CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 20-989

APPROVAL LETTER

NDA 20-989

SnowBrand Pharmaceuticals, Inc.
Attention: William C. Govier, M.D., Ph.D.
President and CEO
2001 Commonwealth Blvd., Suite 205
Ann Arbor, MI 48105

Dear Dr. Govier:

Please refer to your new drug application (NDA) dated August 26, 1998, received August 27, 1998, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for EVOXAC™ (cevimeline HCl) Capsules, 30 mg, originally submitted for EVOXAC™ (cevimeline HCl) Capsules, [ ] 30 mg.

We acknowledge receipt of your submissions dated September 1 and 10, October 18, November 11 and 16, December 13, 14, 20 and 28, 1999; and January 11, 2000 (facsimile). Your submission of November 11, 1999, constituted a complete response to our August 27, 1999, action letter.

This new drug application provides for the use of EVOXAC™ (cevimeline HCl) Capsules, 30 mg, for the treatment of symptoms of dry mouth in patients with Sjögren's Syndrome.

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 described in the agreed upon enclosed labeling text (text for the package insert, immediate container and carton labels). 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, 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 20-989." Approval of this submission by FDA is not required before the labeling is used.

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-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 Olga Cintron, Project Manager, at (301) 827-2020.

Sincerely,

Robert J. DeLap, M.D., Ph.D.
Director
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: 20-989

APPROVABLE LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

NDA 20-989

AUG 27 1999

SnowBrand Pharmaceuticals, Inc.
Attention: William C. Govier, M.D., Ph.D.
President and CEO
2001 Commonwealth Blvd., Suite 205
Ann Arbor, MI 48105

Dear Dr. Govier:

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We acknowledge receipt of your submissions dated August 26, September 30, October 15, December 22, 28 and 29, 1998; January 7, April 21 and 30, May 3, 24 and 26, June 3, 16, 21, 22 and 25, July 6, 7, 8, 12, 13 and 21, August 3 and 27 (facsimile), 1999.

We have completed the review of this application, as amended, and it is approvable. Before this application may be approved, however, it will be necessary for you to submit revised draft labeling for the drug. The labeling should be identical in content to the enclosed labeling (text for the package insert, immediate container and carton labels).

If additional information relating to the safety or effectiveness of this drug becomes available, revision of the labeling may be required.

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, contact Olga Cintron, Project Manager, at (301) 827-2020.

Sincerely,

/S/

Robert J. DeLap, M.D., Ph.D.
Director
Office of Drug Evaluation V
Center for Drug Evaluation and Research

Enclosure

APPEARS THIS WAY
ON ORIGINAL

15 Page(s) Redacted

Draft

Labeling