

**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.

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.

Patients with hepatic and renal 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 eyelash growth, darkening of the eyelid skin and increased iris pigmentation, since these have been observed during treatment with LUMIGAN. Some of these changes may be permanent, and may lead to differences in appearance between the eyes when only one eye is treated. 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. Periorbital tissue pigmentation has been reported to be reversible in some patients.

Cystoid macular oedema has been uncommonly reported ( $\geq 1/1,000$  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

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.

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 ( $\geq 1/10$ ); common ( $\geq 1/100$  to  $< 1/10$ ); uncommon ( $\geq 1/1,000$  to  $< 1/100$ ); rare ( $\geq 1/10,000$  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 in order of decreased seriousness within each frequency grouping.

**Table 1.**

<b><u>System Organ class</u></b>	<b><u>Frequency</u></b>	<b><u>Adverse reaction</u></b>
<i>Nervous system disorders</i>	uncommon	headache
<i>Eye disorders</i>	very common	conjunctival hyperaemia
	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, periorbital and lid changes including deepening of the eyelid sulcus, dry eye
<i>Respiratory, thoracic and mediastinal disorders</i>	not known	asthma, asthma exacerbation, COPD exacerbation and dyspnoea
<i>Gastrointestinal disorders</i>	uncommon	nausea
<i>Skin and subcutaneous tissue disorders</i>	common	skin hyperpigmentation, hypertrichosis
	uncommon	dry skin, eyelid margin crusting, pruritus
<i>General disorders and administration site conditions</i>	common	instillation site irritation
<i>Immune system disorders</i>	not known	Hypersensitivity reaction including signs and symptoms of eye allergy and allergic dermatitis

In clinical studies, over 1800 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.**

<b>System Organ class</b>	<b>Frequency</b>	<b>Adverse reaction</b>
<i>Nervous system disorders</i>	common	headache
	uncommon	dizziness
<i>Eye disorders</i>	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
<i>Vascular disorders</i>	common	hypertension
<i>Skin and subcutaneous tissue disorders</i>	uncommon	hirsutism
<i>General disorders and administration site conditions</i>	uncommon	asthenia
<i>Investigations</i>	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<sup>2</sup> 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, prostaglandin analogues, 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<sub>2a</sub> (PGF<sub>2a</sub>), 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.

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<sub>max</sub> and AUC<sub>0-24hrs</sub> 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<sub>0-24hr</sub> 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 <sup>3</sup> 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 <sup>3</sup> 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**

Allergan Pharmaceuticals Ireland  
Castlebar Road  
Westport  
Co. Mayo  
Ireland

### **8. MARKETING AUTHORISATION NUMBER**

EU/1/02/205/003-004

### **9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

07 January 2010

### **10. DATE OF REVISION OF THE TEXT**

Detailed information on this product is available on the website of the European Medicines Agency  
<http://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.

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.

Patients with hepatic and renal 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 eyelash growth, darkening of the eyelid skin and increased iris pigmentation, since these have been observed during treatment with LUMIGAN. Some of these changes may be permanent, and may lead to differences in appearance between the eyes when only one eye is treated. 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 0.3mg/ml was 1.5% (see section 4.8) and did not increase following 3 years treatment. Periorbital tissue pigmentation has been reported to be reversible in some patients.

Cystoid macular oedema has been uncommonly reported ( $\geq 1/1,000$  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

In clinical studies, over 1800 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.

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 ( $\geq 1/10$ ); common ( $\geq 1/100$  to  $< 1/10$ ); uncommon ( $\geq 1/1,000$  to  $< 1/100$ ); rare ( $\geq 1/10,000$  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.

<b>System Organ class</b>	<b>Frequency</b>	<b>Adverse reaction</b>
<i>Nervous system disorders</i>	common	headache
	uncommon	dizziness
<i>Eye disorders</i>	very common	conjunctival hyperaemia, ocular pruritus, growth of eyelashes
	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	periorbital and lid changes including deepening of the eyelid sulcus
<i>Vascular disorders</i>	common	hypertension
<i>Respiratory, thoracic and mediastinal disorders</i>	not known	asthma, asthma exacerbation, COPD exacerbation and dyspnoea
<i>Gastrointestinal disorders</i>	uncommon	nausea
<i>Skin and subcutaneous tissue disorders</i>	common	pigmentation of periocular skin
	uncommon	hirsutism
<i>General disorders and administration site conditions</i>	uncommon	asthenia
<i>Investigations</i>	common	liver function test abnormal
<i>Immune system disorders</i>	not known	Hypersensitivity reaction including signs and symptoms of eye allergy and allergic dermatitis

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<sup>2</sup> 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, prostaglandin analogues, 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<sub>2a</sub> (PGF<sub>2a</sub>), 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.

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 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  $AUC_{0-24hrs}$  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  $AUC_{0-24hr}$  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 <sup>3</sup> 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 <sup>3</sup> 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**

Allergan Pharmaceuticals Ireland  
Castlebar Road  
Westport  
Co. Mayo  
Ireland

## **8. MARKETING AUTHORISATION NUMBER**



EU/1/02/205/001-002

**9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

8 March 2002 / 20 February 2007

**10. DATE OF REVISION OF THE TEXT**

Detailed information on this product is available on the website of the European Medicines Agency  
<http://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.

#### Patients with hepatic and renal 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 eyelash growth, darkening of the eyelid skin and increased iris pigmentation, since these have been observed during treatment with LUMIGAN. Some of these changes may be permanent, and may lead to differences in appearance between the eyes when only one eye is treated. 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. Periorbital tissue pigmentation has been reported to be reversible in some patients.

Cystoid macular oedema has been uncommonly reported ( $\geq 1/1,000$  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. 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**

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 conjunctival 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.

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 ( $\geq 1/10$ ); common ( $\geq 1/100$  to  $< 1/10$ ); uncommon ( $\geq 1/1,000$  to  $< 1/100$ ); rare ( $\geq 1/10,000$  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**

<b>System Organ class</b>	<b>Frequency</b>	<b>Adverse reaction</b>
<i>Nervous system disorders</i>	uncommon	headache
<i>Eye disorders</i>	very common	conjunctival hyperaemia
	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
<i>Respiratory, thoracic and mediastinal disorders</i>	not known	asthma, asthma exacerbation, COPD exacerbation and dyspnoea
<i>Skin and subcutaneous tissue disorders</i>	common	skin hyperpigmentation (periocular)
	uncommon	hair growth abnormal
<i>Immune system disorders</i>	not known	Hypersensitivity reaction including signs and symptoms of eye allergy and allergic dermatitis

In clinical studies, over 1800 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**

<b>System Organ class</b>	<b>Frequency</b>	<b>Adverse Reaction</b>
<i>Nervous system disorders</i>	common	headache
<i>Eye disorders</i>	very common	ocular pruritus, growth of eyelashes
	common	asthenopia, conjunctival oedema, photophobia, tearing, increased iris pigmentation; blurred vision
<i>Skin and subcutaneous tissue disorders</i>	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**

<b>System Organ class</b>	<b>Frequency</b>	<b>Adverse Reaction</b>
<i>Nervous system disorders</i>	uncommon	dizziness
<i>Eye disorders</i>	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
	not known	periorbital and lid changes including deepening of the eyelid sulcus
<i>Vascular disorders</i>	common	hypertension
<i>Gastrointestinal disorders</i>	uncommon	nausea
<i>Skin and subcutaneous tissue disorders</i>	not known	periobital erythema
<i>General disorders and administration site conditions</i>	uncommon	asthenia
<i>Investigations</i>	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, prostaglandin analogues, 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<sub>2a</sub> (PGF<sub>2a</sub>), 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.

## 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  $AUC_{0-24hrs}$  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  $AUC_{0-24hr}$  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 <sup>3</sup> 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 <sup>3</sup> 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 tray 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:

Cartons containing 5 single-dose containers,  
Carton containing 30 single-dose containers in a tray,  
Carton containing 90 single-dose containers in 3 trays.  
Not all pack sizes may be marketed.

### **6.6 Special precautions for disposal**

No special requirements for disposal.

## **7. MARKETING AUTHORISATION HOLDER**

Allergan Pharmaceuticals Ireland  
Castlebar Road  
Westport  
Co. Mayo  
Ireland

**8. MARKETING AUTHORISATION NUMBER**

EU/1/02/205/005-007

**9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

8 March 2002 / 20 February 2007

**10. DATE OF REVISION OF THE TEXT**

Detailed information on this product is available on the website of the European Medicines Agency:  
<http://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 HOLDER**
- D. CONDITIONS OR RESTRICTIONS WITH REGARD 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**

The marketing authorisation holder shall submit a periodic safety update report for this product in accordance set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and 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 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

**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**

Allergan Pharmaceuticals Ireland  
Castlebar Road  
Westport  
Co. Mayo  
Ireland

**12. MARKETING AUTHORISATION NUMBER(S)**

EU/1/02/205/003

**13. BATCH NUMBER**

Batch:

**14. GENERAL CLASSIFICATION FOR SUPPLY**

Medicinal product subject to medical prescription

**15. INSTRUCTIONS ON USE**

**16. INFORMATION IN BRAILLE**

LUMIGAN 0.1 mg/ml



**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

**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**

Allergan Pharmaceuticals Ireland  
Castlebar Road  
Westport  
Co. Mayo  
Ireland

**12. MARKETING AUTHORISATION NUMBER(S)**

EU/1/02/205/004

**13. BATCH NUMBER**

Batch:

**14. GENERAL CLASSIFICATION FOR SUPPLY**

Medicinal product subject to medical prescription

**15. INSTRUCTIONS ON USE**

**16. INFORMATION IN BRAILLE**

LUMIGAN 0.1 mg/ml

**MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS**

**BOTTLE**

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

LUMIGAN 0.1 mg/ml, eye drops, solution  
Bimatoprost  
Ocular use

**2. METHOD OF ADMINISTRATION**

Read the package leaflet before use.

**3. EXPIRY DATE**

Exp:  
Discard 4 weeks after first opening

**4. BATCH NUMBER**

Batch:

**5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT**

3 ml

**6. OTHER**

**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

**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**

Allergan Pharmaceuticals Ireland  
Castlebar Road  
Westport  
Co. Mayo  
Ireland

**12. MARKETING AUTHORISATION NUMBER(S)**

EU/1/02/205/001

**13. BATCH NUMBER**

Batch:

**14. GENERAL CLASSIFICATION FOR SUPPLY**

Medicinal product subject to medical prescription

**15. INSTRUCTIONS ON USE**

**16. INFORMATION IN BRAILLE**

LUMIGAN 0.3 mg/ml

**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

**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 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**

Allergan Pharmaceuticals Ireland  
Castlebar Road  
Westport  
Co. Mayo  
Ireland

**12. MARKETING AUTHORISATION NUMBER(S)**

EU/1/02/205/002

**13. BATCH NUMBER**

Batch:

**14. GENERAL CLASSIFICATION FOR SUPPLY**

Medicinal product subject to medical prescription

**15. INSTRUCTIONS ON USE**

**16. INFORMATION IN BRAILLE**

LUMIGAN 0.3 mg/ml

**MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS**  
**BOTTLE**

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

LUMIGAN 0.3 mg/ml, eye drops, solution  
Bimatoprost  
Ocular use

**2. METHOD OF ADMINISTRATION**

Read the package leaflet before use.

**3. EXPIRY DATE**

Discard 4 weeks after first opening  
Exp:

**4. BATCH NUMBER**

Batch:

**5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT**

3 ml

**6. OTHER**



**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**

Allergan Pharmaceuticals Ireland  
Castlebar Road,  
Westport,  
Co. Mayo,  
Ireland

**12. MARKETING AUTHORISATION NUMBER(S)**

EU/1/02/205/005

**13. BATCH NUMBER**

Lot

**14. GENERAL CLASSIFICATION FOR SUPPLY**

Medicinal product subject to medical prescription

**15. INSTRUCTIONS ON USE**

For single use only

**16. INFORMATION IN BRAILLE**

LUMIGAN 0.3 mg/mL single-dose

**PARTICULARS TO APPEAR ON THE OUTER PACKAGING**

**OUTER CARTON CONTAINING 30 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

**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 tray 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**

Allergan Pharmaceuticals Ireland  
Castlebar Road  
Westport  
Co. Mayo  
Ireland

**12. MARKETING AUTHORISATION NUMBER(S)**

EU/1/02/205/006

**13. BATCH NUMBER**

Lot

**14. GENERAL CLASSIFICATION FOR SUPPLY**

Medicinal product subject to medical prescription

**15. INSTRUCTIONS ON USE**

For single use only

**16. INFORMATION IN BRAILLE**

LUMIGAN 0.3 mg/mL single-dose

**PARTICULARS TO APPEAR ON THE OUTER PACKAGING**

**OUTER CARTON CONTAINING 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  
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 tray 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**

Allergan Pharmaceuticals Ireland  
Castlebar Road  
Westport  
Co. Mayo  
Ireland

**12. MARKETING AUTHORISATION NUMBER(S)**

EU/1/02/205/007

**13. BATCH NUMBER**

Lot

**14. GENERAL CLASSIFICATION FOR SUPPLY**

Medicinal product subject to medical prescription

**15. INSTRUCTIONS ON USE**

For single use only

**16. INFORMATION IN BRAILLE**

LUMIGAN 0.3 mg/mL single-dose

**PARTICULARS TO APPEAR ON THE OUTER PACKAGING FOR 30 AND 90 PACK  
LID OF TRAY CONTAINING 30 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

**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 tray 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**

Allergan Pharmaceuticals Ireland  
Castlebar Road,  
Westport,  
Co. Mayo,  
Ireland

**12. MARKETING AUTHORISATION NUMBER(S)**

**13. BATCH NUMBER**

Lot

**14. GENERAL CLASSIFICATION FOR SUPPLY**

Medicinal product subject to medical prescription

**15. INSTRUCTIONS ON USE**

For single use only

**16. INFORMATION IN BRAILLE**

Justification for not including Braille accepted



**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 user**

### **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 0.1 mg/ml is and what it is used for
2. What you need to know before you use LUMIGAN 0.1 mg/ml
3. How to use LUMIGAN 0.1 mg/ml
4. Possible side effects
5. How to store LUMIGAN 0.1 mg/ml
6. Contents of the pack and other information

#### **1. What LUMIGAN 0.1 mg/ml 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 0.1 mg/ml**

##### **Do not use LUMIGAN 0.1 mg/ml:**

- if you are allergic (hypersensitive) to bimatoprost or any of the other ingredients of LUMIGAN.
- 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 0.1 mg/ml

Talk to your doctor, 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 "Important information about some of the ingredients of LUMIGAN 0.1 mg/ml")
- You have or have had low blood pressure or low heart rate
- You have had a viral infection or inflammation of the eye

LUMIGAN may 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 over time. These changes may be permanent. The change 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.

### **Important information about some of the ingredients of LUMIGAN 0.1 mg/ml**

Do not use the drops when you are wearing your lenses. Wait 15 minutes after using the drops before you put your lenses back in. A preservative in LUMIGAN called benzalkonium chloride may cause eye irritation and can discolour soft contact lenses.

## **3. How to use LUMIGAN 0.1 mg/ml**

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 0.1 mg/ml 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 0.1 mg/ml**

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 0.1 mg/ml**

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.

If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet.

**Very common side effects**

These may affect one or more users in 10

Affecting the eye

- Slight redness (up to 29 % of people)

**Common side effects**

These may affect 1 to 9 users in 100

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 side effects**

These may affect 1 to 9 users in 1000

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

### **Side effects where the frequency is not known**

#### Affecting the eye

- Macular oedema (swelling of the retina at the back of the eye which may lead to worsening vision)
- Darker eyelid colour
- Eyes appear sunken
- Dryness

#### 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)

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):

- Dizziness
- 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
- A feeling that something is in your eye
- Sensitivity to light
- Tears
- Sticky eyes
- 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
- Increased blood pressure
- 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 side effects

If any of the side effects get serious, or if you notice any side effects not mentioned in this leaflet, please tell your doctor or pharmacist. You can also report side effects directly via [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 0.1 mg/ml**

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 0.1 mg/ml 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.

#### **What LUMIGAN 0.1 mg/ml 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.

#### **Marketing Authorisation Holder and Manufacturer**

Allergan Pharmaceuticals Ireland  
Castlebar Road  
Westport  
Co. Mayo  
Ireland.

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

**België/Belgique/Belgien**  
**Luxembourg/Luxemburg/Nederland**  
Allergan n.v.  
Tél/Tel: +32 (0)2 351 24 24

**Ísland**  
Actavis ehf.  
Sími: +354 550 3300

**България**

Алерган България ЕООД  
Тел.: +359 (0) 800 20 280

**Česká republika**

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Allergan Norden AB  
Tlf/Puh/Tel: +46 (0)8 594 100 00

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**Ελλάδα/Κύπρος**

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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: <http://www.ema.europa.eu>.



## Package leaflet: Information for the user

### 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 0.3 mg/ml is and what it is used for
2. What you need to know before you use LUMIGAN 0.3 mg/ml
3. How to use LUMIGAN 0.3 mg/ml
4. Possible side effects
5. How to store LUMIGAN 0.3 mg/ml
6. Contents of the pack and other information

#### **1. What LUMIGAN 0.3 mg/ml 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 0.3 mg/ml**

##### **Do not use LUMIGAN 0.3 mg/ml:**

- if you are allergic (hypersensitive) to bimatoprost or any of the other ingredients of LUMIGAN.
- 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 0.3 mg/ml:

- **Talk to your doctor, 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 "Important information about some of the ingredients of LUMIGAN 0.3 mg/ml")
  - You have or have had low blood pressure or low heart rate

- You have had a viral infection or inflammation of the eye

LUMIGAN may 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 over time. These changes may be permanent. The change 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.

### **Important information about some of the ingredients of LUMIGAN 0.3 mg/ml**

Do not use the drops when you are wearing your lenses. Wait 15 minutes after using the drops before you put your lenses back in. A preservative in LUMIGAN called benzalkonium chloride may cause eye irritation and can discolour soft contact lenses.

## **3. How to use LUMIGAN 0.3 mg/ml**

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 0.3 mg/ml 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 0.3 mg/ml**

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 0.3 mg/ml**

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.

If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet.

**Very common side effects**

These may affect one or more users in 10

Affecting the eye

- Longer eyelashes (up to 45% of people)
- Slight redness (up to 44% of people)
- Itchiness (up to 14% of people)

**Common side effects**

These may affect 1 to 9 users in 100

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 side effects**

These may affect 1 to 9 users in 1000

#### 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

#### **Side effects where the frequency is not known**

#### Affecting the eye

- Eyes appear sunken

#### 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)

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 side effects

If any of the side effects get serious, or if you notice any side effects not mentioned in this leaflet, please tell your doctor or pharmacist. You can also report side effects directly via [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 0.3 mg/ml

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 0.3 mg/ml 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.

### What LUMIGAN 0.3 mg/ml 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.

### Marketing Authorisation Holder and Manufacturer

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Castlebar Road  
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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:

<http://www.ema.europa.eu/>

## Package Leaflet: Information for the user

### 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 0.3 mg/mL single-dose is and what it is used for
2. What you need to know before you use LUMIGAN 0.3 mg/mL single-dose
3. How to use LUMIGAN 0.3 mg/mL single-dose
4. Possible side effects
5. How to store LUMIGAN 0.3 mg/mL single-dose
6. Contents of the pack and other information

#### **1. What LUMIGAN 0.3 mg/mL single-dose is and what it is used for**

LUMIGAN 0.3 mg/mL single-dose is an antiglaucoma preparation. It belongs to a group of medicines called prostamides.

LUMIGAN 0.3 mg/mL 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 0.3 mg/mL single-dose**

##### **Do not use this medicine:**

- If you are allergic to the active ingredient bimatoprost or any of the other ingredients of this medicine (listed in section 6).

##### **Warnings and precautions**

Talk to your doctor or pharmacist before you use LUMIGAN 0.3 mg/mL single-dose.

##### **Please tell your doctor or pharmacist, 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

LUMIGAN 0.3 mg/mL single-dose may 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 over time. These changes may be permanent. The change may be more noticeable if you are only treating one eye.

### **Children and adolescents**

LUMIGAN 0.3 mg/mL 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 0.3 mg/mL single-dose:**

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

### **Pregnancy and 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 0.3 mg/mL 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 0.3 mg/mL single-dose. You should not drive or use machines until your sight is clear again.

## **3. How to use LUMIGAN 0.3 mg/mL single-dose**

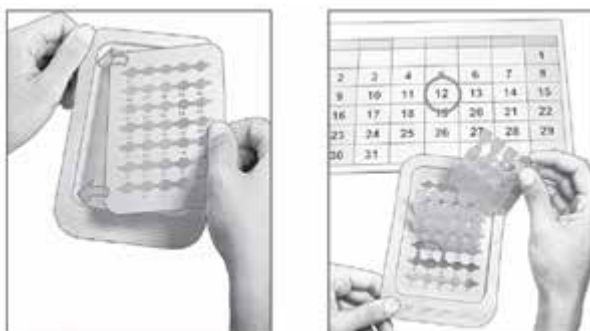
Always use this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

The recommended dose is one drop once daily, in the evening, once daily in each eye that needs treatment. LUMIGAN 0.3 mg/mL single-dose should only be applied to the eye

If you use LUMIGAN 0.3 mg/mL single-dose with another eye medicine, wait at least 5 minutes between using LUMIGAN 0.3 mg/mL single-dose and the other eye medicine.

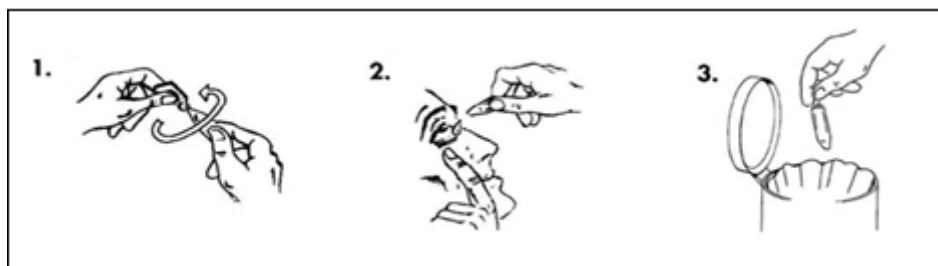
Do not use more than once a day as the effectiveness of treatment may be reduced.

A calendar card is provided in the pack, numbered 1-31 for each day of the month. Place the calendar card on the top of the plastic tub and push down to snap it into place. The 30 vials in the pack should be separated from each other and fitted into the numbered spaces starting with the space that is numbered with today's date. If you have any remaining vials, start over with the spot labelled "1" which will take you into the next month. Each day, the vial should be taken from the numbered spot that matches the calendar day to make sure a daily dose is not missed.





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 numbered spot that matches the calendar day 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). Blink your eye(s) a few times.
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 0.3 mg/mL single-dose 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 0.3 mg/mL single-dose**

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 0.3 mg/mL single-dose**

LUMIGAN 0.3 mg/mL single-dose should be used every day to work properly. If you stop using LUMIGAN 0.3 mg/mL 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.

If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet.

**Very common side effects**

These may affect one or more users in 10

Affecting the eye

- Slight redness (up to 24% of people)

**Common side effects**

These may affect 1 to 9 users in 100

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 side effects**

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

### **Side effects where the frequency is not known**

#### 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)

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:

- Dizziness
- Burning sensation in the eye
- An allergic reaction in the eye
- Inflamed eyelids
- Difficulty in seeing clearly
- Sticky eyes
- 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
- Eyes appear sunken
- Increased blood pressure
- 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 side effects

If any of the side effects get serious, or if you notice any side effects not mentioned in this leaflet, please tell your doctor or pharmacist. You can also report side effects directly via [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 0.3 mg/mL single-dose**

#### **Keep 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 tray after the expiry date (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 pack 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 0.3 mg/mL 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 0.3 mg/mL 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.

Each pack contains 5,30 or 90 single-dose containers. Not all pack sizes may be marketed.

#### **Marketing Authorisation Holder and Manufacturer**

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This leaflet is available in all EU/EEA languages on the European Medicines Agency website.

**ANNEX IV**

**SCIENTIFIC CONCLUSIONS AND GROUNDS FOR THE VARIATION TO THE  
TERMS OF THE MARKETING AUTHORISATION(S)**

## **Scientific conclusions**

Taking into account the PRAC Assessment Report on the PSUR for bimatoprost, the scientific conclusions of CHMP are as follows:

During the reporting period of this PSUR, a certain number of cases from routine pharmacovigilance activities were reported and indicated a causal relationship with the use of bimatoprost containing medicinal products. Based on the available data and analysis presented in this PSUR, the PRAC considered that the summary of product characteristics and package leaflet of bimatoprost (all formulations) containing medicinal products should be amended to reflect the following adverse drug reactions: hypersensitivity reaction including signs and symptoms of eye allergy and allergic dermatitis, asthma, asthma exacerbation, COPD exacerbation and dyspnea, with a frequency not known. The summary of product characteristics and package leaflet of bimatoprost (formulations 0.01%) should be amended to reflect the following adverse drug reactions: iris hyperpigmentation with a frequency uncommon and macular oedema, blepharal pigmentation, periorbital and lid changes including deepening of the eyelid sulcus and dry eye with a frequency not known. Therefore, in view of the data presented in the reviewed PSUR(s), the PRAC considered that changes to the product information of medicinal products containing bimatoprost were warranted.

The CHMP agrees with the scientific conclusions made by the PRAC.

## **Grounds for the variation to the terms of the Marketing Authorisation(s)**

On the basis of the scientific conclusions for bimatoprost the CHMP is of the opinion that the benefit-risk balance of the medicinal product(s) containing bimatoprost is favourable subject to the proposed changes to the product information

The CHMP recommends that the terms of the Marketing Authorisation(s) should be varied.