CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number 20-985

APPROVAL LETTER

NDA 20-985

Dermik Laboratories, Inc.
Attention: Mr. James Thompson
Manager, Regulatory Affairs
1050 Westlakes Drive
Berwyn, PA 19312

Dear Mr. Thompson:

Please refer to your new drug application (NDA) dated October 28, 1999, received October 28, 1999, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for TRADENAME (fluorouracil cream) Cream, 0.5%.

We acknowledge receipt of your submissions dated December 7 and 10, 1999; January 18 (two) and 25, February 1, March 3, June 9, 21, 22, and 26, July 7, 14, and 25, August 2, 4, and 14 (facsimile), September 29 (facsimile), October 17, 23, and 24 (one official and one facsimile), 25 (three official and one facsimile), and 26 (facsimile), 2000.

This new drug application provides for the use of TRADENAME (fluorouracil cream) Cream, 0.5%, for the topical treatment of multiple actinic or solar keratosis of the face and anterior scalp.

We have completed the review of this application, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the agreed upon enclosed labeling text. Accordingly, the application is approved effective on the date of this letter.

According to "Guidance for Industry, Changes to an Approved NDA or ANDA," dated November 1999, you will need to submit a labeling supplement for a tradename. The reporting category for a tradename qualifies as a major change requiring a Prior Approval Supplement.

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert, text for the patient package insert, immediate container and carton labels). Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

Please submit 20 paper copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. Alternatively, you may submit the FPL electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDAs* (January 1999).

For administrative purposes, this submission should be designated "FPL for approved NDA 20-985." Approval of this submission by FDA is not required before the labeling is used.

We remind you of your Phase 4 commitments specified in your submission dated October 25, 2000. These commitments, along with any completion dates agreed upon, are listed below.

The Phase 4 study should include the following:

1. Because the number of subjects studied with the to-be-marketed formulation under labeled conditions does not reach the numbers recommended in the ICH E1A guidance, additional safety data for the treatment of actinic keratosis lesions located on the face is needed. In addition, because the safety and efficacy of TRADENAME has not been characterized for some common skin surface areas at risk for development of actinic keratosis, e.g., ears, scalp (other than anterior), and other sun-exposed areas, an appropriate study to address these informational needs should be conducted.
2. The study should include no less than one year safety and efficacy post-treatment and follow-up for incidence of recurrence,
3. The study should include an assessment of the safety and efficacy of re-treatment of actinic keratoses with TRADENAME cream
4. Particular attention should be paid to an assessment of the potential for eye irritation and the actions patients can take to minimize this potential.

The study protocol or protocols will be submitted to the Agency for review prior to the conduct of said study or studies to assure that the study or studies will address the concerns of the Agency with regard to the use of the product for the treatment of actinic keratosis. The studies or studies will be initiated within one year following this letter. The study or studies will be completed no later than three years after initiation, and the results submitted to the Agency within one year after completion.

Protocols, data, and final reports should be submitted to your IND for this product and a copy of the cover letter sent to this NDA. If an IND is not required to meet your Phase 4 commitments, please submit protocols, data and final reports to this NDA as correspondence. In addition, under 21 CFR 314.81(b)(2)(vii), we request that you include a status summary of each commitment in your annual report to this NDA. The status summary should include the number of patients entered in each study, expected completion and submission dates, and any changes in plans since the last annual report. For administrative purposes, all submissions, including labeling supplements relating to these Phase 4 commitments must be clearly designated "Phase 4 Commitments."

Validation of the regulatory methods has not been completed. At the present time, it is the policy of the Center not to withhold approval because the methods are being validated. Nevertheless, we expect your continued cooperation to resolve any problems that may be identified.

Be advised that, as of April 1, 1999, all applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to

contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred (63 *FR* 66632). We are waiving the pediatric study requirement for this application as the necessary studies are impossible or highly impractical to conduct because the number of patients is too small.

In addition, please submit three copies of the introductory promotional materials that you propose to use for this product. All proposed materials should be submitted in draft or mock-up form, not final print. Please submit one copy to this Division and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising, and Communications, HFD-42
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

Please note, if you choose to use a proprietary name for this product, the name and its use in the label must conform to the specifications under 21 CFR 201.10 and 201.15. We recommend that you submit any proprietary name to the Agency for our review prior to its implementation.

Please submit one market package of the drug product when it is available.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, please call Victoria Lutwak, Project Manager, at 301-827-2073.

Sincerely,

Jonathan K. Wilkin, M.D.
Director
Division of Dermatologic and Dental Drug Products
Office of Drug Evaluation V
Center for Drug Evaluation and Research

Enclosure

APPEARS THIS WAY
ON ORIGINAL