# CENTER FOR DRUG EVALUATION AND RESEARCH

*APPLICATION NUMBER:*

**21-563**

# APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-563

Schering Corporation
2000 Galloping Hill Road
Kenilworth, NJ 07033

Attention: Carlos Langezaal, Ph.D.

Dear Dr. Langezaal,

Please refer to your new drug application (NDA) dated December 4, 2002, received December 4, 2002, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Clarinex (desloratadine) Syrup 0.5 mg/mL.

We also refer to your amendments dated March 13, 2003, and February 27, June 24, July 29, August 30, and 31 and September 1, 2004.

The February 27, 2004, submission constituted a complete response to our October 2, 2002, action letter.

This new drug application provides for the relief of the nasal and non-nasal symptoms of perennial allergic rhinitis, and the symptomatic relief of pruritus, reduction in the number of hives, and size of hives, in patients with chronic idiopathic urticaria in children 6 months to 2 years of age.

We completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text and with the minor editorial revisions listed below, as agreed during our telephone discussion on August 30, 2004.

1. Remove the [redacted] from the carton labeling.
2. Replace the [redacted] with the approved name, Clarinex.
3. Remove the phrase, [redacted] from the carton and container.

The final printed labeling (FPL) must be identical to, except for including the revisions listed, the enclosed labeling (text for the package insert submitted August 30, 2004) and submitted labeling (carton and container label submitted August 30, 2004). These revisions are terms of the NDA approval. Marketing the product before making the revisions, exactly as stated, in the product's labeling may render the product misbranded and an unapproved new drug.

Please submit an electronic version of the FPL according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA.* 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. Individually mount 15 of the copies on heavy-weight paper or similar material. For administrative purposes, designate this

submission "**FPL for approved NDA 21-563**." Approval of this submission by FDA is not required before the labeling is used.

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. We note that you have fulfilled the pediatric study requirement for this application in ages 6 months and above. We are waiving the pediatric requirement for the application in children less than 6 months of age.

Please submit three copies of the introductory promotional materials that you propose to use for this product. Submit all proposed materials in draft or mock-up form, not final print. Send one copy to the Division of Pulmonary and Allergy Drug Products 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, MD 20857

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

If you have any questions, call Anthony M. Zeccola, Regulatory Management Officer, at (301) 827-1058.

Sincerely,

*{See appended electronic signature page}*

Badrul A. Chowdhury, M.D., Ph.D.
Director
Division of Pulmonary and Allergy Drug Products
Center for Drug Evaluation and Research

Enclosure

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/s/

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Badrul Chowdhury
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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 21-563

Schering Corporation
2000 Galloping Hill Road
Kenilworth, NJ 07033

Attention: Joseph F. Lamendola, Ph.D.
Vice President
U.S. Regulatory Affairs

Dear Dr. Lamendola:

Please refer to your new drug application (NDA) dated December 4, 2002, received December 4, 2002, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Clarinex Syrup (desloratadine) 0.5 mg/ml.

We acknowledge receipt of your submission dated March 13, 2003.

We have completed our review of this application, as amended, and it is approvable. Before the application may be approved, however, it will be necessary for you to:

1. Provide a complete response to the deficiencies listed in our Approvable letter for NDA 21-300 dated October 2, 2001 and CMC discipline review letter dated November 19, 2001.

2. The proposed dose for younger children will be 2 ml and 2.5 ml. Provide a discussion of how these small volumes will be measured and delivered by caregivers, and how this will be addressed in the labeling.

In addition, it will be necessary for you to submit draft labeling revised as follows:

3. Throughout the labeling, patients should be referred to as 6 to 11 months of age or 12 to 23 months of age.

4. Under the Adverse Reactions section, the listing of adverse events should be divided into those that were seen in patients 6 to 11 months of ages and those that were seen in patients 12 to 23 months of age.

5. Under the Precautions: Pediatric Use subsection, indicate that not only the tablet but also the syrup formulation has not been demonstrated to be safe and effective for patients less than 6 months of age.

6. The title of table 5 should be changed to read, "Incidence of Adverse Events Reported by 2% or More Allergic Rhinitis Patient in Placebo-Controlled, Multiple Dose Clinical Studies with the Tablet Formulation of Clarinex."

7. Revise the Dosage and Administration section as follows:

   **Adults and children 12 years of age and over:** the recommended dose of CLARINEX Tablets is one 5 mg tablet once daily or 2 teaspoonfuls (5 mg in 10 ml) of CLARINEX Syrup once daily.

   **Children 6 to 11 years of age:** The recommended dose of CLARINEX Syrup is 1 teaspoonful (2.5 mg in 5 ml) once daily.

   **Children 12 months to 5 years of age:** The recommended dose of CLARINEX Syrup is 1/2 teaspoonful (1.25 mg in 2.5 ml) once daily.

   **Children 6 months to less than 1 year of age**: The recommended dose of CLARINEX Syrup is 2 ml (1.0 mg in 2 ml) once daily.

   In adult patients with liver or renal impairment, a starting dose of one 5 mg tablet every other day is recommended based on pharmacokinetic data. Dosing recommendation for children with liver or renal impairment cannot be made due to lack of data.

8. In line 238 of the draft label included in the December 4, 2002, submission, delete the word "aged."

We may have additional labeling comments following our review of your response to the deficiencies listed the Approvable letter mentioned above.

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

When you respond to the above deficiencies, include a safety update as described at 21 CFR 314.50(d)(5)(vi)(b). You are advised to contact the Division regarding the extent and format of your safety update prior to responding to this letter.

Within 10 days after the date of this letter, you are required to amend this application, notify us of your intent to file amendments, or follow one of your other options under 21 CFR 314.110. If you do not follow one of these options, we will consider your lack of response a request to withdraw the application under 21 CFR 314.65. 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), you may request an informal meeting or telephone conference with this Division to discuss what 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, call Anthony M. Zeccola, Regulatory Management Officer, at (301) 827-1058.

Sincerely,

{See appended electronic signature page}

Badrul A. Chowdhury, M.D., Ph.D.
Director
Division of Pulmonary and Allergy Drug Products
Center for Drug Evaluation and Research Drug Products

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/s/

Badrul Chowdhury
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