

Tafluprost Formulation

Version 4.0 Revision Date: 05/02/2017 SDS Number: 558030-00004 Date of last issue: 02/07/2017
Date of first issue: 03/15/2016

SECTION 1. IDENTIFICATION

Product name : Tafluprost Formulation

Manufacturer or supplier's details

Company name of supplier : Merck & Co., Inc

Address : 2000 Galloping Hill Road
Kenilworth - New Jersey - USA 1685

Telephone : 908-740-4000

Telefax : 908-735-1496

Emergency telephone : 1-908-423-6000

E-mail address : EHSDATASTEWARD@merck.com

Recommended use of the chemical and restrictions on use

Recommended use : Pharmaceutical

SECTION 2. HAZARDS IDENTIFICATION**GHS classification in accordance with 29 CFR 1910.1200**

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

Hazardous ingredients

| Chemical name | CAS-No. | Concentration (% w/w) |
|---------------|-------------|-----------------------|
| Glycerine | 56-81-5 | ≥ 1 - < 5 |
| Tafluprost | 209860-87-7 | < 0.1 |

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.

Tafluprost Formulation

| | | | |
|---------|----------------|--------------|---------------------------------|
| Version | Revision Date: | SDS Number: | Date of last issue: 02/07/2017 |
| 4.0 | 05/02/2017 | 558030-00004 | Date of first issue: 03/15/2016 |

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

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

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

Tafluprost Formulation

Version 4.0 Revision Date: 05/02/2017 SDS Number: 558030-00004 Date of last issue: 02/07/2017
 Date of first issue: 03/15/2016

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 : Handle in accordance with good industrial hygiene and safety practice.
 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

SECTION 8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Ingredients with workplace control parameters

| Ingredients | CAS-No. | Value type (Form of exposure) | Control parameters / Permissible concentration | Basis |
|--------------------------------|-------------|---------------------------------|--|----------|
| Glycerine | 56-81-5 | TWA (mist, respirable fraction) | 5 mg/m ³ | OSHA Z-1 |
| | | TWA (mist, total dust) | 15 mg/m ³ | OSHA Z-1 |
| Tafluprost | 209860-87-7 | TWA | 0.002 µg/m ³ (OEB 5) | Merck |
| Further information: Skin, Eye | | | | |
| | | Wipe limit | 0.02 µg/100 cm ² | Merck |

Engineering measures : Ensure adequate ventilation, especially in confined areas.
 Minimize workplace exposure concentrations.

Tafluprost Formulation

| | | | |
|---------|----------------|--------------|---------------------------------|
| Version | Revision Date: | SDS Number: | Date of last issue: 02/07/2017 |
| 4.0 | 05/02/2017 | 558030-00004 | Date of first issue: 03/15/2016 |

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

Remarks : Wash hands before breaks and at the end of workday.

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

Skin and body protection : Skin should be washed after contact.

Hygiene measures : Ensure that eye flushing systems and safety showers are located 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 : clear

Odor : No information 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

Tafluprost Formulation

| | | | |
|---------|----------------|--------------|---------------------------------|
| Version | Revision Date: | SDS Number: | Date of last issue: 02/07/2017 |
| 4.0 | 05/02/2017 | 558030-00004 | Date of first issue: 03/15/2016 |

| | | |
|--|---|--|
| 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 | : | 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. |

Tafluprost Formulation

| | | | |
|---------|----------------|--------------|---------------------------------|
| Version | Revision Date: | SDS Number: | Date of last issue: 02/07/2017 |
| 4.0 | 05/02/2017 | 558030-00004 | Date of first issue: 03/15/2016 |

SECTION 11. TOXICOLOGICAL INFORMATION**Information on likely routes of exposure**

Inhalation
Skin contact
Ingestion
Eye contact

Acute toxicity

Not classified based on available information.

Ingredients:**Glycerine:**

Acute oral toxicity : LD50 (Rat): > 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.

Ingredients:**Glycerine:**

Result: No skin irritation

Serious eye damage/eye irritation

Not classified based on available information.

Ingredients:**Glycerine:**

Result: No eye irritation

Tafluprost:

Species: Monkey
Result: No eye irritation

Respiratory or skin sensitization**Skin sensitization**

Not classified based on available information.

Tafluprost Formulation

| | | | |
|---------|----------------|--------------|---------------------------------|
| Version | Revision Date: | SDS Number: | Date of last issue: 02/07/2017 |
| 4.0 | 05/02/2017 | 558030-00004 | Date of first issue: 03/15/2016 |

Respiratory sensitization

Not classified based on available information.

Ingredients:**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.

Ingredients:**Glycerine:**

Genotoxicity in vitro : Test Type: In vitro mammalian cell gene mutation test
Method: OECD Test Guideline 476
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.

Ingredients:**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

Tafluprost Formulation

| | | | |
|---------|----------------|--------------|---------------------------------|
| Version | Revision Date: | SDS Number: | Date of last issue: 02/07/2017 |
| 4.0 | 05/02/2017 | 558030-00004 | Date of first issue: 03/15/2016 |

Exposure time: 18 Months
Result: negative

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

Not classified based on available information.

Ingredients:**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: Rabbit
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: Rat
Application Route: Intravenous injection
Developmental Toxicity: NOAEL: 3 µg/kg

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

Tafluprost Formulation

| | | | |
|---------|----------------|--------------|---------------------------------|
| Version | Revision Date: | SDS Number: | Date of last issue: 02/07/2017 |
| 4.0 | 05/02/2017 | 558030-00004 | Date of first issue: 03/15/2016 |

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.

Ingredients:**Tafluprost:**

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

STOT-repeated exposure

Not classified based on available information.

Ingredients:**Tafluprost:**

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

Repeated dose toxicity**Ingredients:****Glycerine:**

Species: Rat
NOAEL: 167 mg/m³
LOAEL: 660 mg/m³
Application Route: inhalation (dust/mist/fume)
Exposure time: 13 Weeks
Symptoms: Local irritation

Tafluprost:

Species: Rat
LOAEL: 0.01 mg/kg
Application Route: Intravenous
Exposure time: 6 Months

Tafluprost Formulation

| | | | |
|---------|----------------|--------------|---------------------------------|
| Version | Revision Date: | SDS Number: | Date of last issue: 02/07/2017 |
| 4.0 | 05/02/2017 | 558030-00004 | Date of first issue: 03/15/2016 |

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, Eyes

Symptoms: Dilatation of the pupil

Aspiration toxicity

Not classified based on available information.

Experience with human exposure**Ingredients:****Tafluprost:**

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

SECTION 12. ECOLOGICAL INFORMATION**Ecotoxicity****Ingredients:****Glycerine:**

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

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

Toxicity to microorganisms : NOEC (Pseudomonas putida): > 10,000 mg/l
Exposure time: 16 h

Persistence and degradability**Ingredients:****Glycerine:**

Biodegradability : Result: Readily biodegradable.
Biodegradation: 94 %
Exposure time: 1 d

Bioaccumulative potential**Ingredients:****Glycerine:**

Partition coefficient: n- : log Pow: -1.76
octanol/water

SAFETY DATA SHEET



Tafluprost Formulation

Version 4.0 Revision Date: 05/02/2017 SDS Number: 558030-00004 Date of last issue: 02/07/2017
Date of first issue: 03/15/2016

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

49 CFR

Not regulated as a dangerous good

SECTION 15. REGULATORY INFORMATION

EPCRA - Emergency Planning and Community Right-to-Know

CERCLA Reportable Quantity

| Ingredients | CAS-No. | Component RQ (lbs) | Calculated product RQ (lbs) |
|-----------------------------------|-----------|--------------------|-----------------------------|
| Ethylene diamine tetraacetic acid | 60-00-4 | 5000 | * |
| Sodium hydroxide | 1310-73-2 | 1000 | * |
| Hydrochloric acid | 7647-01-0 | 5000 | * |

*: Calculated RQ exceeds reasonably attainable upper limit.

SARA 304 Extremely Hazardous Substances Reportable Quantity

This material does not contain any components with a section 304 EHS RQ.

SAFETY DATA SHEET



Tafluprost Formulation

Version 4.0 Revision Date: 05/02/2017 SDS Number: 558030-00004 Date of last issue: 02/07/2017
Date of first issue: 03/15/2016

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 : No SARA Hazards

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 |
| Glycerine | 56-81-5 |
| Ethylene diamine tetraacetic acid | 60-00-4 |

California Prop. 65

This product does not contain any chemicals known to the State of California to cause cancer, birth, or any other reproductive defects.

California Permissible Exposure Limits for Chemical Contaminants

| | |
|-----------|---------|
| Glycerine | 56-81-5 |
|-----------|---------|

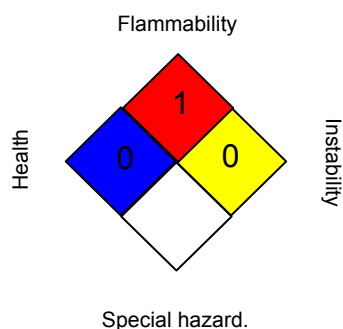
The ingredients of this product are reported in the following inventories:

| | |
|-------|------------------|
| AICS | : not determined |
| DSL | : not determined |
| IECSC | : not determined |

SECTION 16. OTHER INFORMATION

Further information

NFPA:



HMIS® IV:

| | | |
|-----------------|---|---|
| HEALTH | / | 0 |
| FLAMMABILITY | | 1 |
| PHYSICAL HAZARD | | 0 |

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

Tafluprost Formulation

| | | | |
|---------|----------------|--------------|---------------------------------|
| Version | Revision Date: | SDS Number: | Date of last issue: 02/07/2017 |
| 4.0 | 05/02/2017 | 558030-00004 | Date of first issue: 03/15/2016 |

OSHA Z-1 : USA. Occupational Exposure Limits (OSHA) - Table Z-1 Limits for Air Contaminants
OSHA Z-1 / TWA : 8-hour time weighted average

AICS - Australian Inventory of Chemical Substances; 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; 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; 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 : Internal technical data, data from raw material SDSs, OECD eChem Portal search results and European Chemicals Agency, <http://echa.europa.eu/>

Revision Date : 05/02/2017

Items where changes have been made to the previous version are highlighted in the body of this document by two vertical lines.

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



Tafluprost Formulation

| | | | |
|---------|----------------|--------------|---------------------------------|
| Version | Revision Date: | SDS Number: | Date of last issue: 02/07/2017 |
| 4.0 | 05/02/2017 | 558030-00004 | Date of first issue: 03/15/2016 |

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