SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Travoprost Aspire 30 micrograms/ml eye drops, solution

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

One ml of solution contains 30 micrograms of travoprost.

Excipients with known effect
One ml of solution contains 7.5 mg propylene glycol and 5 mg macrogolglycerol hydroxystearate 40 (see section 4.4).

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Eye drops, solution (eye drops)

Clear, colorless aqueous solution, free from foreign particles

pH: 6.3-7.3
Osmolality: 252-308 mOsm/Kg

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Decrease of elevated intraocular pressure in adult patients with ocular hypertension or open-angle glaucoma (see section 5.1).

Decrease of elevated intraocular pressure in paediatric patients aged 3 years to < 18 years with ocular hypertension or paediatric glaucoma (see section 5.1).

4.2 Posology and method of administration

Posology

Use in adults, including elderly patients

The dose is one drop of travoprost in the conjunctival sac of the affected eye(s) once daily. Optimal effect is obtained if the dose is administered in the evening.

Nasolacrimal occlusion or gently closing the eyelid after administration is recommended. This may reduce the systemic absorption of medicinal products administered via the ocular route and result in a decrease in systemic adverse reactions.

If more than one topical ophthalmic medicinal product is being used, the medicinal products must be administered at least 5 minutes apart.

If a dose is missed, treatment should be continued with the next dose as planned. The dose should not exceed one drop in the affected eye(s) daily.

When substituting another ophthalmic antiglaucoma medicinal product with Travoprost, the other medicinal product should be discontinued and Travoprost should be started the following day.

Hepatic and renal impairment
Travoprost 30 µg/ml has not been studied in patients with hepatic or renal impairment. However, travoprost 40 µg/ml has been studied in patients with mild to severe hepatic impairment and in patients with mild to severe renal impairment (creatinine clearance as low as 14 ml/min). No dosage adjustment is necessary in these patients (see section 5.2). Therefore, no need for dose adjustment at the lower concentration of active ingredient is anticipated.

Paediatric population
Travoprost can be used in paediatric patients from 3 years to < 18 years at the same posology as in adults (see section 5.1).

The safety and efficacy of travoprost 30 µg/ml in children below the age of 3 years have not been established. Currently available data are described in section 5.1 but no recommendation on a posology below the age of 3 years can be made.

Method of administration
For ocular use.

For patients who wear contact lenses, please refer to section 4.4.

The patient should remove the protective sachet immediately prior to initial use. After cap is removed, Travoprost eye drops solution is ready for use. To prevent contamination of the dropper tip and solution, care must be taken not to touch the eyelids, surrounding areas or other surfaces with the dropper tip of the bottle.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Eye colour change

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 a permanent change in eye colour. 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. 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 eye lid changes

In controlled clinical trials, periorbital and/or eyelid skin darkening in association with the use of travoprost has been reported in 0.2% of patients.

Periorbital and lid changes including deepening of the eyelid sulcus have been observed with prostaglandin analogues.

Travoprost may gradually change eyelashes in the treated eye(s); these changes were observed in about half of the patients in clinical trials and include: increased length, thickness, pigmentation, and/or number of lashes. The mechanism of eyelash changes and their long term consequences are currently unknown.

There is no experience of travoprost in inflammatory ocular conditions; nor in neovascular, angle-closure, narrow-angle or congenital glaucoma and only limited experience in thyroid eye disease, in open-angle glaucoma of pseudophakic patients and in pigmentary or pseudoexfoliative glaucoma.

Aphakic patients

Caution is recommended when using travoprost in aphakic patients, pseudophakic patients with a torn posterior lens capsule or anterior chamber lenses, or in patients with known risk factors for cystoid macular oedema.

Iritis/uveitis

In patients with known predisposing risk factors for iritis/uveitis, travoprost can be used with caution.

Contact with the skin

Skin contact with travoprost must be avoided as transdermal absorption of travoprost has been demonstrated in rabbits.

Prostaglandins and prostaglandin analogues are biologically active materials that may be absorbed through the skin. Women who are pregnant or attempting to become pregnant should exercise appropriate precautions to avoid direct exposure to the contents of the bottle. In the unlikely event of coming in contact with a substantial portion of the contents of the bottle, thoroughly cleanse the exposed area immediately.

Contact lenses
Patients must be instructed to remove contact lenses prior to application of Travoprost and wait 15 minutes after instillation of the dose before reinsertion.

Excipients
Travoprost contains propylene glycol which may cause skin irritation.
Travoprost contains macrogolglycerol hydroxystearate 40 which may cause skin reactions.

Paediatric population
No long-term safety data are available in the paediatric population.

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed.

4.6 Fertility, pregnancy and lactation

Women of child-bearing potential/contraception
Travoprost must not be used in women of child bearing age/potential unless adequate contraceptive measures are in place (see section 5.3).

Pregnancy
Travoprost has harmful pharmacological effects on pregnancy and/or the foetus/new-born child. Travoprost should not be used during pregnancy unless clearly necessary.

Breastfeeding
It is unknown whether travoprost from eye drops is excreted in human breast milk. Animal studies have shown excretion of travoprost and metabolites in breast milk. The use of travoprost by breast-feeding mothers is not recommended.

Fertility
There are no data on the effects of travoprost on human fertility. Animal studies showed no effect of travoprost on fertility at doses more than 250 times the maximum recommended human ocular dose.

4.7 Effects on ability to drive and use machines

Travoprost has no or negligible influence on the ability to drive and use machines.
Temporary blurred vision or other visual disturbances may affect the ability to drive or use machines. If blurred vision occurs at instillation, the patient must wait until the vision clears before driving or using machines.

4.8 Undesirable effects

Summary of the safety profile
In a clinical trial of 3 months duration (N = 442) involving travoprost 30 μg/ml as monotherapy, the most common adverse reaction observed was hyperaemia of the eye (ocular or conjunctival) reported in approximately 12% of the patients.

Tabulated list of adverse reactions
The following adverse reactions were assessed to be related with travoprost 30 μg/ml monotherapy and are classified according to the following convention: very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1,000 to <1/100), rare (≥1/10,000 to <1/1,000) and very rare (<1/10,000). Within each frequency grouping in Table 1, adverse reactions are presented in decreasing order of seriousness.

Table 1: Travoprost 30 μg/ml eye drops, solution

System Organ class	Frequency	Adverse reaction
Eye disorders	Very common	ocular hyperaemia
	Common	dry eye, eye pruritus, ocular discomfort
	Uncommon	punctate keratitis, anterior chamber inflammation, blepharitis, eye pain, photophobia, visual impairment, vision blurred, conjunctivitis, eyelid oedema, eyelid margin crusting, eye discharge, dark circles under eyes, growth of eyelashes, eyelash thickening
Skin and subcutaneous tissue disorders	Uncommon	pruritus, rash

The following adverse reactions were assessed to be related with Travoprost 40 μg/ml eye drops, solution (either BAK or Polyquad- preserved) and are classified according to the following convention: very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1,000 to <1/100), rare (≥1/10,000

to <1/1,000), very rare (<1/10,000) and not known (cannot be estimated from the available data). Within each frequency grouping in Table 2, adverse reactions are presented in decreasing order of seriousness.

Table 2: Travoprost 40 μg/ml eye drops, solution

System Organ class	Frequency	Adverse reaction
Infections and infestations	Uncommon	herpes simplex, keratitis herpetic
Immune system disorders	Uncommon	hypersensitivity, drug hypersensitivity, seasonal allergy
Nervous system disorders	Common	headache
	Uncommon	dysgeusia, dizziness, visual field defect
Eye disorders	Very common	ocular hyperaemia, iris hyperpigmentation
	Common	punctate keratitis, anterior chamber inflammation, eye pain, photophobia, eye discharge, ocular discomfort, visual acuity reduced, vision blurred, dry eye, eye pruritus, lacrimation increased, erythema of eyelid, eyelid oedema, growth of eyelashes, eyelash discolouration, eye irritation
	Uncommon	corneal erosion, uveitis, keratitis, eye inflammation, photopsia, blepharitis, conjunctival oedema, halo vision, conjunctivitis, conjunctival follicles, hypoaesthesia eye, meibomianitis, ectropion, anterior chamber pigmentation, mydriasis, cataract, eyelid margin crusting, asthenopia
	Not known	macular oedema, sunken eyes
Ear and labyrinth disorders	Not known	vertigo, tinnitus
Cardiac disorders	Uncommon	heart rate irregular, palpitations, heart rate decreased
	Not known	chest pain, bradycardia, tachycardia
Vascular disorders	Uncommon	blood pressure decreased, blood pressure increased, hypotension, hypertension

Respiratory, thoracic and mediastinal disorders	Uncommon	dyspnoea, asthma, respiratory disorder, oropharyngeal pain, cough, dysphonia, nasal congestion, throat irritation
	Not known	asthma aggravated

Gastrointestinal disorders	Uncommon	peptic ulcer reactivated, dry mouth gastrointestinal disorder, constipation
Skin and subcutaneous tissue disorders	Common	skin hyperpigmentation (periocular), skin discolouration
	Uncommon	dermatitis allergic, periorbital oedema, dermatitis contact, erythema, rash, hair colour changes, hair texture abnormal, hypertrichosis, madarosis
	Not known	hair growth abnormal
Musculoskeletal, connective tissue and bone disorders	Uncommon	musculoskeletal pain
General disorders and administrative site conditions	Uncommon	asthenia, malaise
Investigations	Not known	prostatic specific antigen increased

Paediatric Population

In a 3 month phase 3 study and a 7 days pharmacokinetic study, involving 102 paediatric patients (aged between 3 months and 17 years) exposed to travoprost 40 μg/ml eye drops, solution, the types and characteristics of adverse reactions reported were similar to what has been observed in adult patients. The short-term safety profiles in the different paediatric subsets were also similar (see section 5.1). The most frequent adverse reactions reported in the paediatric population were ocular hyperaemia (16.9%) and growth of eyelashes (6.5%). In a similar 3 month study in adult patients, these events occurred at an incidence of 11.4% and 0.0%, respectively.

Additional adverse drug reactions reported in paediatric patients in the 3 month paediatric study (n=77) compared to a similar trial in adults (n=185) included erythema of eyelid, keratitis, lacrimation increased, and photophobia all reported as single events with an incidence of 1.3% versus 0.0% seen in adults.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via Yellow Card Scheme at www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store

4.9 Overdose

A topical overdose is not likely to occur or to be associated with toxicity. A topical overdose of travoprost may be flushed from the eye(s) with lukewarm water. Treatment of a suspected oral ingestion is symptomatic and supportive.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Ophthalmologicals, antiglaucoma preparations and miotics, ATC code: S01EE04

Mechanism of action

Travoprost, a prostaglandin $F_{2\alpha}$ analogue, is a highly selective full agonist which has a high affinity for the prostaglandin FP receptor, and reduces the intraocular pressure by increasing the outflow of aqueous humour via trabecular meshwork and uveoscleral pathways. Reduction of the intraocular pressure in man starts about 2 hours after administration and maximum effect is reached after 12 hours. Significant lowering of intraocular pressure can be maintained for periods exceeding 24 hours with a single dose.

Clinical efficacy and safety

In a clinical trial, patients with open-angle glaucoma or ocular hypertension treated with travoprost 30 µg/ml dosed once-daily in the evening, demonstrated intraocular pressure lowering equivalent to travoprost 40 µg/ml eye drops, solution at all on-therapy visits and time points (95% CI within ±1.0 mmHg). The mean reduction from baseline in IOP ranged from 7.1 to 8.2 mmHg as summarised in Table 3. The mean percent reductions in IOP from baseline to each study visit and assessment time point ranged from 28.4% to 30.7%.

Table 3: IOP Change from Baseline (mmHg) for travoprost 30 µg/ml

Visit		8 AM	10 AM	4 PM
Week 2	Mean	-8.0	-7.3	-7.1
(N=442)	95% CI	(-8.3, -7.7)	(-7.6, -7.0)	(-7.4, -6.8)
Week 6	Mean	-8.1	-7.4	-7.2
(N=440*)	95% CI	(-8.4, -7.9)	(-7.6, -7.1)	(-7.5, -6.9)
Month 3	Mean	-8.2	-7.5	-7.1
(N=432*)	95% CI	(-8.6, -7.9)	(-7.9, -7.2)	(-7.4, -6.8)

*One subject had missing data at 8 AM at Week 6; one had missing data at 4 PM at Month 3.

An improved safety profile has been observed for travoprost 30 µg/ml when compared to the marketed travoprost 40 µg/ml eye drops, solution (benzalkonium chloride preserved or polyquaternium-1 preserved). The most common adverse reaction associated with both travoprost 30 µg/ml and travoprost 40 µg/ml eye drops, solution is hyperaemia. Hyperaemia (ocular or conjunctival) was observed in 11.8% of patients (N = 442) exposed to travoprost 30 µg/ml compared with 14.5% observed for patients exposed to travoprost 40 µg/ml eye drops, solution, benzalkonium chloride preserved.

Secondary pharmacology
Travoprost significantly increased optic nerve head blood flow in rabbits following 7 days of topical ocular administration (1.4 micrograms, once-daily).

Travoprost 40 μg/ml eye drops, solution preserved with polyquaternium-1 induced minimal ocular surface toxicity, compared to eye drops preserved with benzalkonium chloride, on cultured human corneal cells and following topical ocular administration in rabbits.

Paediatric population
Travoprost 30 μg/ml has not been specifically studied in a clinical trial involving paediatric subjects. However, a modelling approach demonstrated that IOP lowering would be expected to be equivalent in paediatric patients aged 3 years and above using both travoprost 30 μg/ml and travoprost 40 μg/ml eye drops, solution. The studies used in the model were two dose response trials, one Phase III study using travoprost 30 μg/ml and a paediatric study using travoprost 40 μg/ml eye drops, solution.

The efficacy of travoprost 40 μg/ml eye drops, solution in paediatric patients from 2 months to less than 18 years of age was demonstrated in a 12-week, double-masked clinical study of travoprost compared with timolol in 152 patients diagnosed with ocular hypertension or paediatric glaucoma. Patients received either travoprost 0.004% once daily or timolol 0.5% (or 0.25% for subjects younger than 3 years old) twice daily. The primary efficacy endpoint was the intraocular pressure (IOP) change from baseline at Week 12 of the study. Mean IOP reductions in the travoprost and timolol groups were similar (see Table 4).

In the age groups 3 to < 12 years (n=36) and 12 to <18 years (n=26), mean IOP reduction at Week 12 in the travoprost group was similar to that in the timolol group. Mean IOP reduction at Week 12 in the 2 months to < 3 years of age group was 1.8 mmHg in the travoprost group and 7.3 mmHg in the timolol group. IOP reductions for this group were based on only 6 patients in the timolol group and 9 patients in the travoprost group where 4 patients in the travoprost group versus 0 patients in the timolol group had no relevant mean IOP reduction at Week 12. No data are available for children less than 2 months old.

The effect on IOP was seen after the second week of treatment and was consistently maintained throughout the 12 week period of study for all age groups.

Table 4 – Comparison of Mean IOP Change from Baseline (mmHg) at Week 12

Travoprost		**Timolol**			
N	**Mean (SE)**	**N**	**Mean (SE)**	**Mean Difference[a]**	**(95% CI)**

53	-6.4 (1.05)	60	-5.8 (0.96)	-0.5	(-2.1, 1.0)

SE = Standard Error; CI = Confidence Interval;
[a]Mean difference is Travoprost – Timolol. Estimates based on least squares means derived from a statistical model that accounts for correlated IOP measurements within patient where primary diagnosis and baseline IOP stratum are in the model.

5.2 Pharmacokinetic properties

Absorption
Travoprost is an ester prodrug. It is absorbed through the cornea where the isopropyl ester is hydrolysed to the active free acid. Studies in rabbits have shown peak concentrations of 20 ng/g of the free acid in aqueous humour one to two hours after topical dosing of travoprost 40 μg/ml eye drops, solution. Aqueous humour concentrations declined with a half-life of approximately 1.5 hours.

Distribution
Following topical ocular administration of travoprost 40 μg/ml eye drops, solution to healthy volunteers, low systemic exposure to active free acid was demonstrated. Peak active free acid plasma concentrations of 25 pg/ml or less were observed between 10 and 30 minutes post-dose. Thereafter, plasma levels declined rapidly to below the 10 pg/ml assay quantitation limit before 1 hour post-administration. Due to the low plasma concentrations and rapid elimination following topical dosing, the elimination half-life of active free acid in man could not be determined.

Biotransformation
Metabolism is the major route of elimination of both travoprost and the active free acid. The systemic metabolic pathways parallel those of endogenous prostaglandin $F_{2\alpha}$ which are characterised by reduction of the double bond in position C13-C14, oxidation of the 15-hydroxyl and β-oxidative cleavages of the upper side chain.

Elimination
Travoprost free acid and its metabolites are mainly excreted by the kidneys. Travoprost 40 μg/ml eye drops, solution has been studied in patients with mild to severe hepatic impairment and in patients with mild to severe renal impairment (creatinine clearance as low as 14 ml/min). No dosage adjustment is necessary in these patients.

Paediatric population
A pharmacokinetic study of travoprost 40 μg/ml eye drops, solution in paediatric patients aged 2 months to <18 years demonstrated low plasma exposure to travoprost free acid, with concentrations ranging from below the 10 pg/ml assay limit of quantitation (BLQ) to 54.5 pg/ml.

5.3 Preclinical safety data

In ocular toxicity studies in monkeys, administration of travoprost at a dose of 0.45 microgram, twice a day, was shown to induce increased palpebral fissure. Topical ocular administration of travoprost to monkeys at concentrations of up to 0.012% to the right eye, twice daily for one year resulted in no systemic toxicity.

Increased palpebral fissure observed in monkeys were not seen in rabbits or in the clinical trials with travoprost products and is considered to be species specific.

Reproduction toxicity studies have been undertaken in rat, mice and rabbit by systemic route. Findings are related to FP receptor agonist activity in uterus with early embryolethality, post-implantation loss, foetotoxicity. In pregnant rat, systemic administration of travoprost at doses more than 200 times the clinical dose during the period of organogenesis resulted in an increased incidence of malformations. Low levels of radioactivity were measured in amniotic fluid and foetal tissues of pregnant rats administered ^{3}H-travoprost. Reproduction and development studies have demonstrated a potent effect on foetal loss with a high rate observed in rats and mice (180 pg/ml and 30 pg/ml plasma, respectively) at exposures 1.2 to 6 times the clinical exposure (up to 25 pg/ml).

Data to evaluate a potential effect on the environment are currently limited.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Polyquaternium-1
Macrogolglycerol hydroxystearate 40
Sodium chloride
Propylene glycol (E1520)
Boric acid (E284)
Sodium hydroxide (for pH adjustment)
Water for injections

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

30 months.

Travoprost eye drops solution should be used no longer than 4 weeks after first opening of the multidose container.

6.4 Special precautions for storage

Before opening, keep the bottle in the sachet in order to avoid evaporation. This medicinal product does not require any special temperature storage conditions.

After first opening, this medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

2.5 ml solution in a 5 ml PP bottle sealed with a LDPE nozzle and a white opaque HDPE/LDPE screw cap with tamper proof seal. Each bottle is packaged in a sachet (PET/ /ALU /PE).

Pack sizes:

Cartons containing 1 or 3 bottles.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Aspire Pharma Ltd
Unit 4, Rotherbrook Court,
Bedford Road,
Petersfield,
Hampshire,
GU32 3QG
United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

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9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

04/02/2025

10 DATE OF REVISION OF THE TEXT

02/03/2026