

Timolol Formulation

Version 2.7 Revision Date: 10.10.2020 SDS Number: 1609225-00009 Date of last issue: 13.09.2019
Date of first issue: 01.05.2017

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

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 :



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.

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Other hazards which do not result in classification

None known.

SECTION 3. COMPOSITION/INFORMATION ON INGREDIENTS

Substance / Mixture : Mixture

Components

Chemical name	CAS-No.	Concentration (% w/w)
(S)-3-[3-(tert-butylamino)-2-hydroxypropoxy]-4-morpholino-1,2,5-thiadiazole monomaleate	26921-17-5	>= 0,1 -< 1

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 fire fighting : Exposure to combustion products may be a hazard to health.
- Hazardous combustion products : Carbon oxides
Metal oxides
Phosphorus compounds

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- 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.

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Materials to avoid : Store in accordance with the particular national regulations.
 : Do not store with the following product types:
 Strong oxidizing agents
 Organic peroxides
 Explosives
 Gases

SECTION 8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Ingredients with workplace control parameters

Components	CAS-No.	Value type (Form of exposure)	Control parameters / Permissible concentration	Basis
(S)-3-[3-(tert-butylamino)-2-hydroxypropoxy]-4-morpholino-1,2,5-thiadiazole monomaleate	26921-17-5	TWA	10 µg/m ³ (OEB 3)	Internal
Further information: Eye, Skin				
		Wipe limit	100 µg/100 cm ²	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

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

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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

Partition coefficient: n-octanol/water : No data available

Autoignition 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 : Not applicable

Particle size : Not applicable

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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

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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

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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

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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 : EC50 (Daphnia magna (Water flea)): 161 mg/l
aquatic invertebrates : 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

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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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IECSC : not determined

SECTION 16. OTHER INFORMATION**Further information**Sources of key data used to compile the Material Safety Data Sheet : Internal technical data, data from raw material SDSs, OECD eChem Portal search results and European Chemicals Agency, <http://echa.europa.eu/>**Full text of other abbreviations**

AllC - 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; KECl - 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

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.

SAFETY DATA SHEET



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