

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use LUMIGAN® 0.03% safely and effectively. See full prescribing information for LUMIGAN® 0.03%.

LUMIGAN® (bimatoprost ophthalmic solution) 0.03% for topical ophthalmic use
Initial U.S. Approval: 2001

RECENT MAJOR CHANGES

Contraindications, Hypersensitivity (4) 07/2017

INDICATIONS AND USAGE

LUMIGAN® 0.03% is a prostaglandin analog indicated for the reduction of elevated intraocular pressure in patients with open angle glaucoma or ocular hypertension. (1)

DOSAGE AND ADMINISTRATION

One drop in the affected eye(s) once daily in the evening. (2)

DOSAGE FORMS AND STRENGTHS

Ophthalmic solution containing 0.3 mg/mL bimatoprost. (3)

CONTRAINDICATIONS

Hypersensitivity. (4)

WARNINGS AND PRECAUTIONS

- **Pigmentation.**
Pigmentation of the iris, periorbital tissue (eyelid) and eyelashes can occur. Iris pigmentation is likely to be permanent. (5.1)
- **Eyelash Changes.**
Gradual change to eyelashes including increased length, thickness and number of lashes. Usually reversible. (5.2)

ADVERSE REACTIONS

Most common adverse reaction is conjunctival hyperemia (45%). (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Allergan at 1-800-678-1605 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

USE IN SPECIFIC POPULATIONS

Use in pediatric patients below the age of 16 years is not recommended because of potential safety concerns related to increased pigmentation following long-term chronic use. (8.4)

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 07/2017

FULL PRESCRIBING INFORMATION: CONTENTS*

1 INDICATIONS AND USAGE	10 OVERDOSAGE
2 DOSAGE AND ADMINISTRATION	11 DESCRIPTION
3 DOSAGE FORMS AND STRENGTHS	12 CLINICAL PHARMACOLOGY
4 CONTRAINDICATIONS	12.1 Mechanism of Action
5 WARNINGS AND PRECAUTIONS	12.3 Pharmacokinetics
5.1 Pigmentation	13 NONCLINICAL TOXICOLOGY
5.2 Eyelash Changes	13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
5.3 Intraocular Inflammation	14 CLINICAL STUDIES
5.4 Macular Edema	16 HOW SUPPLIED/STORAGE AND HANDLING
5.5 Bacterial Keratitis	17 PATIENT COUNSELING INFORMATION
5.6 Use with Contact Lenses	
6 ADVERSE REACTIONS	
6.1 Clinical Trials Experience	
6.2 Postmarketing Experience	
8 USE IN SPECIFIC POPULATIONS	
8.1 Pregnancy	
8.2 Lactation	
8.4 Pediatric Use	
8.5 Geriatric Use	

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

LUMIGAN[®] (bimatoprost ophthalmic solution) 0.03% is indicated for the reduction of elevated intraocular pressure in patients with open angle glaucoma or ocular hypertension.

2 DOSAGE AND ADMINISTRATION

The recommended dosage is one drop in the affected eye(s) once daily in the evening. **LUMIGAN**[®] 0.03% (bimatoprost ophthalmic solution) should not be administered more than once daily since it has been shown that more frequent administration of prostaglandin analogs may decrease the intraocular pressure lowering effect.

Reduction of the intraocular pressure starts approximately 4 hours after the first administration with maximum effect reached within approximately 8 to 12 hours.

LUMIGAN[®] 0.03% may be used concomitantly with other topical ophthalmic drug products to lower intraocular pressure. If more than one topical ophthalmic drug is being used, the drugs should be administered at least five (5) minutes apart.

3 DOSAGE FORMS AND STRENGTHS

Ophthalmic solution containing bimatoprost 0.3 mg/mL

4 CONTRAINDICATIONS

LUMIGAN[®] 0.03% is contraindicated in patients with hypersensitivity to bimatoprost or to any of the ingredients [see *Adverse Reactions (6.2)*].

5 WARNINGS AND PRECAUTIONS

5.1 Pigmentation

Bimatoprost ophthalmic solution has been reported to cause changes to pigmented tissues. The most frequently reported changes have been increased pigmentation of the iris, periorbital tissue (eyelid) and eyelashes. Pigmentation is expected to increase as long as bimatoprost is administered. The pigmentation change is due to increased melanin content in the melanocytes rather than to an increase in the number of melanocytes. After discontinuation of bimatoprost, pigmentation of the iris is likely to be permanent, while pigmentation of the periorbital tissue and eyelash changes have been reported to be reversible in some patients. Patients who receive treatment should be informed of the possibility of increased pigmentation. The long term effects of increased pigmentation are not known.

Iris color change 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 of the iris become more brownish. Neither nevi nor freckles of the iris appear to be affected by treatment. While treatment with **LUMIGAN**[®] (bimatoprost ophthalmic solution) 0.03% can be continued in patients who develop noticeably increased iris pigmentation, these patients should be examined regularly [see *Patient Counseling Information (17)*].

5.2 Eyelash Changes

LUMIGAN[®] 0.03% may gradually change eyelashes and vellus hair in the treated eye. These changes include increased length, thickness, and number of lashes. Eyelash changes are usually reversible upon discontinuation

5.3 Intraocular Inflammation

Prostaglandin analogs, including bimatoprost, have been reported to cause intraocular inflammation. In addition, because these products may exacerbate inflammation, caution should be used in patients with active intraocular inflammation (e.g., uveitis).

5.4 Macular Edema

Macular edema, including cystoid macular edema, has been reported during treatment with bimatoprost ophthalmic solution. LUMIGAN® 0.03% should be used with caution in aphakic patients, in pseudophakic patients with a torn posterior lens capsule, or in patients with known risk factors for macular edema.

5.5 Bacterial Keratitis

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 corneal disease or a disruption of the ocular epithelial surface [see *Patient Counseling Information (17)*].

5.6 Use with Contact Lenses

LUMIGAN® 0.03% contains benzalkonium chloride, which may be absorbed by and cause discoloration of soft contact lenses. Contact lenses should be removed prior to instillation of LUMIGAN® 0.03% and may be reinserted 15 minutes following its administration.

6 ADVERSE REACTIONS

The following adverse reactions are described elsewhere in the labeling:

- Pigmentation [see Warnings and Precautions (5.1)]
- Eyelash Changes [see Warnings and Precautions (5.2)]
- Intraocular Inflammation [see Warnings and Precautions (5.3)]
- Macular Edema [see Warnings and Precautions (5.4)]
- Hypersensitivity [see Contraindications (4)]

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

In clinical trials, the most frequent events associated with the use of LUMIGAN® (bimatoprost ophthalmic solution) 0.03% occurring in approximately 15% to 45% of patients, in descending order of incidence, included conjunctival hyperemia, growth of eyelashes, and ocular pruritus. Approximately 3% of patients discontinued therapy due to conjunctival hyperemia.

Ocular adverse events occurring in approximately 3 to 10% of patients, in descending order of incidence, included ocular dryness, visual disturbance, ocular burning, foreign body sensation, eye pain, pigmentation of the periocular skin, blepharitis, cataract, superficial punctate keratitis, periorbital erythema, ocular irritation, and eyelash darkening. The following ocular adverse events reported in approximately 1 to 3% of patients, in descending order of incidence, included: eye discharge, tearing, photophobia, allergic conjunctivitis, asthenopia, increases in iris pigmentation, and conjunctival edema. In less than 1% of patients, intraocular inflammation was reported as iritis.

Systemic adverse events reported in approximately 10% of patients were infections (primarily colds and upper respiratory tract infections). The following systemic adverse events reported in approximately 1 to 5% of patients, in descending order of incidence, included headaches, abnormal liver function tests, asthenia and hirsutism.

6.2 Postmarketing Experience

The following adverse reactions have been identified during postapproval use of **LUMIGAN**[®] 0.03%. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure. The reactions, which have been chosen for inclusion due to either their seriousness, frequency of reporting, possible causal connection to **LUMIGAN**[®], or a combination of these factors, include: abnormal hair growth, asthma-like symptoms, dizziness, dyspnea, eyelid edema, hypersensitivity reaction including signs and symptoms of eye allergy and allergic dermatitis, hypertension, nausea, and periorbital and lid changes including deepening of the eyelid sulcus.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no adequate and well-controlled studies of **LUMIGAN**[®] (bimatoprost ophthalmic solution) 0.03% administration in pregnant women. There is no increase in the risk of major birth defects or miscarriages based on bimatoprost postmarketing experience.

In embryofetal developmental studies, administration of bimatoprost in pregnant mice and rats during organogenesis, resulted in abortion and early delivery at oral doses at least 33 times (mice) or 94 times (rats) the human exposure at the recommended clinical dose (based on blood area under the curve [AUC] levels). These adverse effects were not observed at 2.6 times (mice) and 47 times (rats) the human exposure at the recommended clinical dose.

In pre/postnatal development studies, administration of bimatoprost to pregnant rats from organogenesis to the end of lactation resulted in reduced gestation length and fetal body weight, and increased fetal and pup mortality at oral doses at least 41 times the human systemic exposure at the recommended clinical dose (based on blood AUC levels). No adverse effects were observed in rat offspring at exposures estimated at 14 times the human exposure at the recommended clinical dose (based on blood AUC levels).

Because animal reproductive studies are not always predictive of human response **LUMIGAN**[®] 0.03% should be administered during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Data

Animal Data

In an embryofetal development rat study, abortion was observed in pregnant rats administered bimatoprost orally during organogenesis at 0.6 mg/kg/day (94 times the human systemic exposure at the recommended human ophthalmic dose [RHOD], based on AUC). The No Observed Adverse Effect Level (NOAEL) for abortion was 0.3 mg/kg/day (estimated at 47 times the human systemic exposure at the RHOD, based on AUC). No abnormalities were observed in rat fetuses at doses up to 0.6 mg/kg/day.

In an embryofetal development mouse study, abortion and early delivery were observed in pregnant mice

the human systemic exposure at the RHOD, based on AUC). The NOAEL for abortion and early delivery was 0.1 mg/kg/day (2.6 times the human systemic exposure at the RHOD, based on AUC). No abnormalities were observed in mouse fetuses at doses up to 0.6 mg/kg/day (72 times the human systemic exposure at the RHOD, based on AUC).

In a pre/postnatal development study, treatment of pregnant rats with bimatoprost orally from gestation day 7 to lactation day 20 resulted in reduced gestation length, increased late resorptions, fetal deaths, and postnatal pup mortality, and reduced pup body weight at doses greater than or equal to 0.3 mg/kg/day. These effects were observed at exposures at least 41 times the human systemic exposure at the RHOD, based on AUC. The NOAEL for postnatal development and mating performance of the offspring was 0.1 mg/kg/day (estimated at 14 times the human systemic exposure at the RHOD, based on AUC).

8.2 Lactation

Risk Summary

It is not known whether topical ocular treatment with **LUMIGAN**[®] 0.03% could result in sufficient systemic absorption to produce detectable quantities in human milk. In animal studies, bimatoprost has been shown to be present in breast milk of lactating rats at an intravenous dose (i.e., 1 mg/kg) 324 times the RHOD (on a mg/m basis), however no animal data is available at clinically relevant doses.

The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for **LUMIGAN**[®] 0.03% and any potential adverse effects on the breastfed child from **LUMIGAN**[®] 0.03%.

8.4 Pediatric Use

Use in pediatric patients below the age of 16 years is not recommended because of potential safety concerns related to increased pigmentation following long-term chronic use.

8.5 Geriatric Use

No overall clinical differences in safety or effectiveness have been observed between elderly and other adult patients.

10 OVERDOSAGE

No information is available on overdosage in humans. If overdose with **LUMIGAN**[®] (bimatoprost ophthalmic solution) 0.03% occurs, treatment should be symptomatic.

In oral (by gavage) mouse and rat general toxicity studies, doses up to 100 mg/kg/day did not produce any toxicity. This dose expressed as mg/m² is at least 70 times higher than the accidental dose of one bottle of **LUMIGAN**[®] 0.03% for a 10 kg child.

11 DESCRIPTION

LUMIGAN[®] (bimatoprost ophthalmic solution) 0.03% is a synthetic prostamide analog with ocular hypotensive activity. Its chemical name is (Z)-7-[(1R,2R,3R,5S)-3,5-Dihydroxy-2-[(1E,3S)-3-hydroxy-5-phenyl-1-pentenyl]cyclopentyl]-5-N-ethylheptenamide, and its molecular weight is 415.58. Its molecular formula is C₂₅H₃₇NO₄. Its chemical structure is:

Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts



Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research



With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips



Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS

Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS

Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS

Sync your system to PACER to automate legal marketing.