CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

Application Number: NDA 20-886

Trade Name: PANRETIN GEL 0.1%

Generic Name:(alitretinoin)

Sponsor: Ligand Pharmaceuticals

Approval Date: February 2, 1999

Indication: Provides for the use of Panretin (alitretinoin) gel 0.1% for topical treatment of cutaneous lesions in patients with AIDS-related Kaposi's sarcoma.

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APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

NDA 20-886

FEB 2 1999

Ligand Pharmaceuticals
Attention: Howard T. Holden, Ph.D.
Vice President, Regulatory Affairs and Compliance
10275 Science Center Drive
San Diego, California 92121-1117

Dear Dr. Holden:

Please refer to your new drug application (NDA) dated May 26, 1998, received May 27, 1998, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Panretin (alitretinoin) gel 0.1%.

We acknowledge receipt of your submissions dated November 12, 17 and 19; December 2, 21, and 28, 1998; January 7, 8, 11, and 13, 1999.

This new drug application provides for the use of Panretin (alitretinoin) gel 0.1% for topical treatment of cutaneous lesions in patients with AIDS-related Kaposi's sarcoma.

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 enclosed labeling text. Accordingly, the application is approved effective on the date of this letter.

The current tube and carton labeling submitted in the amendment of January 11, 1999, may now be used. However, the following labeling changes should be made at the next production of the tube and cartons:

1. The space between the term "Store at 25°C (77°F); excursions permitted to 15-30°C (59-86°F)" and the term "[see USP Controlled Room Temperature]" should be deleted.

2. The phrase "dehydrated alcohol, polyethylene glycol 400, hydroxypropyl cellulose, and butylated hydroxytoluene" should be changed to the phrase "dehydrated alcohol USP, polyethylene glycol 400 NF, hydroxypropyl cellulose NF, and butylated hydroxytoluene NF."

An expiration dating period of 15 months is granted at this time. The expiration dating period could be extended, based on real-time stability data obtained from three primary stability batches 9709-003, 9711-005 and CPDU001. However, the expiration dating period may not be extended beyond 18 months because the proposed commercial stability protocol covers only up to 18 months.

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 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. For administrative purposes, this submission should be designated "FPL for approved NDA 20-886." Approval of this submission by FDA is not required before the labeling is used.

We remind you of your Phase 4 commitment specified in your submission dated January 7, 1999. This commitment, along with any completion dates agreed upon, is listed below:

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 314.82(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.

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 send one copy to the Division of Oncology Drug Products and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising, and Communications, HFD-40
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, contact Amy Chapman, Consumer Safety Officer, at (301) 594-5771.

Sincerely,

/S/

Robert Temple, M.D.
Director
Office of Drug Evaluation I
Center for Drug Evaluation and Research

Enclosure