

DUOTRAV[®]
Travoprost 0.004% and timolol 0.5% Eye Drops

Presentation

Duotrav is a combination eye drop containing a topical prostaglandin analogue, travoprost 0.004% and a topical beta-adrenergic receptor blocking agent, timolol maleate 0.68% (equivalent to timolol 0.5%).

Duotrav Eye Drops is a sterile, isotonic aqueous solution of travoprost and timolol maleate with a buffered pH of approximately 6.0 and an osmolality of approximately 290 mOsmol/kg for topical application to the eye.

Uses

Actions

Duotrav contains two active components, travoprost and timolol, which lower intraocular pressure (IOP) by complementary mechanisms of action. Following the administration of Duotrav, the reduction in IOP starts within 30 minutes and the maximum effect is reached after 12 hours. Significant IOP reduction is maintained for at least 24 hours after multiple treatments.

Glaucoma is defined as an optic neuropathy resulting in optic nerve head damage and visual field loss. The pathogenesis of glaucoma is multi-factorial; the primary risk factors, however, are considered to be sustained elevated IOP and poor ocular perfusion. Clinical studies have shown that Duotrav results in additional IOP reduction compared to either component administered alone and that the IOP-lowering effect is comparable to Travatan (travoprost 0.004%) and timolol 0.5% administered concomitantly once daily.

Travoprost: Travoprost is an ester prodrug of a PGF_{2α} analogue and is hydrolysed to the active acid. The free acid is a prostaglandin FP receptor agonist. PGF_{2α} analogues are believed to reduce the intraocular pressure (IOP) by increasing uveoscleral outflow. Reduction of IOP in man starts about 2 hours after administration and maximum effect is reached after twelve hours. Pressure reduction is maintained for at least twenty-four hours. Pivotal clinical studies have demonstrated that Travatan Eye Drops are effective as monotherapy at reducing intraocular pressure. Repeated observations over a period of one year indicate that the IOP-lowering effect of travoprost is well maintained. In addition, travoprost slightly, but significantly, increased optic nerve head blood flow in a single study in rabbits.

Timolol: Timolol maleate is a non-selective β₁- and β₂-adrenergic receptor blocking agent that does not have significant intrinsic sympathomimetic, direct myocardial depressant, or local anaesthetic (membrane stabilising) activity. Timolol lowers IOP by decreasing the formation of aqueous humour in the ciliary epithelium. The precise mechanism of action is not clearly established.

Pharmacokinetics

Absorption: Travoprost and timolol are absorbed through the cornea. Travoprost undergoes rapid ester hydrolysis in the cornea to the active free acid. Following topical ocular administration of Duotrav once-daily in healthy subjects (n=15) for 3 days, the travoprost free acid was not quantifiable in plasma samples from the majority of subjects (80%) and was not detectable in any samples one hour after dosing. In those subjects in whom travoprost free acid was measurable (≥ 0.01 ng/mL, the assay limit of quantitation), plasma concentration ranged from 0.011 to 0.020 ng/mL. The mean peak timolol steady-state concentration was 0.692 ng/mL after once-daily administration of Duotrav. Timolol T_{max} was observed within one hour after dosing.

Distribution: Travoprost free acid can be measured in the aqueous humour during the first few hours in animals and in human plasma only during the first hour after topical ocular administration of Duotrav. Timolol can be measured in human aqueous humour after topical ocular administration of timolol and in plasma for up to 12 hours after topical ocular administration of Duotrav.

Metabolism: The metabolic pathways of the travoprost free acid parallel those of endogenous $PGF_{2\alpha}$ and are characterised by reduction of the 13-14 double bond, oxidation of the 15-hydroxyl group and β -oxidation of the carboxylic acid chain. The plasma elimination of the free acid was rapid with a mean apparent $t_{1/2}$ of approximately 45 minutes. There was no difference in plasma concentrations between Days 1 and 3, indicating lack of drug accumulation following repeated administration of Duotrav. Timolol is extensively metabolised in the liver. The apparent terminal elimination $t_{1/2}$ of timolol in plasma was approximately 4 hours after topical ocular administration of Duotrav.

Excretion: Travoprost free acid and its metabolites are mainly excreted by the kidneys. In humans, less than 2% of a topical ocular dose of travoprost was recovered in urine as free acid. Timolol and its metabolites are primarily excreted by the kidneys. Approximately 20% of a timolol dose is excreted in the urine unchanged and the remainder excreted in urine as metabolites.

Indications

Reduction of elevated intraocular pressure in patients with open angle glaucoma or ocular hypertension for whom single agent therapy provides insufficient intraocular pressure reduction.

Dosage and administration

Recommended dosage for adults (including the elderly)

Instil one drop of Duotrav once daily at about the same time each day in the conjunctival sac of the affected eye(s).

Duotrav should not be given more than once daily because travoprost is most effective at this dosage. If there is inadequate response to Duotrav, consideration should be given to using the individual agents with timolol dosed twice daily.

If more than one topical ophthalmic product is being used, the eye drop products should be administered at least five minutes apart.

Switching to therapy with Duotrav

When substituting another ophthalmic antiglaucoma agent with Duotrav, discontinue the other agent and start the following day with Duotrav.

Contraindications

Duotrav Eye Drops are contraindicated in patients with a known hypersensitivity to travoprost, timolol or any of the excipients in Duotrav (see **List of excipients**).

Duotrav Eye Drops are also contraindicated in pregnant women or women attempting to become pregnant (see **Use in Pregnancy**).

Reactive airway disease including bronchial asthma, a history of bronchial asthma, or severe chronic obstructive pulmonary disease.

Sinus bradycardia, second or third degree atrioventricular block, overt cardiac failure or cardiogenic shock.

Warnings and precautions

Not for injection or oral ingestion.

Cardiovascular/respiratory reaction: Like other topically applied ophthalmic agents, Duotrav may be absorbed systemically. Due to the beta-adrenergic component timolol, the same types of adverse reactions seen with systemic beta-blockers may occur including aggravation of Prinzmetal angina, aggravation of severe peripheral and central circulatory disorders, bradycardia and hypotension.

Respiratory and cardiac reactions, including death due to bronchospasm in patients with asthma and rarely death associated with cardiac failure have been reported following administration of timolol. Cardiac failure should be adequately controlled before treatment.

Anaphylactic reactions: While taking beta-blockers patients with a history of atopy or a history of severe anaphylactic reaction to a variety of allergens may be more reactive to repeated challenge with such allergens, whether accidental, diagnostic or therapeutic. In addition, such patients may be unresponsive to the usual doses of adrenaline used to treat anaphylactic reactions.

Concomitant therapy: Timolol may react with other drugs (see **Interactions**). The effect on IOP or the known effects of systemic beta-blockade may be exaggerated when Duotrav is given to patients already receiving an oral beta-blocking agent. The use of two topical beta-blockers or topical prostaglandins is not recommended.

The use of Duotrav may be considered in patients who require both timolol and travoprost, but it is unknown whether patients who are adequately controlled with timolol given twice

daily plus travoprost given once daily will be as well controlled with Duotrav given once daily. Duotrav should not be used to initiate therapy.

Additional effects of beta-blockade: Beta-blockers should be administered with caution in patients subject to spontaneous hypoglycaemia or to diabetic patients (especially those with labile diabetes) who are receiving insulin or oral hypoglycaemic agents. Beta-blockers may mask the signs and symptoms of acute hypoglycemia.

Therapy with beta-blockers may mask certain symptoms of hyperthyroidism and abrupt withdrawal of therapy may precipitate a worsening of symptoms.

Therapy with beta-blockers may aggravate symptoms of myasthenia gravis.

Ocular effects. Travoprost may gradually change the eye colour by increasing the number of melanosomes (pigment granules) in melanocytes. Before treatment is instituted patients must be informed of the possibility of these changes. Unilateral treatment can result in permanent heterochromia. The long term effects on the melanocytes and any consequences thereof are currently unknown. The change in iris colour occurs slowly and may not be noticeable for months to years. It may be permanent. The change in eye colour has predominantly been seen in patients with mixed coloured irides, i.e. blue-brown, grey-brown, yellow-brown and green-brown; however, it has also been observed in patients with brown eyes. 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. After discontinuation of therapy, no further increase in brown iris pigment has been observed.

Periorbital and/or eyelid skin darkening has been reported in association with the use of Travoprost.

Eyelash changes occurred in over a third of patients treated with Duotrav. These changes include: increased length, thickness, pigmentation, and/or number of lashes.

There is no experience of Duotrav in inflammatory ocular conditions, inflammatory, neovascular, angle-closure or congenital glaucoma and only limited experience in open-angle glaucoma of pseudophakic patients and in pigmentary glaucoma.

Although not reported during pivotal clinical trials with Duotrav, macular oedema, including cystoid macular oedema, has been reported during treatment with prostaglandin $F_{2\alpha}$ analogues. These reports have mainly occurred in aphakic patients, pseudophakic patients with a torn posterior lens capsule, or in patients with known risk factors for macular oedema. Duotrav should be used with caution in these patients.

Benzalkonium chloride, which is commonly used as a preservative in ophthalmic products, has been reported to cause punctate keratopathy and/or toxic ulcerative keratopathy. Since Duotrav contains benzalkonium chloride, close monitoring is required with frequent or prolonged use in dry eye patients, or in conditions where the cornea is compromised.

Actions the health care professional should take

Systemic absorption can be minimised if patients are instructed to gently occlude the nasolacrimal ducts for two minutes immediately after instillation of the eye drop.

Use in Pregnancy - Category C

No adequate and well-controlled studies have been performed in pregnant women. Duotrav may interfere with the maintenance of pregnancy. It should not be used by women during pregnancy or by women attempting to become pregnant.

Travoprost. The human dose of travoprost with the recommended dosage of Duotrav is 2.2 µg/day or 0.044 µg/kg/day, with plasma concentrations of up to 0.020 ng/mL. Travoprost and/or its metabolites crossed the placenta in rats. Travoprost was teratogenic in rats at intravenous doses of 10 µg/kg/day, equivalent to 98 times the human exposure; it increased the incidence of hydrocephaly and bone abnormalities (e.g. vertebral malformations). Travoprost was not teratogenic in rats at intravenous doses of up to 3 µg/kg/day (29 times the human exposure). When administered to rats during organogenesis (gestation days 6 to 17), travoprost produced increases in post-implantation loss and early delivery at intravenous doses of 10 µg/kg/day (98 times the human exposure). Post-implantation loss increased in rats at subcutaneous doses of 10 µg/kg/day (54 times human exposure) administered from 2 weeks prior to mating to gestation day 7. Travoprost was not teratogenic in mice at subcutaneous doses of up to 0.3 µg/kg/day; post-implantation loss and early delivery were increased in mice at subcutaneous doses of 1 µg/kg/day (5.8 times the human exposure), but not at 0.3 µg/kg/day (1.7 times the human exposure).

Travoprost eye drops, 0.003% administered to rabbits during organogenesis, appeared to increase incidence of fetal loss.

In rats administered travoprost from gestation day 7 to lactation day 21 by subcutaneous injection, abortions occurred at 0.72 µg/kg/day (4 times human exposure), and decreased gestation length and increased still births (see also Use in Lactation) occurred at ≥ 0.12 µg/kg/day (0.65 times human exposure).

Timolol: Timolol maleate was not teratogenic in mice, rats and rabbits, and mice and rabbits showed no evidence of embryofetal toxicity at doses up to 50 mg/kg/day. At higher doses, increases in resorptions and foetal variations (14 ribs and hypoplastic sternebrae) were noted in mice (1,000 mg/kg/day) and increased resorption in rabbits (≥ 90 mg/kg/day). In rats, delayed ossification was seen at ≥ 50 mg/kg/day and a decreased number of caudal vertebral bodies and arches and an increase in hypoplastic sternebrae were noted at 500 mg/kg/day.

Use in Lactation

Nursing women who use Duotrav should use caution because of the potential for serious adverse reactions from Duotrav in breastfeeding infants.

Travoprost: There are no data on the excretion of travoprost into human milk or on the safety of travoprost exposure in infants. Because many drugs are excreted in human milk and adverse effects in rat pups were observed at low doses of travoprost (see below), nursing women who use Duotrav should stop breastfeeding. A study in rats showed that travoprost and/or its metabolites were excreted in milk. Increased pup mortality and depressed pup growth and development occurred in rats where the dams were subcutaneously administered travoprost from gestation day 7 to lactation day 21 at greater than or equal to 0.12 µg/kg/day, corresponding to 2.7 the expected human dose.

Timolol: Timolol maleate has been detected in human milk following oral and ocular administration.

Paediatric use

Duotrav is not recommended for use in children. The safety and effectiveness in paediatric patients have not been established.

Use in the Elderly

No overall differences in safety and effectiveness have been reported between elderly and other adult patients.

Hepatic/Renal Impairment

No dosage alteration of Duotrav is necessary in these patients.

Carcinogenicity

Carcinogenicity studies with Duotrav have not been conducted.

Travoprost: Long term studies in mice and rats at subcutaneous doses up to 100 µg/kg/day did not provide any evidence of carcinogenic potential. These doses correspond to exposure levels over 200 times human exposure at the maximum recommended human ophthalmic dose, based on plasma active drug levels.

Timolol: No evidence of carcinogenicity was observed with timolol maleate at oral doses up to 100 mg/kg/day in rats and 50 mg/kg/day in mice. However, there was a statistically significant increase in the incidence of adrenal pheochromocytomas in male rats administered 300 mg/kg/day. In female mice, statistically significant increases in the incidence of benign and malignant pulmonary tumours, benign uterine polyps and mammary carcinomas were found at 500 mg/kg/day. The increased incidence of mammary tumours was considered to be attributed to a species elevation in serum prolactin.

Genotoxicity

Mutagenicity studies with Duotrav have not been conducted.

Travoprost: Travoprost did not cause gene mutation in bacteria or *in vivo* chromosomal aberrations in bone marrow cells of mice and rats. A slight increase in mutation frequency was observed in one of two *in vitro* mouse lymphoma L5178Y assays. Weight of evidence indicates that travoprost is unlikely to pose a genotoxic risk from clinical use.

Timolol: *In vitro* and *in vivo* studies with timolol maleate did not reveal a mutagenic potential.

Effects on fertility

There are no human data on the effects of Duotrav on male or female fertility.

Travoprost. Travoprost had no effects on mating behaviour or fertility in male and female rats at subcutaneous doses up to 10 µg/kg/day (equivalent to 54 times the human exposure), although embryofetal resorption was increased at 10 µg/kg/day (further information on effects on pregnancy is included under **Use in Pregnancy**).

Timolol. Timolol maleate alone had no effects on male or female fertility when administered at 300 mg/kg/day, orally.

Adverse effects

In clinical trials 514 subjects/patients were exposed to Duotrav administered once-daily. No serious ophthalmic or systemic adverse reactions related to Duotrav were reported.

Clinical Trial Adverse Drug Reactions

The most frequently reported treatment-related adverse drug reaction was ocular hyperaemia (15.6%).

Treatment-related adverse drug reactions that occurred at an incidence of $\geq 10\%$ included the following:

Eye disorders: ocular hyperaemia

Treatment-related adverse drug reactions that occurred at an incidence of $\geq 1.0\%$ to $<10\%$ included the following:

Eye disorders: abnormal sensation in eye, anterior chamber cell, anterior chamber flare, eye irritation, eye pain, eye pruritus, keratoconjunctivitis sicca, growth of eyelashes, photophobia, punctate keratitis, vision blurred

Investigations: corneal staining

Nervous system disorders: headache

Treatment-related adverse drug reactions that occurred at an incidence of $\geq 0.1\%$ to $<1.0\%$ included the following:

Eye disorders: asthenopia, conjunctivitis allergic, conjunctival haemorrhage, dermatitis eyelid, erythema of eyelid, eyelid irritation, eyelid oedema, eyelid pain, eyelids pruritus, eye swelling, lacrimation increased, ocular discomfort, periorbital disorder, visual acuity reduced, visual disturbance

General disorders and administration site conditions: thirst

Immune system disorders: urticaria

Infections and infestations: laryngitis, otitis media, skin infection

Investigations: alanine aminotransferase increased, aspartate aminotransferase increased, blood pressure diastolic decreased, blood pressure diastolic increased, blood pressure increased, heart rate decreased, heart rate irregular, intraocular pressure decreased

Musculoskeletal and connective tissue disorders: pain in extremity

Nervous system disorders: disturbance in attention, dizziness

Psychiatric disorders: nervousness

Renal and urinary disorders: chromaturia

Respiratory, thoracic and mediastinal disorders: postnasal drip, bronchospasm, cough, dyspnoea, throat irritation

Skin and subcutaneous tissue disorders: dermatitis contact

Interactions

No pharmacokinetic interactions were observed between travoprost and timolol following topical ocular administration of Duotrav. No specific interaction studies were performed with Duotrav and other drugs.

Travoprost

The plasma protein binding of the active free acid form of travoprost is moderate (approximately 80%) and, therefore, drug-drug interactions involving protein binding are unlikely.

Timolol

The potential exists for additive effects resulting in hypotension, and/or marked bradycardia when timolol ophthalmic drops are administered with oral calcium channel blockers, catecholamine depleting drugs or β -adrenergic blocking agents, antiarrhythmics (including amiodarone and quinidine), digitalis glycosides, parasymptomimetics, narcotics and monoamine oxidase inhibitors (MAOIs).

Although Duotrav used alone has little or no effect on pupil size, mydriasis has occasionally been reported when timolol is given with adrenaline.

β -blockers may increase the hypoglycaemic effect of antidiabetic agents.

Effects on ability to drive and use machines

As with other ophthalmic medications, patients should be advised to exercise caution if they experience transient blurred vision following instillation of eye drops. Patients should wait until their vision clears before driving or using machinery.

Overdosage

There are no human data available on overdosage with Duotrav, although overdosage data are available on timolol, one of its individual active constituents.

A topical overdose of Duotrav may be flushed from the eyes with warm tap water.

If Duotrav is accidentally ingested the following information should be useful. One 2.5 mL bottle contains travoprost 0.1 mg and timolol 12.5 mg. The oral bioavailability of timolol is good, while that of travoprost is negligible or very low. Both timolol and travoprost are extensively metabolised in the liver.

Travoprost

A single-dose intravenous study in rats was conducted to elucidate maximal acute hazard. The dose employed was 250,000 times the proposed daily clinical exposure and over 5,000 times the possible exposure from the entire contents of one product container. No treatment related pharmacotoxic signs were present in the animals receiving travoprost.

Timolol

The usual daily oral therapeutic dose of timolol is 20 – 40 mg/day, or about 1.5 – 3 times the maximum possible dose from a single DUOTRAV dispenser. Symptoms of systemic timolol

overdosage are bradycardia, hypotension, bronchospasm and cardiac arrest. If such symptoms occur, treatment should be symptomatic and supportive. Studies have shown that timolol is not readily dialyzable.

If overdosage with Duotrav occurs, treatment should be symptomatic.

Pharmaceutical precautions

Store below 25 °C. Discard four weeks after opening.

Medicine classification

Prescription Medicine.

Package quantities

Duotrav Eye Drops: 2.5 mL oval DROP-TAINER® dispenser.

Consumer Medicine Information is supplied with this product.

Further information

Clinical Studies

Adult patients with diagnoses of predominately primary open angle glaucoma, ocular hypertension or pigmentary glaucoma participated in three randomised, double-masked, parallel group multicenter studies (n=982) to demonstrate the safety and efficacy of Duotrav (travoprost 0.004% and timolol 0.5%). These studies evaluated the IOP-lowering effect of Duotrav dosed once daily (morning) over three-months compared to:

- monotherapy with its individual components (mean baseline intraocular pressures of 27 to 30 mmHg), travoprost 0.004% dosed once daily (evening) and timolol 0.5% dosed twice daily (contribution-of-elements; Study 1)
- concomitant administration of travoprost 0.004% and timolol 0.5% (mean baseline intraocular pressures of 23 to 26 mmHg), both dosed once daily (evening and morning, respectively; Study 2). One study also used timolol 0.5% dosed twice daily (Study 3).

The primary efficacy parameter for all studies was mean IOP at 8 AM, 10 AM and 4 PM. The proportion of patients with IOP < 18 mm Hg was measured as a secondary efficacy parameter.

Approximately 22% to 37% of the patients included in the studies were treatment naïve patients. All other patients were receiving monotherapy (49% to 57%) with either timolol, a prostaglandin or other medication; two medications (11% to 17%) or three plus medications (2% to 4%).

In the contribution-of-elements study (Study 1), the mean IOP-lowering effect of Duotrav dosed once-daily in the morning was 8.7 to 11.5 mmHg, and was 0.4 to 1.8 mmHg greater than Travatan 0.004% dosed once daily in the evening and 1.5 to 2.7 mmHg greater than that of timolol 0.5% dosed twice-daily. However there are no data to show the optimal dose of these agents in combination. In the two concomitant administration studies, the mean IOP reductions of Duotrav were similar to those achieved by concomitant therapy with Travatan dosed once daily in the evening and timolol dosed once daily in the morning (see Table 1). Differences in mean IOP change from baseline at 10 AM and 4 PM were approximately 1 mmHg, favouring concomitant therapy. No differences were observed at 8 AM. When Duotrav was compared to concomitant therapy (Study 2 and Study 3), non-inferiority was not demonstrated at all time points. However pooled analyses revealed non-inferiority. Six month extension data was consistent with previous findings in the individual studies.

Duotrav yielded IOP < 18 mmHg at one or more time-points at all visits throughout the entire 3-month period for 50% of patients in the contribution-of-elements study, and for 74% of patients in a pooled analysis of the concomitant administration studies.

Table 1 Mean IOP (mmHg) for Study 2 and Study 3

| Visit | Time point | Mean IOP (mmHg) | | | |
|----------|------------|-----------------|-------------------------------|-----------------|-------------------------------|
| | | Study 2 | | Study 3 | |
| | | Duotrav (n=151) | TRAVATAN + Timolol qd (n=142) | Duotrav (n=155) | TRAVATAN + Timolol qd (n=151) |
| Baseline | 8AM | 25.2 | 25.1 | 25.6 | 25.0 |
| | 10AM | 24.0 | 23.9 | 24.0 | 23.9 |
| | 4PM | 23.0 | 23.1 | 23.1 | 22.9 |
| Week 2 | 8AM | 16.2 | 16.0 | 17.5 | 16.8 |
| | 10AM | 15.5 | 15.2 | 16.8 | 15.7 |
| | 4PM | 15.2 | 14.8 | 16.2 | 15.4 |
| Week 6 | 8AM | 15.9 | 15.7 | 17.0 | 16.6 |
| | 10AM | 15.8 | 14.8 | 16.6 | 15.6 |
| | 4PM | 15.6 | 14.7 | 16.2 | 15.5 |
| Month 3 | 8AM | 16.6 | 16.0 | 17.1 | 16.7 |
| | 10AM | 16.1 | 15.1 | 16.5 | 15.8 |
| | 4PM | 15.6 | 14.7 | 16.3 | 15.5 |

Double-masked extensions of the three studies mentioned above were conducted for up to an additional three months. The IOP-lowering effect of Duotrav was maintained during this period.

A separate dosing study (morning or evening) confirmed that the IOP-lowering efficacy of once-daily Duotrav is independent of the time of dosing.

A similar safety profile was observed comparing therapy with Duotrav to concomitant therapy with the individual components (travoprost 0.004% + timolol 0.5%) or to monotherapy with each component (travoprost 0.004%; timolol 0.5%).

Contact lenses

If patients continue to wear soft (hydrophilic) contact lenses while under treatment with Duotrav they should remove their lens(es) prior to instilling Duotrav in the affected eye(s) and should not insert their lens(es) until 15 minutes after instillation of the eye drops.

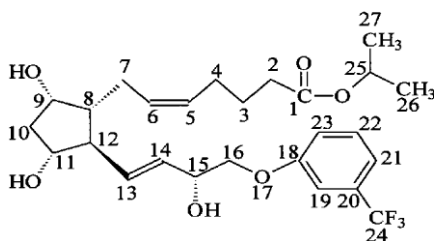
List of excipients

Each mL of Duotrav contains 40 micrograms travoprost and 6.83 mg timolol maleate (equivalent to 5 mg timolol) together with castor oil-ethoxylated hydrogenated, disodium edetate, boric acid, trometamol, mannitol and purified water. The solution is preserved with benzalkonium chloride (0.15 mg/mL).

Note: For further information about the active components contained in Duotrav, refer to the individual data sheet documents.

Pharmaceutical

Travoprost is a clear to slightly opalescent, colourless to yellow oil. Travoprost is practically insoluble in water (approximately 44 ppm). The chemical structure of travoprost is:



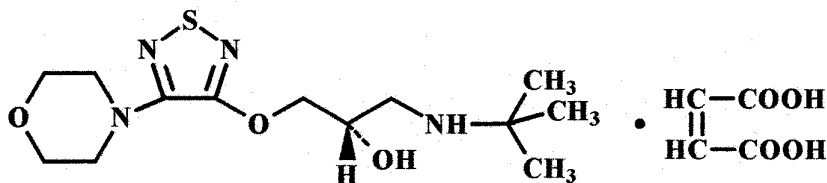
Molecular weight: 500.56

Empirical formula: C₂₆H₃₅F₃O₆

Chemical name: (5Z,13E)-(9S,11R,15R)-9,11,15-Trihydroxy-16-(*m*-trifluoromethylphenoxy) 17,18,19,20-tetranor-5,13-prostadienoic acid, isopropyl ester.

CAS Number: 157283-68-6

Timolol maleate is a white to off-white, crystalline powder which is soluble in water, alcohol and practically insoluble in ether. The chemical structure of timolol maleate is:



Molecular weight: 432.50
Empirical formula: $C_{13}H_{24}N_4O_3S \cdot C_4H_4O_4$
Chemical name: (S)-1-(tert-butylamino)-3-[(4-morpholino-1,2,5-thiadiazol-3-yl) oxy]-2-propanol maleate (1:1) (salt).
CAS Number: 26921-17-5

Name and address

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