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

Material Name: Latanoprost-Timolol Ophthalmic 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

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

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

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.
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/m³

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 >10µg/m³ to < 100µg/m³)

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
Molecular Formula: Mixture
Color: Clear, colorless
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

<table>
<thead>
<tr>
<th>Duration</th>
<th>Species</th>
<th>Route</th>
<th>Dose (mg/kg/day)</th>
<th>End Point</th>
<th>Target Organ(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4 Week(s)</td>
<td>Rabbit</td>
<td>Ocular</td>
<td>0.00125</td>
<td>NOEL</td>
<td>None identified</td>
</tr>
<tr>
<td>52 Week(s)</td>
<td>Rabbit</td>
<td>Ocular</td>
<td>30 uL</td>
<td>NOEL</td>
<td>None identified</td>
</tr>
</tbody>
</table>

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)**

<table>
<thead>
<tr>
<th>Compound</th>
<th>Study Type</th>
<th>Species</th>
<th>Route</th>
<th>Dose (mg/kg/day)</th>
<th>End Point</th>
<th>Target Organ</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium chloride</td>
<td>Eye Irritation</td>
<td>Rabbit</td>
<td>Moderate</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Skin Irritation</td>
<td>Rabbit</td>
<td>Mild</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**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**

<table>
<thead>
<tr>
<th>Duration</th>
<th>Species</th>
<th>Route</th>
<th>Dose (mg/kg/day)</th>
<th>NOAEL</th>
<th>Effect(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>28 Day(s)</td>
<td>Rat</td>
<td>Oral</td>
<td>0.2</td>
<td>NOAEL</td>
<td>None identified</td>
</tr>
<tr>
<td>13 Week(s)</td>
<td>Rat</td>
<td>Oral</td>
<td>0.2</td>
<td>NOAEL</td>
<td>None identified</td>
</tr>
<tr>
<td>13 Week(s)</td>
<td>Dog</td>
<td>Intravenous</td>
<td>0.001</td>
<td>NOAEL</td>
<td>None identified</td>
</tr>
<tr>
<td>2 Year(s)</td>
<td>Rat</td>
<td>Oral</td>
<td>0.2</td>
<td>NOAEL</td>
<td>None identified</td>
</tr>
</tbody>
</table>

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

**Latanoprost**

Fertility and Embryonic Development  Rabbit  Intravenous  0.001  NOAEL  Embryotoxicity
Reproductive & Fertility  Rat  Intravenous  0.035  NOAEL  Paternal toxicity, Not Teratogenic
Prenatal & Postnatal Development  Rat  Intravenous  0.01  NOAEL  No effects at maximum dose

Embryo / Fetal Development  Rat  Intravenous  0.05  NOAEL  Paternal toxicity, Not Teratogenic

**Timolol Maleate**

Embryo / Fetal Development  Rabbit  Oral  100  LOAEL  Fetotoxicity
Embryo / Fetal Development  Rabbit  Oral  50  NOEL  Not Teratogenic

Embryo / Fetal Development  Rat  Oral  50  NOEL  Not Teratogenic

Embryo / Fetal Development  Mouse  Oral  50  NOEL  Not Teratogenic

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

**Latanoprost**

Bacterial Mutagenicity (Ames)  Bacteria  Negative
11. TOXICOLOGICAL INFORMATION

**Carcinogenicity:**

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

**Timolol Maleate**
- **Mouse (In Vivo):** Micronucleus Negative
- **Mouse (In Vivo):** Cytogenetics Negative
- **Mouse (In Vivo):** Cell Transformation Assay Negative

**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

Pfizer Inc believes that the information contained in this Material Safety Data Sheet is accurate, and while it is provided in good faith, it is without warranty of any kind, expressed or implied. If data for a hazard are not included in this document there is no known information at this time.

End of Safety Data Sheet