PT. Pfizer Indonesia
Local Product Document

Generic Name: Latanoprost-Timolol Maleate Ophthalmic Solution
Trade Name: XALACOM®
CDS Effective Date: February 25, 2022
Superseded: September 01, 2016

Special Warning and Special Precaution For Use:
Benzalkonium chloride, which is commonly used as a preservative in ophthalmic products, has been reported to cause punctuate keratopathy and/or toxic ulcerative keratopathy. Since this drug contains benzalkonium chloride, close monitoring is required with frequent or prolonged use in dry eye patients, or in conditions where the cornea is compromised.

Contact Lenses
Patients should be advised not to wear a contact lens if their eye is red. This drug should not be used to treat contact lens related irritation. The preservative in this drug, benzalkonium chloride, may be absorbed by soft contact lenses. Patients who wear soft contact lenses and **whose eyes are not red** should be instructed to wait at least ten minutes after instilling this drug before they insert their contact lenses.

1. NAME OF THE MEDICINAL PRODUCT
XALACOM® eye drops, solution.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
1 mL solution contains latanoprost 50 micrograms and timolol maleate 6.8 mg equivalent to 5 mg timolol.

For excipients, see Section **6.1 List of Excipients**.

3. PHARMACEUTICAL FORM
Eye drops, solution

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications
Reduction of intraocular pressure (IOP) in patients with open-angle glaucoma and ocular hypertension who are insufficiently responsive to timolol or and latanoprost.

4.2 Posology and Method of Administration
Recommended dosage for adults (including the elderly):
Recommended therapy is one eye drop in the affected eye(s) once daily in the morning.
If one dose is missed, treatment should continue with the next dose as planned. The dose should not exceed one drop in the affected eye(s) daily.

Administration:
If more than one topical ophthalmic drug is being used, they should be administered at least five minutes apart.

When using nasolacrimal occlusion or closing the eyelids for 2 minutes, the systemic absorption is reduced. This may result in a decrease in systemic side effects and an increase in local activity.

Use in children and adolescents:
Safety and effectiveness in children and adolescents has not been established.

4.3 Contraindications

- Reactive airway disease including bronchial asthma or a history of bronchial asthma, severe chronic obstructive pulmonary disease.
- Sinus bradycardia, sick sinus syndrome, sino-atrial block, second or third-degree atrioventricular block not controlled with pace-maker, overt cardiac failure, cardiogenic shock.
- Hypersensitivity to the active substances or any of the excipients.

4.4 Special Warnings and Special Precautions for Use
Timolol Maleate

Cardiovascular and Respiratory reactions

The same adverse reactions found with systemic administration of beta-adrenergic blocking agents may occur with their topical administration. Patients with a history of severe cardiac disease should be monitored closely for signs of cardiac failure. The following cardiac and respiratory reactions may occur after topical application of timolol maleate:

- Aggravation of Prinzmetal's angina.
- Aggravation of peripheral and central circulatory disorders.
- Hypotension.
- Cardiac failure resulting in death.
- Severe respiratory reactions, including fatal bronchospasm in patients with asthma.
- Bradycardia.

In patients with cardiovascular diseases (e.g., coronary heart disease, Prinzmetal's angina and cardiac failure) and hypotension therapy with beta-blockers should be critically assessed and the therapy with other active substances should be considered. Patients with cardiovascular diseases should be watched for signs of deterioration of these diseases and of adverse reactions.

Due to its negative effect on conduction time, beta-blockers should only be given with caution to patients with first degree heart block.

Patients with severe peripheral circulatory disturbance/disorders (i.e. severe forms of Raynaud's disease or Raynaud's syndrome) should be treated with caution.

Timolol maleate should be used with caution, in patients with mild/moderate chronic obstructive pulmonary disease (COPD) and only if the potential benefit outweighs the potential risk.

A gradual withdrawal of beta-adrenergic blocking agents prior to major surgery should be considered. Beta-adrenergic blocking agents impair the ability of the heart to respond to beta-adrenergically mediated reflex stimuli, which may augment the risk of general anesthesia in surgical procedures. Protracted severe hypotension during anesthesia and difficulty restarting and maintaining the heartbeat have been reported. During surgery, the effects of beta-adrenergic blocking agents may be reversed by sufficient doses of adrenergic agonists.

Beta-blocking ophthalmological preparations may block systemic beta-agonist effects e.g., of adrenaline. The anesthesiologist should be informed when the patient is receiving timolol.

Hypoglycaemia

Beta-adrenergic blocking agents may increase the hypoglycaemic effect of agents used to treat diabetes, and can mask the signs and symptoms of hypoglycaemia. They should be used with caution in patients with spontaneous hypoglycaemia or diabetes (especially those with labile diabetes), who are receiving insulin or oral hypoglycaemic agents.

Hyperthyroidism

Therapy with beta-adrenergic blocking agents may mask certain signs and symptoms of hyperthyroidism. Abrupt withdrawal of therapy may precipitate a worsening of this condition.

Hypersensitivity reactions

When treated with beta-adrenergic blocking agents, patients with a history of atopy or severe anaphylactic reaction to a variety of allergens may be more reactive to repeated challenge with such allergens. They may be unresponsive to the usual dose of epinephrine used to treat anaphylactic reactions.

Myasthenia gravis

Timolol maleate has been reported to rarely increase muscle weakness in some patients with myasthenia gravis or myasthenic symptoms (e.g., diplopia, ptosis, generalized weakness).

Choroidal detachment and Corneal disease

Choroidal detachment has been reported with administration of aqueous suppressant therapy (e.g., timolol, acetazolamide) after filtration procedures.

Ophthalmic beta-blockers may induce dryness of eyes. Patients with corneal diseases should be treated with caution.

Latanoprost

Iris pigmentation changes

Latanoprost may gradually change the eye colour by increasing the amount of the brown pigment of the iris. Similar to experience with latanoprost eye drops, increased iris pigmentation was seen in 16%-20% of all patients treated with XALACOM® for up to one year (based on photographs). This effect has predominantly been seen in patients with mixed-color irides; i.e. green-brown, yellow-brown or blue/grey-brown, and is due to increased melanin content in the stromal melanocytes of the iris. Typically the brown pigmentation around the pupil spreads concentrically towards the periphery in affected eyes, but the entire iris or parts of it may become more brownish. In patients with homogenously blue, grey, green or brown eyes, the change has only rarely been seen during two years of treatment in clinical trials with latanoprost.

The change in iris colour occurs slowly and may not be noticeable for several months to years and it has not been associated with any symptom or pathological changes. No further increase in brown iris pigment has been observed after discontinuation of treatment, but the resultant colour change may be permanent. Neither nevi nor freckles of the iris have been affected by treatment. Accumulation of pigment in the trabecular meshwork or elsewhere in the anterior chamber has not been observed but patients should be examined regularly and, depending on the clinical situation, treatment may be stopped if increased iris pigmentation ensues. Before treatment is instituted patients should be informed of the possibility of a change in eye colour. Unilateral treatment can result in permanent heterochromia.

The potential for heterochromia exists for patients receiving unilateral treatment.

Eyelid and Eyelash changes

Eyelid skin darkening, which may be reversible, has been reported in association with the use of latanoprost.

Glaucoma

There is no documented experience with latanoprost in inflammatory, neovascular, chronic angle closure or glaucoma, in open angle glaucoma of pseudophakic patients and in pigmentary glaucoma. Latanoprost has no or little effect on the pupil but there is no documented experience in acute attacks of closed angle glaucoma. Therefore it is recommended that XALACOM® should be used with caution in these conditions until more experience is obtained.

Herpetic keratitis

Latanoprost may gradually change eyelashes and vellus hair in the treated eye; these changes include increased length, thickness, pigmentation, and number of lashes or hairs, and misdirected growth of eyelashes. Eyelash changes are reversible upon discontinuation of treatment.

Macular oedema

Macular oedema, including cystoid macular oedema, has been reported during treatment with latanoprost. These reports have mainly occurred in aphakic patients, in pseudophakic patients with torn posterior lens capsule, or in patients with known risk factors for macular oedema. XALACOM® should be used with caution in these patients.

Herpetic keratitis
Latanoprost should be used with caution in patients with a history of herpetic keratitis, and should be avoided in cases of active herpes simplex keratitis and in patients with a history of recurrent herpetic keratitis specifically associated with prostaglandin analogues.

General
Use of Contact Lenses
XALACOM® contains benzalkonium chloride which may be absorbed by contact lenses. This may cause discoloration of soft contact lenses. Benzalkonium chloride may also cause eye irritation. The contact lenses should be removed before instillation of the eye drops and may be reinserted after 15 minutes.

4.5 Interaction with Other Medicinal Products and Other Forms of Interaction
Specific medicinal product interaction studies have not been performed with XALACOM®.

The effect on intraocular pressure or the known effects of systemic beta-blockade may be potentiated when latanoprost-timolol maleate is given to patients already receiving an oral beta-adrenergic blocking agent, and the use of two or more topical beta-adrenergic blocking agents is not recommended.

There have been reports of paradoxical elevations in IOP following the concomitant ophthalmic administration of two prostaglandin analogs. Therefore, the use of two or more prostaglandins, prostaglandin analogs, or prostaglandin derivatives is not recommended.

Mydriasis has occasionally been reported when timolol maleate was given with epinephrine.

There is a potential for additive effects resulting in hypotension and/or marked bradycardia when eye drops with timolol are administered concomitantly with oral calcium channel blockers, beta-adrenergic blocking agents, antiarrhythmics (including amiodarone), digitalis glycosides, parasympathomimetics or guanethidine.

Potentiated systemic beta blockade (e.g., decreased heart rate, depression) has been reported during combined treatment with CYP2D6 inhibitors (e.g., quinidine, fluoxetine, paroxetine) and timolol.

The hypertensive reaction to sudden withdrawal of clonidine can be potentiated when taking beta-blockers.

Beta-blockers may increase the hypoglycaemic effect of antidiabetic agents. Beta-blockers can mask the signs and symptoms of hypoglycaemia (see Section 4.4 – Timolol Maleate).

4.6 Fertility, Pregnancy and Lactation

Fertility:
Latanoprost has not been found to have any effect on male or female fertility in animal studies. Timolol showed no effects on male and female fertility in rats or teratogenic potential in mice, rats and rabbits (see Section **5.3 Preclinical Safety Data**).

Pregnancy:
Latanoprost
There are no adequate and well-controlled studies in pregnant women. Studies in animal have shown reproductive toxicity (see Section **5.3 Preclinical Safety Data**). The potential risk for humans is unknown.

Timolol
Well–controlled epidemiological studies with systemic use of beta-blockers did not indicate malformative effects, but some pharmacological effects such as bradycardia have already been observed in foetuses or neonates.

Consequently XALACOM® should not be used during pregnancy (see Section **5.3 Preclinical Safety Data**).

Lactation:
Timolol is excreted into breast milk**.** Latanoprost and its metabolites may pass into breast milk. Because of the potential for serious adverse reactions in nursing infants, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother. XALACOM® should therefore not be used in women who are breast feeding.

4.7 Effects on Ability to Drive and Use Machines
Instillation of eye drops may cause transient blurring of vision. Until this has resolved, patients should not drive or use machines.

4.8 Undesirable Effects

Latanoprost / timolol Maleate:

The following adverse drug reactions have been observed in clinical trials with latanoprost / timolol maleate.

Adverse Drug Reaction Table 1: ADRs by SOC and CIOMS frequency category for latanoprost / timolol maleate listed in order of decreasing medical seriousness or clinical importance within each frequency category and SOC.

System Organ Class	Common ≥ 1/100 to < 1/10	Uncommon ≥ 1/1,000 to < 1/100	Frequency not known (cannot be estimated from the available data)
Nervous system disorders	Headache		
Eye Disorders	Corneal disorder,	Conjunctival	Abnormal vision,

System Organ Class	Common ≥ 1/100 to < 1/10	Uncommon ≥ 1/1,000 to < 1/100	Frequency not known (cannot be estimated from the available data)
	Keratitis, Conjunctivitis, Blepharitis, Eye pain, Eye irritation, Eye hyperaemia, Iris hyperpigmentation	disorder Hypertrichosis (eyelash and vellus hair changes of the eyelid; increased length, thickness, pigmentation, and number of eyelashes), Photophobia	Errors of refraction
Vascular disorders	Hypertension		
Skin and subcutaneous tissue disorders		Rash, Skin disorder	

The following are adverse events that have been observed in clinical trials with latanoprost / timolol maleate.

Infections and infestations: infection, sinusitis, upper respiratory tract infection

Metabolism and nutrition disorders: diabetes mellitus, hypercholesterolemia

Psychiatric disorders: depression

Eye disorders: cataract, visual field defect

Musculoskeletal and connective tissue disorders: arthritis

Latanoprost:

Additional adverse drug reactions have been observed in clinical trials and postmarketing with the single component latanoprost.

Adverse Drug Reaction Table 2: Latanoprost

System Organ Class	Adverse Drug Reactions
Infections and infestations	Herpetic keratitis*
Nervous system disorders	Dizziness*

Adverse Drug Reaction Table 2: Latanoprost

System Organ Class	Adverse Drug Reactions
Eye disorders	Macular oedema including cystoid macular oedema*; corneal erosion*; punctate keratitis*; corneal oedema*; uveitis*; iritis*; pseudopemphigoid of ocular conjunctiva*; trichiasis*; photophobia*; eye irritation (burning, grittiness, itching, stinging and foreign body sensation); vision blurred*; eyelid oedema; eyelash and vellus hair changes of the eyelid (increased length, thickness, pigmentation, and number of eyelashes)*; localised skin reaction on the eyelids*; iris cyst*; periorbital and lid changes resulting in deepening of the eyelid sulcus*; darkening of the palpebral skin of the eyelids*
Cardiac disorders	Angina unstable*, angina*; palpitations*
Respiratory, thoracic and mediastinal disorders	Acute asthma attacks*, asthma aggravation*; asthma*; dyspnoea*
Gastrointestinal disorders	Vomiting*; nausea*
Skin and subcutaneous tissue disorders	Rash; pruritus*
Musculoskeletal and connective tissue disorders	Myalgia*; arthralgia*
General disorders and administration site conditions	Chest pain*

*ADR identified post-marketing

Timolol Maleate (Ocular Administration):

Additional adverse drug reactions have been observed with the single component timolol maleate when used by ocular administration

Adverse Drug Reaction Table 3: Timolol Maleate (ocular administration)

System Organ Class	Adverse Drug Reactions
Immune system disorders	Signs and symptoms of systemic allergic reactions including anaphylaxis; angioedema; urticaria; pruritus; localised and generalised rash
Metabolism and nutrition disorders	Masked symptoms of hypoglycaemia in diabetic patients; anorexia
Psychiatric disorders	Behavioral changes and psychic disturbances including, confusion, hallucinations, anxiety, disorientation, nervousness, and memory loss; insomnia; depression; nightmares
Nervous system disorders	Cerebral vascular accident; cerebral ischemia; dizziness; increase in signs and symptoms of myasthenia gravis;

Adverse Drug Reaction Table 3: Timolol Maleate (ocular administration)

System Organ Class	Adverse Drug Reactions
	paraesthesia; somnolence; headache; syncope
Eye disorders	Cystoid macular edema; choroidal detachment following filtration surgery; corneal erosion; keratitis; diplopia; decreased corneal sensitivity; signs and symptoms of ocular irritation (e.g., burning, stinging, itching, tearing, redness); dry eyes; ptosis; blepharitis; visual disturbances including refractive changes; vision blurred
Ear and labyrinth disorders	Tinnitus
Cardiac disorders	Cardiac arrest; cardiac failure; heart block; atrioventricular block; congestive heart failure; worsening of angina pectoris; arrhythmia; bradycardia; palpitation
Vascular disorders	Claudication; cold hands and feet; hypotension; Raynaud's phenomenon
Respiratory, thoracic and mediastinal disorders	Respiratory failure; pulmonary oedema; bronchospasm (predominantly in patients with pre-existing bronchospastic disease); cough; dyspnoea; nasal congestion
Gastrointestinal disorders	Retroperitoneal fibrosis; abdominal pain; vomiting; diarrhoea; dry mouth; dysgeusia; dyspepsia; nausea
Skin and subcutaneous tissue disorders	Rash; psoriasiform rash; pseudopemphigoid; exacerbation of psoriasis; alopecia
Musculoskeletal and connective tissue disorders	Myalgia, systemic lupus erythematosus
Reproductive system and breast disorders	Sexual dysfunction; decreased libido; impotence; Peyronie's disease
General disorders and administration site conditions	Chest pain; oedema; asthenia; fatigue

Adverse reactions reported with the use of eyedrops containing phosphate buffers

Cases of corneal calcification have been reported very rarely in association with the use of phosphate-containing eye drops in some patients with significantly damaged corneas.

4.9 Overdose
No data are available in humans with regards to overdose with XALACOM®.

Timolol Maleate:
Symptoms of systemic timolol overdose are: dizziness, headache, bradycardia, hypotension, broncospasm and cardiac arrest. If such symptoms occur the treatment should be symptomatic and supportive.

An *in vitro* hemodialysis study demonstrated that timolol was readily dialyzed from human plasma or whole blood.

Studies have shown that timolol does not dialysis readily.

Latanoprost:
Apart from ocular irritation and conjunctival hyperaemia no other ocular or systemic side effects are known if latanoprost is overdosed.

If latanoprost is accidentally ingested orally the following information may be useful: Treatment gastric lavage if needed. Intravenous infusion of 3 micrograms/kg in healthy volunteers induced no symptoms but a dose of 5.5 -10 micrograms/kg caused nausea, abdominal pain, dizziness, fatigue, hot flushes and sweating. If overdosage with X ALACOM® occurs, treatment should be symptomatic.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic Properties
Pharmacodynamic group:
Opthalmological-beta blocking agents-timolol, combinations.
ATC code: S01ED51.

Mechanism of Action:
XALACOM® consists of two components: latanoprost and timolol maleate. These two components decrease elevated Intra Ocular Pressure (IOP) by different mechanisms of action and the combined effect results in additional IOP reduction compared to either compound administered alone.

Latanoprost:
The active substance latanoprost, a prostaglandin $F_{2\alpha}$ analogue, is a selective prostanoid FP receptor agonist that reduces the IOP by increasing the outflow of aqueous humor. The main mechanism of action is increased uveoscleral outflow. Additionally, some increase in outflow facility (decrease in trabecular outflow resistance) has been reported in man.

Latanoprost has no significant effect on the production of aqueous humour, the blood-aqueous barrier or the intraocular blood circulation.

Chronic treatment with latanoprost in monkey eyes which had undergone extracapsular lens extraction did not affect the retinal blood vessels as determined by fluorescein angiography.

Latanoprost has not induced fluorescein leakage in the posterior segment of pseudophakic human eyes during short-term treatment.

Timolol Maleate:
Timolol is a beta-1 and beta-2 (non-selective) adrenergic receptor blocking agent that has no significant intrinsic sympathomimetic, direct myocardial depressant, or local anesthetic (membrane-stabilizing) activity.

Timolol lowers IOP by decreasing the formation of aqueous in the ciliary epithelium. The precise mechanism of action is not clearly established, but inhibition of the increased cyclic

AMP synthesis caused by endogenous beta-adrenergic stimulation is probable. Timolol has not been found to significantly affect the permeability of the blood-aqueous barrier to plasma proteins. In rabbits, timolol was without effect on the regional ocular blood flow after chronic treatment.

Pharmacodynamics effects
Clinical Effects:
In dose finding studies, XALACOM® produced significantly greater decreases in mean diurnal IOP compared to latanoprost and timolol maleate administered once daily as monotherapy. In two well controlled, double masked six-month clinical studies the IOP reducing effect of XALACOM® was compared with latanoprost and timolol maleate monotherapy in patients with an IOP of at least 25 mmHg or greater. Following a 2 to 4 week run-in with timolol maleate (mean decrease in IOP from enrollment of 5 mmHg), additional decreases in mean diurnal IOP of 3.1, 2.0 and 0.6 mmHg were observed after 6-months of treatment with XALACOM® and latanoprost and timolol maleate (twice daily), respectively. The IOP lowering effect of X ALACOM® was maintained in a 6-month open label extension of these studies.

Onset of action of XALACOM® is within one hour and maximal effect occurs within six to eight hours. Adequate IOP reducing effect has been shown to be present up to 24 hours post-dosage after multiple treatments.

5.2 Pharmacokinetics Properties

Latanoprost

Absorption:
Latanoprost is an isopropyl ester prodrug, which *per se* is inactive but after hydrolysis by esterases in the cornea to the acid of latanoprost, becomes biologically active. The prodrug is well absorbed through the cornea and all drug that enters the aqueous humour is hydrolysed during the passage through the cornea. Studies in man indicate that the maximum concentration in the aqueous humour, approximately 15-30 ng/mL, is reached about two hours after topical administration of latanoprost alone.

Distribution:
After topical application in monkeys latanoprost is distributed primarily in the anterior segment, the conjunctivae and the eye lids.

The acid of latanoprost has a plasma clearance of 0.40 L/h/kg and a small volume of distribution, 0.16 L/h/kg, resulting in a rapid half-life in plasma, 17 minutes. After topical ocular administration the systemic bioavailability of the acid of latanoprost is 45%. The acid of latanoprost has a plasma protein binding of 87%.

Metabolism:
There is practically no metabolism of the acid of latanoprost in the eye. The main metabolism occurs in the liver. The main metabolites, the 1,2-dinor and 1,2,3,4-tetranor metabolites, exert no or only weak biological activity in animal studies and are excreted primarily in the urine.

Excretion:
The elimination of the acid of latanoprost from human plasma is rapid ($t_{1/2}$ =17 min) after both intravenous and topical administration. Systemic clearance is approximately 7 mL/min/kg. Following hepatic β-oxidation, the metabolites are mainly eliminated via the kidneys. Approximately 88% and 98% of the administered dose is recovered in the urine after topical and intravenous dosing, respectively.

Timolol Maleate
The maximum concentration of timolol maleate in the aqueous humor is reached about one hour after topical administration of eye drops. Part of the dose is absorbed systemically and a maximum plasma concentration of 1 ng/mL is reached 10 to 20 minutes after topical administration of one eye drop to each eye once daily (300 micrograms/day). The half-life of timolol maleate in plasma is about six hours. Timolol maleate is extensively metabolized in the liver. The metabolites are excreted in the urine together with some unchanged timolol maleate.

XALACOM®
No pharmacokinetic interactions between latanoprost and timolol maleate were observed, although there was an approximate two-fold increased concentration of the acid of latanoprost in aqueous humour 1 to 4 hours after administration of XALACOM® compared to monotherapy.

5.3 Preclinical Safety Data
The ocular and systemic safety profile of the individual components is well established. No adverse ocular or systemic effects were seen in rabbits treated topically with the fixed combination or with concomitantly administered latanoprost and timolol ophthalmic solutions. Safety pharmacology, genotoxicity and carcinogenicity studies with each of the components revealed no special hazards for humans. Latanoprost did not affect corneal wound healing in the rabbit eye, whereas timolol inhibited the process in the rabbit and the monkey eye when administered more frequently than once a day.

For Latanoprost, no effects on male and female fertility in rats and no teratogenic potential in rats and rabbits have been established. No embryotoxicity was observed in rats after intravenous doses of up to 250 micrograms/kg/day. However, latanoprost caused embryofetal toxicity, characterized by increased incidence of late resorption and abortion and by reduced foetal weight, in rabbits at intravenous doses of 5 micrograms/kg/day (approximately 100 times the clinical dose) and above.

Timolol showed no effects on male and female fertility in rats or teratogenic potential in mice, rats and rabbits.

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients
Sodium chloride.
Benzalkonium chloride.
Sodium dihydrogen phosphate monohydrate.
Disodium phosphate anhydrous.

Water for injection

6.2 Incompatibilities
In vitro studies have shown that precipitation occurs when eye drops containing thiomersal are mixed with XALACOM®. If such drugs are used concomitantly with XALACOM®, the eye drops should be administered with an interval of at least five minutes.

6.3 Shelf-life
3 years
After opening of container: 4 weeks.

6.4 Special Precautions for Storage
Store at temperature 2°C - 8°C. Protect from light.
After first opening the container, store at or below 25°C and use within four weeks.

6.5 Instruction for Use and Handling
The tamper evident overcap should be removed before use.

Supply
XALACOM® Eye Drops; Box, plastic bottle @ 2.5 mL; DKI0386101146A1

HARUS DENGAN RESEP DOKTER

Manufactured by:
Pfizer Manufacturing Belgium NV/SA
Rijksweg 12, 2870 Puurs, Belgium

Imported by:
PT. Pfizer Indonesia
Jakarta, Indonesia

Leaflet kemasan: Informasi untuk pengguna

XALACOM® 50 mcg/ml dan 5 mg/ml obat tetes mata, larutan

Latanoprost-Timolol Maleat

Baca semua bagian leaflet ini dengan cermat sebelum mulai menggunakan obat ini karena berisi informasi penting bagi Anda.
- Simpan leaflet ini. Anda mungkin perlu membacanya kembali.
- Jika Anda memiliki pertanyaan lebih lanjut, tanyakan kepada dokter, apoteker, atau perawat Anda.
- Obat ini telah diresepkan hanya untuk Anda. Jangan memberikannya kepada orang lain. Obat ini dapat membahayakan mereka, sekali pun gejala-gejala penyakit mereka sama dengan Anda.
- Jika Anda mengalami efek samping apa pun, konsultasikan dengan dokter, apoteker, atau perawat Anda. Termasuk setiap kemungkinan efek samping yang tidak tercantum dalam leaflet ini. Lihat bagian 8.

Isi leaflet ini:
1. Nama produk
2. Deskripsi produk
3. Apa kandungan obat ini?
4. Kekuatan obat
5. Apa kegunaan obat ini?
6. Berapa banyak dan seberapa sering Anda seharusnya menggunakan obat ini? Apa yang harus dilakukan jika ada dosis yang terlewat?
7. Kapan seharusnya Anda tidak menggunakan obat ini?
8. Apa yang harus dipertimbangkan saat menggunakan obat ini?
9. Apa saja obat lain atau makanan yang harus dihindari selama menggunakan obat ini?
10. Apakah obat tersebut aman bagi ibu hamil dan menyusui?
11. Apakah pasien diizinkan mengemudi dan mengoperasikan mesin saat menggunakan obat ini?
12. Apa saja potensi efek yang tidak diinginkan dari penggunaan obat ini?
13. Tanda-tanda dan gejala-gejala overdosis
14. Apa yang harus dilakukan jika Anda menggunakan lebih dari dosis yang dianjurkan?
15. Bagaimana cara menyimpan obat ini?
16. Nomor Izin Edar
17. Nama produsen/importir/Pemilik Izin Edar
18. Tanggal revisi
19. Peringatan khusus

1. Nama produk

XALACOM® obat tetes mata, larutan.

2. Deskripsi produk

XALACOM® berisi dua jenis obat yaitu latanoprost dan timolol. Latanoprost termasuk dalam golongan obat yang disebut sebagai analog prostaglandin. Timolol termasuk dalam golongan obat yang disebut sebagai penghambat beta.

3. Apa kandungan obat ini?

1 ml larutan mengandung latanoprost 50 mikrogram dan timolol maleat 6,8 mg yang setara dengan 5 mg timolol.

4. Kekuatan obat

Latanoprost 50 mikrogram/ml dan timolol maleate 5 mg/ml

5. Apa kegunaan obat ini?

XALACOM® digunakan untuk mengurangi tekanan di dalam mata Anda jika Anda mengalami kondisi yang dikenal dengan istilah glaukoma sudut terbuka atau hipertensi okular. Kedua kondisi ini dikaitkan dengan peningkatan tekanan di dalam mata Anda yang pada akhirnya memengaruhi penglihatan Anda. Dokter Anda biasanya akan meresepkan XALACOM® untuk Anda jika pengobatan menggunakan Latanoprost dan atau timolol maleate tidak responsif.

6. Berapa banyak dan seberapa sering Anda seharusnya menggunakan obat ini? Apa yang harus dilakukan jika ada dosis yang terlewat?

Gunakan obat ini tepat sesuai anjuran dokter atau apoteker Anda. Tanyakan kepada dokter atau apoteker jika Anda merasa tidak yakin.

Dosis yang dianjurkan untuk dewasa (termasuk lansia) adalah satu tetes sekali sehari di pagi hari pada mata yang sakit.

Jangan menggunakan XALACOM® lebih dari sekali sehari, karena efektivitas pengobatannya dapat menurun jika Anda menggunakannya lebih sering.

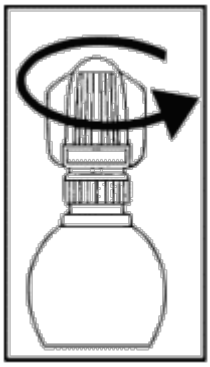
Gunakan XALACOM® sesuai arahan dokter Anda hingga dokter memberi tahu Anda untuk menghentikannya.

Pengguna lensa kontak

Jika Anda memakai lensa kontak, Anda harus melepaskannya sebelum menggunakan XALACOM®. Setelah menggunakan XALACOM® Anda harus menunggu selama 15 menit sebelum memasang lensa kontak Anda kembali.

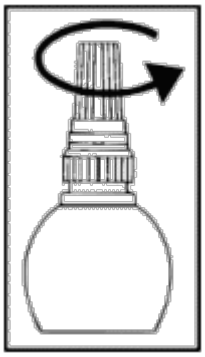
Petunjuk penggunaan

1. Cuci kedua tangan Anda dan duduklah atau berdirilah dengan nyaman.
2. Putar penutup luarnya hingga terlepas (dapat dibuang).



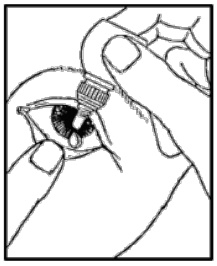
Gambar 1

3. Buka sungkup pelindung dalam. Sungkup pelindung harus tetap disimpan.



Gambar 2

4. Gunakan jari Anda untuk menarik kelopak mata bawah dengan lembut pada mata yang sakit.
5. Dekatkan ujung botol tetapi jangan sampai menyentuh mata Anda.
6. Pencet botol perlahan sehingga hanya satu tetes yang masuk ke dalam mata Anda, lalu lepaskan kelopak mata bawah.



Gambar 3

7. Setelah menggunakan XALACOM®, tekan sudut mata Anda di dekat hidung menggunakan satu jari (gambar 4) selama 2 menit. Langkah ini membantu menghentikan latanoprost + timolol agar tidak masuk ke bagian tubuh Anda lainnya.

Gambar 4

8. Ulangi pada mata yang lainnya jika dokter memerintahkan Anda untuk melakukannya.
9. Pasang kembali sungkup pelindung dalam pada botol.

Jika Anda menggunakan XALACOM® bersama obat tetes mata lainnya

Tunggu minimal 5 menit setelah menggunakan XALACOM® dan lanjutkan dengan menggunakan obat tetes mata lainnya.

Jika XALACOM® tertelan

Jika XALACOM® tidak sengaja tertelan, Anda harus menghubungi dokter Anda untuk meminta saran. Jika XALACOM® yang tertelan cukup banyak, Anda dapat merasa mual, sakit perut, merasa lelah, wajah memerah, pusing, dan mulai berkeringat.

Jika Anda lupa menggunakan XALACOM®

Lanjutkan dengan dosis normal pada waktu yang semestinya. Jangan menggunakan dosis ganda untuk mengejar dosis yang terlewatkan. Jika Anda merasa ragu, konsultasikan dengan dokter atau apoteker Anda.

7. Kapan seharusnya Anda tidak menggunakan obat ini?

Jangan menggunakan XALACOM®
- jika Anda alergi (hipersensitif) terhadap obat mana pun yang terkandung di dalam XALACOM® (latanoprost atau timolol), penghambat beta, atau bahan apa pun yang terkandung di dalam XALACOM® (dicantumkan di bagian 3)
- jika saat ini Anda menderita atau sebelumnya pernah menderita gangguan pernapasan seperti asma, bronkitis obstruktif kronis berat (penyakit paru berat yang dapat menyebabkan mengi, kesulitan bernapas, dan/atau batuk berkepanjangan)
- jika Anda mengalami gangguan jantung berat atau kelainan irama jantung

8. Apa yang harus dipertimbangkan saat menggunakan obat ini?

Peringatan dan tindakan pencegahan

Konsultasikan dengan dokter atau apoteker Anda sebelum menggunakan XALACOM® jika saat ini Anda menderita atau sebelumnya pernah menderita:
- penyakit jantung koroner (gejalanya antara lain dapat berupa nyeri dada atau dada rasa tertekan, sesak napas, atau tersedak), gagal jantung, tekanan darah rendah
- gangguan denyut jantung seperti denyut jantung lambat
- gangguan pernapasan, asma, atau penyakit paru obstruktif kronis
- penyakit sirkulasi darah yang buruk (seperti penyakit Raynaud atau sindrom Raynaud)
- diabetes karena timolol dapat menyamarkan tanda-tanda dan gejala-gejala gula darah rendah
- aktivitas kelenjar tiroid yang berlebihan karena timolol dapat menyamarkan tanda-tanda dan gejalanya
- Anda akan menjalani pembedahan mata apa pun (termasuk bedah katarak) atau Anda pernah menjalani pembedahan mata apa pun sebelumnya
- Anda menderita gangguan mata (seperti nyeri mata, iritasi mata, peradangan mata, atau penglihatan kabur)
- Anda mengetahui bahwa Anda menderita mata kering
- Anda mengenakan lensa kontak. Anda tetap dapat menggunakan XALACOM®, tetapi ikuti petunjuk untuk pengguna lensa kontak di bagian 6
- Anda mengetahui bahwa Anda menderita angina (khususnya jenis yang disebut sebagai Prinzmetal angina)

- Anda mengetahui bahwa Anda menderita reaksi alergi berat yang biasanya memerlukan perawatan di rumah sakit
- Anda pernah menderita atau saat ini menderita infeksi virus pada mata yang disebabkan oleh virus herpes simpleks (HSV)

9. Apa saja obat lain atau makanan yang harus dihindari selama menggunakan obat ini?

Beri tahu dokter atau apoteker jika Anda menggunakan, baru saja menggunakan, atau mungkin menggunakan obat-obatan lain, termasuk obat tetes mata dan obat-obatan yang diperoleh tanpa resep dokter.

XALACOM® dapat memengaruhi atau dipengaruhi oleh obat-obatan lain yang Anda gunakan, termasuk obat tetes mata lainnya, untuk mengobati glaukoma. Beri tahu dokter Anda jika Anda sedang menggunakan atau bermaksud untuk menggunakan obat-obatan untuk menurunkan tekanan darah, obat jantung, atau obat-obatan untuk mengobati diabetes.

Secara khusus, konsultasikan dengan dokter atau apoteker Anda jika Anda mengetahui bahwa Anda sedang menggunakan jenis obat mana pun berikut ini:
- Prostaglandin, analog prostaglandin, atau turunan prostaglandin
- Penghambat beta
- Epinefrin
- Obat-obatan yang digunakan untuk mengobati tekanan darah tinggi seperti penghambat saluran kalsium oral, guanetidin, antiaritmia, glikosida digitalis, atau parasimpatomimetik
- Kuinidin (digunakan untuk mengobati kondisi jantung dan beberapa jenis malaria)
- Antidepresan yang dikenal dengan nama fluoksetin dan paroksetin

10. Apakah Obat tersebut aman bagi ibu hamil dan menyusui?

Kehamilan

Jangan menggunakan XALACOM® jika Anda sedang hamil kecuali jika dokter Anda menganggapnya perlu. Beri tahu dokter Anda segera jika Anda sedang hamil, mengira diri Anda hamil, atau berencana untuk hamil.

Menyusui

Jangan menggunakan XALACOM® jika Anda sedang menyusui. XALACOM® dapat dialirkan melalui ASI. Mintalah saran dari dokter Anda sebelum menggunakan obat apa pun selama menyusui.

Kesuburan

Latanoprost dan timolol telah terbukti tidak berpengaruh terhadap kesuburan dalam penelitian terhadap hewan jantan atau betina.

11. Apakah pasien diizinkan mengemudi dan mengoperasikan mesin saat menggunakan obat ini?

Mengemudi dan menggunakan mesin

Saat Anda menggunakan XALACOM® penglihatan Anda mungkin akan menjadi kabur selama beberapa saat. Jika Anda mengalami hal ini, jangan mengemudi atau menggunakan peralatan atau mesin apa pun hingga penglihatan Anda jelas kembali.

XALACOM® mengandung benzalkonium klorida dan bufer fosfat

Obat ini mengandung 0,2 mg benzalkonium klorida dalam setiap mililiter.

Benzalkonium klorida dapat diserap oleh lensa kontak lunak dan dapat mengubah warna lensa kontak. Anda harus melepaskan lensa kontak sebelum menggunakan obat ini dan memasangnya kembali 15 menit sesudahnya.

Benzalkonium klorida juga dapat menyebabkan iritasi mata, khususnya jika Anda menderita mata kering atau kelainan pada kornea (lapisan bening di bagian depan mata). Jika Anda merasakan sensasi mata yang tidak normal, sensasi tersengat atau nyeri pada mata setelah menggunakan obat ini, konsultasikan dengan dokter Anda.

Obat ini mengandung 6,3 mg fosfat dalam setiap mililiter yang setara dengan 0,2 mg per tetes.

Jika Anda menderita kerusakan berat pada lapisan bening di bagian depan mata (kornea), dalam kasus yang sangat jarang terjadi, fosfat dapat menyebabkan bercak keruh pada kornea akibat penumpukan kalsium selama pengobatan.

12. Apa saja potensi efek yang tidak diinginkan dari penggunaan obat ini?

Seperti obat-obatan lainnya, obat ini dapat menimbulkan efek samping, sekali pun tidak semua orang mengalaminya.

Anda biasanya tetap dapat melanjutkan penggunaan obat tetes mata, kecuali jika efeknya serius. Jika Anda khawatir, konsultasikan dengan dokter atau apoteker. Jangan berhenti menggunakan XALACOM® tanpa berkonsultasi dengan dokter Anda terlebih dahulu.

Yang tertera di bawah ini adalah efek samping yang diketahui dari penggunaan XALACOM®. Efek samping yang paling penting adalah kemungkinan perubahan permanen yang bertahap pada warna mata Anda. Ada kemungkinan juga XALACOM® menimbulkan perubahan serius dalam mekanisme kerja jantung Anda. Jika Anda mengalami perubahan denyut jantung atau fungsi jantung, Anda harus berkonsultasi dengan dokter dan memberi tahu mereka bahwa Anda telah menggunakan XALACOM®.

Berikut ini adalah efek samping yang diketahui dari penggunaan XALACOM®:

Umum (dapat dialami hingga 1 di antara 10 orang):

- Perubahan bertahap pada warna mata Anda dengan meningkatnya kadar pigmen coklat dalam bagian mata Anda yang berwarna yang disebut sebagai iris. Jika Anda memiliki mata dengan warna campuran (biru-cokelat, abu-abu-cokelat, kuning-cokelat, atau hijau-cokelat) semakin besar kemungkinan Anda mengalami perubahan ini dibandingkan jika Anda memiliki mata dengan satu warna (biru, abu-abu, hijau, atau cokelat). Perubahan

apa pun pada warna mata Anda mungkin membutuhkan waktu hingga bertahun-tahun. Perubahan warna mata bisa bersifat permanen dan akan semakin terlihat jika Anda menggunakan XALACOM® hanya pada satu mata. Tampaknya tidak ada masalah yang berhubungan dengan perubahan warna mata. Perubahan warna mata tidak akan berlanjut setelah pengobatan dengan XALACOM® dihentikan.
- Iritasi mata (rasa panas, sensasi pasir dalam mata, gatal, sensasi tersengat, atau seperti ada benda asing di dalam mata) dan nyeri mata.
- Sakit kepala
- Peningkatan tekanan darah
- Kemerahan pada mata, infeksi mata (konjungtivitis), mata berair, peradangan kelopak mata, iritasi, atau gangguan permukaan mata

Tidak umum (dapat dialami hingga 1 di antara 100 orang):
- Ruam kulit
- Kelainan konjungtiva (kemerahan dan iritasi hingga kotoran mata, kelopak mata membengkak, sensasi panas, dan nyeri)
- Hipertrikosis (perubahan bulu mata dan rambut vellus pada kelopak mata; bertambahnya panjang, ketebalan, pigmentasi, dan jumlah bulu mata),
- Sensitivitas terhadap cahaya (fotofobia)

Frekuensi tidak diketahui (tidak dapat diperkirakan dari data yang tersedia):
- Penglihatan tidak normal
- Kesalahan refraksi (penglihatan kabur)

Efek samping lainnya

Meskipun tidak terlihat dalam penggunaan XALATAN®, efek samping tambahan berikut telah dijumpai dalam penggunaan obat-obatan yang terkandung di dalam XALACOM® (latanoprost dan timolol) sehingga mungkin saja terjadi jika Anda menggunakan XALACOM®. Efek samping yang dicantumkan mencakup reaksi yang terlihat dalam golongan penghambat beta (mis., timolol) jika digunakan untuk mengobati kondisi mata:
- Munculnya infeksi virus pada mata yang disebabkan oleh virus herpes simpleks (HSV).
- Reaksi alergi umum yang mencakup pembengkakan di bawah kulit yang terjadi di area seperti wajah dan anggota gerak dan dapat menghambat jalan napas yang dapat mengakibatkan kesulitan menelan atau bernapas, kaligata atau ruam gatal, ruam lokal dan menyebar, gatal-gatal, reaksi alergi berat yang terjadi tiba-tiba dan mengancam jiwa.
- Kadar gula darah rendah.
- Pusing.
- Sulit tidur (insomnia), depresi, mimpi buruk, kehilangan memori, halusinasi.
- Pingsan, stroke, menurunnya pasokan darah ke otak, meningkatnya tanda-tanda dan gejala-gejala miastenia gravis (kelainan otot), sensasi yang tidak biasa seperti kesemutan, dan sakit kepala.
- Pembengkakan pada bagian belakang mata (edema makular), kista berisi cairan di dalam bagian mata yang berwarna (kista iris), sensitivitas terhadap cahaya (fotofobia), mata terlihat cekung (peningkatan kedalaman sulkus mata).
- Tanda-tanda dan gejala-gejala iritasi mata (misalnya rasa panas, sensasi tersengat, gatal-gatal, berair, kemerahan), peradangan kelopak mata, peradangan pada kornea, penglihatan kabur, dan terlepasnya lapisan di bawah retina yang mengandung pembuluh darah setelah

pembedahan filtrasi yang dapat menyebabkan gangguan penglihatan, penurunan sensitivitas kornea, mata kering, erosi kornea (kerusakan pada lapisan depan bola mata), kelopak mata atas terkulai (sehingga membuat mata tertutup sebagian), penglihatan ganda.
- Menggelapnya kulit di sekeliling mata, perubahan pada bulu mata dan rambut-rambut halus di sekeliling mata (meningkatnya jumlah, panjang, ketebalan, dan kegelapan), perubahan arah pertumbuhan bulu mata, pembengkakan di sekeliling mata, pembengkakan bagian berwarna pada mata (iritis/uveitis), jaringan parut pada permukaan mata.
- Telinga berdenging (tinitus).
- Angina, memburuknya angina pada pasien yang sudah menderita penyakit jantung
- Denyut jantung lambat, nyeri dada, palpitasi (bisa merasakan irama jantung), edema (penumpukan cairan), perubahan pada irama atau kecepatan detak jantung, gagal jantung kongestif (penyakit jantung disertai sesak napas dan pembengkakan kaki dan tungkai akibat penumpukan cairan), sejenis gangguan irama jantung, serangan jantung, gagal jantung.
- Tekanan darah rendah, peredaran darah yang buruk sehingga membuat jari-jari tangan dan kaki kebas dan pucat, telapak tangan dan kaki terasa dingin.
- Sesak napas, penyempitan jalan napas pada paru (terutama pada pasien yang sebelumnya sudah menderita penyakit), kesulitan bernapas, batuk, asma, memburuknya asma.
- Gangguan indra perasa, mual, gangguan pencernaan, diare, mulut kering, sakit perut, muntah.
- Rambut rontok, ruam kulit disertai munculnya bercak putih keperakan (ruam psoriasiform) atau memburuknya psoriasis, ruam kulit.
- Nyeri sendi, nyeri otot yang bukan disebabkan oleh olahraga, kelemahan otot, kelelahan.
- Disfungsi seksual, menurunnya libido.

Dalam kasus yang sangat jarang terjadi, sebagian pasien dengan kerusakan berat pada lapisan bening di bagian depan mata (kornea) mengalami kemunculan bercak keruh pada kornea akibat penumpukan kalsium selama pengobatan.

Melaporkan efek samping
Jika Anda mengalami efek samping apa pun, konsultasikan dengan dokter, apoteker, atau perawat Anda. Termasuk setiap kemungkinan efek samping yang tidak tercantum dalam leaflet ini. Dengan melaporkan efek samping, Anda bisa membantu memberikan informasi lebih lanjut mengenai keamanan obat ini.

13. Tanda-tanda dan gejala-gejala overdosis

Jika Anda meneteskan terlalu banyak obat pada mata Anda, Anda mungkin akan mengalami iritasi ringan dan mata Anda dapat berair dan berubah kemerahan. Kondisi ini akan mereda, tetapi jika Anda khawatir silakan menghubungi dokter Anda untuk meminta saran.

14. Apa yang harus dilakukan jika Anda menggunakan lebih dari dosis yang dianjurkan?

Jika terlihat tanda-tanda dan gejala-gejala overdosis, segera hubungi dokter Anda atau langsung datang ke unit gawat darurat di rumah sakit terdekat. Tunjukkan kepada mereka kemasan XALACOM®.

15. Bagaimana cara menyimpan obat ini?

- Jauhkan obat ini dari pandangan dan jangkauan anak-anak.
- Jangan gunakan obat ini setelah melewati tanggal kedaluwarsa yang tertera pada kemasan luar dan label botol setelah tulisan EXP. Tanggal kedaluwarsa mengacu pada tanggal terakhir di bulan tersebut.
- Simpan pada suhu 2 °C–8 °C. Lindungi dari paparan cahaya.
- Setelah kemasan dibuka untuk pertama kali, simpan pada atau di bawah suhu 25 °C dan gunakan dalam waktu empat minggu.

Jangan buang obat melalui saluran pembuangan air atau bersama sampah rumah tangga. Tanyakan kepada apoteker mengenai cara membuang obat yang sudah tidak digunakan lagi. Langkah-langkah ini akan membantu melindungi lingkungan.

16. Nomor Izin Edar

XALACOM® Obat Tetes Mata; Dus, botol plastik @ 2,5 ml; DKI0386101146A1

17. Nama produsen/importir/Pemegang Hak Pemasaran

Diproduksi oleh:
Pfizer Manufacturing Belgium NV/SA
Rijksweg 12, 2870 Puurs, Belgium

Diimpor oleh:
PT Pfizer Indonesia
Jakarta Indonesia

18. Tanggal revisi

09/2022

19. Peringatan khusus

HARUS DENGAN RESEP DOKTER