DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

TRANSMITTED BY FACSIMILE

Barbara Spallitta
Regulatory Compliance Manager
DOAK DERMATOLOGICS
383 Route 46 West
Fairfield, NJ 07004-2402

RE: NDA # 21-005
Solaraze (diclofenac sodium) Gel, 3%
MACMIS ID #15348

Dear Ms. Spallitta:

The Division of Drug Marketing, Advertising, and Communications (DDMAC) of the U.S. Food and Drug Administration (FDA) has reviewed a detail aid (PA1629) for Solaraze® (diclofenac sodium) Gel, 3% (Solaraze Gel), submitted under cover of Form FDA-2253 by Doak Dermatologics, and a journal ad for Solaraze Gel (IL206A). These promotional materials for Solaraze Gel recommend or suggest uses for Solaraze Gel that have not been approved by FDA, and thus create new "intended uses" for the drug for which the product lacks adequate directions, broaden the indication for Solaraze Gel, and omit important risk information for the drug. Therefore, the pieces misbrand Solaraze Gel in violation of the Federal Food, Drug, and Cosmetic Act (Act), 21 U.S.C. 352(a), (f)(1), & (n); 321(n); and FDA's implementing regulations. S*ee* 21 CFR 201.128; 202.1(e)(5) & (6)(i). Furthermore, the journal ad was not submitted to FDA under cover of Form FDA-2253 as required by 21 CFR 314.81(b)(3)(i).

Background

According to the **INDICATIONS AND USAGE** section of the approved product labeling (PI), "Solaraze® (diclofenac sodium) Gel is indicated for the topical treatment of actinic keratoses (AK). Sun avoidance is indicated during therapy."

Additionally, the **WARNINGS** and **PRECAUTIONS** sections of the PI state:

> **WARNINGS**
> As with other NSAIDs, anaphylactoid reactions may occur in patients without prior exposure to diclofenac. Diclofenac sodium should be given with caution to patients with the aspirin triad. The triad typically occurs in asthmatic patients who experience rhinitis with or without nasal polyps, or who exhibit severe, potentially fatal bronchospasm after taking aspirin or other NSAIDs.

PRECAUTIONS
Solaraze® (diclofenac sodium) Gel should be used with caution in patients with active gastrointestinal ulceration or bleeding and severe renal or hepatic impairments. Solaraze® should not be applied to open skin wounds, infections, or exfoliative dermatitis. It should not be allowed to come in contact with the eyes.

The safety of the concomitant use of sunscreens, cosmetics or other topical medications and Solaraze® is unknown.

Finally, the **DOSAGE** AND **ADMINISTRATION** section of the PI states in relevant part "Solaraze® Gel is applied to lesion areas twice daily. It is to be smoothed onto the affected skin gently. The amount needed depends upon the size of the lesion site. Assure that enough Solaraze® Gel is applied to adequately cover each lesion."

Broadening of Indication

The detail aid and journal ad are misleading because they suggest that Solaraze Gel is approved for use in the treatment of AK when used in combination with cryotherapy. However, Solaraze Gel is approved for the treatment of AK only when used as monotherapy. The detail aid, entitled "Treat The Field Sequential Treatment Cryotherapy followed by Solaraze Gel®, Diclofenac Sodium-3%," includes claims such as "'Treat The Field' is the successful operative removal of obvious actinic keratoses, enhanced by treating the source of the lesions after cryotherapy with Solaraze® Gel to eliminate the potential for additional AK development or recurrence." and **"CRYOTHERAPY to treat defined AK lesions and Solaraze® Gel to treat the field of lesions you can't see or feel**" (emphasis original). The journal ad which also is entitled "Treat the Field" includes the claim, "A recent study showed that for patients with multiple actinic keratosis (AK) lesions, '**Treating the Field'*** utilizing a sequential treatment of **Solaraze® Gel** subsequent to cryotherapy is likely more effective than cryotherapy alone[1]" (emphasis original). Furthermore, both pieces present a bar graph entitled "Average Percent Reduction in Total Lesions in Target Area" that presents data for patients who were treated with either cryotherapy alone or cryotherapy, with two week healing, followed by Solaraze Gel therapy for three months. Finally, the detail aid includes before and after pictures for two patients who received cryotherapy followed by treatment with Solaraze Gel.

As stated above, Solaraze Gel is approved only as monotherapy for AK, it is not approved for use in combination with other treatment methods as your promotional materials suggest. The PI does not include any information on the safety and efficacy of Solaraze Gel when used in combination with cryotherapy or any other dermal products. In fact, the Precautions section of the PI specifically states "Safety and efficacy of the use of Solaraze® together with other dermal products, including cosmetics, sunscreens, and other topical medications on the area being treated, have not been studied." Therefore, your claims and presentations in the detail aid and journal ad contradict Solaraze Gel's PI, and cause the PI to lack adequate directions for the use recommended in your promotional materials.

[1] Lebwohl M, Zeichner J. Ten patients treated with cryotherapy with two week healing followed by Solaraze Gel for three months, or cryotherapy alone. Study data compiled December 2005 from: An Assessment of the Safety and Efficacy of Cryotherapy Alone Compared to Sequential Treatment with Solaraze Gel (diclofenac sodium 3%) After Cryotherapy for the Treatment of Actinic Keratoses. Study conducted at Mount Sinai School of Medicine, Department of Dermatology: New York, NY.

Furthermore, the reference provided is a single, open-label, pilot trial that included 10 patients in each of two treatment arms: (1) cryotherapy with two week healing followed by Solaraze Gel application twice daily for three months, or (2) cryotherapy alone. This trial is not substantial evidence or substantial clinical experience to support efficacy claims for the combined use of cryotherapy and Solaraze Gel since the trial failed to demonstrate a statistically significant benefit for combination therapy. The cited reference itself states that "the data are not statistically significant…."

Omission of Risk Information

Promotional materials are misleading if they fail to reveal facts that are material in light of the representations made by the materials or with respect to the consequences that may result from the use of the drug as recommended or suggested by the materials. Although the promotional materials include information regarding the need to administer Solaraze Gel with caution to patients with the aspirin triad, they fail to mention that "The triad typically occurs in asthmatic patients who experience rhinitis with or without nasal polyps, or who exhibit severe, potentially fatal bronchospasm after taking aspirin or other NSAIDs." Furthermore, the promotional materials fail to include the Precautions that "Solaraze® (diclofenac sodium) Gel should be used with caution in patients with active gastrointestinal ulceration or bleeding and severe renal or hepatic impairments," that Solaraze Gel "should not be allowed to come in contact with the eyes," and that "The safety of the concomitant use of sunscreens, cosmetics or other topical medications and Solaraze® is unknown." (*See* background section). The statements "Please see package insert attached for full Prescribing Information." and "Please see package insert on adjacent page for full Prescribing Information." provided in the detail aid and journal ad, respectively, do not mitigate these misleading presentations. As a result, the promotional materials misleadingly suggest that Solaraze Gel is safer than has been demonstrated by substantial evidence or substantial clinical experience.

Failure to Submit

FDA regulations require you to submit specimens of mailing pieces and any other labeling or advertising devised for promotion of the drug product at the time of initial dissemination of the labeling and at the time of initial publication of the advertisement for a prescription drug product. Each submission is required to be accompanied by a completed transmittal Form FDA-2253 (Transmittal of Advertisements and Promotional Labeling for Drugs and Biologics for Human Use) and is required to include a copy of the product's current professional labeling. Your journal ad which appeared on the back cover of the October 2006 issue of the *Journal of the American Academy of Dermatology* (Volume 55, Number 4), was not submitted to FDA on Form FDA-2253, as required by 21 CFR 314.81(b)(3)(i).

Conclusion and Requested Action

For the reasons discussed above, your journal ad and detail aid misbrand Solaraze Gel in violation of the Act, 21 U.S.C. 352(a), (f)(1), & (n); 321(n); and FDA's implementing regulations. S*ee* 21 CFR 201.128; 202.1(e)(5) & (6)(i). Furthermore, the journal ad was not submitted to FDA under cover of Form FDA-2253, as required by 21 CFR 314.81(b)(3)(i).

DDMAC requests that Doak Dermatologics immediately cease the dissemination of violative promotional materials for Solaraze Gel the same as or similar to those described above. Please submit a written response to this letter on or before July 31, 2007, stating whether you intend to comply with

this request, listing all violative promotional materials for Solaraze Gel such as those described above, and explaining your plan for discontinuing use of such materials.

Please direct your response to the undersigned at the Food and Drug Administration, Center for Drug Evaluation and Research, Division of Drug Marketing, Advertising, and Communications, 5901-B Ammendale Road, Beltsville, MD 20705-1266, facsimile at 301-796-9877. In all future correspondence regarding this matter, please refer to MACMIS ID #15348 in addition to the NDA number. We remind you that only written communications are considered official.

The violations discussed in this letter do not necessarily constitute an exhaustive list. It is your responsibility to ensure that your promotional materials for Solaraze Gel comply with each applicable requirement of the Act and FDA implementing regulations.

Sincerely,

{See appended electronic signature page}

Andrew S.T. Haffer, PharmD
Regulatory Review Officer
Division of Drug Marketing,
Advertising, and Communications

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Andrew Haffer

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