SDS: Zioptan® (tafluprost ophthalmic solution)

SAFETY DATA SHEET

1. Identification

Product Identifier:	Zioptan® (tafluprost ophthalmic solution)
Synonyms:	Tafluprost: 1-methylethyl (5Z)-7-{(1R, 2R, 3R, 5S)-2-[(1E)-3,3-difluoro-4-phenoxy-1-butenyl}-3,5-dihydroxycyclopentyl]-5-heptenoate
National Drug Code (NDC):	17478-609-30 17478-609-90
Recommended Use:	Pharmaceutical.
Company:	Oak Pharmaceuticals, Inc. (Subsidiary of Akorn, Inc.) 1925 West Field Court, Suite 300 Lake Forest, Illinois 60045
Contact Telephone:	1-800-932-5676
E mail:	customer.service@akorn.com
Emergency Phone Number:	CHEMTREC 1-800-424-9300 (U.S. and Canada)

2. Hazard(s) Identification

Physical Hazards:	Not classifiable.
Health Hazards:	Not classifiable.
Symbol(s):	None.
Signal Word:	Warning.
Hazard Statement(s):	This product is hazardous according to OSHA 29CFR 1910.1200.
Precautionary Statement(s):	None.
Hazards Not Otherwise Classified:	Not classifiable.
Supplementary Information:	None.

3. Composition/Information on Ingredients

General Information:	The formulation for this product is proprietary information. Only hazardous ingredients in concentrations of 1% or greater and/or carcinogenic ingredients in concentrations of 0.1% or greater are listed in the composition table. Active ingredients in any concentration are listed.

Chemical Name	CAS Number	Synonyms	Chemical Formula	Molecular Weight	Percentage
Tafluprost	209860-87-7	Tafluprost: 1-methylethyl (5Z)-7-{(1R, 2R, 3R, 5S)-2-[(1E)-3,3-difluoro-4-phenoxy-1-butenyl}-3,5-dihydroxycyclopentyl]-5-heptenoate	$C_{25}H_{34}F_2O_5$	452.53	0.0015%

*The formula also contains Glycerol, Sodium Dihydrogen Phosphate Dihydrate, Disodium Edetate, Polysorbate 80, Hydrochloric Acid and/or Sodium Hydroxide (to adjust pH) and Water for Injection. ZIOPTAN does not contain a preservative.

4. First Aid Measures

General: CAUTION! First aid personnel must be aware of own risk during rescue! If medical advice is needed, have product container or label at hand.

Ingestion: Do not induce vomiting unless directed to do so by medical personnel. If a person vomits place them in the recovery position so that vomit will not reenter the mouth and throat. Rinse mouth with water. If swallowed, seek medical advice immediately and show the container or label. Treat symptomatically and supportively. Ensure that medical personnel are aware of the material(s) involved and take precautions to protect themselves.

Eye Contact: Remove from source of exposure. Flush with copious amounts of water for at least 15 minutes. If irritation persists or signs of toxicity occur, seek medical attention. Provide symptomatic/supportive care as necessary. Ensure that medical personnel are aware of the material(s) involved and are aware of precautions to protect themselves.

Skin Contact: Remove from source of exposure. Remove and isolate contaminated clothing and shoes. Flush with copious amounts of water for at least 20 minutes. Use soap. If irritation persists or signs of toxicity occur, seek medical attention. Provide symptomatic/supportive care as necessary. Ensure that medical personnel are aware of the material(s) involved and are aware of precautions to protect themselves.

Inhalation: Remove from source of exposure. Move individual(s) to fresh air. Give artificial respiration if individual(s) are not breathing and call emergency medical service. If signs of toxicity occur, seek medical attention. Provide symptomatic/supportive care as necessary. Ensure that medical personnel are aware of the material(s) involved and are aware of precautions to protect themselves.

Protection of First-Aiders: Use personal protective equipment (see section 8).

Signs and Symptoms:	In clinical use the most frequently reported adverse effect was conjunctival hyperemia. Other common ocular adverse events include eye pruritis, eye irritation, eye pain, changes in eyelashes (increased length, thickness, and number of lashes), dry eye, eyelash discoloration, foreign body sensation in eye, photophobia, and blurred vision. Some of the eyelash, eyelid, and irital changes may be permanent and alter the appearance of the eyes. Changes in iris pigmentation occur slowly and may not be noticed for several months. Reported adverse experiences included constipation, headache, musculoskeletal pain, dizziness, nausea, blood in urine, and nasopharyngitis.
Medical Conditions Aggravated by Exposure:	Not determined.
Notes to Physician:	Indicated for the treatment of open-angle glaucoma (OAG) and ocular hypertension (OHT). Adverse health effects may occur at exposures above the OEC due to direct ocular contact with aerosols or contaminated surfaces and/or absorption following inhalation. Treat supportively and symptomatically.

5. Firefighting Measures

Suitable Extinguishing Media:	Water spray, fog CO2, dry chemical, or alcohol resistant foam. CAUTION: Carbon dioxide will displace air in confined spaces and may cause oxygen deficient atmosphere.
Unsuitable Extinguishing Media:	Not determined.

Specific Hazards Arising from the Chemical:

Hazardous Combustion Products:	Emits toxic fumes under fire conditions.
Other Specific Hazards:	Not determined.
Special Protective Equipment Precautions for Firefighters:	Wear self-contained breathing apparatus and full and protective gear.

6. Accidental Release Measures

Personal Precautions:	Use personal protective equipment recommended in Section 8 of this document and isolate the hazard area.
Personal Protective Equipment:	For personal protection see section 8.
Methods for Cleaning Up:	Absorb up with sand or other non-combustible absorbent material. Large quantities should not be discharged into the drain but removed with absorbing material.
Environmental Precautions:	Prevent runoff from entering drains, sewers, or streams.

Other Information: A spill of this material does not need to be reported to the National Response Center.

Reference to Other Sections: Refer to Sections 8, 12 and 13 for further information.

7. Handling and Storage

Precautions for Safe Handling: Avoid breathing mists or vapors. Avoid contact with eyes, skin, and clothing. Wash thoroughly after handling. Handle in accordance with product label and/or product insert information. Handle in accordance with good industrial hygiene and safety practices.

Conditions for Safe Storage, Including Any Incompatibilities: Refrigeration required (2°C – 8°C). Do not store above 25°C. Keep container tightly closed. Store according to label and/or product insert information.

Specific End Use: Pharmaceuticals.

8. Exposure Controls/Personal Protection

Occupational Exposure Guidelines:

Common or Chemical Name	Employee Exposure Limits
Tafluprost	OEL (Merck): 0.0015 µg/m^{3*} TWA Wipe Lilit (Merck): 0.015 µg/100 cm^2
Glycerin	ACGIH TLV: 10 mg/m^3 – (Mist) OSHA PEL: 5 mg/m^3 – (Respirable fraction) OSHA PEL: 15 mg/m^3 – (Total dust)

OEB Category 5 is an internal Merck control band and corresponds to the 8-hour TWA (time weighted average) and concentration of < 1 µg/m^3. Refer to recommendation below.

*****An eye notation has been assigned to this compound because absorption through the eyes may contribute significantly to the overall exposure and produce systemic effects.

Engineering Controls: No open handling permitted. Use a properly designed containment device. Use appropriate engineering controls and manufacturing technologies to control airborne concentrations (e.g., seal less pumps, all welded piping system, lock ring fittings, etc.).If handled in a laboratory, use a properly designed biosafety cabinet, fume hood, or other containment device if the potential exists for aerosolization. If this potential does not exist, handle over lined trays or benchtops.

Respiratory Protection: Where respirators are deemed necessary to reduce or control occupational exposures, use NIOSH-approved respiratory protection and have an effective respirator program in place (applicable U.S. regulation OSHA 29 CFR 1910.134).

Eyes Protection:	Safety glasses with side shields are recommended. Face shields or goggles may be required if splash potential exists or if corrosive materials are present. Approved eye protection (e.g., bearing the ANSI Z87 or CSA stamp) is preferred. Maintain eyewash facilities in the work area.
Hand Protection:	Wear chemically compatible gloves. For handling solutions, ensure that the glove material is protective against the solvent being used. Use handling practices that minimize direct hand contact. Employees who are sensitive to natural rubber (latex) should use nitrile or other synthetic non-latex gloves. Use of powdered latex gloves should be avoided due to the risk of latex allergy.
Skin Protection:	Wear protective laboratory coat, apron, or disposable garment when working with large quantities.
Hygiene Measures:	Wash skin thoroughly with soap and water.

9. Physical and Chemical Properties

Physical State/Color:	Liquid. Colorless solution.
Odor:	No data available.
Odor Threshold:	No data available.
pH:	5.5 – 6.7.
Melting Point:	No data available.
Freezing Point:	No data available.
Boiling Point:	No data available.
Flash Point:	No data available.
Evaporation Rate:	No data available.
Flammability (solid, gas):	No data available.
Flammability Limit - Lower:	No data available.
Flammability Limit - Upper:	No data available.
Vapor Pressure:	No data available.
Vapor Density:	No data available.
Relative Density:	No data available.
Solubility(ies):	No data available.
Partition Coefficient (n-octanol/water):	No data available.
Auto-Ignition Temperature:	No data available.
Decomposition Temperature:	No data available.
Viscosity:	No data available.

10. Stability and Reactivity

Reactivity:	No data available.
Chemical Stability:	Stable under recommended storage conditions.
Possibility of Hazardous Reactions:	No data available.
Conditions to Avoid (e.g., static discharge, shock, or vibration):	None at ambient temperatures.
Incompatible Materials:	No data available.

Hazardous Decomposition Products: Thermal decomposition or combustion may liberate carbon oxides and other toxic gases or vapors.

11. Toxicological Information

Information on the Likely Routes of Exposure:

Inhalation: No data available for finished product. Active pharmaceutical ingredient: May cause bronchoconstriction.

Ingestion: No data available for finished product. The bioavailability is expected to be very low.

Skin Contact: No data available for finished product.

Eye Contact: In clinical use the most frequently reported adverse event was conjunctival hyperemia. Other common ocular adverse events include eye pruritis, eye irritation, eye pain, changes in eyelashes (increased length, thickness, and number of lashes), dry eye, eyelash discoloration, foreign body sensation in eye, photophobia, and blurred vision. Some of the eyelash, eyelid, and irital changes may be permanent and alter the appearance of the eyes. Changes in iris pigmentation occur slowly and may not be noticed for several months.

Symptoms Related to the Physical, Chemical and Toxicological Characteristics: See Section 4. To the best of our knowledge, the chemical, physical and toxicological properties have not been thoroughly investigated.

Delayed and Immediate Effects of Exposure: No data available.

Acute Toxicity:

Compound	Species	Route	Type	Dose
Glycerin	Rat	Oral	LD_{50}	12,600 mg/kg
Glycerin	Rat	Oral	LD_{50}	10,000 mg/kg
Tafluprost	Rat	Oral	LD_{50}	665 mg/kg (as Prostaglandin F-2 alpha salt, a tafluprost analogue.
Tafluprost	Rat	Oral	Acute	100 mg/kg No mortality observed

Repeated Dose Toxicity:

Compound	Species	Route	Type	Dose	Duration	Target Organ
Glycerin	Rat	Inhalation	NOAEL	0.167 mg/l	6 h/day; 5 d/week	Minimal to mild squamous cell metaplasia at the base of the epiglottis.
Glycerin	Rat	Oral	Carcinogenicity	5 – 10g/kg	730 days	No increase in tumor incidence.
Glycerin	Rat	Oral	Two generation study	~0.2 g/kg	56 – 84 days, daily	None identified
Tafluprost	Monkey	Ocular	NOAEL	0.005%	365 days, daily	Caused significant changes to the eyes.
Tafluprost	Dog	Intravenous	NOAEL	1.0 ug/kg	90 days, daily	Caused significant changes in the cardiovascular system, pulmonary system, and eyes.
Tafluprost	Rat	Intravenous	NOAEL	10 ug/kg	168 days, daily	Caused significant changes in the heart, blood, spleen, liver, kidneys, and bone marrow.

Acute Toxicity – Dermal: No data available.
Acute Toxicity – Inhalation: No data available.
Corrosivity: No data available.
Dermal Irritation: No data available.

Eye Irritation: Cause eye irritation.

Sensitization: No data available.
Toxicokinetics/Metabolism: No data available.

Target Organ Effects: Eyes.

Reproductive Effects: Possible risk of harm to the unborn child. Mating performance and fertility in rats were unaffected by intravenous treatment with 100 ug/kg/day. Effects on post-natal development and maternal function (e.g., nursing behavior) were observed in rats. Active pharmaceutical ingredient: In rabbits, intravenous administration caused increased in abortion and pre - and post-implantation loss. Significant malformations of the skulls, brain, spine, and eye were observed in rats.

PREGNANCY CATEGORY C – Animal reproduction studies have not been conducted with adenosine; nor have studies been performed in pregnant women. Because it is not known whether adenosine can cause fetal harm when administered to pregnant women, adenosine should be used during pregnancy only if clearly needed.

Other Effects: The most common reported non-ocular adverse events regardless of causality have been headaches, nasopharyngitis and fatigue.

Carcinogenicity: Does not contain any carcinogens.

National Toxicology Program (NTP): Not considered to be a carcinogen.

International Agency for Research on Cancer (IARC): Not considered to be a carcinogen.

Occupational Safety and Health Administration (OSHA): Not considered to be a carcinogen.

Mutagenicity: Active pharmaceutical ingredient: Negative in a battery of in vitro and in vivo genotoxicity assays.

Aspiration Hazard: Based on available data, the classification criteria are not met.

12. Ecological Information

Ecotoxicity

General Information: The environmental hazards and fate of this material have not been characterized. The information presented below pertains to the individual ingredients, and not to the mixture(s) or final formulation.

Aquatic: No data available.

Acute Toxicity:

Compound	Species	Type	Dose	Duration
Glycerin	Carp (Leuciscus idus melanotus)	LC_{50}	>10,000 mg/l Mortality	48 Hours
Glycerin	Rainbow trout, Donaldson trout (Oncorhynchus mykiss	LC_{50}	51,000-57,000 mg/l Mortality	96 Hours
Glycerin	Goldfish (Carassius auratus)	LC_{50}	>5,000 mg/l Mortality	24 Hours
Glycerin	Water flea (Daphnia magna)	LC_{50}	>10,000 mg/l Mortality	24 Hours

Terrestrial: No data available.
Persistence and Degradability: No data available.
Bioaccumulative Potential: No data available.
Mobility in Soil: No data available.
Mobility in Environment: No data available.
Other Adverse Effects: No data available.

13. Disposal Considerations

Dispose of all waste in accordance with Federal, State and Local regulations.

14. Transport Information

UN Number:	Not applicable.
UN Proper Shipping Name:	Not applicable.
Transport Hazard Class(es):	Not applicable.
Packing Group:	Not applicable.
Department of Transportation:	Not regulated as a hazardous material.
International Air Transport Association (IATA):	Not regulated as a dangerous good.
International Maritime Dangerous Good (IMDG):	Not regulated as a dangerous good.

15. Regulatory Information

US Federal Regulations:

Toxic Substance Control Act (TSCA):	Not listed.
Clean Water Act Section 311 Hazardous Substances:	Ethylenediaminetertraacetic Acid: 5,000 lbs. Sodium Hydroxide: 1,000 lbs. Hydrochloric Acid: 5,000 lbs.
Clean Air Act (CAA) Section 112 Accidental Release Prevention:	Hydrochloric Acid: 5,000 lbs. Hydrochloric Acid: 15,000 lbs.
CERCLA Hazardous Substance and Reportable Quantity:	Not listed.
SARA 313:	Not listed.
SARA 302:	Not listed.

State Regulations

Massachusetts:	Ethylenediaminetetraacetic Acid: Listed Glycerin: Listed Sodium Hydroxide: Listed Hydrochloric Acid: Listed
Pennsylvania:	Glycerin listed.
California Proposition 65:	Not listed.

16. Other Information

NFPA Rating:

Health:	2
Flammability:	0
Reactivity:	0

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