DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

TRANSMITTED BY FACSIMILE

Bobbi Woodward, MS, RAC
Manager, Regulatory Affairs
Galderma Laboratories, L.P.
14501 North Freeway
Fort Worth, TX 76177-3304

RE: NDA 20-922
Solagé™ (mequinol 2%, tretinoin 0.01%) Topical Solution
MACMIS ID#: 11668

Dear Ms. Woodward:

This letter objects to Galderma Laboratories, L.P.'s (Galderma) dissemination of promotional materials for Solagé Topical Solution that violate the Federal Food, Drug, and Cosmetic Act (Act) and its implementing regulations. As part of its routine monitoring program, the Division of Drug Marketing, Advertising, and Communications (DDMAC) has identified a patient tear sheet, "How Should I Use Solagé Solution?" that is provided by Galderma to healthcare providers for dissemination to patients. The patient tear sheet is misleading because it omits a serious risk associated with the use of Solagé Topical Solution. Our specific objections follow:

Failure to Reveal Material Facts/Minimization of Risk

Promotional materials are misleading if they fail to reveal material facts with respect to consequences that may result from use of the drug as recommended or suggested by the materials. Sections 502(a) and 201(n) of the Act (21 U.S.C. §§352(a) and 321(n)); 21 C.F.R. 1.21. Specifically, the patient tear sheet omits information from Solagé's approved product labeling (PI) regarding the contraindication in women of childbearing potential and thereby minimizes the risk associated with the use of Solagé.

According to the Contraindications section of the PI for Solagé:

> "The combination of mequinol and tretinoin may cause fetal harm when administered to a pregnant woman. Due to the known effects of these active ingredients, Solagé Topical Solution should not be used in women of childbearing potential."

In addition, the Precautions section of the PI, under the **Pregnancy: Teratogenic effects: Pregnancy Category X** (the most serious pregnancy warning category) header, states:

> "Although the magnitude of the potential for teratogenicity may not be well-defined, Solagé Solution is labeled as an "X" because **the potential risk of the use of this drug to treat this particular indication (solar lentigines) in a pregnant woman clearly outweighs any possible benefit**." (emphasis added)

Furthermore, the section entitled *What is the Most Important Information about Solagé Solution?* of the approved patient labeling (PPI), states in bolded type:

> "**Warning: Solagé Solution should not be used if you are pregnant, attempting to become pregnant, or at a high risk of pregnancy. Consult your doctor for adequate birth control measures if you are a female of child-bearing potential**."

Although the patient tear sheet discloses certain Warning and Dosage and Administration information concerning limitations to Solagé use (such as avoiding application to surrounding, normally-colored skin; using excessive amounts of Solagé to affected areas; and applying Solagé to the mucous membranes, lips, and the nose), the tear sheet fails to disclose the contraindication of use of Solagé in women of childbearing potential, and the serious potential for fetal harm. Contraindications and warnings about pregnancy are material facts to a female of childbearing potential who uses Solagé. Therefore, the patient tear sheet is misleading because it minimizes the risks of Solagé by its omission of material facts regarding this critically important risk information.

Requested Action

Galderma should immediately cease the dissemination of this violative patient tear sheet and all other promotional materials for Solagé that omit this risk information. On or before September 3, 2003, please submit a written response to DDMAC describing your intent and plans to comply with the above. In this letter, please also include a list of all discontinued promotional materials and the discontinuation date of each.

If you have any questions or comments, please contact the undersigned by facsimile at (301) 594-6759, or in writing at the Division of Drug Marketing, Advertising, and Communications, HFD-42, Room 8B-45, 5600 Fishers Lane, Rockville, Maryland 20857. In all future correspondence on this matter, please refer to **MACMIS #11668** and **NDA 20-922**. DDMAC reminds Galderma that only written communication is considered official.

Sincerely,

{See appended electronic signature page}

Jennifer C. Murphy, Pharm.D.
Consumer Promotion Analyst
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.

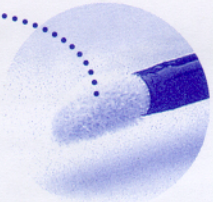
/s/

Jennifer Murphy
8/19/03 02:59:27 PM

HOW SHOULD I USE SOLAGÉ™ SOLUTION?

TOPICAL SOLUTION
Solagé™
mequinol 2%
tretinoin 0.01%

1. Solagé™ Solution is to be used twice daily, at least 8 hours apart.
2. Apply Solagé™ Solution to the age spots using the applicator provided with the medication.
3. Avoid application of Solagé™ Solution to the surrounding, normally colored skin.
4. Only enough Solagé™ Solution should be applied to make the lesion appear moist – running or dripping of the medication should be avoided.
5. Applications of larger amounts of Solagé™ Solution, or more frequent applications than recommended, will not lead to more rapid or better results, and marked redness, peeling, irritation or hypopigmentation may occur.



6. You should not shower or bathe the treatment area for at least 6 hours after application of Solagé™ Solution.
7. Solagé™ Solution is a drug for topical use only and is not a cosmetic preparation.
8. Do not use Solagé™ Solution around your eyes, lips, creases of the nose or mucous membranes.
9. Solagé™ Solution may cause severe redness, itching, burning, stinging, and peeling if applied to these areas.
10. If the product gets in your eyes, rinse thoroughly with water and contact your doctor.

Please see additional information on reverse side.

www.solage.com

Solagé™ TOPICAL SOLUTION
mequinol 2%
tretinoin 0.01%

- Stop treating any age spots that become the same color or lighter than your normally colored skin. If the skin surrounding an age spot becomes lighter than your normally colored skin, stop treating that age spot and contact your doctor regarding continued use of Solagé™ Solution to treat that age spot.
- If you forget or miss a dose of Solagé™ Solution, do not try to "make it up." Return to your normal application schedule as soon as you can.
- If sensitivity or increased irritation occurs, stop use of Solagé™ Solution and contact your doctor.
- If the age spots become darker with treatment, stop use of Solagé™ Solution and contact your doctor.
- Do not use Solagé™ Solution for any condition other than for which it was prescribed by your doctor. Do not give it to other persons or allow other persons to use it.
- You may use cosmetics after applying Solagé™ Solution but you should wait 30 minutes before applying.
- Solagé™ Solution increases your sensitivity to sunlight. Sun exposure (natural or artificial) to areas of the skin treated with Solagé™ Solution should be avoided. Wear protective clothing if exposure to the sun cannot be avoided. Patients using Solagé™ Solution should practice a comprehensive sun protection program. Following discontinuation of Solagé™ Solution, patients should continue to practice a comprehensive sun protection program using broad spectrum sunscreens with an SPF or 30 or higher.