SAFETY DATA SHEET

Tafluprost Formulation

SECTION 1. PRODUCT AND COMPANY IDENTIFICATION

Product name: Tafluprost Formulation

Manufacturer or supplier’s details

Company name of supplier: MSD
Address: Avenida 16 de Septiembre No. 301
Xaltocan - Xochimilco Mexico 16090
Telephone: 52 55 57284444
Telefax: 908-735-1496
Emergency telephone: 1-908-423-6000
E-mail address: EHSDATASTEWAR@msd.com

Recommended use of the chemical and restrictions on use

Recommended use: Pharmaceutical

SECTION 2. HAZARDS IDENTIFICATION

GHS Classification
Not a hazardous substance or mixture.

GHS label elements
Not a hazardous substance or mixture.

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>Glycerine</td>
<td>56-81-5</td>
<td>&gt;= 1 - &lt; 5</td>
</tr>
<tr>
<td>Tafluprost</td>
<td>209860-87-7</td>
<td>&lt; 0.1</td>
</tr>
</tbody>
</table>

SECTION 4. FIRST AID MEASURES

If inhaled: If inhaled, remove to fresh air. Get medical attention if symptoms occur.

In case of skin contact: Wash with water and soap as a precaution. Get medical attention if symptoms occur.

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 if symptoms occur. Rinse mouth thoroughly with water.

Most important symptoms and effects, both acute and delayed: None known.

Protection of first-aiders: No special precautions are necessary for first aid responders.

Notes to physician: Treat symptomatically and supportively.

SECTION 5. FIRE-FIGHTING MEASURES
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Version 1.8  Revision Date: 09/13/2019  SDS Number: 558026-00009  Date of last issue: 24.04.2019  Date of first issue: 15.03.2016

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  
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: Wear self-contained breathing apparatus for firefighting if necessary.  Use personal protective equipment.  

SECTION 6. ACCIDENTAL RELEASE MEASURES

Personal precautions, protective equipment and emergency procedures: Follow safe handling advice and personal protective equipment recommendations.  
Environmental precautions: Discharge into the environment must be avoided.  Prevent further leakage or spillage if safe to do so.  Prevent spreading over a wide area (e.g., by containment or oil barriers).  Retain and dispose of contaminated wash water.  Local authorities should be advised if significant spillages cannot be contained.  
Methods and materials for containment and cleaning up: Soak up with inert absorbent material.  For large spills, provide 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.
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Advice on safe handling:
Handle in accordance with good industrial hygiene and safety practice, based on the results of the workplace exposure assessment.
Take care to prevent spills, waste and minimize release to the environment.

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.

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

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>Glycerine</td>
<td>56-81-5</td>
<td>VLE-PPT (Mist)</td>
<td>10 mg/m³</td>
<td>NOM-010-STPS-2014</td>
</tr>
<tr>
<td>Tafluprost</td>
<td>209860-87-7</td>
<td>TWA</td>
<td>0.002 µg/m³ (OEB 5)</td>
<td>Internal</td>
</tr>
</tbody>
</table>

Further information: Skin, Eye
Wipe limit 0.02 µg/100 cm² Internal

Engineering measures:
Use closed processing systems or containment technologies to control at source (e.g., glove boxes/isolators) and to prevent leakage of compounds into the workplace.
All engineering controls should be implemented by facility design and operated in accordance with GMP principles to protect products, workers, and the environment.
No open handling permitted.
Totally enclosed processes and materials transport systems are required.
Operations require the use of appropriate containment technology designed to prevent leakage of compounds into the workplace.

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: Organic vapor Type
Hand protection:
Material : Chemical-resistant gloves

Remarks : Consider double gloving.
Eye protection : Wear safety glasses with side shields or goggles.
If the work environment or activity involves dusty conditions, mists or aerosols, wear the appropriate goggles.
Wear a faceshield or other full face protection if there is a potential for direct contact to the face with dusts, mists, or aerosols.
Skin and body protection : Work uniform or laboratory coat.
Additional body garments should be used based upon the task being performed (e.g., sleevelets, apron, gauntlets, disposable suits) to avoid exposed skin surfaces.
Use appropriate degowning techniques to remove potentially contaminated clothing.

SECTION 9. PHYSICAL AND CHEMICAL PROPERTIES

Appearance : Aqueous solution
Color : clear
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
Relative density : No data available
Density : No data available
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Solubility(ies)
Water solubility: No data available

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: No data available

Particle size: No data available

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:

Glycerine:
Acute oral toxicity: LD50 (Rat): > 5,000 mg/kg

Acute dermal toxicity: LD50 (Guinea pig): > 5,000 mg/kg

Tafluprost:
Acute oral toxicity: LD50 (Rat): 665 mg/kg

LD50 (Rat): > 100 mg/kg
Remarks: No mortality observed at this dose.

Acute toxicity (other routes of administration): (Dog): 3 mg/kg  
Application Route: Intravenous  
Target Organs: Cardio-vascular system

Skin corrosion/irritation  
Not classified based on available information.

Components:

Glycerine:  
Species: Rabbit  
Result: No skin irritation

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

Components:

Glycerine:  
Species: Rabbit  
Result: No eye irritation

Tafluprost:  
Species: Monkey  
Result: No eye irritation

Respiratory or skin sensitization

Skin sensitization  
Not classified based on available information.

Respiratory sensitization  
Not classified based on available information.

Components:

Tafluprost:  
Test Type: Maximization Test  
Routes of exposure: Dermal  
Species: Guinea pig  
Result: Not a skin sensitizer.

Germ cell mutagenicity  
Not classified based on available information.

Components:

Glycerine:  
Genotoxicity in vitro: Test Type: In vitro mammalian cell gene mutation test  
Result: negative
Test Type: Bacterial reverse mutation assay (AMES)
Result: negative

Test Type: Chromosome aberration test in vitro
Result: negative

Test Type: DNA damage and repair, unscheduled DNA synthesis in mammalian cells (in vitro)
Result: negative

**Tafluprost:**
Genotoxicity in vitro: Test Type: Bacterial reverse mutation assay (AMES)
Result: negative

Test Type: Chromosome aberration test in vitro
Result: negative

Genotoxicity in vivo: Test Type: Mammalian erythrocyte micronucleus test (in vivo cytogenetic assay)
Species: Mouse
Application Route: Intraperitoneal injection
Result: negative

**Carcinogenicity**
Not classified based on available information.

**Components:**

**Glycerine:**
Species: Rat
Application Route: Ingestion
Exposure time: 2 Years
Result: negative

**Tafluprost:**
Species: Rat
Application Route: Subcutaneous
Exposure time: 24 Months
Result: negative

Species: Mouse
Application Route: Subcutaneous
Exposure time: 18 Months
Result: negative

**Reproductive toxicity**
Not classified based on available information.

**Components:**

**Glycerine:**
Effects on fertility: Test Type: Two-generation reproduction toxicity study
Species: Rat
Application Route: Ingestion
Result: negative

Effects on fetal development:
Test Type: Embryo-fetal development
Species: Rat
Application Route: Ingestion
Result: negative

Tafluprost:

Effects on fertility:
Test Type: Fertility/early embryonic development
Species: Rat
Application Route: Intravenous injection
Fertility: NOAEL: 100 µg/kg
Result: No effects on fertility.

Effects on fetal development:
Test Type: Embryo-fetal development
Species: Rat
Application Route: Intravenous injection
Developmental Toxicity: LOAEL: 10 µg/kg
Result: Malformations were observed., Reduced fetal weight.

Test Type: Embryo-fetal development
Species: Rabbit
Application Route: Intravenous injection
Developmental Toxicity: LOAEL: 0.03 µg/kg
Result: Malformations were observed.

Test Type: Embryo-fetal development
Species: Rabbit
Application Route: Intravenous injection
Developmental Toxicity: NOAEL: 0.01 µg/kg

Test Type: Embryo-fetal development
Species: Rat
Application Route: Intravenous injection
Developmental Toxicity: LOAEL: 1 µg/kg

Test Type: Embryo-fetal development
Species: Rat
Application Route: Intravenous injection
Developmental Toxicity: NOAEL: 0.3 µg/kg

Reproductive toxicity - Assessment:
Clear evidence of adverse effects on development, based on animal experiments.

STOT-single exposure
Not classified based on available information.
## Components:

### Tafluprost:
- **Target Organs**: Lungs, Cardio-vascular system
- **Assessment**: Causes damage to organs.

### STOT-repeated exposure
Not classified based on available information.

### Repeated dose toxicity

#### Components:

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

#### Glycerine:
- **Species**: Rat
- **NOAEL**: 0.167 mg/l
- **LOAEL**: 0.622 mg/l
- **Application Route**: inhalation (dust/mist/fume)
- **Exposure time**: 13 Weeks

- **Species**: Rat
- **NOAEL**: 8,000 - 10,000 mg/kg
- **Application Route**: Ingestion
- **Exposure time**: 2 y

- **Species**: Rabbit
- **NOAEL**: 5,040 mg/kg
- **Application Route**: Skin contact
- **Exposure time**: 45 Weeks

### Tafluprost:
- **Species**: Rat
- **LOAEL**: 0.01 mg/kg
- **Application Route**: Intravenous
- **Exposure time**: 6 Months
- **Target Organs**: Cardio-vascular system, Blood, Bone marrow, Kidney, Liver, spleen

- **Species**: Dog
- **NOAEL**: 0.0001 mg/kg
- **LOAEL**: 0.001 mg/kg
- **Application Route**: Intravenous
- **Exposure time**: 39 Weeks
- **Target Organs**: Cardio-vascular system, Eye
- **Symptoms**: Dilatation of the pupil
**Aspiration toxicity**
Not classified based on available information.

**Experience with human exposure**

**Components:**

**Tafluprost:**
Eye contact  
Symptoms: dryness of the eyes, Blurred vision

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### SECTION 12. ECOLOGICAL INFORMATION

#### Ecotoxicity

**Components:**

**Glycerine:**
Toxicity to fish  
LC50 (Oncorhynchus mykiss (rainbow trout)): 54,000 mg/l  
Exposure time: 96 h

Toxicity to daphnia and other aquatic invertebrates  
EC50 (Daphnia magna (Water flea)): 1,955 mg/l  
Exposure time: 48 h

Toxicity to microorganisms  
NOEC (Pseudomonas putida): > 10,000 mg/l  
Exposure time: 16 h  
Method: DIN 38 412 Part 8

#### Persistence and degradability

**Components:**

**Glycerine:**
Biodegradability  
Result: Readily biodegradable.  
Biodegradation: 92%  
Exposure time: 30 d  
Method: OECD Test Guideline 301D

#### Bioaccumulative potential

**Components:**

**Glycerine:**
Partition coefficient: n-octanol/water  
log Pow: -1.75

**Tafluprost:**
Partition coefficient: n-octanol/water  
log Pow: 4.5

**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.

Domestic regulation
NOM-002-SCT
Not regulated as a dangerous good

Special precautions for user
Not applicable

SECTION 15. REGULATORY INFORMATION

Safety, health and environmental regulations/legislation specific for the substance or mixture
Federal Law for the control of chemical precursors, essential chemical products and machinery for producing capsules, tablets and pills.

The ingredients of this product are reported in the following inventories:
AICS : not determined
DSL : not determined
IECSC : not determined

SECTION 16. OTHER INFORMATION

Full text of other abbreviations
NOM-010-STPS-2014 : Mexico. Norm NOM-010-STPS-2014 on Chemicals Polluting the Work Environment - Identification, Assessment and Con-
AICS - Australian Inventory of Chemical Substances; ANTT - National Agency for Transport by Land of Brazil; ASTM - American Society for the Testing of Materials; bw - Body weight; CMR - Carcinogen, Mutagen or Reproductive Toxicant; DIN - Standard of the German Institute for Standardisation; DSL - Domestic Substances List (Canada); ECx - Concentration associated with x% response; ELx - Loading rate associated with x% response; EmS - Emergency Schedule; ENCS - Existing and New Chemical Substances (Japan); ErCx - Concentration associated with x% growth rate response; ERG - Emergency Response Guide; GHS - Globally Harmonized System; GLP - Good Laboratory Practice; IARC - International Agency for Research on Cancer; IATA - International Air Transport Association; IBC - International Code for the Construction and Equipment of Ships carrying Dangerous Chemicals in Bulk; IC50 - Half maximal inhibitory concentration; ICAO - International Civil Aviation Organization; IECSC - Inventory of Existing Chemical Substances in China; IMDG - International Maritime Dangerous Goods; IMO - International Maritime Organization; ISHL - Industrial Safety and Health Law (Japan); ISO - International Organisation for Standardization; KECI - Korea Existing Chemicals Inventory; LC50 - Lethal Concentration to 50% of a test population; 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 Substances 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


Revision Date: 09/13/2019

The information is considered as correct, but not exhaustive, and will be used only as a guide, which is based in the current knowledge of the substance or mixture, and is applicable to proper safety precautions for the product.

MX / Z8