<tr>
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<tr>
<td>pH</td>
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<td>Flash point</td>
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<tr>
<td>Evaporation rate</td>
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<td>Flammability (solid, gas)</td>
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<td>Flammability (liquids)</td>
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<td>Upper explosion limit / Upper flammability limit</td>
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<tr>
<td>Lower explosion limit / Lower flammability limit</td>
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<tr>
<td>Vapor pressure</td>
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</tr>
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<td>Solubility(ies)</td>
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<tr>
<td>Decomposition temperature</td>
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<tr>
<td>Oxidizing properties</td>
<td>The substance or mixture is not classified as oxidizing.</td>
</tr>
</tbody>
</table>
SAFETY DATA SHEET

Dorzolamide Formulation

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

IARC
No ingredient of this product present at levels greater than or equal to 0.1% is identified as probable, possible or confirmed human carcinogen by IARC.

OSHA
No component of this product present at levels greater than or equal to 0.1% is on OSHA’s list of regulated carcinogens.

NTP
No ingredient of this product present at levels greater than or equal to 0.1% is identified as a known or anticipated carcinogen by NTP.

Reproductive toxicity
Not classified based on available information.

Components:

**Dorzolamide:**

**Effects on 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**
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

Test Type: Development
Species: Rabbit
Application Route: Oral
Developmental Toxicity: LOAEL: 2.5 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**
May cause damage to organs (Central nervous system, Gastrointestinal tract, Bone, Blood, Bladder) through prolonged or repeated exposure.

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.

Domestic regulation

49 CFR
Not regulated as a dangerous good
SECTION 15. REGULATORY INFORMATION

EPCRA - Emergency Planning and Community Right-to-Know

CERCLA Reportable Quantity
This material does not contain any components with a CERCLA RQ.

SARA 304 Extremely Hazardous Substances Reportable Quantity
This material does not contain any components with a section 304 EHS RQ.

SARA 302 Extremely Hazardous Substances Threshold Planning Quantity
This material does not contain any components with a section 302 EHS TPQ.

SARA 311/312 Hazards : Specific target organ toxicity (single or repeated exposure)

SARA 313 : This material does not contain any chemical components with known CAS numbers that exceed the threshold (De Minimis) reporting levels established by SARA Title III, Section 313.

US State Regulations

Pennsylvania Right To Know
Water 7732-18-5

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**

**Dorzolamide Formulation**

**Version 6.3**

**Revision Date:** 03/23/2020

**SDS Number:** 29001-00015

**Date of last issue:** 09/13/2019

**Date of first issue:** 11/07/2014

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**NFPA 704:**

<table>
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<tr>
<th>Flammability</th>
<th>Health</th>
<th>Instability</th>
</tr>
</thead>
<tbody>
<tr>
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</tr>
</tbody>
</table>

**HMIS® IV:**

<table>
<thead>
<tr>
<th>Health</th>
<th>Flammability</th>
<th>Physical Hazard</th>
</tr>
</thead>
<tbody>
<tr>
<td>*</td>
<td>2</td>
<td>1</td>
</tr>
</tbody>
</table>

**HMIS® ratings are based on a 0-4 rating scale, with 0 representing minimal hazards or risks, and 4 representing significant hazards or risks. The "*" represents a chronic hazard, while the "/" represents the absence of a chronic hazard.**

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**Full text of other abbreviations**

AICS - Australian Inventory of Chemical Substances; ASTM - American Society for the Testing of Materials; bw - Body weight; CERCLA - Comprehensive Environmental Response, Compensation, and Liability Act; CMR - Carcinogen, Mutagen or Reproductive Toxicant; DIN - Standard of the German Institute for Standardisation; DOT - Department of Transportation; DSL - Domestic Substances List (Canada); ECx - Concentration associated with x% response; EHS - Extremely Hazardous Substance; 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; HMIS - Hazardous Materials Identification System; 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; MSHA - Mine Safety and Health Administration; n.o.s. - Not Otherwise Specified; NFPA - National Fire Protection Association; NO(A)EC - No Observed (Adverse) Effect Concentration; NO(A)EL - No Observed (Adverse) Effect Level; NOELR - No Observable Effect Loading Rate; 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; RCRA - Resource Conservation and Recovery Act; REACH - Regulation (EC) No 1907/2006 of the European Parliament and of the Council concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals; RQ - Reportable Quantity; SADT - Self-Accelerating Decomposition Temperature; SARA - Superfund Amendments and Reauthorization Act; SDS - Safety Data Sheet; TCSI - Taiwan Chemical Substance 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
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.