DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

TRANSMITTED BY FACSIMILE

Dave Garbe
Director, Scientific Information and Medical Communications
Allergan, Inc.
2525 Dupont Drive
PO Box 19534
Irvine, CA 92623-9534

RE: **NDA 21-275** Lumigan (bimatoprost ophthalmic solution) 0.03%
MACMIS # 9867

Dear Mr. Garbe:

This letter objects to Allergan, Inc.'s (Allergan), dissemination of violative promotional materials for Lumigan. We specifically refer to a "Dear Doctor" letter dated March 19, 2001, from Scott M. Whitcup, MD, Vice President, Ophthalmology, Therapeutic Area, Allergan, Inc. The Division of Drug Marketing, Advertising, and Communications (DDMAC) reviewed the promotional letter and concluded that it is false or misleading under the Federal Food, Drug, and Cosmetic Act and its implementing regulations. Our specific objections follow:

Minimization of Risk

Your letter lacks fair balance and is misleading because it minimizes important risk information contained in a bolded warning in the approved product labeling (PI) for Lumigan. This bolded warning concerns possible permanent changes to pigmented eye tissues such as increased pigmentation of the iris and periorbital tissue (eyelid skin), and increased pigmentation and growth of eyelashes. Your letter fails to present this important risk information with a prominence and readability reasonably comparable to the effectiveness claims (i.e., the effectiveness claims are presented in the body of the letter, whereas the bolded warning is presented in small print after the signature block and the reference to the enclosure).

Misleading Superiority Claim

In the letter, you claim that Lumigan was superior to timolol 0.5% dosed bid in clinical trials. This claim is misleading because you compare the effectiveness of two products that have dissimilar indications. Timolol is indicated as a first line therapy whereas Lumigan is indicated as a second-line therapy. Further, the two drugs have very different adverse events, warnings, and contraindications. Thus, this comparison implies that Lumigan is indicated as a first line therapy, which is an unapproved indication. We note that we communicated this objection to you in our March 15, 2001, comment letter.

Overstatement of Efficacy

In the letter, you state that patients reached target IOPs of ≤17 and 15 mmHg. These statements are misleading because imply that Lumigan is more effective than has been shown by substantial evidence. The PI for Lumigan states that patients in the clinical trials had a baseline IOP of 26 mmHg, and that the IOP lowering effect of Lumigan was 7-8 mmHg. Thus, your claim that patients reached target IOPs of 15-17mmHg is inconsistent with the approved product labeling.

Requested Actions

In order to address these objections, we request that you immediately cease the dissemination of this violative promotional materials and all similar promotional materials that contain the same or similar messages.

You should respond in writing to us regarding this issue by April 9, 2001. Your response should include Allergan's intent to comply with the above request, the date that it ceased disseminating these and any other violative promotional materials with the same or similar messages, and a list of the discontinued materials.

If you have any questions, please contact me by facsimile at (301) 594-6771, or by written communication at the Division of Drug Marketing, Advertising, and Communications, HFD-42; Room 17B-20; 5600 Fishers Lane; Rockville, MD 20857. DDMAC reminds Allergan that only written communications are considered official.

In all future correspondence regarding this matter, please refer to MACMIS # 9867 and NDA 21-275.

Sincerely,

{See appended electronic signature page}

Warren Rumble
Regulatory Review Officer
Division of Drug Marketing,
Advertising, and Communications

/s/

Warren Rumble
3/26/01 10:42:42 AM

ALLERGAN

2525 Dupont Drive, P.O. Box 19534, Irvine, California, USA 92623-9534 Telephone: (714) 246-4500 Web site: www.allergan.com

March 2001

Dear Doctor:

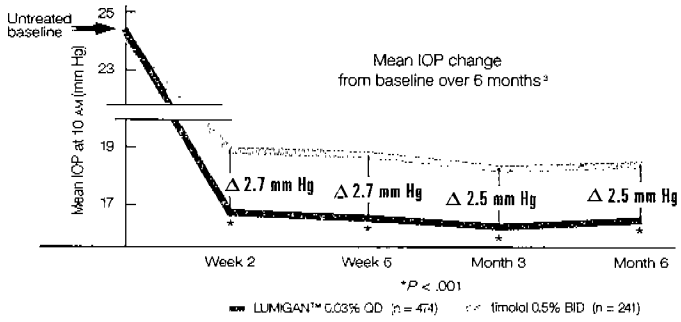
Allergan, Inc., is pleased to announce the availability of an exciting new treatment for lowering intraocular pressure (IOP). LUMIGAN™ (bimatoprost ophthalmic solution) 0.03% is indicated for the reduction of elevated IOP in patients with open-angle glaucoma or ocular hypertension who are intolerant of other IOP-lowering medications or insufficiently responsive (failed to achieve target IOP determined after multiple measurements over time) to another IOP-lowering medication. New LUMIGAN™ will be available in pharmacies soon.

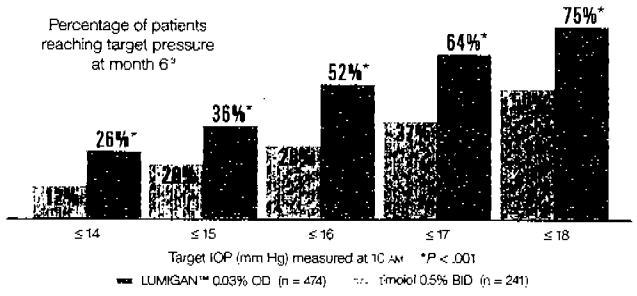
LUMIGAN™ ophthalmic solution is a synthetic prostamide analog. Discovered by Allergan, LUMIGAN™, which mimics the activity of newly identified prostamides, effectively lowers IOP.[1] Recent studies suggest that LUMIGAN™ enhances outflow through both the trabecular-meshwork and uveoscleral routes.[1,2]

In 2 well-controlled clinical trials involving 715 patients, LUMIGAN™ QD produced a 33% reduction in IOP vs 23% achieved with timolol BID (8.1 mm Hg vs 5.6 mm Hg) after 6 months of therapy.[3]

In addition, LUMIGAN™ ophthalmic solution demonstrated consistent 7 mm Hg to 8 mm Hg IOP reduction over 6 months.[3]

LUMIGAN™ achieves lower target pressure in more patients than timolol. In phase-III studies, 64% of LUMIGAN™ patients reached target IOP of ≤ 17 mm Hg, and 36% of LUMIGAN™ patients reached target IOP of ≤ 15 mm Hg.[3] The demonstrated ability of LUMIGAN™ ophthalmic solution to achieve lower target pressure in more patients should make it a valuable addition to your clinical practice.



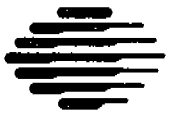


LUMIGAN™ ophthalmic solution is also safe and well tolerated. Patients receiving LUMIGAN™ responded favorably to treatment. Minimal systemic side effects were observed after 12 months of therapy.[1] The most frequently reported adverse events occurring in approximately 15% to 45% of patients dosed once daily, in descending order of incidence, were conjunctival hyperemia, growth of eyelashes, and ocular pruritus.[1] Conjunctival hyperemia was primarily trace to mild, with only 3% of patients discontinuing.[1] Additionally, there was a low incidence of iris pigmentation—only 1.5% observed after 12 months.[1]

LUMIGAN™ ophthalmic solution also offers the enhanced convenience of QD dosing and requires no refrigeration. It is available in 2.5-mL and 5-mL sizes. Please see full prescribing information enclosed.

ALLERGAN

2525 Dupont Drive, P.O. Box 19534, Irvine, California, USA 92623-9534 Telephone: (714) 246-4500 Web site: www.allergan.com



We believe that LUMIGAN™ represents an exciting breakthrough in IOP-lowering therapy. Data from the AGIS Investigators support the suggestive evidence from earlier studies that achieving low levels of IOP slows the progression of glaucomatous optic neuropathy.[4]

Your Allergan representative will soon be contacting you with more information regarding LUMIGAN™. You may also contact our Scientific Information and Medical Compliance Department at (800) 433-8871. Thank you for your support of Allergan products, and as always, please let your representative know how we can best continue to serve you and your patients.

Sincerely,

Scott M Whitcup

Scott M. Whitcup, MD
Vice President
Ophthalmology, Therapeutic Area

Enclosure

Gradual eyelash growth (lengthening, darkening, and thickening) and darkening of the eyelid skin have been reported after treatment with LUMIGAN™. Darkening of the iris has been reported in 1.5% of patients treated for 12 months with LUMIGAN™. Some of these changes may be permanent.

1. LUMIGAN™ Prescribing Information.
2. Brubaker RF, Schoff EO, Nau CB, Carpenter SP, Chen K, Vandenburgh AM. Effects of AGN 192024, a new ocular hypotensive agent, on aqueous dynamics. *Am J Ophthalmol.* 2001;131(1):19-24.
3. Data on file, Allergan, Inc.
4. The AGIS Investigators. The Advanced Glaucoma Intervention Study (AGIS):7. The relationship between control of intraocular pressure and visual field deterioration. *Am J Ophthalmol.* 2000;130(4):429-440.