

Generic Name: Latanoprost-Timolol Maleate Ophthalmic Solution
Trade Name: XALACOM®
CDS Effective Date: September 01, 2016
Superseded: August 07, 2013
Approved by BPOM: January 16, 2019

**PT. Pfizer Indonesia
Local Product Document**

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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.

Generic Name: Latanoprost-Timolol Maleate Ophthalmic Solution

Trade Name: XALACOM®

CDS Effective Date: September 01, 2016

Superseded: August 07, 2013

Approved by BPOM: January 16, 2019

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.

Generic Name: Latanoprost-Timolol Maleate Ophthalmic Solution

Trade Name: XALACOM®

CDS Effective Date: September 01, 2016

Superseded: August 07, 2013

Approved by BPOM: January 16, 2019

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.

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.

Generic Name: Latanoprost-Timolol Maleate Ophthalmic Solution

Trade Name: XALACOM®

CDS Effective Date: September 01, 2016

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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

Generic Name: Latanoprost-Timolol Maleate Ophthalmic Solution

Trade Name: XALACOM®

CDS Effective Date: September 01, 2016

Superseded: August 07, 2013

Approved by BPOM: January 16, 2019

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 discolouration 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 Medicaments 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

Generic Name: Latanoprost-Timolol Maleate Ophthalmic Solution

Trade Name: XALACOM®

CDS Effective Date: September 01, 2016

Superseded: August 07, 2013

Approved by BPOM: January 16, 2019

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,

Generic Name: Latanoprost-Timolol Maleate Ophthalmic Solution

Trade Name: XALACOM®

CDS Effective Date: September 01, 2016

Superseded: August 07, 2013

Approved by BPOM: January 16, 2019

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*

Generic Name: Latanoprost-Timolol Maleate Ophthalmic Solution
 Trade Name: XALACOM®
 CDS Effective Date: September 01, 2016
 Superseded: August 07, 2013
 Approved by BPOM: January 16, 2019

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*;
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; paraesthesia; somnolence; headache; syncope

Generic Name: Latanoprost-Timolol Maleate Ophthalmic Solution

Trade Name: XALACOM®

CDS Effective Date: September 01, 2016

Superseded: August 07, 2013

Approved by BPOM: January 16, 2019

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

System Organ Class	Adverse Drug Reactions
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; psoriasisiform 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, bronchospasm 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.

Generic Name: Latanoprost-Timolol Maleate Ophthalmic Solution
Trade Name: XALACOM®
CDS Effective Date: September 01, 2016
Superseded: August 07, 2013
Approved by BPOM: January 16, 2019

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:

Ophthalmological-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 mechanism 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_{2α} 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

Generic Name: Latanoprost-Timolol Maleate Ophthalmic Solution
Trade Name: XALACOM®
CDS Effective Date: September 01, 2016
Superseded: August 07, 2013
Approved by BPOM: January 16, 2019

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:

Generic Name: Latanoprost-Timolol Maleate Ophthalmic Solution

Trade Name: XALACOM®

CDS Effective Date: September 01, 2016

Superseded: August 07, 2013

Approved by BPOM: January 16, 2019

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.

Hydrochloric acid solution (for adjustment to pH 6.0)

Generic Name: Latanoprost-Timolol Maleate Ophthalmic Solution
Trade Name: XALACOM®
CDS Effective Date: September 01, 2016
Superseded: August 07, 2013
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Sodium hydroxide solution (for adjustment to pH 6.0)
Water for injection

6.2 Incompatibilities

In vitro studies have shown that precipitation occurs when eye drops containing thiomersal are mixed with XALATAN®. 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