SECTION 1. PRODUCT AND COMPANY IDENTIFICATION

Product name : Timolol Formulation

Manufacturer or supplier’s details
Company : MSD
Address : 855 Leandro N. Alem St., 8 Floor
          Buenos Aires, Argentina C1001AFB
Telephone : 908-740-4000
Emergency telephone : 1-908-423-6000
E-mail address : EHSDATASTEWARD@msd.com
Telefax : 908-735-1496

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

SECTION 2. HAZARDS IDENTIFICATION

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

GHS label elements
Hazard pictograms : ![Danger symbol]
Signal Word : Danger
Hazard Statements : H372 Causes damage to organs (Cardio-vascular system, Lungs) through prolonged or repeated exposure.
Precautionary Statements : Prevention:
P260 Do not breathe mist or vapors.
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.
SAFETY DATA SHEET

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Other hazards which do not result in classification
None known.

SECTION 3. COMPOSITION/INFORMATION ON INGREDIENTS

<table>
<thead>
<tr>
<th>Components</th>
<th>Chemical name</th>
<th>CAS-No.</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<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>

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: 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

Unsuitable extinguishing media: None known.

Specific hazards during firefighting: Exposure to combustion products may be a hazard to health.

Hazardous combustion products: Carbon oxides
Metal oxides
Phosphorus compounds
SECTION 6. ACCIDENTAL RELEASE MEASURES

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 7. HANDLING AND STORAGE

Technical measures: See Engineering measures under EXPOSURE CONTROLS/PERSOAL 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.
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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</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>
</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: 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: 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
### Timolol Formulation

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Appearance</strong></td>
<td>Aqueous solution</td>
</tr>
<tr>
<td><strong>Color</strong></td>
<td>Colorless to pale yellow</td>
</tr>
<tr>
<td><strong>Odor</strong></td>
<td>No data available</td>
</tr>
<tr>
<td><strong>Odor Threshold</strong></td>
<td>No data available</td>
</tr>
<tr>
<td><strong>pH</strong></td>
<td>No data available</td>
</tr>
<tr>
<td><strong>Melting point/freezing point</strong></td>
<td>No data available</td>
</tr>
<tr>
<td><strong>Initial boiling point and boiling range</strong></td>
<td>No data available</td>
</tr>
<tr>
<td><strong>Flash point</strong></td>
<td>No data available</td>
</tr>
<tr>
<td><strong>Evaporation rate</strong></td>
<td>No data available</td>
</tr>
<tr>
<td><strong>Flammability (solid, gas)</strong></td>
<td>Not applicable</td>
</tr>
<tr>
<td><strong>Flammability (liquids)</strong></td>
<td>No data available</td>
</tr>
<tr>
<td><strong>Upper explosion limit / Upper flammability limit</strong></td>
<td>No data available</td>
</tr>
<tr>
<td><strong>Lower explosion limit / Lower flammability limit</strong></td>
<td>No data available</td>
</tr>
<tr>
<td><strong>Vapor pressure</strong></td>
<td>No data available</td>
</tr>
<tr>
<td><strong>Relative vapor density</strong></td>
<td>No data available</td>
</tr>
<tr>
<td><strong>Density</strong></td>
<td>No data available</td>
</tr>
<tr>
<td><strong>Solubility(ies)</strong></td>
<td></td>
</tr>
<tr>
<td>Water solubility</td>
<td>soluble</td>
</tr>
<tr>
<td><strong>Partition coefficient: n-octanol/water</strong></td>
<td>No data available</td>
</tr>
<tr>
<td><strong>Autoignition temperature</strong></td>
<td>No data available</td>
</tr>
<tr>
<td><strong>Decomposition temperature</strong></td>
<td>No data available</td>
</tr>
<tr>
<td><strong>Viscosity</strong></td>
<td></td>
</tr>
<tr>
<td>Viscosity, kinematic</td>
<td>No data available</td>
</tr>
<tr>
<td><strong>Explosive properties</strong></td>
<td>Not explosive</td>
</tr>
<tr>
<td><strong>Oxidizing properties</strong></td>
<td>The substance or mixture is not classified as oxidizing.</td>
</tr>
<tr>
<td><strong>Molecular weight</strong></td>
<td>Not applicable</td>
</tr>
<tr>
<td><strong>Particle size</strong></td>
<td>Not applicable</td>
</tr>
</tbody>
</table>
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
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:

(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.

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.
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.

SECTION 15. REGULATORY INFORMATION

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

Argentina. Carcinogenic Substances and Agents Registry : Not applicable

Control of precursors and essential chemicals for the preparation of drugs : Not applicable

International Regulations

The ingredients of this product are reported in the following inventories:

AICS : not determined

DSL : not determined
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SECTION 16. OTHER INFORMATION

Further information

Full text of other abbreviations

AIC - Australian Inventory of Industrial Chemicals; 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; 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; 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

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