SAFETY DATA SHEET
according to Regulation (EC) No. 1907/2006

Timolol / Dorzolamide Formulation

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

1.1 Product identifier
   Trade name : Timolol / 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
             Shotton Lane
             NE23 3JU Cramlington NU - Great Britain
   Telephone : 44 1 670 59 30 00
   Telefax : 908-735-1496
   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)
   Specific target organ toxicity - repeated exposure, Category 1, Cardio-vascular system, Central nervous system, Gastro-intestinal tract, Lungs
   H372: Causes damage to organs through prolonged or repeated exposure.

2.2 Label elements
   Labelling (REGULATION (EC) No 1272/2008)
   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:
SAFETY DATA SHEET
according to Regulation (EC) No. 1907/2006

Timolol / Dorzolamide Formulation

Version 3.9  Revision Date: 16.10.2020  SDS Number: 28818-00017  Date of last issue: 23.03.2020

Date of first issue: 06.11.2014

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.

2.3 Other hazards
None known.

SECTION 3: Composition/information on ingredients

3.2 Mixtures

<table>
<thead>
<tr>
<th>Components</th>
<th>Chemical name</th>
<th>CAS-No.</th>
<th>EC-No.</th>
<th>Index-No.</th>
<th>Registration number</th>
<th>Classification</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Dorzolamide</td>
<td>130693-82-2</td>
<td></td>
<td></td>
<td></td>
<td>Acute Tox. 4; H302 STOT RE 2; H373 (Central nervous system, Gastrointestinal tract, Bone, Blood, Bladder)</td>
<td>&gt;= 1 - &lt; 10</td>
</tr>
<tr>
<td></td>
<td>(S)-3-[3-(tert-butylamino)-2-hydroxypropoxy]-4-morpholino-1,2,5-thiadiazole monomaleate</td>
<td>26921-17-5 248-111-5</td>
<td></td>
<td></td>
<td></td>
<td>Acute Tox. 4; H302 Repr. 2; H361d STOT RE 1; H372 (Lungs, Cardiovascular system)</td>
<td>&gt;= 0,1 - &lt; 1</td>
</tr>
</tbody>
</table>

For explanation of abbreviations see section 16.

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.

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.

4.2 Most important symptoms and effects, both acute and delayed
Risks: Causes damage to organs through prolonged or repeated exposure.

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

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 certain local or national requirements.

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. Wash skin thoroughly after handling. Handle in accordance with good industrial hygiene and safety practice, based on the results of the workplace exposure assessment. Do not eat, drink or smoke when using this product. 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, Organic peroxides, Explosives, Gases

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>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>Dorzolamide</td>
<td>130693-82-2</td>
<td>TWA</td>
<td>10 µg/m³ (OEB 3)</td>
<td>Internal</td>
</tr>
<tr>
<td>Further information: Eye</td>
<td></td>
<td></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>
<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>Further information: Eye, Skin</td>
<td></td>
<td></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>

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.

Equipment should conform to NS EN 143

**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>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 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>
<tr>
<td>Flammability (solid, gas)</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Upper explosion limit / Upper flammability limit</td>
<td>No data available</td>
</tr>
<tr>
<td>Lower explosion limit / Lower flammability limit</td>
<td>No data available</td>
</tr>
</tbody>
</table>
Timolol / Dorzolamide Formulation

Vapour pressure : No data available
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.

9.2 Other information
Flammability (liquids) : No data available
Molecular weight : No data available
Particle size : No data available

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

**(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:**

**(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:

**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:

**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
**SAFETY DATA SHEET**

according to Regulation (EC) No. 1907/2006

---

## 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>3.9</td>
<td>16.10.2020</td>
<td>28818-00017</td>
<td>23.03.2020</td>
<td>06.11.2014</td>
</tr>
</tbody>
</table>

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

**Genotoxicity in vitro**
- **Test Type:** Bacterial reverse mutation assay (AMES)
- **Method:** OECD Test Guideline 471
- **Result:** negative

**Genotoxicity in vivo**
- **Test Type:** In vivo micronucleus test
- **Species:** Mouse
- **Method:** OECD Test Guideline 474
- **Result:** negative

### Carcinogenicity

Not classified based on available information.

### Components:

#### Dorzolamide:

<table>
<thead>
<tr>
<th>Species</th>
<th>Rat, male</th>
</tr>
</thead>
<tbody>
<tr>
<td>Application Route</td>
<td>Oral</td>
</tr>
<tr>
<td>Exposure time</td>
<td>2 Years</td>
</tr>
<tr>
<td>Result</td>
<td>negative</td>
</tr>
<tr>
<td>Remarks</td>
<td>The mechanism or mode of action may not be relevant in humans.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Species</th>
<th>Mouse</th>
</tr>
</thead>
<tbody>
<tr>
<td>Application Route</td>
<td>Oral</td>
</tr>
<tr>
<td>Exposure time</td>
<td>21 month(s)</td>
</tr>
<tr>
<td>Result</td>
<td>negative</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Species</th>
<th>Rat</th>
</tr>
</thead>
<tbody>
<tr>
<td>Application Route</td>
<td>Oral</td>
</tr>
<tr>
<td>Exposure time</td>
<td>2 Years</td>
</tr>
<tr>
<td>LOAEL</td>
<td>300 mg/kg body weight</td>
</tr>
<tr>
<td>Result</td>
<td>negative</td>
</tr>
<tr>
<td>Target Organs</td>
<td>Adrenal gland</td>
</tr>
<tr>
<td>Remarks</td>
<td>The significance of these findings for humans is not certain.</td>
</tr>
</tbody>
</table>

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

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

### Reproductive toxicity

Not classified based on available information.
Components:

**Dorzolamide:**

<table>
<thead>
<tr>
<th>Effect on fertility</th>
<th>Test Type:</th>
<th>Fertility</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Species:</td>
<td>Rat, male and female</td>
</tr>
<tr>
<td></td>
<td>Application Route:</td>
<td>Oral</td>
</tr>
<tr>
<td>Fertility: NOAEL:</td>
<td>7,5 mg/kg body weight</td>
<td></td>
</tr>
</tbody>
</table>

Result: Animal testing did not show any effects on fertility.

<table>
<thead>
<tr>
<th>Effect on foetal development</th>
<th>Test Type:</th>
<th>Development</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Species:</td>
<td>Rabbit</td>
</tr>
<tr>
<td></td>
<td>Application Route:</td>
<td>Oral</td>
</tr>
<tr>
<td>Developmental Toxicity:</td>
<td>NOAEL: 1 mg/kg body weight</td>
<td></td>
</tr>
</tbody>
</table>

Result: Embryotoxic effects and adverse effects on the offspring were detected only at high maternally toxic doses.

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

<table>
<thead>
<tr>
<th>Effect on fertility</th>
<th>Test Type:</th>
<th>Fertility/early embryonic development</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Species:</td>
<td>Rat</td>
</tr>
<tr>
<td></td>
<td>Application Route:</td>
<td>Oral</td>
</tr>
<tr>
<td>Fertility: NOAEL Mating/Fertility:</td>
<td>150 mg/kg body weight</td>
<td></td>
</tr>
<tr>
<td>Early Embryonic Development:</td>
<td>NOAEL F1: 150 mg/kg body weight</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Effect on foetal development</th>
<th>Test Type:</th>
<th>Embryo-foetal development</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Species:</td>
<td>Rabbit</td>
</tr>
<tr>
<td></td>
<td>Developmental Toxicity:</td>
<td>LOAEL F1: 50 mg/kg body weight</td>
</tr>
</tbody>
</table>

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:**

<table>
<thead>
<tr>
<th>Target Organs</th>
<th>Cardio-vascular system, Central nervous system, Gastrointestinal tract, Lungs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Assessment</td>
<td>Causes damage to organs through prolonged or repeated exposure.</td>
</tr>
</tbody>
</table>
Timolol / Dorzolamide Formulation

Components:

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

(S)-3-[3-(tert-butylamino)-2-hydroxypropoxy]-4-morpholino-1,2,5-thiadiazole monomaleate:
Target Organs: Lungs, Cardio-vascular system
Assessment: Causes 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

(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.
Timolol / Dorzolamide Formulation

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

**(S)-3-[3-(tert-butylamino)-2-hydroxypropoxy]-4-morpholino-1,2,5-thiadiazole monomaleate:**
Eye contact: Symptoms: burning or stinging of the eye, dryness of the eyes, Headache, Nausea, Dizziness, dry mouth, changes in libido, hair loss, Allergic reactions

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

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

**(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
12.2 Persistence and degradability

**Components:**

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

**(S)-3-[3-(tert-buty lamino)-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

12.3 Bioaccumulative potential

**Components:**

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

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

12.4 Mobility in soil
- No data available

12.5 Results of PBT and vPvB assessment
- Not relevant

12.6 Other adverse effects
- No data available

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.

SECTION 15: Regulatory information

15.1 Safety, health and environmental regulations/legislation specific for the substance or mixture

REACH - Restrictions on the manufacture, placing on the market and use of certain dangerous substances, preparations and articles (Annex XVII) : Conditions of restriction for the following entries should be considered: Number on list 3
REACH - Candidate List of Substances of Very High Concern for Authorisation (Article 59). : Not applicable
REACH - List of substances subject to authorisation (Annex XIV) : Not applicable
Regulation (EC) No 1005/2009 on substances that deplete the ozone layer : Not applicable
Regulation (EU) 2019/1021 on persistent organic pollutants (recast) : Not applicable
Regulation (EC) No 649/2012 of the European Parliament and the Council concerning the export and import of dangerous chemicals : Not applicable

Other regulations:
Young people under the age of 18 are not allowed to use or be exposed to the product professionally. Young people above the age of 15 are, however, except from this rule if the product is a necessary part of their education.

The components of this product are reported in the following inventories:
AICS : not determined
DSL : not determined
SAFETY DATA SHEET
according to Regulation (EC) No. 1907/2006

Timolol / Dorzolamide Formulation

Version 3.9    Revision Date: 16.10.2020    SDS Number: 28818-00017    Date of last issue: 23.03.2020

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.
H361d: Suspected of damaging the unborn child.
H372: Causes damage to organs through prolonged or repeated exposure.
H373: May cause damage to organs through prolonged or repeated exposure.

Full text of other abbreviations

Acute Tox.: Acute toxicity
Repr.: Reproductive 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; EnS - 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 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; RID - Regulations concerning the International Carriage of Dangerous Goods by Rail; SADT - Self-Accelerating Decomposition Temperature; SDS - Safety Data Sheet;
SVHC - Substance of very high concern; 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 Bio-accumulative

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

Classification of the mixture:
STOT RE 1
H372

Classification procedure:
Based on product data or assessment

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.

NO / EN