SECTION 1. IDENTIFICATION

Product name: Timolol Formulation

Manufacturer or supplier's details
Company name of supplier: Merck & Co., Inc
Address: 126 E. Lincoln Avenue, Rahway, New Jersey U.S.A. 07065
Telephone: 908-740-4000
Emergency telephone: 1-908-423-6000
E-mail address: EHSDATASTEWARD@merck.com

Recommended use of the chemical and restrictions on use
Recommended use: Pharmaceutical
Restrictions on use: Not applicable

SECTION 2. HAZARDS IDENTIFICATION

GHS classification in accordance with the OSHA Hazard Communication Standard (29 CFR 1910.1200)
Reproductive toxicity: Category 2
Specific target organ toxicity - repeated exposure: Category 1 (Cardio-vascular system, Lungs)

GHS label elements
Hazard pictograms: 

Signal Word: Danger
Hazard Statements: H361d Suspected of damaging the unborn child.
H372 Causes damage to organs (Cardio-vascular system, Lungs) through prolonged or repeated exposure.

Precautionary Statements: Prevention:
P201 Obtain special instructions before use.
P202 Do not handle until all safety precautions have been read and understood.
P260 Do not breathe mist or vapors.
P264 Wash skin thoroughly after handling.
P270 Do not eat, drink or smoke when using this product.
P280 Wear protective gloves, protective clothing, eye protection and face protection.

Response:
P308 + P313 IF exposed or concerned: Get medical attention.

Storage:
P405 Store locked up.

Disposal:
P501 Dispose of contents and container to an approved waste disposal plant.

Other hazards
None known.

SECTION 3. COMPOSITION/INFORMATION ON INGREDIENTS

Substance / Mixture : Mixture

Components

<table>
<thead>
<tr>
<th>Chemical name</th>
<th>CAS-No.</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(S)-3-[3-(tert-butylamino)-2-hydroxypropoxy]-4-morpholino-1,2,5-thiadiazole monomaleate</td>
<td>26921-17-5</td>
<td>&gt;= 0.1 - &lt; 1</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.

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:
Suspected of damaging the unborn child. 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.

SECTION 5. FIRE-FIGHTING MEASURES

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

Unsuitable extinguishing media: None known.
Specific hazards during fire fighting: Exposure to combustion products may be a hazard to health.
Hazardous combustion products:
- Carbon oxides
- Metal oxides
- Phosphorus compounds

Specific extinguishing methods: Use extinguishing measures that are appropriate to local circumstances and the surrounding environment. Use water spray to cool unopened containers. Remove undamaged containers from fire area if it is safe to do so. Evacuate area.

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

SECTION 6. ACCIDENTAL RELEASE MEASURES

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

Environmental precautions: Avoid release to the environment. Prevent further leakage or spillage if safe to do so. Prevent spreading over a wide area (e.g., by containment or oil barriers). Retain and dispose of contaminated wash water. Local authorities should be advised if significant 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.

SECTION 7. HANDLING AND STORAGE

Technical measures: See Engineering measures under EXPOSURE CONTROLS/PERSONAL PROTECTION section.
Local/Total ventilation: Use only with adequate ventilation.
Advice on safe handling:
- Do not breathe mist or vapors.
- Do not swallow.
- Avoid contact with eyes.
- Avoid prolonged or repeated contact with skin.
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.

**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
  - Self-reactive substances and mixtures
  - Organic peroxides
  - Explosives
  - Gases

### 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>(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></td>
<td></td>
</tr>
</tbody>
</table>

**Further information:**

- **Eye, Skin:**
  - Wipe limit 100 µg/100 cm² Internal

**Engineering measures:**

- Ensure adequate ventilation, especially in confined areas.
- Minimize workplace exposure concentrations.

**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:**

- Choose gloves to protect hands against chemicals depending on the concentration specific to place of work. Breakthrough time is not determined for the product. Change gloves often! For special applications, we recommend clarifying the
resistance to chemicals of the aforementioned protective gloves with the glove manufacturer. Wash hands before breaks and at the end of workday.

Eye protection :  Wear the following personal protective equipment:
                   Safety glasses

Skin and body protection :  Select appropriate protective clothing based on chemical resistance data and an assessment of the local exposure potential.
                           Skin contact must be avoided by using impervious protective clothing (gloves, aprons, boots, etc).

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.

SECTION 9. PHYSICAL AND CHEMICAL PROPERTIES

Appearance :  Aqueous solution
Color :  Colorless to pale yellow
Odor :  No data available
Odor Threshold :  No data available
pH :  No data available
Melting point/freezing point :  No data available
Initial boiling point and boiling range :  No data available
Flash point :  No data available
Evaporation rate :  No data available
Flammability (solid, gas) :  Not applicable
Flammability (liquids) :  No data available
Upper explosion limit / Upper flammability limit :  No data available
Lower explosion limit / Lower flammability limit :  No data available
Vapor pressure :  No data available
Relative vapor density :  No data available
Density :  No data available
Solubility(ies)
   Water solubility :  soluble
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.

Components:

(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:**
(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 sensitization**

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

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

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

**Components:**
(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:**
(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
SAFETY DATA SHEET

Timolol Formulation

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

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
Suspected of damaging the unborn child.

Components:
(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 fetal development : Test Type: Embryo-fetal 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, Lungs) through prolonged or repeated exposure.
SAFETY DATA SHEET

Timolol Formulation

Version 5.9 Revision Date: 04/04/2023 SDS Number: 1598341-00015 Date of last issue: 10/01/2022 Date of first issue: 05/01/2017

Product:
Target Organs: Cardio-vascular system, Lungs
Assessment: Causes damage to organs through prolonged or repeated exposure.

Components:
(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:
(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:
General Information: May cause Stomach/intestinal disorders
Respiratory disorders
Symptoms: Irregular cardiac activity, central nervous system effects
Eye contact: Symptoms: burning or stinging of the eye

Components:
(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

Ecotoxicity

Components:

(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:

(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:

(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

Other adverse effects:

No data available

SECTION 13. DISPOSAL CONSIDERATIONS

Disposal methods:

Waste from residues:
Dispose of in accordance with local regulations.
Do not dispose of waste into sewer.

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

Special precautions for user
Not applicable

SECTION 15. REGULATORY INFORMATION

CERCLA Reportable Quantity
Listed substances in the product are at low enough levels to not be expected to exceed the 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
Reproductive toxicity
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
Disodium hydrogenorthophosphate 7558-79-4

California List of Hazardous Substances
Disodium hydrogenorthophosphate 7558-79-4

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

NFPA 704:

HMIS® IV:

Health

FLAMMABILITY

PHYSICAL HAZARD

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.

Full text of other abbreviations

AIIIC - Australian Inventory of Industrial Chemicals; 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;
SAFETY DATA SHEET

Timolol Formulation

Version 5.9  Revision Date: 04/04/2023  SDS Number: 1598341-00015  Date of last issue: 10/01/2022

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; TECI - Thailand Existing Chemicals 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

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

Revision Date: 04/04/2023

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.

US / Z8