DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

AUG 15 1997

**TRANSMITTED VIA FACSIMILE**

Donald H. Chmielewski
Director, Regulatory Affairs
Bausch & Lomb Pharmaceuticals, Inc.
Pharmaceutical Division
8500 Hidden River Parkway
Tampa, FL 33637

**RE: ANDA 74-443**
Crolom (cromolyn sodium ophthalmic solution, USP, 4%)
MACMIS # 5721

Dear Mr. Chmielewski:

This letter is in reference to Bausch & Lomb's (B&L) submission, dated June 25, 1997, of promotional materials under cover of Form FDA 2253 for Crolom (cromolyn sodium ophthalmic solution, USP, 4%). This submission included two flash cards identified as PH0998-1 and titled "The role of mast cells, chemical mediators and selected products," and PH0998-2 and titled "By stabilizing mast cells, Crolom can prevent chemical mediators from being released." The Division of Drug Marketing, Advertising and Communications (DDMAC) considers the flash cards to be false and/or misleading under the Federal Food, Drug, and Cosmetic Act and its implementing regulations. Our specific objections follow:

Misleading Claim of Superiority

In flash card PH0998-1, B&L graphically represents specific pathways and chemical mediators by which mast cells can release chemical mediators that result in the ocular effects of itching, watering, pain, and redness. B&L identifies points in the pathways where Crolom, Pred Forte, Acular, and Livostin have an effect. The graphic shows that Crolom can prevent the mast cell chemical mediators from being released (by blocking the whole cascade), but in comparison, the graphic presents the competitor's product as affecting only one pathway to the final ocular effects. DDMAC considers this misleading because this graphic implies that Crolom is superior to the other products in preventing the ocular effects of itching, watering, pain, and redness. At least one of these drug products is indicated for the temporary relief of the signs and symptoms of seasonal allergic conjunctivitis which would include itching, watering, pain, and redness.

B&L has not provided clinical support for this superiority claim. Claims of superiority require substantial evidence (i.e., generally two adequate and well-controlled, head-to-head studies).

Promotion of New Uses for Crolom

In the flash card identified as PH0998-2 and titled "By stabilizing mast cells, Crolom can prevent chemical mediators from being released," B&L lists four drug products--Crolom, Acular, Livostin, and Patanol, and indicates each drug's blocked pathway. In the flash card PH0998-1 described under "Misleading Claims of Superiority", B&L compares the effect of Crolom, Pred Forte, Acular, and Livostin. However, both flash cards compare drugs that do not have the same indications for use. Crolom is indicated in the treatment of ocular disorders referred to by the terms vernal keratoconjunctivitis, vernal conjunctivitis, and vernal keratitis, but Acular is indicated for the relief of ocular itching due to seasonal allergic conjunctivitis; Patanol is indicated for the temporary prevention of itching of the eye due to allergic conjunctivitis; Livostin is indicated for the temporary relief of the signs and symptoms of seasonal allergic conjunctivitis; and Pred Forte is indicated for the treatment of steroid responsive inflammation of the conjunctiva, cornea, and anterior segment of the globe. Because these drugs do not have the same indications for use, and because B&L has not demonstrated that Crolom is safe and effective for the indicated uses of these other drug products, DDMAC considers this comparison between them to be misleading and the promotion of unapproved uses for Crolom.

B&L should instruct its sales force to immediately discontinue the use of the above flash cards, and any other promotional materials that make false and/or misleading claims or promote unapproved uses for Crolom. B&L should respond to DDMAC regarding these violations by August 29, 1997. In its response, B&L should state which promotional pieces it has discontinued.

If you have any questions, please contact me by telephone at (301) 827-2831, by facsimile at (301) 827-2831, or by written communication at the Division of Drug Marketing, Advertising, and Communications, HFD-40; Room 17B-20; 5600 Fishers Lane; Rockville, MD 20857.

In all future correspondence regarding this matter, please refer to MACMIS # 5721 and ANDA 74-443.

Sincerely,

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