DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

SEP - 2 1997

TRANSMITTED VIA FACSIMILE

Dr. Wael El-Amin
Medical Advisor
Leiras, Inc.
1850 Centennial Park Drive
Suite 450
Reston, VA 22091

RE: NDA 20-439
Betimol (timolol ophthalmic solution)
MACMIS File ID# 5492

Dear Dr. El-Amin:

This letter is in reference to Leiras, Inc.'s (Leiras) promotional campaign for Betimol (timolol ophthalmic solution) 0.25% and 0.5%. The Division of Drug Marketing, Advertising, and Communications (DDMAC) has concluded that Leiras is disseminating promotional materials that are false and/or misleading under the Federal Food, Drug, and Cosmetic Act and its implementing regulations. Our specific objections follow:

Superiority of Betimol over timolol maleate

In an advertisement published in the May 15, 1997, edition of Ocular Surgery News, Leiras represents that Betimol is superior to generic timolol. The theme of the brochure is that a health practitioner should prescribe Betimol so the patient won't get a generic drug as one might get if the practitioner prescribed Timoptic. In the following statements and representations, Leiras claims there is a benefit of getting the name brand drug Betimol without a generic substitute: "Write Timoptic And You May Get..." (followed by a dark picture of many unidentifiable ophthalmic bottles); "Write Betimol And You Get Betimol," and "Count On These Benefits For You And Your Patients -- Brand Quality--No generic substitutes."

In a similar brochure identified as 080788, Leiras makes similar claims that Betimol is superior to generic timolol by stating "benefits for you and your patients," "no generic substitutes," and "Stay in control. Write Betimol. Get Betimol." Leiras makes these same statements in a brochure identified as 080787 and titled, "Stay in control. Write Betimol. Get Betimol."

DDMAC considers these statements and representations to imply that Leiras's form of timolol hemihydrate is superior to generic timolol maleate products that are rated therapeutically equivalent to Timoptic. This representation is false and/or misleading because there is no evidence to demonstrate that Betimol is superior to Timoptic or other beta-blocking drugs. Leiras's suggestion that generic products are less beneficial for the practitioner and patient is false and misleading. All Food and Drug Administration (FDA) approved dosage forms of generic drugs classified as therapeutically equivalent to branded products coded AB under an ingredient and dosage form heading can be substituted with the full expectation that the substituted product will produce the same clinical effect and safety profile as the branded drug[1].

Unsupported Claim

In the "branded quality" section of the brochure identified as 080787 cited above, Leiras claims under the "potential results when a generic is prescribed" heading, that the patient may be confused due to getting different packaging, but that the patient will benefit from getting Betimol because they will get the same bottle and packaging every time they receive a prescription. Under the same heading Leiras claims that the doctor "has less knowledge of what brand the patient is taking." Leiras has not provided adequate substantiation for this claim. In the absence of such substantiation, DDMAC considers this claim to be misleading.

Cost Comparisons

In the "affordability" section of the brochure cited above and identified as 080788, Leiras claims that Betimol is "competitively priced," and that "Betimol is priced comparably with timolol maleate generics." Leiras then presents a table on the opposite page of the spread with 10 beta-blocking intraocular pressure reducing drugs, but with only one generic product. DDMAC considers the headline regarding generic prices that references a table with only one generic drug to be misleading.

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[1]According to the Approved Drug Products, 15th Edition, 1995; all drug products that are rated bioequivalent have demonstrated that they are: 1) safe and effective; 2) pharmaceutical equivalents in that they contain identical amounts of the same active drug ingredient in the same dosage form and route of administration, and meet compendial or other applicable standards of strength, quality, purity, and identity; 3) bioequivalent in that they do not present a known or potential bioequivalence problem, and they meet an acceptable *in vitro* standard, or if they do present such a known or potential problem, they are shown to meet an appropriate bioequivalence standard; 4) adequately labeled; and 5) manufactured in compliance with Current Good Manufacturing Practice regulations.

Patient Compliance

In the "affordability" section of the brochure, Leiras claims that "lower price encourages long-term patient compliance." Leiras has not provided adequate substantiation for this claim. In the absence of such substantiation, DDMAC considers this claim to be misleading.

Previous Notice

DDMAC notified Leiras on February 26, 1996, of similar violative claims of superiority of Betimol over generic timolol products. In conclusion, once again, DDMAC requests that Leiras cease promoting Betimol as being superior to generic timolol. In addition, Leiras should cease using all promotional materials that include these or similar violative claims, and should respond to DDMAC in writing by September 16, 1997, detailing which promotional materials make these claims and stating its commitment to discontinue the use of these violative pieces. DDMAC further requests that Leiras submit its reference "Pharmaceutical Research Corporation, July and November 1996," so that we can complete our review of Leiras' claims regarding price, drop size, and patient use.

If you have any questions, please contact the undersigned by telephone at (301) 827-2831, facsimile (301) 594-6771, or by written communication at the Division of Drug Marketing, Advertising, and Communications, HFD-40, Room 17B-20, 5600 Fishers Lane; Rockville, MD 20857. DDMAC reminds Leiras that only written communications are considered official. In all future correspondence regarding this matter, please refer to MACMIS #5492 and NDA 20-439.

Sincerely,

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