CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 21-005

APPROVAL LETTER

NDA 21-005

SkyePharma Inc.
Attention: Gordon L. Schooley, Ph.D.
Senior Vice President, Clinical Research & Regulatory Affairs
10450 Science Center Drive
San Diego, CA 92121

Dear Dr. Schooley:

Please refer to your new drug application (NDA) dated October 20, 1998, received October 22, 1998, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Solaraze (diclofenac sodium) Gel, 3%.

Please refer to our action letters dated October 21, 1999, and July 19, 2000.

We acknowledge receipt of your submissions dated July 28, August 15, September 22, and October 3, 2000. Your submission of August 15, 2000, received August 16, 2000, constituted a complete response to our July 19, 2000 action letter.

This new drug application provides for the use of Solaraze (diclofenac sodium) Gel for the topical treatment of actinic keratoses.

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.

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert, text for the patient package insert, and immediate container and carton labels) as agreed to in your facsimiles dated October 12 and 16, 2000. 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 21-005." Approval of this submission by FDA is not required before the labeling is used.

We remind you of your post marketing commitments specified in your submission dated July 28, 2000. You have agreed to complete and submit the following Phase 4 studies within 12 months of the approval of this application:

1. To further investigate the possible [ ].

2. Specifications for [ ].

3. Provide an updated stability protocol consistent with the revised drug product specifications.

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 post marketing 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 post marketing commitments must be clearly designated "Post Marketing 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 action on this application.

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 inserts directly to:

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

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 Kevin Darryl White, Project Manager, at (301) 827-2020.

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

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 21-005

APPROVABLE LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

NDA 21-005

SkyePharma Inc.
Attention: Gordon L. Schooley, Ph.D.
Senior Vice President, Clinical Research & Regulatory Affairs
10450 Science Center Drive
San Diego, CA 92121

JUL 19 2000

Dear Dr. Schooley:

Please refer to your new drug application (NDA) dated October 20, 1998, received October 22, 1998, submitted pursuant to section 505(b) of the Federal Food, Drug, and Cosmetic Act for Solarase (diclofenac sodium) Gel, 3%.

Please refer to our action letter dated October 21, 1999.

We acknowledge receipt of your submissions dated October 8 and 29, 1999; and January 21, April 3 and 24, May 18, June 2, 23 and 27, and July 17, 2000.

Your submission of January 21, 2000, received January 24, 2000, constituted a complete response to our October 21, 1999 action letter.

We have completed the review of this application, as amended, and it is approvable. Before the application may be approved, however, it will be necessary for you to submit revised draft labeling including proof copies of the immediate container and carton labels. Should additional information relating to the safety or effectiveness of this drug product become available, further revisions of the labeling may be required.

To support the safety of Solarase Gel, 3%, you should commit to complete and submit the following as Phase 4 studies within 12 months of the approval of this application:

1. To further investigate the possible [redacted]

2. Specifications for [redacted]

3. Provide an updated stability protocol consistent with the revised drug product specifications.

Under 21 CFR 314.50(d)(5)(vi)(*b*), we request that you update your NDA by submitting all safety information you now have regarding your new drug. Please provide updated information as listed below.

The update should cover all studies and uses of the drug including: (1) those involving indications not being sought in the present submission, (2) other dosage forms, and (3) other dose levels, etc.

1. Retabulation of all safety data including results of trials that were still ongoing at the time of NDA submission. The tabulation can take the same form as in your initial submission. Tables comparing adverse reactions at the time the NDA was submitted versus now will certainly facilitate review.

2. Retabulation of drop-outs with new drop-outs identified. Discuss, if appropriate.

3. Details of any significant changes or findings.

4. Summary of worldwide experience on the safety of this drug.

5. Case report forms for each patient who died during a clinical study or who did not complete a study because of an adverse event.

6. English translations of any approved foreign labeling not previously submitted.

7. Information suggesting a substantial difference in the rate of occurrence of common, but less serious, adverse events.

Within 10 days after the date of this letter, you are required to amend the application, notify us of your intent to file an amendment, or follow one of your other options under 21 CFR 314.110. In the absence of any such action FDA may proceed to withdraw the application.
Any amendment should respond to all the deficiencies listed. We will not process a partial reply as a major amendment nor will the review clock be reactivated until all deficiencies have been addressed.

Under 21 CFR 314.102(d) of the new drug regulations, you may request an informal meeting or telephone conference with this Division to discuss what further steps need to be taken before the application may be approved.

The drug product may not be legally marketed until you have been notified in writing that the application is approved.

If you have any questions, please contact Kevin Darryl White, Project Manager, at (301) 827-2020.

Sincerely,

/S/

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

APPEARS THIS WAY
ON ORIGINAL