DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

JUL 24 2000

TRANSMITTED VIA FACSIMILE

David Garbe
Director, Scientific Information and Medical Compliance
Allergan
2525 Dupont Drive TL-1L
P.O. Box 19534
Irvine, CA 92623-9534

RE: NDA 20-428
Azelex (Azelaic Acid) 20% Cream
MACMIS# 8735

Dear Mr. Garbe:

As part of our routine monitoring program, the Division of Drug Marketing, Advertising, and Communications (DDMAC) has become aware of promotional materials for Azelex (Azelaic Acid) 20% Cream by Allergan, Inc. that violate the Federal Food, Drug and Cosmetic Act (Act) and its implementing regulations. Reference is made to selected promotional materials for Azelex, including sales aid SIMCOO-099, journal advertisement SIMCOO-089, and "Dear Doctor" sample letter SIMC99561 submitted under cover of Form FDA 2253. We have reviewed these materials and have determined that they promote an unapproved new drug, namely the combination of Azelex and 4% Benzoyl Peroxide (Azelex/BPO)[1].

Unapproved New Drug

In your promotional materials, you make several claims and presentations relating to the safety and efficacy of Azelex/BPO as if it were an approved product. Examples include, "A winning combination," "Azelex and BPO: A winning combination vs. Benzamycin[2]," and " Play your cards right with Azelex and BPO." These claims and representations promote an unapproved new drug, in violation of the Act.

[1] In certain promotional materials, Brevoxyl® of Stiefel Laboratories, Inc. is referenced as the 4% Benzoyl peroxide used in the Azelex/BPO combination.
[2] Benzamycin® of Dermik Laboratories, Inc. is an approved drug combination product of 3% erythromycin and 5% benzoyl peroxide

Comparative superiority claim of unapproved drug vs. approved drug

In your promotional materials, you make several superiority claims comparing an unapproved drug (Azelex/BPO), with an approved drug, Benzamycin. These claims include, but are not limited to:

- Effective: Greater reduction in mean inflammatory lesions at all time points
- Well Tolerated: Less dryness, burning, and scaling at all time points
- Significantly greater decrease in mean overall disease severity score at week 8
- Significantly greater increase in mean overall global improvement score at weeks 8 and 12
- Higher overall patient preference rating

These superiority claims for Azelex/BPO are false or misleading because the safety and efficacy of Azelex/BPO, an unapproved new drug, has not been established.

Action Requested

You should immediately cease distribution of these promotional materials and all other promotional materials for Azelex that contain the same or similar claims or presentations cited in this letter. You should submit a written response to us, on or before 10 business days, describing your intent and plans to comply with the above. In your letter to us, you should include a list of all promotional materials that were discontinued, and the discontinuation dates.

You should direct your response to me by facsimile at (301) 594-6771, or at the Food and Drug Administration, Division of Drug Marketing, Advertising, and Communications, HFD-42, Rm. 17B-20, 5600 Fishers Lane, Rockville, MD 20857. We remind you that only written communications are considered official. In all correspondence regarding this particular submission, please refer to MACMIS ID# 8735 in addition to the NDA number.

Sincerely,

/S/

Cheryl Y. Roberts
Regulatory Review Officer
Division of Drug Marketing,
Advertising and Communications

ALLERGAN
SKIN CARE
Leader in Retinoid and AHA Research

2525 Dupont Drive
P.O. Box 19534
Irvine, California 92623-9534
Telephone: (714) 246-4500
Fax: (714) 246-4764

December 6, 1999

John Q. Sample, M.D.
1234 Main Street
Anytown, US 12345

Dear Dr. Sample:

Thank you for meeting with me recently to discuss the results of a study comparing AZELEX® (azelaic acid cream) 20% in combination with Brevoxyl® (4% benzoyl peroxide) gel versus Benzamycin® (3% erythromycin, 5% benzoyl peroxide) gel alone for treating mild to moderate inflammatory acne.

Unlike Benzamycin®, which only targets *Propionibacterium acnes,* AZELEX® targets 2 pathogenic factors in acne: *P acnes* and abnormal keratinization. (The exact mechanism of action and clinical significance are unknown.)

Based on a randomized, physician-masked, parallel-group clinical study (N = 58), the AZELEX®/Brevoxyl® combination was found to be as effective, safe, and well tolerated as Benzamycin® gel for treating mild to moderate inflammatory acne.[1]

AZELEX®/Brevoxyl® produced a significantly greater reduction in mean overall disease severity at week 8 ($P = .005$) and week 12 ($P = .058$) (Figure 1) and a significantly lower mean inflammatory lesion count at week 8 ($P = .004$) (Figure 2) than Benzamycin® alone. The treatment success rate—percentage of patients with 75% improvement or above—was also greater in the AZELEX®/Brevoxyl® group than the Benzamycin® group throughout the study (Figure 3). And the AZELEX®/Brevoxyl® combination had a higher patient preference rating than Benzamycin® (Figure 4).[1]

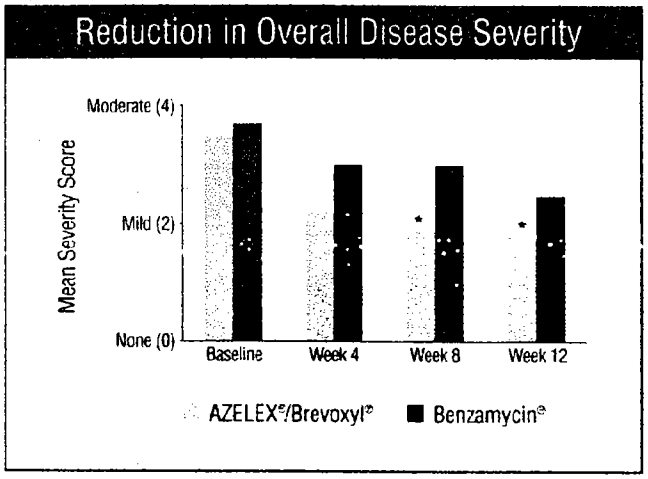

Figure 1

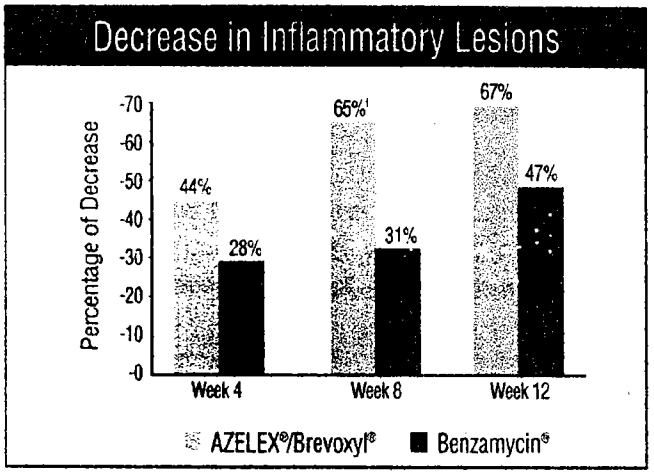

Figure 2

*The reduction in disease severity was greater in the AZELEX®/Brevoxyl® group throughout the study and statistically significant at week 8 ($P = .005$) and week 12 ($P = .058$).[1]

†Mean inflammatory lesion count was significantly lower in the AZELEX®/Brevoxyl® group at week 8 ($P = .004$).[1]

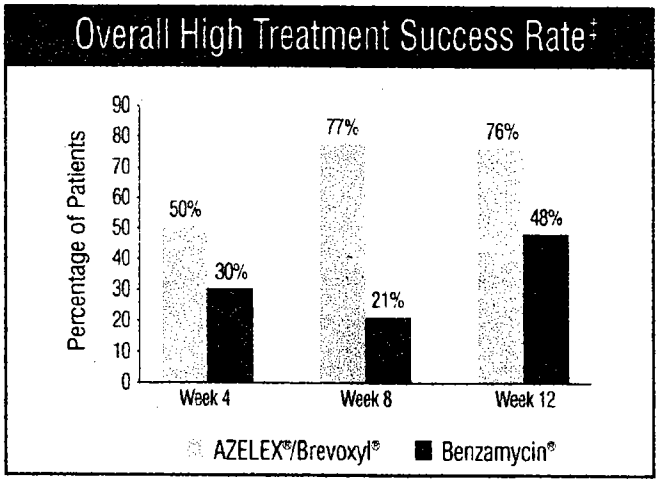

Figure 3

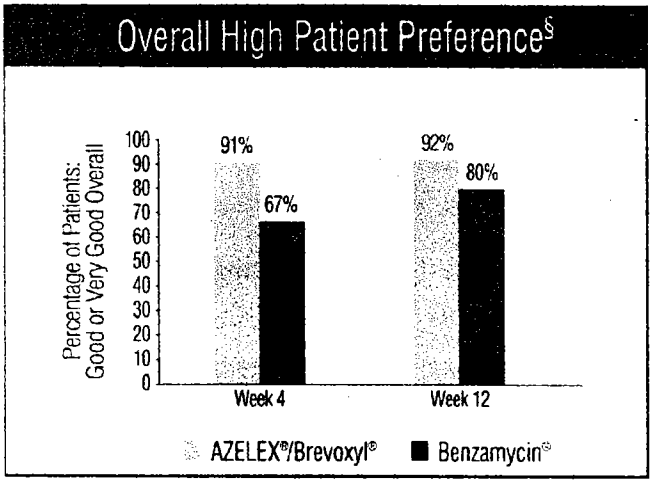

Figure 4

‡Treatment success defined as percentage of patients with ≥75% improvement. Treatment success rate was greater in the AZELEX®/Brevoxyl® group throughout the treatment period and statistically significant at week 8 ($P = .003$) and week 12 ($P = .024$).[1]

§More patients using AZELEX®/Brevoxyl® rated their medication as good or very good overall.[1]

Also noteworthy, the AZELEX®/Brevoxyl® combination produced excellent results with minimal irritation. There was no significant difference between treatment groups in redness, oiliness, peeling, burning, and itching.[1]

You'll be pleased to know that AZELEX® comes in a cosmetically elegant, noncomedogenic, emollient formulation that can easily be worn under makeup.

Full prescribing information for AZELEX® is enclosed for your reference. Adverse reactions are generally mild and transient in nature. The most common adverse reactions—pruritus, burning, stinging, and tingling—occur in approximately 1% to 5% of patients. Patients with dark complexions should be monitored for early signs of hypopigmentation.

Dr. Sample, I am confident you will appreciate the many benefits of AZELEX® in combination with Brevoxyl®. If you have any questions or comments, or if you would like to receive samples of AZELEX®, please contact me at 1-800-669-6890, extension 1234.

Sincerely,

John Q. Rep
Territory Manager

Enclosure

1. Data on file, Allergan, Inc.

A winning combination vs Benzamycin®

In two 12-week, physician-masked clinical studies (N = 133) versus Benzamycin® alone, the combination of AZELEX® and BPO was found to be[1]:

EFFECTIVE: Greater reduction in mean inflammatory lesions at all time points (not statistically significant)

WELL TOLERATED: Less scaling, burning, and dryness at all time points (not statistically significant for scaling at week 12 and burning at week 4)

AZELEX® is indicated for the treatment of mild to moderate inflammatory acne. Adverse reactions are generally mild and transient in nature. Pruritus, burning, stinging, and tingling occur in approximately 1% to 5% of patients. Patients with dark complexions should be monitored for early signs of hypopigmentation.

Please see adjacent page for brief prescribing information.

Benzamycin (3% erythromycin, 5% benzoyl peroxide) is a registered trademark of Dermik Laboratories, Inc.

1. Data on file, Allergan, Inc., 2000. Studies A008 and A008B.

ALLERGAN *50 Years of Growth & Innovation*

AZELEX®
(AZELAIC ACID CREAM) 20%

Available in 30- and 50-g tubes, b.i.d.