CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

20-463/S-002

APPROVAL LETTER

NDA 20-463/S-002

Pharmacia Consumer Healthcare
Attention: Raymond E. Dann, Ph.D.
Director, Regulatory Affairs
100 Route 206 North
Peapack, NJ 07977

27 MAR 2001

Dear Dr. Dann:

Please refer to your new drug application (NDA) dated August 19, 1999, received August 31, 1999, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for NasalCrom Nasal Solution (cromolyn sodium nasal solution) nasal spray.

We acknowledge receipt of your submissions dated October 27, 1999; January 31, February 9, April 4, April 6, April 26 and 27, June 26 and 27, November 22, and December 14, 2000; and February 28, and March 2, 2001. Your submission of March 2, 2001 constituted a complete response to our June 30, 2000 action letter.

This new drug application provides for the use of NasalCrom Nasal Solution (cromolyn sodium nasal solution) nasal spray for use in children down to 2 years of age.

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

The final printed labeling (FPL) must be identical to the submitted draft labeling (immediate container, carton labels and patient package insert submitted February 28, 2001) and must be formatted in accordance with the requirements of 21 CFR 201.66. Marketing the product with FPL that is not identical to the approved labeling text and "Drug Facts" format may render the product misbranded and an unapproved new drug.

Please submit the copies of final printed labeling (FPL) electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA* (January 1999). Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no 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 20-463." Approval of this submission by FDA is not required before the labeling is used.

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 note that you have fulfilled the pediatric study requirement at this time.

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 Babette Merritt, Project Manager, at (301) 827-2222.

Sincerely,

Charles Ganley, M.D.
Director
Division of Over-The-Counter Drug Products
Office of Drug Evaluation V
Center for Drug Evaluation and Research

Robert J. Meyer, M.D.
Director
Division of Pulmonary and Allergy Drug Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

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APPLICATION NUMBER:

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APPROVABLE LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-463/S-002

JUN 30 2000

Pharmacia and Upjohn Company
Attention: Raymond E. Dann, Ph.D.
Director, Regulatory Affairs
100 Route 206 North
Peapack, NJ 07977

Dear Dr. Dann:

Please refer to your new drug application (NDA) dated August 19, 1999, received August 31, 1999, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for NasalCrom Nasal Solution (cromolyn sodium nasal solution) nasal spray.

We acknowledge receipt of your submissions dated October 27, 1999, January 31, 2000. February 9, 2000, April 4, 6, 26, and 27, 2000, June 26 and 27, 2000.

This supplemental new drug application provides for use of the drug product in children 2 years to less than 6 years of age.

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 as specified below:

1. Carton label:

   A. Carton label dated June 26, 2000 with the following changes:

      LEFT SIDE PANEL,
      Nasal Allergy Symptom Prevention -
      insert the word "nasal" before the word "allergies."
      (i.e., ...exposure to the cause of nasal allergies, and will...)

   B. Drug Facts:

      Identical to label dated June 14, 2000, recommended by the Agency.

2. Immediate container label:

   Identical to container label dated June 26, 2000, with no changes.

3. Package insert label:

Package insert label dated June 26, 2000, with the following changes on side 1:

C. How to use NasalCrom Nasal Spray -
insert the word "nasal" before the word "allergens."
(i.e., ... before you are exposed to nasal allergens...)

The use "children's" in the name of the product suggests that this product is specific for use in children. Typically, products that include "children's" in the name offer a formulation that is more acceptable to children to encourage better compliance or ease of administration (e.g. liquid formulation, chewable tablets). In this case, there is no difference in the formulation or dosage regimen from the original NasalCrom Nasal Spray. The "children's" product differs only in the addition of a modified grip that is not necessarily recommended to be used by children. This grip is no specific for use in children and could be of benefit to any other age group. Additionally, the use of "children's" in the name of the product could lead to a proliferation of other products with names based on the age of the population (e.g. "Adolescent NasalCrom", "Elderly NasalCrom"). For these reasons, the use of "children's" in the name is not acceptable because it may be misleading to consumers.

The use of "Allergy Prevention" in the name of the product in conjunction with the changes made to the package insert are not consistent with the approved use of the product. The original approval provided for prevention of nasal allergy symptoms. The term "Allergy Prevention" connotes a broader systemic effect on all allergy symptoms. It also connotes that all allergies are prevented rather than nasal allergy symptoms are prevented. The principle display panel (PDP) does not provide sufficient clarifying information to inform the consumer of these important distinctions. The changes that you have made to the package insert compound our concerns because in many cases the term "allergy prevention" has been substituted for "nasal allergy symptom prevention". Although the name "NasalCrom" suggests use in the nose, the nasal administration of the product alone does not convey sufficient information to consumers to conclude that relief or prevention of symptoms is confined to the nasal passages. There are other products currently available for intranasal administration which treat conditions not confined to the nasal passages or the upper respiratory tract (e.g. sumatriptan nasal spray for treatment of migraine headache). There should be additional information on the PDP that makes the uses

clear to the consumer.

It should be noted that changes you made to the name of the product, to the PDP and to the package insert and submitted in annual reports are more than editorial and should have been submitted as a pre-approval labeling supplement.

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.

Please be reminded that the proposed pediatric use and the approved adult use should be marketed in a single product.

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.

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 Babette Merritt, Project Manager, at (301) 827-2222.

Sincerely,

/S/

Charles Ganley, M.D.
Director
Division of Over-the-Counter Drug Products
Office of Drug Evaluation V
Center for Drug Evaluation and Research

/S/

Robert J. Meyer, M.D.
Director
Division of Pulmonary and Allergy Drug Products
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