

LUMIGAN®

(bimatoprost ophthalmic solution) 0.03%

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.

CONTRAINDICATIONS

LUMIGAN® (bimatoprost ophthalmic solution) 0.03% is contraindicated in patients with hypersensitivity to bimatoprost or any other ingredient in this product.

WARNINGS

LUMIGAN® (bimatoprost ophthalmic solution) 0.03% has been reported to cause changes to pigmented tissues. The most frequently reported changes have been increased pigmentation of the iris, periocular tissue (eyelid) and eyelashes, and growth of eyelashes. Pigmentation is expected to increase as long as LUMIGAN® is administered. After discontinuation of LUMIGAN® pigmentation of the iris is likely to be permanent while pigmentation of the periocular 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 effects of increased pigmentation beyond 5 years are not known.

PRECAUTIONS

General: LUMIGAN® (bimatoprost ophthalmic solution) 0.03% may gradually increase the pigmentation of the iris. The eye color change is due to increased melanin content in the stromal melanocytes of the iris rather than to an increase in the number of melanocytes. This change may not be noticeable for several months to years (see WARNINGS). 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. Whether new or freckles of the iris appear to be affected by treatment. While treatment with LUMIGAN® can be continued in patients who develop noticeably increased iris pigmentation, these patients should be examined regularly.

During clinical trials, the increase in brown iris pigment has not been shown to progress further upon discontinuation of treatment, but the resultant color change may be permanent.

eyelid skin darkening, which may be reversible upon discontinuation of the treatment has been reported in association with the use of LUMIGAN®.

LUMIGAN® 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 of treatment.

LUMIGAN® (bimatoprost ophthalmic solution) 0.03% should be used with caution in patients with active intraocular inflammation (e.g., uveitis).

Macular edema, including cystoid macular edema, has been reported during treatment with bimatoprost ophthalmic solution. LUMIGAN® 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.

LUMIGAN® has not been evaluated for the treatment of angle closure, inflammatory or neovascular glaucoma.

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 PRECAUTIONS, Information for Patients).

Contact lenses should be removed prior to instillation of LUMIGAN® and may be reinserted 15 minutes following its administration (see PRECAUTIONS, Information for Patients).

Information for Patients: (see WARNINGS and PRECAUTIONS) Patients should be advised about the potential for increased brown pigmentation of the iris, which may be permanent. Patients should also be informed about the possibility of eyelid skin darkening, which may be reversible after discontinuation of LUMIGAN®.

Patients should also be informed of the possibility of eyelash and vellus hair changes in the treated eye during treatment with LUMIGAN®. These changes may result in a disparity between eyes in length, thickness, pigmentation, number of eyelashes or vellus hairs, and/or direction of eyelash growth. Eyelash changes are usually reversible upon discontinuation of treatment.

Patients should be instructed to avoid allowing the tip of the dispensing container to contact the eye, surrounding structures, fingers, or any other surface in order to avoid contamination of the solution by common bacteria known to cause ocular infections. Serious damage to the eye and subsequent loss of vision may result from using contaminated solutions.

Patients should also be advised that if they develop an intercurrent ocular condition (e.g., trauma or infection) or have ocular surgery, they should immediately seek their physician's advice concerning the continued use of the multidose container.

Patients should be advised that if they develop any ocular reactions, particularly conjunctivitis and eyelid reactions, they should immediately seek their physician's advice.

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

If more than one topical ophthalmic drug is being used, the drugs should be administered at least five (5) minutes between applications.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Bimatoprost was not carcinogenic in either mice or rats when administered by oral gavage at doses of up to 2 mg/kg/day and 1 mg/kg/day respectively (approximately 192 times and 291 times the recommended human exposure based on blood AUC levels respectively) for 104 weeks.

Bimatoprost was not mutagenic or clastogenic in the Ames test, in the mouse lymphoma test, or in the *in vivo* mouse micronucleus tests.

Bimatoprost did not impair fertility in male or female rats up to doses of 0.6 mg/kg/day (approximately 103 times the recommended human exposure based on blood AUC levels).

Pregnancy: Teratogenic effects: Pregnancy Category C. In embryo/fetal developmental studies in pregnant mice and rats, abortion was observed at oral doses of bimatoprost which achieved at least 33 or 97 times, respectively, the intended human exposure based on blood AUC levels.

At doses 41 times the intended human exposure based on blood AUC levels, the gestation length was reduced in the dams, the incidence of dead fetuses, late resorptions, peri- and postnatal pup mortality was increased, and pup body weights were reduced.

There are no adequate and well-controlled studies of LUMIGAN® administration in pregnant women. Because animal reproductive studies are not always predictive of human response, LUMIGAN® should be administered during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing mothers: It is not known whether LUMIGAN® is excreted in human milk, although in animal studies, bimatoprost has been shown to be excreted in breast milk. Because many drugs are excreted in human milk, caution should be exercised when LUMIGAN® is administered to a nursing woman.

Pediatric Use: Safety and effectiveness in pediatric patients have not been established.

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

ADVERSE REACTIONS

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, eyelid 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.

Rx only

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US Patent 5,688,819 and 6,403,649

9106X



New test helps to detect AMD at home

The device encourages frequent age-related macular degeneration monitoring at home and promotes early detection of CNV.

by Anat Loewenstein, MD

As the baby boomer generation ages and the occurrences of age-related macular degeneration become more frequent, it is important that we take every measure possible to detect the conversion to wet AMD in a timely manner to prevent significant vision loss for our patients.

Once AMD has been detected, a combination of in-office and home monitoring for choroidal neovascularization is extremely important in preserving patients' sight to ensure treatment is administered at the appropriate time. I have found that by using the Foresee Preferential Hyperacuity Perimeter (Notal Vision) in my office, we can monitor for CNV before the patient notices any change in

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— ANAT LOEWENSTEIN, MD

vision. The Foresee PHP is designed specifically to monitor and differentiate between dry AMD and early onset CNV. It offers 82% sensitivity and 88% specificity and is the only device approved by the U.S. Food and Drug Administration to monitor conversion to wet AMD.

To supplement the success of its in-office PHP test, Notal Vision is developing a testing unit — the ForeseeHome — for dry AMD patients to use at home.

The ForeseeHome identifies CNV lesions when they are very small and often before the patient notices any symptoms. According to a 6-month study that followed patients' compli-

ance using the ForeseeHome, the average number of tests per month is 14 (patients were instructed to use the test daily). Because of its testing method and the promise of earlier detection, the ForeseeHome can serve as an incentive for patients to self-test on a regular basis.

Home test supplements in-office test

The data on the ForeseeHome are consistent with previous studies showing that it more accurately detects CNV compared with the Amsler grid. By combining patient interactive software with an innovative algorithm that measures relative photoreceptor field dislocation, the algorithm analyzes the patients' responses based on a comprehensive normative database that define normal/abnormal visual field defects.

In a study that I conducted with colleagues at Tel Aviv Sourasky Medical Center in Israel, researchers examined 35 patients with intermediate dry AMD, as well as 26 newly diagnosed CNV patients, all with an initial visual acuity of 20/200 or better. The participants each went through an examination with the Amsler grid and the ForeseeHome before treatment or routine ophthalmic examination. Patients performed an unsupervised test with the Amsler grid and were thereafter classified as Amsler positive if they reported visual field abnormalities or Amsler negative if no abnormalities were present. This was followed by a self-administered ForeseeHome test, and the result, negative or positive, was noted.

Accurate detection rate

Study results showed that among the 26 CNV patients, 23 were found to be positive with the ForeseeHome, compared with only 15 patients found positive with the Amsler grid. This data yields a sensitivity of 88.4% for the ForeseeHome vs. 57.6% for the Amsler grid.

Additionally, the ForeseeHome indicated no false positives among the group of 35 intermediate AMD patients.

The occurrence of this disease is

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steadily growing. By 2020, the number of patients with advanced AMD is estimated by the Age-Related Eye Disease Study to increase by 50% from the 2004 estimate of 1.75 million, largely because of the aging population of the baby boomers. Utilizing instruments such as the Foresee PHP in-office tool and the ForeseeHome self-testing unit allows us to effectively work with our patients to become proactive in monitoring for CNV conversion and take the steps necessary to save their sight. **OSN**

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