1. PRODUCT AND COMPANY IDENTIFICATION

Product name: Timolol / Dorzolamide Formulation

Manufacturer or supplier's details
Company name of supplier: MSD
Address: Kumagaya, Saitama Prefecture, Xicheng 810 MSD Co., Ltd.
Menuma factory
Telephone: 048-588-8411
E-mail address: EHSDATASTEWARD@msd.com
Emergency telephone number: 1-908-423-6000

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

2. HAZARDS IDENTIFICATION

GHS Classification
Specific target organ toxicity - repeated exposure: Category 1 (Cardio-vascular system, Central nervous system, Gastrointestinal tract, Lungs)

GHS label elements
Hazard pictograms:
Signal word: Danger
Hazard statements: H372 Causes damage to organs (Cardio-vascular system, Central nervous system, Gastrointestinal tract, Lungs) through prolonged or repeated exposure.
Precautionary statements:
Prevention:
P260 Do not breathe mist or vapours.
P264 Wash skin thoroughly after handling.
P270 Do not eat, drink or smoke when using this product.
Response:
P314 Get medical advice/attention if you feel unwell.
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

<table>
<thead>
<tr>
<th>Components</th>
<th>Chemical name</th>
<th>CAS-No.</th>
<th>Concentration (% w/w)</th>
<th>ENCS No.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Benzododecinium chloride</td>
<td>139-07-1</td>
<td>&gt;= 0.0025 - &lt; 0.025</td>
<td>1-215 / 3-2694, 3-326 / 1-215</td>
</tr>
<tr>
<td></td>
<td>Miristalkonium chloride</td>
<td>139-08-2</td>
<td>&gt;= 0.0025 - &lt; 0.025</td>
<td>1-215 / 3-2694, 3-326 / 1-215</td>
</tr>
<tr>
<td></td>
<td>Dorzolamide</td>
<td>130693-82-2</td>
<td>&gt;= 1 - &lt; 10</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(S)-3-[3-(tert-butyiamino)-2-hydroxypropoxy]-4-morpholino-1,2,5-thiadiazole monomaleate</td>
<td>26921-17-5</td>
<td>&gt;= 0.1 - &lt; 1</td>
<td></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 delayed : Causes 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.

5. FIREFIGHTING MEASURES

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

**Timolol / Dorzolamide 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>6.3</td>
<td>09/13/2019</td>
<td>28813-00015</td>
<td>2019/04/24</td>
<td>2014/11/06</td>
</tr>
</tbody>
</table>

**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), Sulphur 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 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 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 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

**Handling**

**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 vapour 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.

Avoidance of contact

Hygiene measures

- Oxidizing agents
- 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.

Storage

Conditions for safe storage

- Keep in properly labelled containers.
- Store in accordance with the particular national regulations.

Materials to avoid

- Do not store with the following product types:
  - Strong oxidizing agents

Packaging material

- Unsuitable material: None known.

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Threshold limit value and permissible exposure limits for each component in the work environment

<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></td>
<td>Further information: Eye</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Wipe limit</td>
<td>100 µg/100 cm²</td>
<td>Internal</td>
</tr>
<tr>
<td>(S)-3-[3-(tert-butylamino)-2-hydroxypropoxy]-4-morpholino-1,2,5-thiadiazole monomaleate</td>
<td>26921-17-5</td>
<td>TWA</td>
<td>10 µg/m³ (OEB 3)</td>
<td>Internal</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Further information: Eye, Skin</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., 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

**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

**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.

### 9. PHYSICAL AND CHEMICAL PROPERTIES

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appearance</td>
<td>liquid</td>
</tr>
<tr>
<td>Colour</td>
<td>colourless</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</td>
<td>No data available</td>
</tr>
<tr>
<td>range</td>
<td></td>
</tr>
<tr>
<td>Flash point</td>
<td>No data available</td>
</tr>
<tr>
<td>Evaporation rate</td>
<td>No data available</td>
</tr>
<tr>
<td>Flammability (solid, gas)</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Flammability (liquids)</td>
<td>No data available</td>
</tr>
<tr>
<td>Upper explosion limit / Upper</td>
<td>No data available</td>
</tr>
<tr>
<td>flammability limit</td>
<td></td>
</tr>
<tr>
<td>Lower explosion limit / Lower</td>
<td>No data available</td>
</tr>
<tr>
<td>flammability limit</td>
<td></td>
</tr>
<tr>
<td>Vapour pressure</td>
<td>No data available</td>
</tr>
</tbody>
</table>
Relative vapour density : No data available
Relative density : 1.02
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.
Molecular weight : No data available
Particle size : No data available

10. STABILITY AND REACTIVITY
Reactivity : Not classified as a reactivity hazard.
Chemical stability : Stable under normal conditions.
Possibility of hazardous reac-
tions : 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.

Product:
Acute oral toxicity : Acute toxicity estimate: > 2,000 mg/kg
  Method: Calculation method
Components:

Benzododecinium chloride:
Acute oral toxicity : LD50 (Rat): > 300 - 2,000 mg/kg
Remarks: Based on data from similar materials

Acute inhalation toxicity : Assessment: Corrosive to the respiratory tract.

Acute dermal toxicity : LD50 (Rabbit): > 2,000 mg/kg
Remarks: Based on data from similar materials

Miristalkonium chloride:
Acute oral toxicity : LD50 (Rat): 397.5 mg/kg
Method: OECD Test Guideline 401
Remarks: Based on data from similar materials

Acute inhalation toxicity : Assessment: Corrosive to the respiratory tract.
Remarks: Based on data from similar materials

Acute dermal toxicity : LD50 (Rabbit): 3,412 mg/kg
Remarks: Based on data from similar materials

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

(S)-3-[3-(tert-butylamino)-2-hydroxypropoxy]-4-morpholino-1,2,5-thiadiazole monomaleate:
Acute oral toxicity : LD50 (Rat): 1,000 mg/kg
LD50 (Mouse): 1,140 mg/kg

Acute toxicity (other routes of administration) : LD50 (Mouse): 300 mg/kg
Application Route: Intraperitoneal
LD50 (Mouse): 800 mg/kg
Application Route: Subcutaneous

Skin corrosion/irritation
Not classified based on available information.

Components:

Benzododecinium chloride:
Species : Rabbit
Result : Corrosive after 3 minutes to 1 hour of exposure
Remarks : Based on data from similar materials
Miristalkonium chloride:
Species: Rabbit
Result: Corrosive after 3 minutes to 1 hour of exposure
Remarks: Based on data from similar materials

(S)-3-[3-(tert-butylamino)-2-hydroxypropoxy]-4-morpholino-1,2,5-thiadiazole monomaleate:
Species: Rabbit
Method: Draize Test
Result: No skin irritation

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

Components:
Benzododecinium chloride:
Species: Rabbit
Result: Irreversible effects on the eye
Remarks: Based on data from similar materials

Miristalkonium chloride:
Species: Rabbit
Result: Irreversible effects on the eye
Remarks: Based on data from similar materials

Dorzolamide:
Species: Monkey
Result: Mild eye irritation

(S)-3-[3-(tert-butylamino)-2-hydroxypropoxy]-4-morpholino-1,2,5-thiadiazole monomaleate:
Species: Rabbit
Result: Mild eye irritation
Species: Dog
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:
Benzododecinium chloride:
Test Type: Buehler Test
Exposure routes: Skin contact
Species: Guinea pig
Method: OECD Test Guideline 406
Result: negative
### Miristalkonium chloride:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Test Type</td>
<td>Buehler Test</td>
<td>Based on data from similar materials</td>
</tr>
<tr>
<td>Exposure routes</td>
<td>Skin contact</td>
<td></td>
</tr>
<tr>
<td>Species</td>
<td>Guinea pig</td>
<td></td>
</tr>
<tr>
<td>Method</td>
<td>OECD Test Guideline 406</td>
<td></td>
</tr>
<tr>
<td>Result</td>
<td>negative</td>
<td></td>
</tr>
<tr>
<td>Remarks</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Dorzolamide:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Test Type</td>
<td>Maximisation Test</td>
<td></td>
</tr>
<tr>
<td>Exposure routes</td>
<td>Skin contact</td>
<td></td>
</tr>
<tr>
<td>Species</td>
<td>Guinea pig</td>
<td></td>
</tr>
<tr>
<td>Result</td>
<td>Weak sensitizer</td>
<td></td>
</tr>
<tr>
<td>Germ cell mutagenicity</td>
<td></td>
<td>Not classified based on available information</td>
</tr>
</tbody>
</table>

### Components:

#### Benzododecinium chloride:

<table>
<thead>
<tr>
<th>Genotoxicity in vitro</th>
<th>Test Type: Bacterial reverse mutation assay (AMES) Method: OECD Test Guideline 471 Result: negative Remarks: Based on data from similar materials</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Test Type: In vitro mammalian cell gene mutation test Method: OECD Test Guideline 476 Result: negative Remarks: Based on data from similar materials</td>
</tr>
<tr>
<td></td>
<td>Test Type: Chromosome aberration test in vitro Method: OECD Test Guideline 473 Result: negative Remarks: Based on data from similar materials</td>
</tr>
</tbody>
</table>

#### Miristalkonium chloride:

<table>
<thead>
<tr>
<th>Genotoxicity in vitro</th>
<th>Test Type: Bacterial reverse mutation assay (AMES) Method: OECD Test Guideline 471 Result: negative Remarks: Based on data from similar materials</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Test Type: In vitro mammalian cell gene mutation test</td>
</tr>
</tbody>
</table>
Method: OECD Test Guideline 476  
Result: negative  
Remarks: Based on data from similar materials

Test Type: Chromosome aberration test in vitro  
Method: OECD Test Guideline 473  
Result: negative  
Remarks: Based on data from similar materials

Genotoxicity in vivo  
Species: Mouse  
Application Route: Ingestion

Test Type: Mammalian erythrocyte micronucleus test (in vivo cytogenetic assay)  
Method: OECD Test Guideline 474  
Result: negative  
Remarks: Based on data from similar materials

Dorzolamide:

Genotoxicity in vitro  
Species: Mouse

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  
Species: Mouse

Test Type: Cytogenetic assay  
Result: negative

(S)-3-[3-(tert-butylamino)-2-hydroxypropoxy]-4-morpholino-1,2,5-thiadiazole monomaleate:

Genotoxicity in vitro  
Species: Mouse

Test Type: Bacterial reverse mutation assay (AMES)  
Method: OECD Test Guideline 471  
Result: negative

Genotoxicity in vivo  
Species: Mouse

Test Type: In vivo micronucleus test  
Method: OECD Test Guideline 474  
Result: negative

Carcinogenicity
Not classified based on available information.

Components:

Benzododecinium chloride:  
Species: Rat
Application Route: Ingestion
Exposure time: 104 weeks
Method: OECD Test Guideline 453
Result: negative
Remarks: Based on data from similar materials

**Miristalkonium chloride:**
Species: Rat
Application Route: Ingestion
Exposure time: 2 y
Method: OECD Test Guideline 453
Result: negative
Remarks: Based on data from similar materials

**Dorzolamide:**
Species: Rat, male
Application Route: Oral
Exposure time: 2 Years
LOAEL: 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

**(S)-3-[3-(tert-butylamino)-2-hydroxypropoxy]-4-morpholino-1,2,5-thiadiazole monomaleate:**
Species: Rat
Application Route: Oral
Exposure time: 2 Years
LOAEL: 300 mg/kg body weight
Result: negative
Target Organs: Adrenal gland
Remarks: The significance of these findings for humans is not certain.

Species: Mouse, female
Application Route: Oral
Exposure time: 18 Months
LOAEL: 500 mg/kg body weight
Result: negative
Target Organs: Lungs, Mammary gland, Uterus (including cervix)
Remarks: The significance of these findings for humans is not certain.

Carcinogenicity - Assessment: Weight of evidence does not support classification as a carcinogen

**Reproductive toxicity**
Not classified based on available information.
## Components:

### Benzododecinium chloride:

<table>
<thead>
<tr>
<th>Effects on fertility</th>
<th>Test Type: Two-generation reproduction toxicity study</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Species: Rat</td>
</tr>
<tr>
<td></td>
<td>Application Route: Ingestion</td>
</tr>
<tr>
<td></td>
<td>Method: OECD Test Guideline 416</td>
</tr>
<tr>
<td></td>
<td>Result: negative</td>
</tr>
<tr>
<td></td>
<td>Remarks: Based on data from similar materials</td>
</tr>
</tbody>
</table>

### Effects on foetal development:

<table>
<thead>
<tr>
<th>Effects on foetal development</th>
<th>Test Type: Embryo-foetal development</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Species: Rabbit</td>
</tr>
<tr>
<td></td>
<td>Application Route: Ingestion</td>
</tr>
<tr>
<td></td>
<td>Method: OECD Test Guideline 414</td>
</tr>
<tr>
<td></td>
<td>Result: negative</td>
</tr>
<tr>
<td></td>
<td>Remarks: Based on data from similar materials</td>
</tr>
</tbody>
</table>

### Miristalkonium chloride:

<table>
<thead>
<tr>
<th>Effects on fertility</th>
<th>Test Type: Two-generation study</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Species: Rat</td>
</tr>
<tr>
<td></td>
<td>Application Route: Ingestion</td>
</tr>
<tr>
<td></td>
<td>Method: OECD Test Guideline 416</td>
</tr>
<tr>
<td></td>
<td>Result: negative</td>
</tr>
<tr>
<td></td>
<td>Remarks: Based on data from similar materials</td>
</tr>
</tbody>
</table>

### Dorzolamide:

<table>
<thead>
<tr>
<th>Effects on fertility</th>
<th>Test Type: Fertility</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Species: Rat, male and female</td>
</tr>
<tr>
<td></td>
<td>Application Route: Oral</td>
</tr>
<tr>
<td></td>
<td>Fertility: NOAEL: 7.5 mg/kg body weight</td>
</tr>
<tr>
<td></td>
<td>Result: Animal testing did not show any effects on fertility.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Effects on foetal development</th>
<th>Test Type: Development</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Species: Rabbit</td>
</tr>
<tr>
<td></td>
<td>Application Route: Oral</td>
</tr>
<tr>
<td></td>
<td>Developmental Toxicity: NOAEL: 1 mg/kg body weight</td>
</tr>
<tr>
<td></td>
<td>Result: Embryotoxic effects and adverse effects on the offspring were detected only at high maternally toxic doses</td>
</tr>
<tr>
<td>Test Type: Development</td>
<td>Species: Rabbit</td>
</tr>
<tr>
<td></td>
<td>Application Route: Oral</td>
</tr>
<tr>
<td></td>
<td>Developmental Toxicity: LOAEL: 2.5 mg/kg body weight</td>
</tr>
<tr>
<td></td>
<td>Result: Embryotoxic effects and adverse effects on the offspring were detected only at high maternally toxic doses</td>
</tr>
</tbody>
</table>
(S)-3-[3-(tert-butylamino)-2-hydroxypropoxy]-4-morpholino-1,2,5-thiadiazole monomaleate:

- **Effects on fertility**
  - Test Type: Fertility/early embryonic development
  - Species: Rat
  - Application Route: Oral
  - Fertility: NOAEL Mating/Fertility: 150 mg/kg body weight
  - Early Embryonic Development: NOAEL F1: 150 mg/kg body weight

- **Effects on foetal development**
  - Test Type: Embryo-foetal development
  - Species: Rabbit
  - Developmental Toxicity: LOAEL F1: 50 mg/kg body weight
  - Result: Some evidence of adverse effects on development, based on animal experiments.

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**
Causes damage to organs (Cardio-vascular system, Central nervous system, Gastrointestinal tract, Lungs) through prolonged or repeated exposure.

**Product:**
- **Target Organs:** Cardio-vascular system, Central nervous system, Gastrointestinal tract, Lungs
- **Assessment:** Causes damage to organs 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.

**Components:**

**Benzododecinium chloride:**
- **Species:** Rat
- **NOAEL:** > 25 mg/kg
- **Application Route:** Ingestion
- **Exposure time:** 52 Weeks
- **Method:** OECD Test Guideline 453

**Repeated dose toxicity**

**Components:**

**Benzododecinium chloride:**
- **Species:** Rat
- **NOAEL:** > 25 mg/kg
- **Application Route:** Ingestion
- **Exposure time:** 52 Weeks
- **Method:** OECD Test Guideline 453
Remarks: Based on data from similar materials

Miristalkonium chloride:
Species: Rat
NOAEL: 56 - 65 mg/kg
LOAEL: 109 - 133 mg/kg
Application Route: Ingestion
Exposure time: 52 Weeks
Remarks: Based on data from similar materials

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

(S)-3-[3-(tert-butylamino)-2-hydroxypropoxy]-4-morpholino-1,2,5-thiadiazole monomaleate:
Species: Rat
NOAEL: 25 mg/kg
Application Route: Oral
Exposure time: 67 Weeks

Species: Dog
NOAEL: 10 mg/kg
Application Route: Oral
Exposure time: 54 Weeks
Target Organs: Kidney

Aspiration toxicity
Not classified based on available information.

Experience with human exposure

Product:
Eye contact: Symptoms: The most common side effects are; bitter taste, burning or stinging of the eye, Blurred vision, Abdominal pain, Dizziness, digestive disorder, eye pain, Headache, hypertension, Nausea, upper respiratory tract infection
Components:

**Dorzolamide:**

**Eye contact:** Symptoms: burning or stinging of the eye, Blurred vision, tearing, asthenia, bitter taste, Nausea, dry mouth, Headache

**Ingestion:** Symptoms: Headache, Fatigue, Respiratory disorders, Gastrointestinal discomfort, Allergic reactions, Rash, hair loss, altered mental status, Dizziness, changes in libido

12. ECOLOGICAL INFORMATION

Ecotoxicity

**Components:**

**Benzododecinium chloride:**

**Toxicity to fish**

\[ \text{LC50: } > 0.1 \text{ - } 1 \text{ mg/l} \]

Exposure time: 96 h

Remarks: Based on data from similar materials

**Toxicity to daphnia and other aquatic invertebrates**

\[ \text{EC50 (Daphnia magna (Water flea)): } > 0.01 \text{ - } 0.1 \text{ mg/l} \]

Exposure time: 48 h

Method: OECD Test Guideline 202

Remarks: Based on data from similar materials

**Toxicity to algae/aquatic plants**

\[ \text{ErC50: } > 0.01 \text{ - } 0.1 \text{ mg/l} \]

Exposure time: 72 h

Remarks: Based on data from similar materials

\[ \text{EC10: } > 0.001 \text{ - } 0.01 \text{ mg/l} \]

Exposure time: 72 h

Remarks: Based on data from similar materials

**M-Factor (Acute aquatic toxicity)**

\[ 10 \]

**Toxicity to fish (Chronic toxicity)**

\[ \text{NOEC (Pimephales promelas (fathead minnow)): } > 0.01 \text{ - } 0.1 \text{ mg/l} \]

Exposure time: 28 d

Remarks: Based on data from similar materials

**Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity)**

\[ \text{NOEC (Daphnia magna (Water flea)): } > 0.001 \text{ - } 0.01 \text{ mg/l} \]

Exposure time: 21 d

Method: OECD Test Guideline 211

Remarks: Based on data from similar materials

**M-Factor (Chronic aquatic toxicity)**

\[ 1 \]

**Toxicity to microorganisms**

\[ \text{EC50: } > 10 \text{ - } 100 \text{ mg/l} \]

Exposure time: 30 min

Method: OECD Test Guideline 209
Remarks: Based on data from similar materials

**Miristalkonium chloride:**

Toxicity to fish: LC50 (Oncorhynchus mykiss (rainbow trout)): 0.85 mg/l
Exposure time: 96 h
Method: OECD Test Guideline 203
Remarks: Based on data from similar materials

Toxicity to daphnia and other aquatic invertebrates: EC50 (Daphnia magna (Water flea)): 0.016 mg/l
Exposure time: 48 h
Method: OECD Test Guideline 202
Remarks: Based on data from similar materials

Toxicity to algae/aquatic plants: ErC50 (Pseudokirchneriella subcapitata (green algae)): 0.049 mg/l
Exposure time: 72 h
Method: OECD Test Guideline 201
Remarks: Based on data from similar materials

NOEC (Pseudokirchneriella subcapitata (green algae)): 0.0012 mg/l
Exposure time: 72 h
Method: OECD Test Guideline 201
Remarks: Based on data from similar materials

M-Factor (Acute aquatic toxicity): 10
M-Factor (Chronic aquatic toxicity): 1

Toxicity to microorganisms: EC10: 4 mg/l
Exposure time: 30 min
Method: OECD Test Guideline 209
Remarks: Based on data from similar materials

**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

**(S)-3-[3-(tert-butylamino)-2-hydroxypropoxy]-4-morpholino-1,2,5-thiadiazole monomaleate:**

Toxicity to fish: LC50 (Pimephales promelas (fathead minnow)): 411 mg/l
Exposure time: 96 h

Toxicity to daphnia and other aquatic invertebrates: EC50 (Daphnia magna (Water flea)): 161 mg/l
Exposure time: 48 h
Method: OECD Test Guideline 202
Toxicity to microorganisms: EC50: > 1,000 mg/l
       Exposure time: 3 h
       Test Type: Respiration inhibition

       EC50 (Photobacterium phosphoreum): > 1,800 mg/l

Persistence and degradability

Components:

Benzododecinium chloride:
Biodegradability: Result: Readily biodegradable.
       Remarks: Based on data from similar materials

Miristalkonium chloride:
Biodegradability: Result: Readily biodegradable.
       Biodegradation: 95.5%
       Exposure time: 28 d
       Method: OECD Test Guideline 301B
       Remarks: Based on data from similar materials

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

(S)-3-[3-(tert-butylamino)-2-hydroxypropoxy]-4-morpholino-1,2,5-thiadiazole monomaleate:
Biodegradability: Result: Not readily biodegradable.
       Biodegradation: 0%
       Exposure time: 30 d

Stability in water: Hydrolysis: 0% (61 d)
       Method: FDA 3.09

Bioaccumulative potential

Components:

Benzododecinium chloride:
Bioaccumulation: Species: Lepomis macrochirus (Bluegill sunfish)
       Bioconcentration factor (BCF): < 500
       Remarks: Based on data from similar materials

Partition coefficient: n-octanol/water: log Pow: < 4
       Remarks: Expert judgement

Miristalkonium chloride:
Bioaccumulation: Species: Lepomis macrochirus (Bluegill sunfish)
       Bioconcentration factor (BCF): 79
Dorzolamide:
Partition coefficient: n-octanol/water  :  log Pow: 0.292

(S)-3-[3-(tert-butylamino)-2-hydroxypropoxy]-4-morpholino-1,2,5-thiadiazole monomaleate:
Partition coefficient: n-octanol/water  :  log Pow: 1.48

Mobility in soil
No data available

Hazardous to the ozone layer
Not applicable

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
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.

National Regulations
Refer to section 15 for specific national regulation.

15. REGULATORY INFORMATION

Related Regulations
Fire Service Law
Not applicable to dangerous materials / designated flammables.

Chemical Substance Control Law
Priority Assessment Chemical Substance
Chemical name | Number
---|---
Salt of alkyl(C=12-16)(benzyl)(dimethyl)ammonium | 184

**Industrial Safety and Health Law**

**Harmful Substances Prohibited from Manufacture**
Not applicable

**Harmful Substances Required Permission for Manufacture**
Not applicable

**Substances Prevented From Impairment of Health**
Not applicable

**Circular concerning Information on Chemicals having Mutagenicity - Annex 2: Information on Existing Chemicals having Mutagenicity**
Not applicable

**Circular concerning Information on Chemicals having Mutagenicity - Annex 1: Information on Notified Substances having Mutagenicity**
Not applicable

**Substances Subject to be Notified Names**
Not applicable

**Substances Subject to be Indicated Names**
Not applicable

**Ordinance on Prevention of Hazards Due to Specified Chemical Substances**
Not applicable

**Ordinance on Prevention of Lead Poisoning**
Not applicable

**Ordinance on Prevention of Tetraalkyl Lead Poisoning**
Not applicable

**Ordinance on Prevention of Organic Solvent Poisoning**
Not applicable

**Enforcement Order of the Industrial Safety and Health Law - Attached table 1 (Dangerous Substances)**
Not applicable

**Poisonous and Deleterious Substances Control Law**
Not applicable

**Act on Confirmation, etc. of Release Amounts of Specific Chemical Substances in the Environment and Promotion of Improvements to the Management Thereof**
Not applicable

**High Pressure Gas Safety Act**
Not applicable

**Explosive Control Law**
Not applicable

**Vessel Safety Law**
Not regulated as a dangerous good
Aviation Law
Not regulated as a dangerous good

Marine Pollution and Sea Disaster Prevention etc Law
Bulk transportation: Not classified as noxious liquid substance
Pack transportation: Not classified as marine pollutant

Narcotics and Psychotropics Control Act
Narcotic or Psychotropic Raw Material (Export / Import Permission)
Not applicable
Specific Narcotic or Psychotropic Raw Material (Export / Import permission)
Not applicable

Waste Disposal and Public Cleansing Law
Industrial waste
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: yyyy/mm/dd

Full text of other abbreviations
AICS - Australian Inventory of Chemical Substances; 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; LSD50 - 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.

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