ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

LUMIGAN 0.1 mg/ml eye drops, solution

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One ml of solution contains 0.1 mg bimatoprost.

Excipient with known effect
One ml of solution contains 0.2 mg benzalkonium chloride.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Eye drops, solution (eye drops)

Colourless solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Reduction of elevated intraocular pressure in chronic open-angle glaucoma and ocular hypertension in adults (as monotherapy or as adjunctive therapy to beta-blockers).

4.2 Posology and method of administration

Posology

The recommended dose is one drop in the affected eye(s) once daily, administered in the evening. The dose should not exceed once daily, as more frequent administration may lessen the intraocular pressure lowering effect.

Paediatric population

The safety and efficacy of LUMIGAN in children aged 0 to 18 years has not yet been established.

Renal and hepatic impairment

LUMIGAN has not been studied in patients with renal or moderate to severe hepatic impairment and should therefore be used with caution in such patients. In patients with a history of mild liver disease or abnormal alanine aminotransferase (ALT), aspartate aminotransferase (AST) and/or bilirubin at baseline, bimatoprost 0.3 mg/ml eye drops, solution had no adverse effect on liver function over 24 months.

Method of administration

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

4.3 Contraindications

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

LUMIGAN 0.1 mg/ml is contraindicated in patients who have had a suspected previous adverse reaction to benzalkonium chloride that has led to discontinuation.

4.4 Special warnings and precautions for use

Ocular

Before treatment is initiated, patients should be informed of the possibility of prostaglandin analogue periorbitopathy (PAP) and increased iris pigmentation, since these have been observed during treatment with LUMIGAN. Some of these changes may be permanent, and may lead to impaired field of vision and differences in appearance between the eyes when only one eye is treated (see section 4.8).

Cystoid macular oedema has been uncommonly reported (≥1/1 000 to <1/100) following treatment with bimatoprost 0.3 mg/ml eye drops, solution. Therefore, LUMIGAN should be used with caution in patients with known risk factors for macular oedema (e.g. aphakic patients, pseudophakic patients with a torn posterior lens capsule).

There have been rare spontaneous reports of reactivation of previous corneal infiltrates or ocular infections with bimatoprost 0.3 mg/ml eye drops, solution. LUMIGAN should be used with caution in patients with a prior history of significant ocular viral infections (e.g. herpes simplex) or uveitis/iritis.

LUMIGAN has not been studied in patients with inflammatory ocular conditions, neovascular, inflammatory, angle-closure glaucoma, congenital glaucoma or narrow-angle glaucoma.

Skin

There is a potential for hair growth to occur in areas where LUMIGAN solution comes repeatedly in contact with the skin surface. Thus, it is important to apply LUMIGAN as instructed and avoid it running onto the cheek or other skin areas.

Respiratory

LUMIGAN has not been studied in patients with compromised respiratory function. While there is limited information available on patients with a history of asthma or COPD, there have been reports of exacerbation of asthma, dyspnoea and COPD, as well as reports of asthma, in post-marketing experience. The frequency of these symptoms is not known. Patients with COPD, asthma or compromised respiratory function due to other conditions should be treated with caution.

Cardiovascular

LUMIGAN has not been studied in patients with heart block more severe than first degree or uncontrolled congestive heart failure. There have been a limited number of spontaneous reports of bradycardia or hypotension with bimatoprost 0.3 mg/ml eye drops, solution. LUMIGAN should be used with caution in patients predisposed to low heart rate or low blood pressure.

Other information

In studies of bimatoprost 0.3 mg/ml in patients with glaucoma or ocular hypertension, it has been shown that the more frequent exposure of the eye to more than one dose of bimatoprost daily may decrease the IOP-lowering effect (see section 4.5). Patients using LUMIGAN with other prostaglandin analogues should be monitored for changes to their intraocular pressure.

LUMIGAN 0.1 mg/ml contains the preservative benzalkonium chloride (200 ppm), which may be absorbed by soft contact lenses. Eye irritation and discolouration of the soft contact lenses may also

occur because of the presence of benzalkonium chloride. Contact lenses should be removed prior to instillation and may be reinserted 15 minutes following administration.

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 LUMIGAN 0.1 mg/ml contains 200 ppm benzalkonium chloride (four times the concentration in bimatoprost 0.3 mg/ml eye drops), it should be used with caution in dry eye patients, in patients where the cornea may be compromised and in patients taking multiple BAK-containing eye drops. In addition, monitoring is required with prolonged use in such patients.

There have been reports of bacterial keratitis associated with the use of multiple dose containers of topical ophthalmic products. These containers had been inadvertently contaminated by patients who, in most cases, had a concurrent ocular disease. Patients with a disruption of the ocular epithelial surface are at greater risk of developing bacterial keratitis.

Patients should be instructed to avoid allowing the tip of the dispensing container to contact the eye or surrounding structures, to avoid eye injury and contamination of the solution.

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed.

No interactions are anticipated in humans, since systemic concentrations of bimatoprost are extremely low (less than 0.2 ng/ml) following ocular dosing with bimatoprost 0.3 mg/ml eye drops, solution. Bimatoprost is biotransformed by any of multiple enzymes and pathways, and no effects on hepatic drug metabolising enzymes were observed in preclinical studies.

In clinical studies, bimatoprost 0.3 mg/ml eye drops, solution was used concomitantly with a number of different ophthalmic beta-blocking agents without evidence of interactions.

Concomitant use of LUMIGAN and antiglaucomatous agents other than topical beta-blockers has not been evaluated during adjunctive glaucoma therapy.

There is a potential for the IOP-lowering effect of prostaglandin analogues (e.g. LUMIGAN) to be reduced in patients with glaucoma or ocular hypertension when used with other prostaglandin analogues (see section 4.4).

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no adequate data from the use of bimatoprost in pregnant women. Animal studies have shown reproductive toxicity at high maternotoxic doses (see section 5.3).

LUMIGAN should not be used during pregnancy unless clearly necessary.

Breast-feeding

It is unknown whether bimatoprost is excreted in human breast milk. Animal studies have shown excretion of bimatoprost in breast milk. A decision must be made whether to discontinue breast-feeding or to discontinue from LUMIGAN therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman.

Fertility

There are no data on the effects of bimatoprost on human fertility.

4.7 Effects on ability to drive and use machines

LUMIGAN has negligible influence on the ability to drive and use machines. As with any ocular treatment, if transient blurred vision occurs at instillation, the patient should wait until the vision clears before driving or using machines.

4.8 Undesirable effects

Summary of the safety profile

In a 12-month Phase III clinical study approximately 38 % of patients treated with LUMIGAN 0.1 mg/ml eye drops, solution experienced adverse reactions. The most frequently reported adverse reaction was conjunctival hyperaemia (mostly trace to mild and of a non-inflammatory nature) occurring in 29 % of patients. Approximately 4 % of patients discontinued due to any adverse event in the 12-month study.

Tabulated list of adverse reactions

The following adverse reactions were reported during clinical trials with LUMIGAN 0.1 mg/ml eye drops, solution or in the post-marketing period. Most were ocular, mild and none was serious:

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); not known (cannot be estimated from available data) adverse reactions are presented according to System Organ Class in Table 1. Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

Table 1. List of adverse reactions

System Organ class	Frequency	Adverse reaction
Nervous system disorders	Uncommon	Headache
	Not known	Dizziness
Eye disorders	Very common	Conjunctival hyperaemia, prostaglandin analogue periorbitopathy
	Common	Punctate keratitis, eye irritation, eye pruritus, growth of eyelashes,eye pain, erythema of eyelid, eyelid pruritus
	Uncommon	Asthenopia, blurred vision, conjunctival disorder, conjunctival oedema, iris hyperpigmentation, madarosis, eyelid oedema
	Not known	Blepharal pigmentation, macular oedema, dry eye, eye discharge, eye oedema, foreign body sensation in eyes, lacrimation increased, ocular discomfort, photophobia
Respiratory, thoracic and mediastinal disorders	Not known	Asthma, asthma exacerbation, COPD exacerbation and dyspnoea
Gastrointestinal disorders	Uncommon	Nausea
Skin and subcutaneous tissue disorders	Common	Skin hyperpigmentation, hypertrichosis
	Uncommon	Dry skin, eyelid margin crusting, pruritus
	Not known	Skin discoloration (periocular)
General disorders and administration site conditions	Common	Instillation site irritation

Immune system disorders	Not known	Hypersensitivity reaction including signs and symptoms of eye allergy and allergic dermatitis
Vascular disorders	Not known	Hypertension

Description of selected adverse reactions

Prostaglandin analogue periorbitopathy (PAP)

Prostaglandin analogues including LUMIGAN can induce periorbital lipodystrophic changes which can lead to deepening of the eyelid sulcus, ptosis, enophthalmos, eyelid retraction, involution of dermatochalasis and inferior scleral show. Changes are typically mild, can occur as early as one month after initiation of treatment with LUMIGAN, and may cause impaired field of vision even in the absence of patient recognition. PAP is also associated with periocular skin hyperpigmentation or discoloration and hypertrichosis. All changes have been noted to be partially or fully reversible upon discontinuation or switch to alternative treatments.

Iris hyperpigmentation

Increased iris pigmentation is likely to be permanent. The pigmentation change is due to increased melanin content in the melanocytes rather than to an increase in the number of melanocytes. The long term effects of increased iris pigmentation are not known. Iris colour changes seen with ophthalmic administration of bimatoprost may not be noticeable for several months to years. Typically, the brown pigmentation around the pupil spreads concentrically towards the periphery of the iris and the entire iris or parts become more brownish. Neither naevi nor freckles of the iris appear to be affected by the treatment. At 12 months, the incidence of iris hyperpigmentation with bimatoprost 0.1 mg/ml eye drops, solution was 0.5%. At 12 months, the incidence with bimatoprost 0.3 mg/ml eye drops, solution was 1.5% (see section 4.8 Table 2) and did not increase following 3 years treatment.

In clinical studies, over 1 800 patients have been treated with LUMIGAN 0.3 mg/ml. On combining the data from phase III monotherapy and adjunctive LUMIGAN 0.3 mg/ml usage, the most frequently reported adverse reactions were:

- growth of eyelashes in up to 45 % in the first year with the incidence of new reports decreasing to 7 % at 2 years and 2 % at 3 years
- conjunctival hyperaemia (mostly trace to mild and thought to be of a non-inflammatory nature) in up to 44 % in the first year with the incidence of new reports decreasing to 13 % at 2 years and 12 % at 3 years
- ocular pruritus in up to 14 % of patients in the first year with the incidence of new reports decreasing to 3 % at 2 years and 0 % at 3 years. Less than 9 % of patients discontinued due to any adverse event in the first year with the incidence of additional patient discontinuations being 3 % at both 2 and 3 years.

Additional adverse reactions reported with LUMIGAN 0.3 mg/ml are presented in Table 2. The table also includes those adverse reactions which occurred with both formulations but at a different frequency. Most were ocular, mild to moderate, and none was serious: With each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

Table 2. List of additional adverse reactions

System Organ class	Frequency	Adverse reaction
Nervous system disorders	Common	Headache
	Uncommon	Dizziness
Eye disorders	Very common	Ocular pruritus, growth of eyelashes
	Common	Corneal erosion, ocular burning, allergic conjunctivitis, blepharitis, worsening of visual acuity, asthenopia, conjunctival oedema, foreign body sensation, ocular dryness, eye pain, photophobia, tearing, eye discharge, visual disturbance/blurred vision, increased iris pigmentation, eyelash darkening
	Uncommon	Retinal haemorrhage, uveitis, cystoid macular oedema, iritis, blepharospasm, eyelid retraction, periorbital erythema
Vascular disorders	Common	Hypertension
Skin and subcutaneous tissue disorders	Uncommon	Hirsutism
General disorders and administration site conditions	Uncommon	Asthenia
Investigations	Common	Liver function test abnormal

Adverse reactions reported in phosphate containing eye drops

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.

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 the national reporting system listed in Appendix V.

4.9 Overdose

No case of overdose has been reported, and is unlikely to occur after ocular administration.

If overdose occurs, treatment should be symptomatic and supportive. If LUMIGAN is accidentally ingested, the following information may be useful: in two-week oral rat and mouse studies, doses up to 100 mg/kg/day did not produce any toxicity. This dose expressed as mg/m^2 is at least 210 times higher than the accidental dose of one bottle of LUMIGAN 0.1 mg/ml eye drops, solution in a 10 kg child.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Ophthalmologicals - antiglaucoma preparations and miotics – prostaglandin analogues – bimatoprost - ATC code: S01EE03.

Mechanism of action

The mechanism of action by which bimatoprost reduces intraocular pressure in humans is by increasing aqueous humour outflow through the trabecular meshwork and enhancing uveoscleral outflow. Reduction of the intraocular pressure starts approximately 4 hours after the first administration and maximum effect is reached within approximately 8 to 12 hours. The duration of effect is maintained for at least 24 hours.

Bimatoprost is a potent ocular hypotensive agent. It is a synthetic prostamide, structurally related to prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$), that does not act through any known prostaglandin receptors. Bimatoprost selectively mimics the effects of newly discovered biosynthesised substances called prostamides. The prostamide receptor, however, has not yet been structurally identified.

Clinical efficacy

During a 12-month pivotal study in adults with LUMIGAN 0.1 mg/ml eye drops, the mean diurnal IOP values measured at any visit over the 12-month study period differed by no more than 1.1 mmHg throughout the day and were never greater than 17.7 mmHg.

LUMIGAN 0.1 mg/ml eye drops contains BAK in a concentration of 200 ppm.

Limited experience is available with the use of LUMIGAN in patients with open-angle glaucoma with pseudoexfoliative and pigmentary glaucoma, and chronic angle-closure glaucoma with patent iridotomy.

No clinically relevant effects on heart rate and blood pressure have been observed in clinical trials.

Paediatric population

The safety and efficacy of LUMIGAN in children aged 0 to less than 18 years has not been established.

5.2 Pharmacokinetic properties

Absorption

Bimatoprost penetrates the human cornea and sclera well *in vitro*. After ocular administration in adults, the systemic exposure of bimatoprost is very low with no accumulation over time. After once daily ocular administration of one drop of 0.3 mg/ml bimatoprost to both eyes for two weeks, blood concentrations peaked within 10 minutes after dosing and declined to below the lower limit of detection (0.025 ng/ml) within 1.5 hours after dosing. Mean C_{max} and AUC $_{0\text{-}24hrs}$ values were similar on days 7 and 14 at approximately 0.08 ng/ml and 0.09 ng•hr/ml respectively, indicating that a steady bimatoprost concentration was reached during the first week of ocular dosing.

Distribution

Bimatoprost is moderately distributed into body tissues and the systemic volume of distribution in humans at steady-state was 0.67 l/kg. In human blood, bimatoprost resides mainly in the plasma. The plasma protein binding of bimatoprost is approximately 88 %.

Biotransformation

Bimatoprost is the major circulating species in the blood once it reaches the systemic circulation following ocular dosing. Bimatoprost then undergoes oxidation, N-deethylation and glucuronidation to form a diverse variety of metabolites.

Elimination

Bimatoprost is eliminated primarily by renal excretion, up to 67 % of an intravenous dose administered to healthy adult volunteers was excreted in the urine, 25 % of the dose was excreted via the faeces. The elimination half-life, determined after intravenous administration, was approximately 45 minutes; the total blood clearance was 1.5 l/hr/kg.

Characteristics in elderly patients

After twice daily dosing with bimatoprost 0.3 mg/ml eye drops, solution, the mean $AUC_{0\text{-}24hr}$ value of 0.0634 ng•hr/ml bimatoprost in the elderly (subjects 65 years or older) were significantly higher than 0.0218 ng•hr/ml in young healthy adults. However, this finding is not clinically relevant as systemic exposure for both elderly and young subjects remained very low from ocular dosing. There was no accumulation of bimatoprost in the blood over time and the safety profile was similar in elderly and young patients.

5.3 Preclinical safety data

Effects in non-clinical studies were observed only at exposures considered sufficiently in excess of the maximum human exposure indicating little relevance to clinical use.

Monkeys administered ocular bimatoprost concentrations of ≥0.3 mg/ml daily for 1 year had an increase in iris pigmentation and reversible dose-related periocular effects characterised by a prominent upper and/or lower sulcus and widening of the palpebral fissure. The increased iris pigmentation appears to be caused by increased stimulation of melanin production in melanocytes and not by an increase in melanocyte number. No functional or microscopic changes related to the periocular effects have been observed, and the mechanism of action for the periocular changes is unknown.

Bimatoprost was not mutagenic or carcinogenic in a series of *in vitro* and *in vivo* studies.

Bimatoprost did not impair fertility in rats up to doses of 0.6 mg/kg/day (at least 103-times the intended human exposure). In embryo/foetal developmental studies abortion, but no developmental effects were seen in mice and rats at doses that were at least 860-times or 1700-times higher than the dose in humans, respectively. These doses resulted in systemic exposures of at least 33- or 97-times higher, respectively, than the intended human exposure. In rat peri/postnatal studies, maternal toxicity caused reduced gestation time, foetal death, and decreased pup body weights at ≥ 0.3 mg/kg/day (at least 41-times the intended human exposure). Neurobehavioural functions of offspring were not affected.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzalkonium chloride
Sodium chloride
Sodium phosphate dibasic heptahydrate
Citric acid monohydrate
Hydrochloric acid or sodium hydroxide (to adjust pH)
Purified water

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years.
4 weeks after first opening.

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

White opaque low density polyethylene bottles with polystyrene screw cap. Each bottle has a fill volume of 3 ml.

The following pack sizes are available: cartons containing 1 or 3 bottles of 3 ml solution. Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements for disposal.

7. MARKETING AUTHORISATION HOLDER

AbbVie Deutschland GmbH & Co. KG
Knollstrasse
67061 Ludwigshafen
Germany

8. MARKETING AUTHORISATION NUMBER

EU/1/02/205/003
EU/1/02/205/004

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 07 January 2010

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency https://www.ema.europa.eu.

1. NAME OF THE MEDICINAL PRODUCT

LUMIGAN 0.3 mg/ml eye drops, solution

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One ml of solution contains 0.3 mg bimatoprost.

Excipient with known effect
One ml of solution contains 0.05 mg benzalkonium chloride.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Eye drops, solution (eye drops)

Colourless solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Reduction of elevated intraocular pressure in chronic open-angle glaucoma and ocular hypertension in adults (as monotherapy or as adjunctive therapy to beta-blockers).

4.2 Posology and method of administration

Posology

The recommended dose is one drop in the affected eye(s) once daily, administered in the evening. The dose should not exceed once daily as more frequent administration may lessen the intraocular pressure lowering effect.

Paediatric population

The safety and efficacy of LUMIGAN in children aged 0 to 18 years has not yet been established.

Renal and hepatic impairment
LUMIGAN has not been studied in patients with renal or moderate to severe hepatic impairment and should therefore be used with caution in such patients. In patients with a history of mild liver disease or abnormal alanine aminotransferase (ALT), aspartate aminotransferase (AST) and/or bilirubin at baseline, bimatoprost 0.3 mg/ml eye drops, solution had no adverse effect on liver function over 24 months.

Method of administration

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

4.3 Contraindications

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

LUMIGAN 0.3 mg/ml is contraindicated in patients who have had a suspected previous adverse reaction to benzalkonium chloride that has led to discontinuation.

4.4 Special warnings and precautions for use

Ocular

Before treatment is initiated, patients should be informed of the possibility of prostaglandin analogue periorbitopathy (PAP) and increased iris pigmentation, since these have been observed during treatment with LUMIGAN. Some of these changes may be permanent, and may lead to impaired field of vision and differences in appearance between the eyes when only one eye is treated (see section 4.8).

Cystoid macular oedema has been uncommonly reported (≥1/1 000 to <1/100) following treatment with bimatoprost 0.3 mg/ml eye drops. Therefore, LUMIGAN should be used with caution in patients with known risk factors for macular oedema (e.g. aphakic patients, pseudophakic patients with a torn posterior lens capsule).

There have been rare spontaneous reports of reactivation of previous corneal infiltrates or ocular infections with bimatoprost 0.3 mg/ml eye drops, solution. LUMIGAN should be used with caution in patients with a prior history of significant ocular viral infections (e.g. herpes simplex) or uveitis/iritis.

LUMIGAN has not been studied in patients with inflammatory ocular conditions, neovascular, inflammatory, angle-closure glaucoma, congenital glaucoma or narrow-angle glaucoma.

Skin

There is a potential for hair growth to occur in areas where LUMIGAN solution comes repeatedly in contact with the skin surface. Thus, it is important to apply LUMIGAN as instructed and avoid it running onto the cheek or other skin areas.

Respiratory

LUMIGAN has not been studied in patients with compromised respiratory function. While there is limited information available on patients with a history of asthma or COPD, there have been reports of exacerbation of asthma, dyspnoea and COPD, as well as reports of asthma, in post-marketing experience. The frequency of these symptoms is not known. Patients with COPD, asthma or compromised respiratory function due to other conditions should be treated with caution.

Cardiovascular

LUMIGAN has not been studied in patients with heart block more severe than first degree or uncontrolled congestive heart failure. There have been a limited number of spontaneous reports of bradycardia or hypotension with bimatoprost 0.3 mg/ml eye drops, solution. LUMIGAN should be used with caution in patients predisposed to low heart rate or low blood pressure.

Other information

In studies of bimatoprost 0.3 mg/ml in patients with glaucoma or ocular hypertension, it has been shown that the more frequent exposure of the eye to more than one dose of bimatoprost daily may decrease the IOP-lowering effect (see section 4.5). Patients using LUMIGAN with other prostaglandin analogues should be monitored for changes to their intraocular pressure.

Bimatoprost 0.3 mg/ml eye drops, solution contains the preservative benzalkonium chloride, which may be absorbed by soft contact lenses. Eye irritation and discolouration of the soft contact lenses may also occur because of the presence of benzalkonium chloride. Contact lenses should be removed prior to instillation and may be reinserted 15 minutes following administration.

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 LUMIGAN contains benzalkonium chloride, monitoring is required with frequent or prolonged use in dry eye patients or where the cornea is compromised.

There have been reports of bacterial keratitis associated with the use of multiple dose containers of topical ophthalmic products. These containers had been inadvertently contaminated by patients who, in most cases, had a concurrent ocular disease. Patients with a disruption of the ocular epithelial surface are at greater risk of developing bacterial keratitis.

Patients should be instructed to avoid allowing the tip of the dispensing container to contact the eye or surrounding structures, to avoid eye injury and contamination of the solution.

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed.

No interactions are anticipated in humans, since systemic concentrations of bimatoprost are extremely low (less than 0.2 ng/ml) following ocular dosing with bimatoprost 0.3 mg/ml eye drops, solution. Bimatoprost is biotransformed by any of multiple enzymes and pathways, and no effects on hepatic drug metabolising enzymes were observed in preclinical studies.

In clinical studies, LUMIGAN was used concomitantly with a number of different ophthalmic beta-blocking agents without evidence of interactions.

Concomitant use of LUMIGAN and antiglaucomatous agents other than topical beta-blockers has not been evaluated during adjunctive glaucoma therapy.
There is a potential for the IOP-lowering effect of prostaglandin analogues (e.g. LUMIGAN) to be reduced in patients with glaucoma or ocular hypertension when used with other prostaglandin analogues (see section 4.4).

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no adequate data from the use of bimatoprost in pregnant women. Animal studies have shown reproductive toxicity at high maternotoxic doses (see section 5.3).

LUMIGAN should not be used during pregnancy unless clearly necessary.

Breast-feeding

It is unknown whether bimatoprost is excreted in human breast milk. Animal studies have shown excretion of bimatoprost in breast milk. A decision must be made whether to discontinue breast-feeding or to discontinue from LUMIGAN therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman.

Fertility

There are no data on the effects of bimatoprost on human fertility.

4.7 Effects on ability to drive and use machines

LUMIGAN has negligible influence on the ability to drive and use machines. As with any ocular treatment, if transient blurred vision occurs at instillation, the patient should wait until the vision clears before driving or using machines.

4.8 Undesirable effects

Summary of the safety profile

In clinical studies, over 1 800 patients have been treated with LUMIGAN 0.3 mg/ml eye drops, solution. On combining the data from phase III monotherapy and adjunctive LUMIGAN 0.3 mg/ml eye drops, solution usage, the most frequently reported treatment-related adverse events were: growth of eyelashes in up to 45% in the first year with the incidence of new reports decreasing to 7% at 2 years and 2% at 3 years, conjunctival hyperaemia (mostly trace to mild and thought to be of a non-inflammatory nature) in up to 44% in the first year with the incidence of new reports decreasing to 13% at 2 years and 12% at 3 years and ocular pruritus in up to 14% of patients in the first year with the incidence of new reports decreasing to 3% at 2 years and 0% at 3 years. Less than 9% of patients discontinued due to any adverse event in the first year with the incidence of additional patient discontinuations being 3% at both 2 and 3 years.

Tabulated list of adverse reactions

The following adverse reactions were reported during clinical trials with LUMIGAN 0.3 mg/ml eye drops, solution or in the post-marketing period. Most were ocular, mild to moderate, and none was serious:

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 available data) adverse reactions are presented according to System Organ Class in Table 1. Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

Table 1. List of adverse reactions

System Organ class	Frequency	Adverse reaction
Nervous system disorders	Common	Headache
	Uncommon	Dizziness
Eye disorders	Very common	Conjunctival hyperaemia, ocular pruritus, growth of eyelashes, prostaglandin analogue periorbitopathy
	Common	Superficial punctate keratitis, corneal erosion, ocular burning, ocular irritation, allergic conjunctivitis, blepharitis, worsening of visual acuity, asthenopia, conjunctival oedema, foreign body sensation, ocular dryness, eye pain, photophobia, tearing, eye discharge, visual disturbance/blurred vision, increased iris pigmentation, eyelash darkening, eyelid erythema, eyelid pruritus
	Uncommon	Retinal haemorrhage, uveitis, cystoid macular oedema, iritis, blepharospasm, eyelid retraction, periorbital erythema, eyelid oedema
	Not known	Ocular discomfort

Vascular disorders	Common	Hypertension
Respiratory, thoracic and mediastinal disorders	Not known	Asthma, asthma exacerbation, COPD exacerbation and dyspnoea
Gastrointestinal disorders	Uncommon	Nausea
Skin and subcutaneous tissue disorders	Common	Pigmentation of periocular skin
	Uncommon	Hirsutism
	Not known	Skin discoloration (periocular)
General disorders and administration site conditions	Uncommon	Asthenia
Investigations	Common	Liver function test abnormal
Immune system disorders	Not known	Hypersensitivity reaction including signs and symptoms of eye allergy and allergic dermatitis

Description of selected adverse reactions

Prostaglandin analogue periorbitopathy (PAP)

Prostaglandin analogues including LUMIGAN can induce periorbital lipodystrophic changes which can lead to deepening of the eyelid sulcus, ptosis, enophthalmos, eyelid retraction, involution of dermatochalasis and inferior scleral show. Changes are typically mild, can occur as early as one month after initiation of treatment with LUMIGAN, and may cause impaired field of vision even in the absence of patient recognition. PAP is also associated with periocular skin hyperpigmentation or discoloration and hypertrichosis. All changes have been noted to be partially or fully reversible upon discontinuation or switch to alternative treatments.

Iris hyperpigmentation

Increased iris pigmentation is likely to be permanent. The pigmentation change is due to increased melanin content in the melanocytes rather than to an increase in the number of melanocytes. The long term effects of increased iris pigmentation are not known. Iris colour changes seen with ophthalmic administration of bimatoprost may not be noticeable for several months to years. Typically, the brown pigmentation around the pupil spreads concentrically towards the periphery of the iris and the entire iris or parts become more brownish. Neither naevi nor freckles of the iris appears to be affected by the treatment. At 12 months, the incidence of iris pigmentation with bimatoprost 0.3 mg/ml was 1.5% (see section 4.8) and did not increase following 3 years treatment.

Adverse reactions reported in phosphate containing eye drops

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.

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 the national reporting system listed in Appendix V.

4.9 Overdose

No case of overdose has been reported, and is unlikely to occur after ocular administration.

If overdose occurs, treatment should be symptomatic and supportive. If LUMIGAN is accidentally ingested, the following information may be useful: in two-week oral rat and mouse studies, doses up to 100 mg/kg/day did not produce any toxicity. This dose expressed as mg/m^2 is at least 70-times higher than the accidental dose of one bottle of LUMIGAN 0.3 mg/ml eye drops, solution in a 10 kg child.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Ophthalmologicals - antiglaucoma preparations and miotics - prostaglandin analogues - bimatoprost - ATC code: S01EE03.

Mechanism of action

The mechanism of action by which bimatoprost reduces intraocular pressure in humans is by increasing aqueous humour outflow through the trabecular meshwork and enhancing uveoscleral outflow. Reduction of the intraocular pressure starts approximately 4 hours after the first administration and maximum effect is reached within approximately 8 to 12 hours. The duration of effect is maintained for at least 24 hours.

Bimatoprost is a potent ocular hypotensive agent. It is a synthetic prostamide, structurally related to prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$), that does not act through any known prostaglandin receptors. Bimatoprost selectively mimics the effects of newly discovered biosynthesised substances called prostamides. The prostamide receptor, however, has not yet been structurally identified.

Clinical efficacy

During 12 months' monotherapy treatment with LUMIGAN 0.3 mg/ml in adults, versus timolol, mean change from baseline in morning (08:00) intraocular pressure ranged from -7.9 to -8.8 mm Hg. At any visit, the mean diurnal IOP values measured over the 12-month study period differed by no more than 1.3 mmHg throughout the day and were never greater than 18.0 mmHg.

In a 6-month clinical study with LUMIGAN 0.3 mg/ml versus latanoprost, a statistically superior reduction in morning mean IOP (ranging from -7.6 to -8.2 mmHg for bimatoprost versus –6.0 to -7.2 mmHg for latanoprost) was observed at all visits throughout the study. Conjunctival hyperaemia, growth of eyelashes, and eye pruritus were statistically significantly higher with bimatoprost than with latanoprost, however, the discontinuation rates due to adverse events were low with no statistically significant difference.

Compared to treatment with beta-blocker alone, adjunctive therapy with beta-blocker and LUMIGAN 0.3 mg/ml lowered mean morning (08:00) intraocular pressure by -6.5 to -8.1 mmHg.

Limited experience is available with the use of LUMIGAN in patients with open-angle glaucoma with pseudoexfoliative and pigmentary glaucoma, and chronic angle-closure glaucoma with patent iridotomy.

No clinically relevant effects on heart rate and blood pressure have been observed in clinical trials.

Paediatric population

The safety and efficacy of LUMIGAN in children aged 0 to less than 18 years has not been established.

5.2 Pharmacokinetic properties

Absorption

Bimatoprost penetrates the human cornea and sclera well *in vitro*. After ocular administration in adults, the systemic exposure of bimatoprost is very low with no accumulation over time. After once daily ocular administration of one drop of LUMIGAN 0.3 mg/ml to both eyes for two weeks, blood

concentrations peaked within 10 minutes after dosing and declined to below the lower limit of detection (0.025 ng/ml) within 1.5 hours after dosing. Mean C_{max} and AUC $_{0\text{-}24hrs}$ values were similar on days 7 and 14 at approximately 0.08 ng/ml and 0.09 ng•hr/ml respectively, indicating that a steady bimatoprost concentration was reached during the first week of ocular dosing.

Distribution

Bimatoprost is moderately distributed into body tissues and the systemic volume of distribution in humans at steady-state was 0.67 l/kg. In human blood, bimatoprost resides mainly in the plasma. The plasma protein binding of bimatoprost is approximately 88%.

Biotransformation

Bimatoprost is the major circulating species in the blood once it reaches the systemic circulation following ocular dosing. Bimatoprost then undergoes oxidation, N-deethylation and glucuronidation to form a diverse variety of metabolites.

Elimination

Bimatoprost is eliminated primarily by renal excretion, up to 67% of an intravenous dose administered to healthy adult volunteers was excreted in the urine, 25% of the dose was excreted via the faeces. The elimination half-life, determined after intravenous administration, was approximately 45 minutes; the total blood clearance was 1.5 l/hr/kg.

Characteristics in elderly patients

After twice daily dosing of LUMIGAN 0.3 mg/ml, the mean $AUC_{0\text{-}24hr}$ value of 0.0634 ng•hr/ml bimatoprost in the elderly (subjects 65 years or older) were significantly higher than 0.0218 ng•hr/ml in young healthy adults. However, this finding is not clinically relevant as systemic exposure for both elderly and young subjects remained very low from ocular dosing. There was no accumulation of bimatoprost in the blood over time and the safety profile was similar in elderly and young patients.

5.3 Preclinical safety data

Effects in non-clinical studies were observed only at exposures considered sufficiently in excess of the maximum human exposure indicating little relevance to clinical use.

Monkeys administered ocular bimatoprost concentrations of ≥0.3 mg/ml daily for 1 year had an increase in iris pigmentation and reversible dose-related periocular effects characterised by a prominent upper and/or lower sulcus and widening of the palpebral fissure. The increased iris pigmentation appears to be caused by increased stimulation of melanin production in melanocytes and not by an increase in melanocyte number. No functional or microscopic changes related to the periocular effects have been observed, and the mechanism of action for the periocular changes is unknown.

Bimatoprost was not mutagenic or carcinogenic in a series of *in vitro* and *in vivo* studies.

Bimatoprost did not impair fertility in rats up to doses of 0.6 mg/kg/day (at least 103-times the intended human exposure). In embryo/foetal developmental studies abortion, but no developmental effects were seen in mice and rats at doses that were at least 860-times or 1700-times higher than the dose in humans, respectively. These doses resulted in systemic exposures of at least 33- or 97-times higher, respectively, than the intended human exposure. In rat peri/postnatal studies, maternal toxicity caused reduced gestation time, foetal death, and decreased pup body weights at ≥0.3 mg/kg/day (at least 41-times the intended human exposure). Neurobehavioural functions of offspring were not affected.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzalkonium chloride
Sodium chloride
Sodium phosphate dibasic heptahydrate
Citric acid monohydrate
Hydrochloric acid or sodium hydroxide (to adjust pH)
Purified water

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years.
4 weeks after first opening.

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

White opaque low density polyethylene bottles with polystyrene screw cap. Each bottle has a fill volume of 3 ml.

The following pack sizes are available: cartons containing 1 or 3 bottles of 3 ml solution. Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements for disposal.

7. MARKETING AUTHORISATION HOLDER

AbbVie Deutschland GmbH & Co. KG
Knollstrasse
67061 Ludwigshafen
Germany

8. MARKETING AUTHORISATION NUMBER

EU/1/02/205/001
EU/1/02/205/002

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation:8 March 2002
Date of latest renewal: 20 February 2007

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency https://www.ema.europa.eu.

1. NAME OF THE MEDICINAL PRODUCT

LUMIGAN 0.3 mg/ml eye drops, solution, in single-dose container

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One ml of solution contains 0.3 mg bimatoprost.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Eye drops, solution, in single-dose container.

Colourless solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Reduction of elevated intraocular pressure in chronic open-angle glaucoma and ocular hypertension in adults (as monotherapy or as adjunctive therapy to beta-blockers).

4.2 Posology and method of administration

Posology

The recommended dose is one drop in the affected eye(s) once daily, administered in the evening. The dose should not exceed once daily as more frequent administration may lessen the intraocular pressure lowering effect.

For single use only, one container is sufficient to treat both eyes. Any unused solution should be discarded immediately after use.

Paediatric population

The safety and efficacy of LUMIGAN in children aged 0 to 18 years has not yet been established.

Renal and hepatic impairment

LUMIGAN has not been studied in patients with renal or moderate to severe hepatic impairment and should therefore be used with caution in such patients. In patients with a history of mild liver disease or abnormal alanine aminotransferase (ALT), aspartate aminotransferase (AST) and/or bilirubin at baseline, bimatoprost 0.3 mg/ml eye drops (multi-dose formulation), solution had no adverse effect on liver function over 24 months.

Method of administration

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

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

Ocular

Before treatment is initiated, patients should be informed of the possibility of prostaglandin analogue periorbitopathy (PAP) and increased iris pigmentation, since these have been observed during treatment with LUMIGAN. Some of these changes may be permanent, and may lead to impaired field of vision and differences in appearance between the eyes when only one eye is treated (see section 4.8).

Cystoid macular oedema has been uncommonly reported (≥1/1 000 to <1/100) following treatment with bimatoprost 0.3 mg/ml eye drops (multi-dose formulation). Therefore, LUMIGAN should be used with caution in patients with known risk factors for macular oedema (e.g. aphakic patients, pseudophakic patients with a torn posterior lens capsule).

There have been rare spontaneous reports of reactivation of previous corneal infiltrates or ocular infections with bimatoprost 0.3 mg/ml eye drops, solution (multi-dose formulation). LUMIGAN should be used with caution in patients with a prior history of significant ocular viral infections (e.g. herpes simplex) or uveitis/iritis.

LUMIGAN has not been studied in patients with inflammatory ocular conditions, neovascular, inflammatory, angle-closure glaucoma, congenital glaucoma or narrow-angle glaucoma.

Skin

There is a potential for hair growth to occur in areas where LUMIGAN solution comes repeatedly in contact with the skin surface. Thus, it is important to apply LUMIGAN as instructed and avoid it running onto the cheek or other skin areas.

Respiratory

LUMIGAN has not been studied in patients with compromised respiratory function. While there is limited information available on patients with a history of asthma or COPD, there have been reports of exacerbation of asthma, dyspnoea and COPD, as well as reports of asthma, in post-marketing experience. The frequency of these symptoms is not known. Patients with COPD, asthma or compromised respiratory function due to other conditions should be treated with caution.

Cardiovascular

LUMIGAN has not been studied in patients with heart block more severe than first degree or uncontrolled congestive heart failure. There have been a limited number of spontaneous reports of bradycardia or hypotension with bimatoprost 0.3 mg/ml eye drops, solution (multi-dose formulation). LUMIGAN should be used with caution in patients predisposed to low heart rate or low blood pressure.

Other information

In studies of bimatoprost 0.3 mg/ml in patients with glaucoma or ocular hypertension, it has been shown that the more frequent exposure of the eye to more than one dose of bimatoprost daily may decrease the IOP-lowering effect (see section 4.5). Patients using LUMIGAN with other prostaglandin analogues should be monitored for changes to their intraocular pressure.

LUMIGAN 0.3 mg/mL single-dose has not been studied in patients wearing contact lenses. Contact lenses should be removed prior to instillation and may be reinserted 15 minutes following administration.

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed.

No interactions are anticipated in humans, since systemic concentrations of bimatoprost are extremely low (less than 0.2 ng/mL) following ocular dosing with bimatoprost 0.3 mg/ml eye drops, solution (multi-dose formulation). Bimatoprost is biotransformed by any of multiple enzymes and pathways, and no effects on hepatic drug metabolising enzymes were observed in preclinical studies.

In clinical studies, LUMIGAN 0.3 mg/mL (multi-dose formulation) was used concomitantly with a number of different ophthalmic beta-blocking agents without evidence of interactions.

Concomitant use of LUMIGAN and antiglaucomatous agents other than topical beta-blockers has not been evaluated during adjunctive glaucoma therapy.

There is a potential for the IOP-lowering effect of prostaglandin analogues (e.g. LUMIGAN) to be reduced in patients with glaucoma or ocular hypertension when used with other prostaglandin analogues (see section 4.4).

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no adequate data from the use of bimatoprost in pregnant women. Animal studies have shown reproductive toxicity at high maternotoxic doses (see section 5.3).

LUMIGAN should not be used during pregnancy unless clearly necessary.

Breast-feeding

It is unknown whether bimatoprost is excreted in human breast milk. Animal studies have shown excretion of bimatoprost in breast milk. A decision must be made whether to discontinue breast-feeding or to discontinue from LUMIGAN therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman.

Fertility

There are no data on the effects of bimatoprost on human fertility.

4.7 Effects on ability to drive and use machines

LUMIGAN has negligible influence on the ability to drive and use machines. As with any ocular treatment, if transient blurred vision occurs at instillation, the patient should wait until the vision clears before driving or using machines.

4.8 Undesirable effects

Summary of safety profile

In a 3 month clinical study, approximately 29% of patients treated with LUMIGAN 0.3 mg/mL single-dose experienced adverse reactions. The most frequently reported adverse reactions were conjuctival hyperaemia (mostly trace to mild and of a non-inflammatory nature) occurring in 24% of patients, and eye pruritis occurring in 4% of patients. Approximately 0.7% of patients in the LUMIGAN 0.3 mg/mL single-dose group discontinued due to any adverse event in the 3 month study.

Tabulated list of adverse reactions

The following adverse reactions were reported during clinical trials with LUMIGAN 0.3 mg/ml single-dose or in the post-marketing period. Most were ocular, mild and none was serious:

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 available data) adverse reactions are presented according to System Organ Class in Table 1. Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

Table 1 List of adverse reactions

System Organ class	Frequency	Adverse reaction
Nervous system disorders	Uncommon	Headache
	not known	Dizziness
Eye disorders	Very common	Conjunctival hyperaemia, prostaglandin analogue periorbitopathy
	Common	Punctate keratitis, eye irritation, foreign body sensation, dry eye, eye pain, eye pruritus, growth of eyelashes, eyelid erythema
	Uncommon	Asthenopia, conjunctival oedema, photophobia, lacrimation increased, iris hyperpigmentation, blurred vision, eyelid pruritus, eyelid oedema
	Not known	Eye discharge, ocular discomfort
Respiratory, thoracic and mediastinal disorders	Not known	Asthma, asthma exacerbation, COPD exacerbation and dyspnoea
Skin and subcutaneous tissue disorders	Common	Skin hyperpigmentation (periocular)
	Uncommon	Hair growth abnormal
	Not known	Skin discoloration (periocular)
Immune system disorders	Not known	Hypersensitivity reaction including signs and symptoms of eye allergy and allergic dermatitis
Vascular disorders	Not known	Hypertension

Description of selected adverse reactions

Prostaglandin analogue periorbitopathy (PAP)

Prostaglandin analogues including LUMIGAN can induce periorbital lipodystrophic changes which can lead to deepening of the eyelid sulcus, ptosis, enophthalmos, eyelid retraction, involution of dermatochalasis and inferior scleral show. Changes are typically mild, can occur as early as one month after initiation of treatment with LUMIGAN, and may cause impaired field of vision even in the absence of patient recognition. PAP is also associated with periocular skin hyperpigmentation or discoloration and hypertrichosis. All changes have been noted to be partially or fully reversible upon discontinuation or switch to alternative treatments.

Iris hyperpigmentation

Increased iris pigmentation is likely to be permanent. The pigmentation change is due to increased melanin content in the melanocytes rather than to an increase in the number of melanocytes. The long term effects of increased iris pigmentation are not known. Iris colour changes seen with ophthalmic administration of bimatoprost may not be noticeable for several months to years. Typically, the brown pigmentation around the pupil spreads concentrically towards the periphery of the iris and the entire iris or parts become more brownish. Neither naevi nor freckles of the iris appear to be affected by the treatment. At 3 months, the incidence of iris hyperpigmentation with bimatoprost 0.3 mg/mL single-dose was 0.3%. At 12 months, the incidence of iris pigmentation with bimatoprost 0.3 mg/mL (multi-dose formulation) was 1.5% (see section 4.8) and did not increase following 3 years treatment.

In clinical studies, over 1 800 patients have been treated with LUMIGAN 0.3 mg/ml (multi-dose formulation). On combining the data from phase III monotherapy and adjunctive LUMIGAN 0.3 mg/ml (multi-dose formulation) usage, the most frequently reported adverse reactions were:

- growth of eyelashes in up to 45% in the first year with the incidence of new reports decreasing to 7% at 2 years and 2% at 3 years
- conjunctival hyperaemia (mostly trace to mild and thought to be of a non-inflammatory nature) in up to 44% in the first year with the incidence of new reports decreasing to 13% at 2 years and 12% at 3 years
- ocular pruritus in up to 14% of patients in the first year with the incidence of new reports decreasing to 3% at 2 years and 0% at 3 years.

Less than 9% of patients discontinued due to any adverse event in the first year with the incidence of additional patient discontinuations being 3% at both 2 and 3 years.

Table 2 lists adverse reactions that were seen in a 12-month clinical study with LUMIGAN 0.3 mg/mL (multi-dose formulation), but were reported at a higher frequency than with LUMIGAN 0.3 mg/mL (single-dose). Most were ocular, mild to moderate, and none were serious.

Table 2 List of adverse reactions with LUMIGAN 0.3 mg/ml (multi-dose formulation)

System Organ class	**Frequency**	**Adverse Reaction**
Nervous system disorders	Common	Headache
Eye disorders	Very common	Ocular pruritus, growth of eyelashes
	Common	Asthenopia, conjunctival oedema, photophobia, tearing, increased iris pigmentation; blurred vision
Skin and subcutaneous tissue disorders	Common	Eyelid pruritus

In addition to the adverse reactions seen with LUMIGAN 0.3 mg/mL single-dose, Table 3 lists additional adverse reactions that were seen with LUMIGAN 0.3 mg/mL (multi-dose formulation). Most were ocular, mild to moderate, and none were serious.

Table 3 Additional adverse reactions seen with LUMIGAN 0.3 mg/ml (multi-dose formulation)

System Organ class	Frequency	Adverse Reaction
Nervous system disorders	Uncommon	Dizziness
Eye disorders	Common	Corneal erosion, ocular burning, allergic conjunctivitis, blepharitis, worsening of visual acuity, eye discharge, visual disturbance, eyelash darkening
	Uncommon	Retinal haemorrhage, uveitis, cystoid macular oedema, iritis, blepharospasm, eyelid retraction
Vascular disorders	Common	Hypertension
Gastrointestinal disorders	Uncommon	Nausea
Skin and subcutaneous tissue disorders	Not known	Periobital erythema
General disorders and administration site conditions	Uncommon	Asthenia
Investigations	Common	Liver function test abnormal

Adverse reactions reported in phosphate containing eye drops

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.

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 the national reporting system listed in Appendix V.

4.9 Overdose

No information is available on overdose in humans; overdose is unlikely to occur after ocular administration.

If overdose occurs, treatment should be symptomatic and supportive. If LUMIGAN 0.3 mg/mL single-dose is accidentally ingested, the following information may be useful: In short term oral (by gavage) mouse and rat studies, doses up to 100 mg/kg/day of bimatoprost did not produce any toxicity. This dose is at least 22 times higher than an accidental dose of the entire content of a pack of LUMIGAN 0.3 mg/mL single-dose (30 x 0.4 mL single-dose containers; 12 mL) in a 10 kg child.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Ophthalmologicals - antiglaucoma preparations and miotics - prostaglandin analogues - bimatoprost - ATC code: S01EE03.

Mechanism of action

The mechanism of action by which bimatoprost reduces intraocular pressure in humans is by increasing aqueous humour outflow through the trabecular meshwork and enhancing uveoscleral

outflow. Reduction of the intraocular pressure starts approximately 4 hours after the first administration and maximum effect is reached within approximately 8 to 12 hours. The duration of effect is maintained for at least 24 hours.

Bimatoprost is a potent ocular hypotensive agent. It is a synthetic prostamide, structurally related to prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$), that does not act through any known prostaglandin receptors. Bimatoprost selectively mimics the effects of newly discovered biosynthesised substances called prostamides. The prostamide receptor, however, has not yet been structurally identified.

Clinical efficacy

A 12 week (double-masked, randomized, parallel group) clinical study compared the efficacy and safety of LUMIGAN 0.3 mg/mL single-dose with LUMIGAN 0.3 mg/mL (multi-dose formulation). LUMIGAN 0.3 mg/mL single-dose achieved non-inferior IOP-lowering efficacy to LUMIGAN 0.3 mg/mL (multi-dose formulation) for worse eye IOP change from baseline in patients with glaucoma or ocular hypertension. LUMIGAN 0.3 mg/mL single-dose also achieved equivalent IOP-lowering efficacy with LUMIGAN 0.3 mg/mL (multi-dose formulation) in average eye IOP at each follow-up timepoint at weeks 2, 6 and 12.

During 12 months' monotherapy treatment with LUMIGAN 0.3 mg/ml (multi-dose formulation) in adults, versus timolol, mean change from baseline in morning (08:00) intraocular pressure ranged from -7.9 to -8.8 mmHg. At any visit, the mean diurnal IOP values measured over the 12-month study period differed by no more than 1.3 mmHg throughout the day and were never greater than 18.0 mmHg.

In a 6-month clinical study with LUMIGAN 0.3 mg/ml (multi-dose formulation), versus latanoprost, a statistically superior reduction in morning mean IOP (ranging from -7.6 to -8.2 mmHg for bimatoprost versus –6.0 to -7.2 mmHg for latanoprost) was observed at all visits throughout the study. Conjunctival hyperaemia, growth of eyelashes, and eye pruritus were statistically significantly higher with bimatoprost than with latanoprost, however, the discontinuation rates due to adverse events were low with no statistically significant difference.

Compared to treatment with beta-blocker alone, adjunctive therapy with beta-blocker and LUMIGAN 0.3 mg/ml (multi-dose formulation) lowered mean morning (08:00) intraocular pressure by -6.5 to -8.1 mmHg.

Limited experience is available in patients with open-angle glaucoma with pseudoexfoliative and pigmentary glaucoma, and chronic angle-closure glaucoma with patent iridotomy.

No clinically relevant effects on heart rate and blood pressure have been observed in clinical trials.

Paediatric population

The safety and efficacy of LUMIGAN in children aged 0 to 18 years has not been established.

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Absorption

Bimatoprost penetrates the human cornea and sclera well *in vitro*. After ocular administration in adults, the systemic exposure of bimatoprost is very low with no accumulation over time. After once daily ocular administration of one drop of LUMIGAN 0.3 mg/ml to both eyes for two weeks, blood concentrations peaked within 10 minutes after dosing and declined to below the lower limit of detection (0.025 ng/ml) within 1.5 hours after dosing. Mean C_{max} and $AUC_{0\text{-}24hrs}$ values were similar on days 7 and 14 at approximately 0.08 ng/ml and 0.09 ng•hr/ml respectively, indicating that a steady bimatoprost concentration was reached during the first week of ocular dosing.

Distribution

Bimatoprost is moderately distributed into body tissues and the systemic volume of distribution in humans at steady-state was 0.67 l/kg. In human blood, bimatoprost resides mainly in the plasma. The plasma protein binding of bimatoprost is approximately 88%.

Biotransformation

Bimatoprost is the major circulating species in the blood once it reaches the systemic circulation following ocular dosing. Bimatoprost then undergoes oxidation, N-deethylation and glucuronidation to form a diverse variety of metabolites.

Elimination

Bimatoprost is eliminated primarily by renal excretion, up to 67% of an intravenous dose administered to healthy adult volunteers was excreted in the urine, 25% of the dose was excreted via the faeces. The elimination half-life, determined after intravenous administration, was approximately 45 minutes; the total blood clearance was 1.5 l/hr/kg.

Characteristics in elderly patients

After twice daily dosing of LUMIGAN 0.3 mg/ml, the mean $AUC_{0\text{-}24hr}$ value of 0.0634 ng•hr/ml bimatoprost in the elderly (subjects 65 years or older) were significantly higher than 0.0218 ng•hr/ml in young healthy adults. However, this finding is not clinically relevant as systemic exposure for both elderly and young subjects remained very low from ocular dosing. There was no accumulation of bimatoprost in the blood over time and the safety profile was similar in elderly and young patients.

5.3 Preclinical safety data

Effects in non-clinical studies were observed only at exposures considered sufficiently in excess of the maximum human exposure indicating little relevance to clinical use.

Monkeys administered ocular bimatoprost concentrations of ≥0.3 mg/ml daily for 1 year had an increase in iris pigmentation and reversible dose-related periocular effects characterised by a prominent upper and/or lower sulcus and widening of the palpebral fissure. The increased iris pigmentation appears to be caused by increased stimulation of melanin production in melanocytes and not by an increase in melanocyte number. No functional or microscopic changes related to the periocular effects were observed, and the mechanism of action for the periocular changes is unknown.

Bimatoprost was not mutagenic or carcinogenic in a series of *in vitro* and *in vivo* studies.

Bimatoprost did not impair fertility in rats up to doses of 0.6 mg/kg/day (at least 103-times the intended human exposure). In embryo/foetal developmental studies abortion, but no developmental effects were seen in mice and rats at doses that were at least 860-times or 1700-times higher than the dose in humans, respectively. These doses resulted in systemic exposures of at least 33- or 97-times higher, respectively, than the intended human exposure. In rat peri/postnatal studies, maternal toxicity caused reduced gestation time, foetal death, and decreased pup body weights at ≥0.3 mg/kg/day (at least 41-times the intended human exposure). Neurobehavioural functions of offspring were not affected.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium chloride
Sodium phosphate dibasic heptahydrate
Citric acid monohydrate
Hydrochloric acid or sodium hydroxide (to adjust pH)
Purified water

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

5 pack – 12 months
30 pack – 18 months
90 pack – 18 months
Once the pouch is opened, the single-dose containers should be used within 30 days.

Discard the opened single-dose container immediately after use.

6.4 Special precautions for storage

5 pack - Do not store above 25°C
30 pack - No special requirements for storage
90 pack - No special requirements for storage

6.5 Nature and contents of container

Clear, single-dose Low Density Polyethylene (LDPE) containers with a twist-off tab.

Each single-dose container contains 0.4 ml solution.

The following pack sizes are available:
Carton containing 5 single-dose containers,
Carton containing 30 or 90 single-dose containers in three or nine aluminium foil pouches, respectively.
Each pouch contains 10 single-dose containers.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements for disposal.

7. MARKETING AUTHORISATION HOLDER

AbbVie Deutschland GmbH & Co. KG
Knollstrasse
67061 Ludwigshafen
Germany

8. MARKETING AUTHORISATION NUMBER

EU/1/02/205/005
EU/1/02/205/006
EU/1/02/205/007

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation:8 March 2002
Date of latest renewal: 20 February 2007

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency https://www.ema.europa.eu.

ANNEX II

A. MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

A. MANUFACTURERS RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer responsible for batch release

Allergan Pharmaceuticals Ireland
Castlebar Road
Westport
County Mayo
Ireland

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to medical prescription.

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

- **Periodic safety update reports (PSURs)**

The requirements for submission of PSURs for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

- **Risk management plan (RMP)**

The marketing authorisation holder (MAH) shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the marketing authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

If the dates for submission of a PSUR and the update of a RMP coincide, they can be submitted at the same time.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON FOR SINGLE BOTTLE

1. NAME OF THE MEDICINAL PRODUCT

LUMIGAN 0.1 mg/ml eye drops, solution
bimatoprost

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One ml of solution contains 0.1 mg bimatoprost

3. LIST OF EXCIPIENTS

Benzalkonium chloride, sodium phosphate dibasic heptahydrate, citric acid monohydrate, sodium chloride, hydrochloric acid or sodium hydroxide (to adjust pH) and purified water. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Eye drops, solution
1 x 3 ml

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Ocular use
Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

Remove contact lenses before use.

8. EXPIRY DATE

EXP
Discard four weeks after first opening.
Opened:

9. SPECIAL STORAGE CONDITIONS

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

AbbVie Deutschland GmbH & Co. KG
Knollstrasse
67061 Ludwigshafen
Germany

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/02/205/003

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

lumigan 0.1 mg/ml

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON CONTAINING THREE BOTTLES

1. NAME OF THE MEDICINAL PRODUCT

LUMIGAN 0.1 mg/ml eye drops, solution
bimatoprost

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One ml of solution contains 0.1 mg bimatoprost

3. LIST OF EXCIPIENTS

Benzalkonium chloride, sodium phosphate dibasic heptahydrate, citric acid monohydrate, sodium chloride, hydrochloric acid or sodium hydroxide (to adjust pH) and purified water. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Eye drops, solution
3 x 3 ml

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Ocular use
Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach and children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

Remove contact lenses before use.

8. EXPIRY DATE

EXP
Discard four weeks after first opening.
Opened (1):
Opened (2):
Opened (3):

9. SPECIAL STORAGE CONDITIONS

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

AbbVie Deutschland GmbH & Co. KG
Knollstrasse
67061 Ludwigshafen
Germany

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/02/205/004

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

lumigan 0.1 mg/ml

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

BOTTLE LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

LUMIGAN 0.1 mg/ml eye drops
bimatoprost
Ocular use

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

3 ml

6. OTHER

AbbVie (as logo)

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON FOR SINGLE BOTTLE

1. NAME OF THE MEDICINAL PRODUCT

LUMIGAN 0.3 mg/ml eye drops, solution
bimatoprost

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One ml of solution contains 0.3 mg bimatoprost

3. LIST OF EXCIPIENTS

Benzalkonium chloride, sodium phosphate dibasic heptahydrate, citric acid monohydrate, sodium chloride, hydrochloric acid or sodium hydroxide (to adjust pH) and purified water. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Eye drops, solution
1 x 3 ml

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Ocular use
Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

Remove contact lenses before use.

8. EXPIRY DATE

EXP
Discard 4 weeks after first opening.
Opened:

9. SPECIAL STORAGE CONDITIONS

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

AbbVie Deutschland GmbH & Co. KG
Knollstrasse
67061 Ludwigshafen
Germany

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/02/205/001

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

lumigan 0.3 mg/ml

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON CONTAINING THREE BOTTLES

1. NAME OF THE MEDICINAL PRODUCT

LUMIGAN 0.3 mg/ml eye drops, solution
bimatoprost

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One ml of solution contains 0.3 mg bimatoprost

3. LIST OF EXCIPIENTS

Benzalkonium chloride, sodium phosphate dibasic heptahydrate, citric acid monohydrate, sodium chloride, hydrochloric acid or sodium hydroxide (to adjust pH) and purified water. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Eye drops, solution
3 x 3 ml

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Ocular use
Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

Remove contact lenses before use.

8. EXPIRY DATE

EXP
Discard 4 weeks after first opening.
Opened (1):
Opened (2):
Opened (3):

9. SPECIAL STORAGE CONDITIONS

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

AbbVie Deutschland GmbH & Co. KG
Knollstrasse
67061 Ludwigshafen
Germany

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/02/205/002

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

lumigan 0.3 mg/ml

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

BOTTLE LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

LUMIGAN 0.3 mg/ml eye drops
bimatoprost
Ocular use

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

3 ml

6. OTHER

AbbVie (as logo)

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON CONTAINING 5 SINGLE-DOSE CONTAINERS

1. NAME OF THE MEDICINAL PRODUCT

LUMIGAN 0.3 mg/ml eye drops, solution, in Single-dose container
bimatoprost

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One ml of solution contains 0.3 mg bimatoprost.

3. LIST OF EXCIPIENTS

Sodium phosphate dibasic heptahydrate, citric acid monohydrate, sodium chloride, hydrochloric acid or sodium hydroxide (to adjust pH) and purified water.

4. PHARMACEUTICAL FORM AND CONTENTS

Eye drops, solution
5 x 0.4 ml

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Ocular use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Do not store above 25°C.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

Discard the opened single-dose container immediately after use.

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

AbbVie Deutschland GmbH & Co. KG
Knollstrasse
67061 Ludwigshafen
Germany

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/02/205/005

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

For single use only

16. INFORMATION IN BRAILLE

lumigan 0.3 mg/ml single-dose

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON CONTAINING 30 or 90 SINGLE-DOSE CONTAINERS

1. NAME OF THE MEDICINAL PRODUCT

LUMIGAN 0.3 mg/ml eye drops, solution, in Single-dose container
bimatoprost

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One ml of solution contains 0.3 mg bimatoprost.

3. LIST OF EXCIPIENTS

Sodium phosphate dibasic heptahydrate, citric acid monohydrate, sodium chloride, hydrochloric acid or sodium hydroxide (to adjust pH) and purified water.

4. PHARMACEUTICAL FORM AND CONTENTS

Eye drops, solution
30 x 0.4 ml
90 x 0.4 ml

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Ocular use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP
Once the pouch is opened, the single-dose containers should be used within 30 days.

9. SPECIAL STORAGE CONDITIONS

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

Discard the opened single-dose container immediately after use.

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

AbbVie Deutschland GmbH & Co. KG
Knollstrasse
67061 Ludwigshafen
Germany

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/02/205/006
EU/1/02/205/007

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

For single use only

16. INFORMATION IN BRAILLE

lumigan 0.3 mg/ml single-dose

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

POUCH CONTAINING 10 SINGLE-DOSE CONTAINERS

1. NAME OF THE MEDICINAL PRODUCT

LUMIGAN 0.3 mg/ml eye drops, solution, in Single-dose container
bimatoprost

2. NAME OF THE MARKETING AUTHORISATION HOLDER

AbbVie (as logo)

3. EXPIRY DATE

EXP
Once the pouch is opened, the single-dose containers should be used within 30 days.

4. BATCH NUMBER

Lot

5. OTHER

Ocular use.
10 single-dose containers.
Single use only.
Read the package leaflet before use.
Discard the opened single-dose container immediately after use.

PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

SINGLE-DOSE CONTAINER

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

LUMIGAN 0.3 mg/ml
bimatoprost

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

6. OTHER

B. PACKAGE LEAFLET

Package leaflet: Information for the patient

LUMIGAN 0.1 mg/ml eye drops, solution
bimatoprost

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What LUMIGAN is and what it is used for

LUMIGAN is an antiglaucoma preparation. It belongs to a group of medicines called prostamides.

LUMIGAN eye drops are used to reduce high pressure in the eye. This medicine may be used on its own or with other drops called beta-blockers which also reduce pressure.

Your eye contains a clear, watery liquid that feeds the inside of the eye. Liquid is constantly being drained out of the eye and new liquid is made to replace this. If the liquid cannot drain out quickly enough, the pressure inside the eye builds up. This medicine works by increasing the amount of liquid that is drained. This reduces the pressure inside the eye. If the high pressure is not reduced, it could lead to a disease called glaucoma and eventually damage your sight.

2. What you need to know before you use LUMIGAN

Do not use LUMIGAN:
- if you are allergic to bimatoprost or any of the other ingredients of this medicine (listed in section 6).
- if you have had to stop using eye drops in the past because of a side effect of the preservative benzalkonium chloride.

Warnings and precautions:
Talk to your doctor or pharmacist before you use LUMIGAN if:
- You have any breathing problems
- You have liver or kidney problems
- You have had a cataract surgery in the past
- You have dry eye
- You have or have had any problems with your cornea (front transparent part of the eye)
- You wear contact lenses (see “Lumigan contains benzalkonium chloride”)
- You have or have had low blood pressure or low heart rate
- You have had a viral infection or inflammation of the eye

During treatment, LUMIGAN may cause a loss of fat around the eye, which may cause your eyelid crease to deepen, your eye to appear sunken (enophthalmos), your upper eyelid to droop (ptosis), the skin around your eye to tighten (involution of dermatochalasis) and the lower white part of your eye to become more visible (inferior scleral show). The changes are typically mild, but if pronounced, they can affect your field of vision. The changes may disappear if you stop taking LUMIGAN. LUMIGAN may also cause your eyelashes to darken and grow, and cause the skin around the eyelid to darken too. The colour of your iris may also go darker. These changes may be permanent. The changes may be more noticeable if you are only treating one eye.

Children and adolescents
LUMIGAN has not been tested in children under the age of 18 and therefore should not be used by patients under 18 years.

Other medicines and LUMIGAN
Tell your doctor or pharmacist if you are taking, have recently taken, or might take any other medicines.

Pregnancy and breast-feeding
If you are pregnant or breast-feeding, think you might be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking any medicine.

LUMIGAN may get into breast milk so you should not breast-feed while you are taking LUMIGAN.

Driving and using machines
Your sight may become blurred for a short time just after using LUMIGAN. You should not drive or use machines until your sight is clear again.

LUMIGAN contains benzalkonium chloride
This medicine contains 0.6 mg benzalkonium chloride in each 3 ml of solution which is equivalent to 0.2 mg/ml.
Do not use the drops when you are wearing your lenses. A preservative in LUMIGAN, benzalkonium chloride may be absorbed by soft contact lenses and may change the colour of the contact lenses. You should remove contact lenses before using this medicine and wait 15 minutes after using the drops before you put your lenses back in. Benzalkonium chloride may also cause eye irritation, especially if you have dry eyes or disorders of the cornea (the clear layer at the front of the eye). If you feel abnormal eye sensation, stinging or pain in the eye after using this medicine, talk to your doctor.

3. How to use LUMIGAN

Always use this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

LUMIGAN should only be applied to the eye. The recommended dose is one drop of LUMIGAN in the evening, once daily in each eye that needs treatment.

If you use LUMIGAN with another eye medicine, wait at least five minutes between using LUMIGAN and the other eye medicine.

Do not use more than once a day as the effectiveness of treatment may be reduced.

Instructions for use:

You must not use the bottle if the tamper-proof seal on the bottle neck is broken before you first use it.

1. 
2. 
3. 
4. 

1. Wash your hands. Tilt your head back and look at the ceiling.
2. Gently pull down the lower eyelid until there is a small pocket.
3. Turn the bottle upside down and squeeze it to release one drop into each eye that needs treatment.
4. Let go of the lower lid, and close your eye for 30 seconds.

Wipe off any excess that runs down the cheek.

If a drop misses your eye, try again.

To help prevent infections and avoid eye injury, do not let the tip of the bottle touch your eye or anything else. Put the cap back on and close the bottle straight after you have used it.

If you use more LUMIGAN than you should
If you use more LUMIGAN than you should, it is unlikely to cause you any serious harm. Put your next dose in at the usual time. If you are worried, talk to your doctor or pharmacist.

If you forget to use LUMIGAN
If you forget to use LUMIGAN, use a single drop as soon as you remember, and then go back to your regular routine. Do not take a double dose to make up for a forgotten dose.

If you stop using LUMIGAN
LUMIGAN should be used every day to work properly. If you stop using LUMIGAN the pressure inside your eye may go up, therefore talk to your doctor before stopping this treatment.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Very common (may affect more than 1 in 10 people)
Affecting the eye
- Slight redness (up to 29 % of people)
- Loss of fat in the eye region which can lead to deepening of your eyelid crease, sunken eye (enophthalmos), drooping eyelid (ptosis), tightening of the skin around your eye (involution of dermatochalasis), and the lower white part of your eye to become more visible (inferior scleral show)

Common (may affect up to 1 in 10 people)
Affecting the eye
- Small breaks in the surface of the eye, with or without inflammation
- Irritation
- Itchy eyes
- Longer eyelashes
- Irritation, when drop is put in the eye
- Eye pain

Affecting the skin
- Red and itchy eyelids
- Darker skin colour around the eye
- Hair growth around the eye

Uncommon (may affect up to 1 in 100 people)
Affecting the eye
- Darker Iris colour
- Tired eye
- Swelling of the surface of the eye
- Blurred vision
- Loss of eye lashes

Affecting the skin
- Dry skin
- Crusting on the edge of the eyelid
- Swelling of the eyelid
- Itching

Affecting the body
- Headache
- Feeling of sickness

Not known (frequency cannot be estimated from the available data**)**
Affecting the eye
- Macular oedema (swelling of the retina at the back of the eye which may lead to worsening vision)
- Darker eyelid colour
- Dryness
- Sticky eyes
- A feeling that something is in your eye
- Swelling of the eye
- Increasing tears
- Ocular discomfort
- Sensitivity to light

Affecting the body
- Asthma
- Worsening of asthma
- Worsening of the lung disease called chronic obstructive pulmonary disease (COPD)
- Shortness of breath
- Symptoms of allergic reaction (swelling, redness of the eye and rash of the skin)
- Dizziness
- Increased blood pressure
- Skin discoloration (periocular)

In addition to the side effects for LUMIGAN 0.1 mg/ml, the following side effects have been seen with another medicine containing a higher strength of bimatoprost (0.3 mg/ml):

- Ocular burning
- An allergic reaction in the eye
- Inflamed eyelids
- Difficulty in seeing clearly
- Worsening of vision
- Swelling of the see-through layer that covers the eye
- Tears
- Darker eyelashes
- Retinal bleeding
- Inflammation within the eye
- Cystoid macular oedema (swelling of the retina within the eye leading to worsening vision)

- Eyelid twitching
- Eyelid shrinking, moving away from surface of the eye
- Skin redness around the eye
- Weakness
- An increase in blood-test results that show how your liver is working

Other side effects reported with eye drops containing phosphates
In very rare cases, some patients with severe damage to the clear layer at the front of the eye (the cornea) have developed cloudy patches on the cornea due to calcium build-up during treatment.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of the medicine.

5. How to store LUMIGAN

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the bottle label and the carton after EXP. The expiry date refers to the last day of that month.

You must throw away the bottle at the latest four weeks after you first opened it, even if there are still some drops left. This will prevent infections. To help you remember, write down the date you opened it in the space on the box.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help to protect the environment.

6. Contents of the pack and other information

What LUMIGAN contains

- The active substance is bimatoprost. One ml of solution contains 0.1 mg bimatoprost.
- The other ingredients are benzalkonium chloride (preservative), sodium chloride, sodium phosphate dibasic heptahydrate, citric acid monohydrate and purified water. Small amounts of hydrochloric acid or sodium hydroxide may be added to keep the level of acid (pH levels) normal (see section 2).

What LUMIGAN looks like and contents of the pack
LUMIGAN is a colourless clear eye drop solution in a pack containing either 1 plastic bottle or 3 plastic bottles each with a screw cap. Each bottle is approximately half full and contains 3 millilitres of solution. This is enough for 4 weeks' usage. Not all pack sizes may be marketed.

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AbbVie Deutschland GmbH & Co. KG
Knollstrasse
67061 Ludwigshafen
Germany

Manufacturer
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Castlebar Road
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Ireland

For any information about this medicine, please contact the local representative of the marketing authorisation holder.

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This leaflet was last revised in

Detailed information on this medicinal product is available on the European Medicines Agency web site: https://www.ema.europa.eu.

To listen to or request a copy of this leaflet in <Braille>, <large print> or <audio>, please contact the local representative of the Marketing Authorisation Holder.

Package leaflet: Information for the patient

LUMIGAN 0.3 mg/ml eye drops, solution
bimatoprost

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What LUMIGAN is and what it is used for

LUMIGAN is an antiglaucoma preparation. It belongs to a group of medicines called prostamides.

LUMIGAN is used to reduce high pressure in the eye. This medicine may be used on its own or with other drops called beta-blockers which also reduce pressure.

Your eye contains a clear, watery liquid that feeds the inside of the eye. Liquid is constantly being drained out of the eye and new liquid is made to replace this. If the liquid cannot drain out quickly enough, the pressure inside the eye builds up. This medicine works by increasing the amount of liquid that is drained. This reduces the pressure inside the eye. If the high pressure is not reduced, it could lead to a disease called glaucoma and eventually damage your sight.

2. What you need to know before you use LUMIGAN

Do not use LUMIGAN:
- if you are allergic to bimatoprost or any of the other ingredients of this medicine (listed in section 6).
- if you have had to stop using eye drops in the past because of a side effect of the preservative benzalkonium chloride.

Warnings and precautions:
Talk to your doctor or pharmacist before you use LUMIGAN if:

- You have any breathing problems
- You have liver or kidney problems
- You have had a cataract surgery in the past
- You have dry eye
- You have or have had any problems with your cornea (front transparent part of the eye)
- You wear contact lenses (see “LUMIGAN contains benzalkonium chloride”)
- You have or have had low blood pressure or low heart rate
- You have had a viral infection or inflammation of the eye

During treatment, LUMIGAN may cause a loss of fat around the eye, which may cause your eyelid crease to deepen, your eye to appear sunken (enophthalmos), your upper eyelid to droop (ptosis), the skin around your eye to tighten (involution of dermatochalasis) and the lower white part of your eye to become more visible (inferior scleral show). The changes are typically mild, but if pronounced, they can affect your field of vision. The changes may disappear if you stop taking LUMIGAN. LUMIGAN may also cause your eyelashes to darken and grow, and cause the skin around the eyelid to darken too. The colour of your iris may also go darker. These changes may be permanent. The changes may be more noticeable if you are only treating one eye.

Children and adolescents
LUMIGAN has not been tested in children under the age of 18 and therefore LUMIGAN should not be used by patients under 18 years.

Other medicines and LUMIGAN
Tell your doctor or pharmacist if you are taking, or have recently taken, or might take any other medicines.

Pregnancy and breast-feeding
If you are pregnant or breast-feeding, think you might be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking any medicine.

LUMIGAN may get into breast milk so you should not breast-feed while you are taking LUMIGAN.

Driving and using machines
Your sight may become blurred for a short time just after using LUMIGAN. You should not drive or use machines until your sight is clear again.

LUMIGAN contains benzalkonium chloride
This medicine contains 0.15 mg benzalkonium chloride in each 3 ml of solution which is equivalent to 0.05 mg/ml.
Do not use the drops when you are wearing your lenses. A preservative in LUMIGAN, benzalkonium chloride may be absorbed by soft contact lenses and may change the colour of the contact lenses. You should remove contact lenses before using this medicine and wait 15 minutes after using the drops before you put your lenses back in. Benzalkonium chloride may also cause eye irritation, especially if you have dry eyes or disorders of the cornea (the clear layer at the front of the eye). If you feel abnormal eye sensation, stinging or pain in the eye after using this medicine, talk to your doctor.

3. How to use LUMIGAN

Always use this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

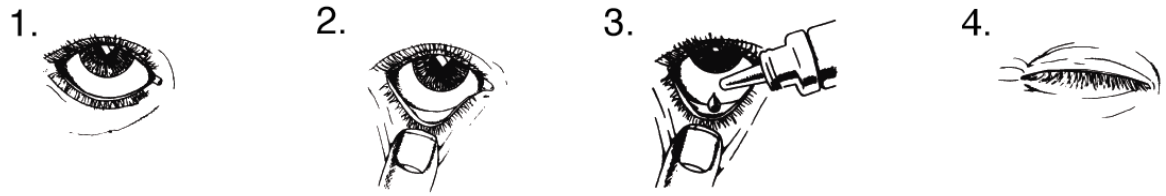
LUMIGAN should only be applied to the eye. The recommended dose is one drop of LUMIGAN in the evening, once daily in each eye that needs treatment.

If you use LUMIGAN with another eye medicine, wait at least five minutes between using LUMIGAN and the other eye medicine.

Do not use more than once a day as the effectiveness of treatment may be reduced.

Instructions for use:

You must not use the bottle if the tamper-proof seal on the bottle neck is broken before you first use it.



1. Wash your hands. Tilt your head back and look at the ceiling.
2. Gently pull down the lower eyelid until there is a small pocket.
3. Turn the bottle upside down and squeeze it to release one drop into each eye that needs treatment.
4. Let go of the lower lid, and close your eye for 30 seconds.

Wipe off any excess that runs down the cheek.

If a drop misses your eye, try again.

To help prevent infections and avoid eye injury, do not let the tip of the bottle touch your eye or anything else. Put the cap back on and close the bottle straight after you have used it.

If you use more LUMIGAN than you should
If you use more LUMIGAN than you should, it is unlikely to cause you any serious harm. Put your next dose in at the usual time. If you are worried, talk to your doctor or pharmacist.

If you forget to use LUMIGAN
If you forget to use LUMIGAN, use a single drop as soon as you remember, and then go back to your regular routine. Do not take a double dose to make up for a forgotten dose.

If you stop using LUMIGAN
LUMIGAN should be used every day to work properly. If you stop using LUMIGAN the pressure inside your eye may go up, therefore talk to your doctor before stopping this treatment.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Very common (may affect more than 1 in 10 people)
Affecting the eye
- Longer eyelashes (up to 45% of people)
- Slight redness (up to 44% of people)
- Itchiness (up to 14% of people)
- Loss of fat in the eye region which can lead to deepening of your eyelid crease, sunken eye (enophthalmos), drooping eyelid (ptosis), tightening of the skin around your eye (involution of dermatochalasis), and the lower white part of your eye to become more visible (inferior scleral show)

Common (may affect up to 1 in 10 people)
Affecting the eye
- An allergic reaction in the eye
- Tired eyes
- Sensitivity to light
- Darker skin colour around the eye

- Darker eyelashes
- Pain
- A feeling that something is in your eye
- Sticky eyes
- Darker iris colour
- Difficulty in seeing clearly
- Irritation
- Burning
- Inflamed, red and itchy eyelids
- Tears
- Dryness
- Worsening of vision
- Blurred vision
- Swelling of the see-through layer which covers the surface of the eye
- Small breaks in the surface of the eye, with or without inflammation

Affecting the body
- Headaches
- An increase in blood-test results that show how your liver is working
- Increased blood pressure

Uncommon (may affect up to 1 in 100 people)
Affecting the eye
- Cystoid macular oedema (swelling of the retina within the eye leading to worsening vision)
- Inflammation within the eye
- Retinal bleeding
- Swollen eyelids
- Eyelid twitching
- Eyelid shrinking, moving away from surface of the eye
- Skin redness around the eye

Affecting the body
- Nausea
- Dizziness
- Weakness
- Hair growth around the eye

Not known (frequency cannot be estimated from the available data)
Affecting the eye
- Ocular discomfort

Affecting the body
- Asthma
- Worsening of asthma
- Worsening of the lung disease called chronic obstructive pulmonary disease (COPD)
- Shortness of breath
- Symptoms of allergic reaction (swelling, redness of the eye and rash of the skin)
- Skin discoloration (periocular)

Other side effects reported with eye drops containing phosphates.
In very rare cases, some patients with severe damage to the clear layer at the front of the eye (the cornea) have developed cloudy patches on the cornea due to calcium build-up during treatment.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of the medicine.

5. How to store LUMIGAN

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the bottle label and the carton after EXP. The expiry date refers to the last day of that month.

You must throw away the bottle, at the latest, four weeks after you first opened it, even if there are still some drops left. This will prevent infections. To help you remember, write down the date you opened it in the space on the box.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help to protect the environment.

6. Contents of the pack and other information

What LUMIGAN contains
- The active substance is bimatoprost. One ml of solution contains 0.3 mg bimatoprost.
- The other ingredients are benzalkonium chloride (preservative), sodium chloride, sodium phosphate dibasic heptahydrate, citric acid monohydrate and purified water. Small amounts of hydrochloric acid or sodium hydroxide may be added to keep the level of acid (pH levels) normal (see section 2).

What LUMIGAN looks like and contents of the pack
LUMIGAN is a colourless clear eye drop solution in a pack containing either 1 plastic bottle or 3 plastic bottles each with a screw cap. Each bottle is approximately half full and contains 3 millilitres of solution. This is enough for 4 weeks' usage. Not all pack sizes may be marketed.

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This leaflet was last revised in

Detailed information on this medicinal product is available on the European Medicines Agency web site:
https://www.ema.europa.eu/

To listen to or request a copy of this leaflet in <Braille>, <large print> or <audio>, please contact the local representative of the Marketing Authorisation Holder.

Package Leaflet: Information for the patient

LUMIGAN 0.3 mg/ml eye drops, solution, in single-dose container
bimatoprost

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What LUMIGAN single-dose is and what it is used for

LUMIGAN single-dose is an antiglaucoma preparation. It belongs to a group of medicines called prostamides.

LUMIGAN single-dose eye drops are used to reduce high pressure in the eye. This medicine may be used on its own or with other drops called beta-blockers which also reduce pressure.

Your eye contains a clear, watery liquid that feeds the inside of the eye. Liquid is constantly being drained out of the eye and new liquid is made to replace this. If the liquid cannot drain out quickly enough, the pressure inside the eye builds up. This medicine works by increasing the amount of liquid that is drained. This reduces the pressure inside the eye. If the high pressure is not reduced, it could lead to a disease called glaucoma and eventually damage your sight.

This medicine does not contain a preservative.

2. What you need to know before you use LUMIGAN single-dose

Do not use LUMIGAN
- If you are allergic to bimatoprost or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions
Talk to you doctor or pharmacist before you use LUMIGAN single-dose if:

- You have any breathing problems
- You have liver or kidney problems
- You have had a cataract surgery in the past
- You have or have had low blood pressure or low heart rate
- You have had a viral infection or inflammation of the eye

During treatment, LUMIGAN may cause a loss of fat around the eye, which may cause your eyelid crease to deepen, your eye to appear sunken (enophthalmos), your upper eyelid to droop (ptosis), the skin around your eye to tighten (involution of dermatochalasis) and the lower white part of your eye to

become more visible (inferior scleral show). The changes are typically mild, but if pronounced, they can affect your field of vision. The changes may disappear if you stop taking LUMIGAN. LUMIGAN single-dose may also cause your eyelashes to darken and grow, and cause the skin around the eyelid to darken too. The colour of your iris may also go darker. These changes may be permanent. The changes may be more noticeable if you are only treating one eye.

Children and adolescents
LUMIGAN single-dose has not been tested in children under the age of 18 and therefore should not be used by patients under 18 years.

Other medicines and LUMIGAN
Tell your doctor or pharmacist if you are taking, have recently taken, or might take any other medicines.

Pregnancy, breast-feeding and fertility
If you are pregnant or breast-feeding, think you might be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

LUMIGAN single-dose may get into breast milk so you should not breast-feed while you are taking this medicine.

Driving and using machines
Your sight may become blurred for a short time just after using LUMIGAN single-dose. You should not drive or use machines until your sight is clear again.

3. How to use LUMIGAN single-dose

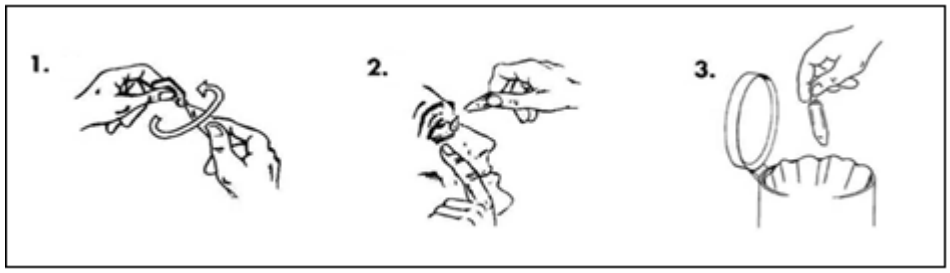
Always use this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

The recommended dose is one drop once daily, in the evening, once daily in each eye that needs treatment. LUMIGAN single-dose should only be applied to the eye.

If you use LUMIGAN single-dose with another eye medicine, wait at least 5 minutes between using LUMIGAN single-dose and the other eye medicine.

Do not use more than once a day as the effectiveness of treatment may be reduced.

Wash your hands before use. Make sure that the single-dose container is intact before use. The solution should be used immediately after opening. To avoid contamination, do not let the open-end of the single-dose container touch your eye or anything else.



1. Take one single-dose container from the pouch and hold it upright (with the cap pointing upwards) and twist-off the cap.
2. Gently pull down the lower eyelid to form a pocket. Turn the single-dose container upside down and squeeze it to release 1 drop into the affected eye(s).
3. Throw away the single-dose container after you have used it, even if there is some solution left.

Wipe off any excess that runs down the cheek.

If you wear contact lenses, take your lenses out before using this medicine. Wait 15 minutes after using the drops, and before you put your lenses back in.

If you use more LUMIGAN than you should
If you use more of this medicine than you should, it is unlikely to cause you any serious harm. Put your next dose in at the usual time. If you are worried, talk to your doctor or pharmacist.

If you forget to use LUMIGAN
If you forget to use this medicine, use a single drop as soon as you remember, and then go back to your regular routine. Do not take a double dose to make up for a forgotten dose.

If you stop using LUMIGAN
LUMIGAN single-dose should be used every day to work properly. If you stop using LUMIGAN single-dose the pressure inside your eye may go up, therefore talk to your doctor before stopping this treatment.

If you have any further questions on the use of this product, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Very common (may affect more than 1 in 10 people)
Affecting the eye
- Slight redness (up to 24% of people)
- Loss of fat in the eye region which can lead to deepening of your eyelid crease, sunken eye (enophthalmos), drooping eyelid (ptosis), tightening of the skin around your eye (involution of dermatochalasis), and the lower white part of your eye to become more visible (inferior scleral show)

Common side (may affect up to 1 in 10 people)
Affecting the eye
- Small breaks in the surface of the eye, with or without inflammation
- Irritation
- Itchy eyes
- Pain
- Dryness
- A feeling that something is in your eye
- Longer eyelashes
- Darker skin colour around the eye
- Red eyelids

Uncommon (may affect up to 1 in 100 people)
These may affect 1 to 9 users in 1000
Affecting the eye
- Tired eyes
- Sensitivity to light
- Darker iris colour
- Itchy and swollen eyelids
- Tears
- Swelling of the see-through layer which covers the surface of the eye
- Blurred vision

Affecting the body
- Headaches
- Hair growth around the eye

Not known (frequency cannot be estimated from the available data)
Affecting the eye
- Sticky eyes
- Ocular discomfort

Affecting the body
- Asthma
- Worsening of asthma
- Worsening of the lung disease called chronic obstructive pulmonary disease (COPD)
- Shortness of breath
- Symptoms of allergic reaction (swelling, redness of the eye and rash of the skin)
- Dizziness
- Increased blood pressure
- Skin discoloration (periocular)

In addition to the side effects for LUMIGAN 0.3 mg/mL single-dose, the following side effects have been seen with the preserved multi-dose formulation of LUMIGAN 0.3 mg/mL and may occur in patients taking LUMIGAN 0.3 mg/mL single-dose:

- Burning sensation in the eye
- An allergic reaction in the eye
- Inflamed eyelids
- Difficulty in seeing clearly
- Worsening vision
- Darker eyelashes
- Retinal bleeding
- Inflammation within the eye
- Cystoid macular oedema (swelling of the retina within the eye leading to worsening vision)
- Iris inflammation
- Eyelid twitching
- Eyelid shrinking, moving away from surface of the eye
- Nausea
- Skin redness around the eye
- Weakness
- An increase in blood-test results that show how your liver is working

Other side effects reported with eye drops containing phosphates
In very rare cases, some patients with severe damage to the clear layer at the front of the eye (the cornea) have developed cloudy patches on the cornea due to calcium build-up during treatment.

Reporting of side effects
If you get any of the side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of the medicine.

5. How to store LUMIGAN single-dose

Keep this medicine out of the sight and reach of children.

This medicine is for single use only and does not contain preservatives. Do not keep any unused solution.

Do not use this medicine after the expiry date which is stated on the single-dose container and the carton after EXP. The expiry date refers to the last day of that month.

This medicinal product does not require any special storage condition. However, once the pouch is opened use within 30 days.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help to protect the environment.

6. Contents of the pack and other information

What LUMIGAN single-dose contains
- The active substance is bimatoprost. One ml of solution contains 0.3 mg bimatoprost.
- The other ingredients are sodium chloride, sodium phosphate dibasic heptahydrate, citric acid monohydrate and purified water. Small amounts of hydrochloric acid or sodium hydroxide may be added to keep the level of acid (pH levels) normal.

What LUMIGAN single-dose looks like and contents of the pack
LUMIGAN 0.3 mg/ml single-dose is a clear, colourless solution supplied in single-dose plastic containers, each containing 0.4 ml of solution.

Pack contains 5-single-dose containers in a carton.

Pack contains 3 or 9 aluminium foil pouches, each containing 10 single-dose containers, for a total of 30 or 90 single-dose containers in a carton, respectively.
Not all pack sizes may be marketed.

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