MATERIAL SAFETY DATA SHEET

1. IDENTIFICATION OF THE SUBSTANCE/PREPARATION AND THE COMPANY/UNDERTAKING

Pfizer Inc
Pfizer Pharmaceuticals Group
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New York, New York 10017
1-212-573-2222

Emergency telephone number:
CHEMTREC (24 hours): 1-800-424-9300
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Sandwich, Kent
CT13 9NJ
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+00 44 (0)1304 616161
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ChemSafe (24 hours): +44 (0)208 762 8322

Material Name: Latanoprost-Timolol Opthalmic Solution

Trade Name: XALACOM; XALCOM; TAVU
Chemical Family: Mixture
Intended Use: Pharmaceutical product for the treatment of glaucoma

2. HAZARDS IDENTIFICATION

Appearance: Clear, colorless solution

Statement of Hazard: Non-hazardous in accordance with international standards for workplace safety.

Additional Hazard Information:
Short Term: Accidental ingestion may cause effects similar to those seen in clinical use.
Long Term: Repeat-dose studies in animals have shown a potential to cause adverse effects on the developing fetus. Suspected of causing cancer. (based on components) .

Known Clinical Effects: Effects reported during clinical use include dizziness, headache, lethargy, changes in blood pressure, nausea, and abdominal pain. Clinical use may cause changes in heart rate. Adverse clinical reactions include the development of hypersensitivity and/or irritation leading to rashes, itching, and burning. Serious allergic reactions, including anaphylaxis, have been reported. Effects include sweating, fatigue, change in eye color, change in eyelash color, change in eyelid color.

EU Indication of danger: Not classified

Note: This document has been prepared in accordance with standards for workplace safety, which require the inclusion of all known hazards of the active substance or its intermediates regardless of the potential risk. The precautionary statements and warnings included may not apply in all cases. Your needs may vary depending upon the potential for exposure in your workplace.

3. COMPOSITION/INFORMATION ON INGREDIENTS

Hazardous

Ingredient	CAS Number	EU EINECS/ELINCS List	Classification	%
Timolol Maleate	26921-17-5	248-111-5	Xn;R22 Carc.Cat.3;R40	0.5
Latanoprost	130209-82-4	Not listed	Repr.Cat.3;R63	0.005
Benzalkonium chloride	8001-54-5	Not listed	Not Listed	*

Ingredient	CAS Number	EU EINECS/ELINCS List	Classification	%
Sodium phosphate, dibasic	7558-79-4	231-448-7	Not Listed	*
Water	7732-18-5	231-791-2	Not Listed	*
Sodium chloride	7647-14-5	231-598-3	Not Listed	*
Sodium Phosphate Monobasic, Monohydrate	10049-21-5	Not listed	Not Listed	*

Additional Information: * Proprietary
Ingredient(s) indicated as hazardous have been assessed under standards for workplace safety.

For the full text of the R phrases mentioned in this Section, see Section 16

4. FIRST AID MEASURES

Eye Contact: Flush with water while holding eyelids open for at least 15 minutes. Seek medical attention immediately.

Skin Contact: Remove contaminated clothing. Flush area with large amounts of water. Use soap. Seek medical attention.

Ingestion: Never give anything by mouth to an unconscious person. Wash out mouth with water. Do not induce vomiting unless directed by medical personnel. Seek medical attention immediately.

Inhalation: Remove to fresh air and keep patient at rest. Seek medical attention immediately.

Symptoms and Effects of Exposure: For information on potential signs and symptoms of exposure, See Section 2 - Hazards Identification and/or Section 11 - Toxicological Information.

5. FIRE FIGHTING MEASURES

Extinguishing Media: Use carbon dioxide, dry chemical, or water spray.

Hazardous Combustion Products: Formation of toxic gases is possible during heating or fire.

Fire Fighting Procedures: During all fire fighting activities, wear appropriate protective equipment, including self-contained breathing apparatus.

Fire / Explosion Hazards: Fine particles (such as dust and mists) may fuel fires/explosions.

6. ACCIDENTAL RELEASE MEASURES

Health and Safety Precautions: Personnel involved in clean-up should wear appropriate personal protective equipment (see Section 8). Minimize exposure.

Measures for Cleaning / Collecting: Contain the source of spill if it is safe to do so. Collect spill with absorbent material. Clean spill area thoroughly.

Measures for Environmental Protections:	Place waste in an appropriately labeled, sealed container for disposal. Care should be taken to avoid environmental release.
Additional Consideration for Large Spills:	Non-essential personnel should be evacuated from affected area. Report emergency situations immediately. Clean up operations should only be undertaken by trained personnel.

7. HANDLING AND STORAGE

General Handling:	Avoid contact with eyes, skin and clothing. Avoid breathing vapor or mist. Wash thoroughly after handling. When handling, use appropriate personal protective equipment (see Section 8). Releases to the environment should be avoided. Review and implement appropriate technical and procedural waste water and waste disposal measures to prevent occupational exposure or environmental releases. Potential points of process emissions of this material to the atmosphere should be controlled with dust collectors, HEPA filtration systems or other equivalent controls.
Storage Conditions:	Store as directed by product packaging.

8. EXPOSURE CONTROLS / PERSONAL PROTECTION

Refer to available public information for specific member state Occupational Exposure Limits.

Sodium chloride

Latvia OEL - TWA	Listed
Lithuania OEL - TWA	Listed

Latanoprost

Pfizer OEL TWA-8 Hr:	0.7µg/m^3

The purpose of the Occupational Exposure Band (OEB) classification system is to separate substances into different Hazard categories when the available data are sufficient to do so, but inadequate to establish an Occupational Exposure Limit (OEL). The OEB given is based upon an analysis of all currently available data; as such, this value may be subject to revision when new information becomes available.

Timolol Maleate

Pfizer Occupational Exposure Band (OEB):	OEB3 (control exposure to the range of >10ug/m^3 to < 100ug/m^3)

Engineering Controls:	Engineering controls should be used as the primary means to control exposures. General room ventilation is adequate unless the process generates dust, mist or fumes. Keep airborne contamination levels below the exposure limits listed above in this section.
Environmental Exposure Controls:	Refer to specific Member State legislation for requirements under Community environmental legislation.
Personal Protective Equipment:	Refer to applicable national standards and regulations in the selection and use of personal protective equipment (PPE).
Hands:	Impervious gloves are recommended if skin contact with drug product is possible and for bulk processing operations.
Eyes:	Wear safety glasses or goggles if eye contact is possible.
Skin:	Impervious protective clothing is recommended if skin contact with drug product is possible and for bulk processing operations.
Respiratory protection:	If the applicable Occupational Exposure Limit (OEL) is exceeded, wear an appropriate respirator with a protection factor sufficient to control exposures to below the OEL.

9. PHYSICAL AND CHEMICAL PROPERTIES

Physical State:	Solution	**Color:**	Clear, colorless
Molecular Formula:	Mixture	**Molecular Weight:**	Mixture

10. STABILITY AND REACTIVITY

Stability: Stable at normal conditions
Conditions to Avoid: Exposure to light
Incompatible Materials: As a precautionary measure, keep away from strong oxidizers

11. TOXICOLOGICAL INFORMATION

General Information: The information in this section includes the potential hazards of the formulated product . The remaining information describes the potential hazards of the individual ingredients.

Product Level Toxicity Data

Irritation / Sensitization

Study Type	Species	Result
Eye Irritation	Rabbit	No effect

Repeated Dose Toxicity

Duration	Species	Route	Dose (mg/kg/day)	End Point	Target Organ(s)
4 Week(s)	Rabbit	Ocular	0.00125	NOEL	None identified
52 Week(s)	Rabbit	Ocular	30 uL	NOEL	None identified

Ingredients:
Acute Toxicity: (Species, Route, End Point, Dose)

Sodium chloride
Rat Oral LD50 3000 mg/kg
Mouse Oral LD50 4000 mg/kg

Latanoprost
Rat Oral LD 50 > 50 mg/kg
Rat Intravenous LD 50 > 2 mg/kg
Mouse Oral LD50 > 50 mg/kg

Sodium phosphate, dibasic
Rat Oral LD 50 17 g/kg

Timolol Maleate
Rat Oral LD 50 1,028 mg/kg
Mouse Oral LD 50 1,137 mg/kg
Rat Intraperitoneal LD 50 381 mg/kg
Mouse Intraperitoneal LD 50 300 mg/kg
Rat Subcutaneous LD 50 881 mg/kg

11. TOXICOLOGICAL INFORMATION

Benzalkonium chloride
Rat Oral LD50 240 mg/kg
Acute Toxicity Comments: A greater than symbol (>) indicates that the toxicity endpoint being tested was not achievable at the highest dose used in the test.

Irritation / Sensitization: (Study Type, Species, Severity)

Sodium chloride
Eye Irritation Rabbit Moderate
Skin Irritation Rabbit Mild

Latanoprost
Skin Irritation Rabbit Slight
Eye Irritation Rabbit No effect
Skin Sensitization - GPMT Guinea Pig Negative
Antigenicity- Passive cutaneous anaphylaxis Mouse Negative
Antigenicity- Passive cutaneous anaphylaxis Guinea Pig Negative

Sodium phosphate, dibasic
Eye Irritation Rabbit Mild
Skin Irritation Rabbit Mild

Benzalkonium chloride
Skin Irritation Rabbit Moderate
Eye Irritation Rabbit Severe

Repeated Dose Toxicity: (Duration, Species, Route, Dose, End Point, Target Organ)

Latanoprost
28 Day(s) Rat Oral 0.2 mg/kg/day NOAEL None identified
13 Week(s) Rat Oral 0.2 mg/kg/day NOAEL None identified
13 Week(s) Dog Intravenous 0.001 mg/kg/day NOAEL None identified
2 Year(s) Rat Oral 0.2 mg/kg/day NOAEL None identified

Reproduction & Developmental Toxicity: (Study Type, Species, Route, Dose, End Point, Effect(s))

Latanoprost
Fertility and Embryonic Development Rabbit Intravenous 0.001 mg/kg/day NOAEL Embryotoxicity
Reproductive & Fertility Rat Intravenous 0.035 mg/kg/day NOAEL Paternal toxicity, Not Teratogenic
Prenatal & Postnatal Development Rat Intravenous 0.01 mg/kg/day NOAEL No effects at maximum dose
Embryo / Fetal Development Rat Intravenous 0.05 mg/kg/day NOAEL Paternal toxicity, Not Teratogenic

Timolol Maleate
Embryo / Fetal Development Rabbit Oral 100 mg/kg/day LOAEL Fetotoxicity
Embryo / Fetal Development Rabbit Oral 50 mg/kg/day NOEL Not Teratogenic
Embryo / Fetal Development Rat Oral 50 mg/kg/day NOEL Not Teratogenic
Embryo / Fetal Development Mouse Oral 50 mg/kg/day NOEL Not Teratogenic

Genetic Toxicity: (Study Type, Cell Type/Organism, Result)

Latanoprost
Bacterial Mutagenicity (Ames) Bacteria Negative

11. TOXICOLOGICAL INFORMATION

In Vitro Mammalian Cell Mutagenicity Mouse Lymphoma Negative
In Vitro Chromosome Aberration Human Lymphocytes Positive without activation
In Vivo Unscheduled DNA Synthesis Rat Hepatocyte Negative
In Vivo Micronucleus Mouse Bone Marrow Negative

Timolol Maleate
In Vivo Micronucleus Mouse Negative
In Vivo Cytogenetics Mouse Negative
In Vitro Cell Transformation Assay Negative

Carcinogenicity: (Duration, Species, Route, Dose, End Point, Effect(s))

Latanoprost
80 Month(s) Mouse Oral 0.2 mg/kg/day NOAEL Not carcinogenic
2 Year(s) Rat Oral 0.2 mg/kg/day NOAEL Not carcinogenic

Timolol Maleate
2 Year(s) Rat Oral 300 mg/kg/day LOEL Tumors, Adrenal gland
2 Year(s) Mouse Oral 500 mg/kg/day LOEL Tumors, Lungs, Mammary gland, Female reproductive system

Carcinogen Status: None of the components of this formulation are listed as a carcinogen by IARC, NTP or OSHA.

12. ECOLOGICAL INFORMATION

Environmental Overview: Environmental properties have not been investigated. Releases to the environment should be avoided.

13. DISPOSAL CONSIDERATIONS

Disposal Procedures: Dispose of waste in accordance with all applicable laws and regulations. Member State specific and Community specific provisions must be considered. Considering the relevant known environmental and human health hazards of the material, review and implement appropriate technical and procedural waste water and waste disposal measures to prevent occupational exposure and environmental release. It is recommended that waste minimization be practiced. The best available technology should be utilized to prevent environmental releases. This may include destructive techniques for waste and wastewater.

14. TRANSPORT INFORMATION

Not regulated for transport under USDOT, EUADR, IATA, or IMDG regulations.

15. REGULATORY INFORMATION

EU Indication of danger: Not classified

15. REGULATORY INFORMATION

OSHA Label:
Non-hazardous in accordance with international standards for workplace safety.

Canada - WHMIS: Classifications

WHMIS hazard class:
Class D, Division 2, Subdivision A

Ingredients:

Timolol Maleate

Australia (AICS):	Listed
EU EINECS/ELINCS List	248-111-5

Sodium phosphate, dibasic

CERCLA/SARA Hazardous Substances and their Reportable Quantities:	2270 kg final RQ 5000 lb final RQ
Inventory - United States TSCA - Sect. 8(b)	Listed
Australia (AICS):	Listed
EU EINECS/ELINCS List	231-448-7

Water

Inventory - United States TSCA - Sect. 8(b)	Listed
Australia (AICS):	Listed
REACH - Annex IV - Exemptions from the obligations of Register:	Present
EU EINECS/ELINCS List	231-791-2

Sodium chloride

Inventory - United States TSCA - Sect. 8(b)	Listed
Australia (AICS):	Listed
EU EINECS/ELINCS List	231-598-3

Latanoprost

Standard for the Uniform Scheduling for Drugs and Poisons:	Schedule 4

Sodium Phosphate Monobasic, Monohydrate

Australia (AICS):	Listed

Benzalkonium chloride

Australia (AICS):	Listed
Standard for the Uniform Scheduling for Drugs and Poisons:	Schedule 5 Schedule 6

16. OTHER INFORMATION

Text of R phrases mentioned in Section 3

R22 - Harmful if swallowed.
R40 - Limited evidence of a carcinogenic effect
R63 - Possible risk of harm to the unborn child.

Data Sources: Pfizer proprietary drug development information. Safety data sheets for individual ingredients. Publicly available toxicity information.

Reasons for Revision: Updated Section 2 - Hazard Identification. Updated Section 3 - Composition / Information on Ingredients. Updated Section 4 - First Aid Measures. Updated Section 7 - Handling and Storage. Updated Section 8 - Exposure Controls / Personal Protection. Updated Section 13 - Disposal Considerations. Updated Section 15 - Regulatory Information.

Prepared by: Toxicology and Hazard Communication
Pfizer Global Environment, Health, and Safety Operations

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End of Safety Data Sheet