CENTER FOR DRUG EVALUATION AND RESEARCH

APPROVAL PACKAGE FOR:

APPLICATION NUMBER 21-165

CORRESPONDENCE

BC

SCHERING CORPORATION

2000 GALLOPING HILL ROAD KENILWORTH, N.J. 07033
TELEPHONE: (908) 298-4000

ORIGINAL

December 20, 2001

Robert Meyer, M.D., Director
Division of Pulmonary and Allergy Drug Products
Food and Drug Administration
Center for Drug Evaluation and Research
Document Control Room (HFD-570)
Parklawn Building, Room 10B05
5600 Fishers Lane
Rockville, MD 20857

NDA 21-165
CLARINEX™
(desloratadine) Tablets, 5 mg

SUBJECT: GENERAL CORRESPONDENCE

Dear Dr. Meyer:

We refer to the meeting held today to discuss the stability data provided to the Agency on December 19, 2001. Based on its review of the stability data, the Agency requested that we make a commitment to address issues related to the degradation products reported.

Schering-Plough commits to the following, which will be completed post-approval of this NDA:

> We agree to review our current procedures for stability methods, and to clarify or revise our procedures, as needed, to ensure appropriate peak labeling, review/approval of peak identity, and proper trending of stability data. We will also review current practice and procedures to ensure that they provide for adequate supervisory oversight. We will re-train as indicated to ensure complete understanding and proper implementation of any revisions made to our existing procedures. This activity will be completed by February 2002.
>
> In addition, we will immediately review the Clarinex stability data generated at Las Piedras to ensure proper identification of all peaks at all testing stations, and will perform trend analyses on all lots in the stability program. We will complete this review by January 15, 2002.

Please contact Dr. A. Giaquinto (980-740-5770) or Dr. N. Pelliccione (908-740-5680) if you have any questions regarding this submission.

Schering Corporation certifies that a copy of this correspondence is being sent to FDA's New Jersey District Office and San Juan, Puerto Rico.

Please be advised that the material and data contained in this submission are considered to be confidential. The legal protection of such confidential commercial material is claimed under applicable provisions of 18 U.S.C., Section 1905 or 21 U.S.C., Section 331(j) as well as the FDA regulations.

Sincerely,

Alexander R. Giaquinto, Ph.D.
Senior Vice President
Worldwide Regulatory Affairs

NP:jc

Attachment

Desk Copies: Dr. Poochikian, Mr. Zeccola

C:\WINDOWS\Profiles\GTrout\Local Settings\Temporary Internet Files\OLK62C4\122001a.doc

SCHERING CORPORATION

2000 GALLOPING HILL ROAD KENILWORTH, N.J. 07033

TELEPHONE: (908) 298-4000

December 18, 2001

Robert Meyer, M.D., Director
Division of Pulmonary and Allergy Drug Products
Food and Drug Administration
Center for Drug Evaluation and Research
Document Control Room (HFD-570)
Parklawn Building, Room 10B05
5600 Fishers Lane
Rockville, MD 20857

NDA 21-165
CLARINEX®
(desloratadine) Tablets, 5 mg

SUBJECT: FINAL DRAFT LABELING

Dear Dr. Meyer,

Enclosed is the final draft labeling for the following CLARINEX Tablets packaging components:

Label for Bottle of 100 Tablets
Label for Bottle of 500 Tablets
Carton for Box of 10 Tablets
Carton for Box of 30 Tablets
Carton for Box of 100 Tablets
Carton for Professional Sample Box of 7 Tablets
Carton for Professional Sample Box of 50 Tablets
Artwork for 10 Tablet Blister
Artwork for 7 Tablet Sample Blister
Artwork for 1 Tablet Sample Blister (Note: No artwork on front panel)
Product Information Sheet (8.5" x 11" format)

Please be advised that the material and data contained in this submission are considered to be confidential. The legal protection of such confidential commercial material is claimed under the applicable provisions of 18 U.S.C., Section 1905 or 21 U.S.C., Section 331(j) as well as the FDA regulations.

Sincerely,

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

RF/sb

SCHERING CORPORATION

2000 GALLOPING HILL ROAD KENILWORTH, N.J. 07033

TELEPHONE: (908) 298-4000

February 13, 2001

Robert Meyer, M.D., Director
Division of Pulmonary and Allergy Drug Products
Food and Drug Administration
Center for Drug Evaluation and Research
Document Control Room (HFD-570)
Parklawn Building, Room 10B03
5600 Fishers Lane
Rockville, MD 20857

NDA 21-165
CLARINEX™TABLET

SUBJECT: DRAFT LABELING

Dear Dr. Meyer:

In response to your approvable letter of January 19, 2001, we are responding to point No. 2.

Enclosed is revised draft labeling (hard copy and electronic versions), including marked-up changes, as per your correspondence. This revised package insert also includes revisions to the OVERDOSAGE section as included in our January 31, 2001 submission of the ECG re-read report.

Please contact Mary Jane Boyle at 908-740-5693, should you have any questions.

Please be advised that the material and data contained in this submission are considered to be confidential. The legal protection of such confidential commercial material is claimed under the applicable provisions of 18 U.S.C., Section 1905 or 21 U.S.C., Section 331(j) as well as the FDA regulations.

Sincerely,

Mary Jane Boyle for

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

MJB:fs
Enclosures

14 pages redacted from this section of the approval package consisted of draft labeling

DUPLICATE

SCHERING CORPORATION

2000 GALLOPING HILL ROAD KENILWORTH, N.J. 07033
TELEPHONE: (908) 298-4000

BL

October 30, 2000

Robert Meyer, M.D., Director
Division of Pulmonary & Allergy Drug Products
Center for Drug Evaluation and Research
HFD-570, Room 10B03
5600 Fishers Lane
Rockville, MD 20857

NDA 21-165
SCH 34117
CLARINEX Tablets

SUBJECT: RESPONSE TO FDA REQUEST

Dear Dr. Meyer:

In response to your October 27 2000 fax, please find new revised labeling. A fully marked up copy of the labeling is being provided. Additions are in highlight; deletions are in strike-out. Revisions include the following, as requested by the Agency:

Mechanism of action: The deletion of the sentence, '

' at the end of the first paragraph.

Effects on QTc: Last paragraph. The sentences, '

were

replaced by '

Overdosage: The use of the word, ' ' in place of ' ' in the sentence,

An electronic Word copy of the labeling is being provided to the electronic file room.

In addition, in response to an October 27, 2000 telecon between Ms. Sandy Barnes and Ms. Mary Jane Boyle, we are providing certification of the following Phase IV commitments:

1. SPRI agrees to submit a final Mouse Carcinogenicity Study Report within three years of NDA Approval.
2. SPRI will investigate the genotype for Allele "Z" and provide documentation within 3 – 4 months after NDA Approval.

Should you have any questions or need additional information, please contact Ms. Bernadette Knott at (908) 740-2452 or Ms. Mary Jane Boyle at (908) 740-5693.

Please be advised that the material and data contained in this submission are considered to be confidential. The legal protection of such confidential commercial material is claimed under the applicable provisions of 18 U.S.C., Section 1905 or 21 U.S.C., Section 331(j) as well as the FDA

Sincerely,

Bernadette Knott for/

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

BK:js
Enclosures

Schering-Plough Research Institute

2000 Galloping Hill Road
Kenilworth, New Jersey 07033

Alexander R. Giaquinto, PhD
Sr. Vice President
Worldwide Regulatory Affairs

TELECOPIER TRANSMITTAL SHEET

(908) 740-5770
(908) 740-4131 FAX
E-mail: alexander.giaquinto@spcorp.com

Please deliver the following 5 pages (including cover page)

If transmittal is incomplete or illegible, please call: Ethel Brady (908) 740-5771

DATE:	October 20, 2000
TO:	Dr. Robert Meyer
FAX:	301-827-1271
SUBJECT:	Clarinex Name

MESSAGE:

As discussed.

Alexander R. Giaquinto, Ph.D.

SCHERING CORPORATION

2000 GALLOPING HILL ROAD KENILWORTH, N.J. 07033
TELEPHONE: (908) 298-4000

October 20, 2000

Robert Meyer, M.D., Director
Division of Pulmonary & Allergy Drug Products
Center for Drug Evaluation and Research
HFD-570, Room 10B03
5600 Fishers Lane
Rockville, MD 20857

NDA 21-165
CLARINEX (desloratadine)
Tablets

SUBJECT: GENERAL CORRESPONDENCE

Dear Dr. Meyer:

As per our discussion, I have obtained the following information. The product name, CLARINEX, is approved for use in only four countries in Europe. These four countries are Denmark, Iceland, Lithuania and Finland. Moreover, in only two of these countries, Denmark and Iceland, is the CLARINEX name used on a marketed product. In both of these countries, the CLARINEX name is used with the loratadine/pseudoephedrine 24-hour combination product, not the individual antihistamine product. Sales of the CLARINEX product
Denmark and Iceland; together the sales total

If the use of CLARINEX with the loratadine/pseudoephedrine product in any of these countries raises a concern about the use of the CLARINEX name with desloratadine, we will, of course, cease using the CLARINEX name in Denmark and Iceland and commit to not using it in Lithuania and Finland.

I trust that this addresses your concerns and will call you to follow-up on this matter next week.

Please be advised that the material and data contained in this submission are considered to be confidential. The legal protection of such confidential commercial material is claimed under the applicable provisions of 18 U.S.C., Section 1905 or 21 U.S.C., Section 331(j) as well as the FDA regulations.

Sincerely,

Alexander R. Giaquinto, Ph.D.
Senior Vice President
Worldwide Regulatory Affairs

js

Toout

AUG 25 2000

NDA 21-165

DISCIPLINE REVIEW LETTER

Schering Corporation
2000 Galloping Hill Road
Kenilworth, NJ 07033

Attention: Nicholas J. Pelliccione, Ph.D.
Vice President, CMC
Worldwide Regulatory Affairs

Dear: Dr. Pelliccione

Please refer to your supplemental new drug application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Clarinex (desloratadine) 5mg Tablet.

We also refer to your submission dated August 2, 2000.

Our review of the Chemistry, Manufacturing, and Controls section of your submission is complete, and we have identified the following deficiencies:

1. Tighten the specification for dissolution rate to Q = [redacted]% at 30 minutes. (Comment 12 of the June 26, 2000, letter).

2. The following pertain to the annual batch stability protocol:

   a. Provide a commitment that the drug product stability protocol on page 206 of the August 2, 2000, amendment (to be updated with dissolution specifications from comment 1) is also the annual batch stability protocol and any changes to this protocol will require a "prior approval" supplement.

   b. Indicate in the annual batch stability protocol the formula used to determine the number of batches to be placed on annual stability.

3. Submit an updated drug product specification sheet, and an updated drug product stability protocol after addressing above comments 1 and 2. (Comment 10 of the June 26, 2000 letter)

4. Provide statistical data sets for evaluation of the expiration dating period.

5. Comments pertaining to drug product impurities and degradants are pending review by Pharmacology-Toxicology. (Comment 13 of the June 26, 2000, letter)

6. Comments regarding the package labeling will be forthcoming after resolution of the pending issues. (Comment 11 of the June 26, 2000, letter)

We are providing these comments to you before we complete our review of the entire application to give you preliminary notice of issues that we have identified. In conformance with the prescription drug user fee reauthorization agreements, these comments do not reflect a final decision on the information reviewed and should not be construed to do so. These comments are preliminary and subject to change as we finalize our review of your application. In addition, we may identify other information that must be provided before we can approve this application. If you respond to these issues during this review cycle, depending on the timing of your response, and in conformance with the user fee reauthorization agreements, we may not be able to consider your response before we take an action on your application during this review cycle.

If you have any questions, call Vicky Borders, Pharm.D., Regulatory Project Manager, at (301) 827-5580.

Sincerely,

/S/

Guirag Poochikian, Ph.D.
Chemistry Team Leader
Division of Pulmonary and Allergy Drug Products, (HFD-570)
DNDC II, Office of New Drug Chemistry
Center for Drug Evaluation and Research

AUG 16 2000

NDA 21-165

Schering Corporation
2000 Galloping Hill Road
Kenilworth, NJ 07033

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

Dear Dr. Lamendola:

Please refer to your October 20, 1999, new drug application (NDA) submitted under serction 505(b) of the Federal Food, Drug and Cosmetic Act for desloratadine tablets.

On August 3, 2000, we received your August 2, 2000, major amendment to this application. The receipt date is within 3 months of the primary and secondary user fee goal dates. Therefore, we are extending the goal dates by three months to provide time for a full review of the submission. The extended primary user fee goal date is November 21, 2000. The extended secondary user fee goal date is January 21, 2000.

If you have questions, call Mrs. Gretchen Trout, Project Manager, at (301) 827-1058.

Sincerely yours,

/S/ 8/17/00

Sandra L. Barnes
Chief Project Management Staff
Division of Allergy and Pulmonary Drug Products
Center for Drug Evaluation and Research
Office of Drug Evaluation II

Trout

IND [ ]

JUN 26 2000

Schering Corporation
2000 Galloping Hill Road
Kenilworth, NJ 07033

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

Dear Dr. Lamendola:

Reference is made to your March 7, 2000, submission to IND [ ] containing proposed trade names for desloratadine.

As discussed in a teleconference on June 16, 2000, between Mary Jane Boyle and myself, the Agency has no objection to the use of the proprietary name "Clarinex" for the desloratadine products at this time. However, depending on the timeframe for approval of the pending NDA 21-165 for desloratadine tablets, the name may have to be reevaluated.

If you have any questions, call me at (301) 827-1058.

Sincerely yours,

/S/

Gretchen Trout
Project Manager
Division of Pulmonary and Allergy Drug Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

TROUT

NDA 21-165

FEB 28 2000

Schering Corporation
2000 Galloping Hill Road
Kenilworth, NJ 07033

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

Dear Dr. Lamendola:

Please refer to your October 20, 1999, new drug application for desloratadine 5 mg tablets.

We are reviewing the pre-clinical pharmacology and clinical pharmacology and biopharmaceutics sections of your submission and have the following information requests. We need your prompt written response to continue our evaluation of your NDA.

1. Clarify the term "mineralization" as related to findings in the ovaries of monkeys (i.e., type of minerals) in the 3-month toxicity study (study P-6976).

2. Provide the in vitro metabolism data using human liver enzymes.

3. Provide in vitro protein binding data.

4. Provide the proposed dissolution specification and rationale for your proposal. Include dissolution media selection criteria and rationale for the selection, dissolution profiles in those media, and individual dissolution data of the biobatches in the selected medium along with mean value.

5. Provide the expected completion date for the pharmacokinetic study in renally impaired patients, and submit the study results as soon as possible.

6. Please provide the individual pharmacokinetic data as an electronic file (e.g., SAS transport files).

If you have any questions, call me at (301) 827-1058.

Sincerely yours,

/S/

Gretchen Trout
Chief, Project Management Staff
Division of Pulmonary and Allergy Drug Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

Treat

NOV 8 1999

NDA 21-165

Schering Corporation
2000 Galloping Hill Road
Kenilworth, NJ 07033

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

Dear Dr. Lamendola:

We have received your new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for the following:

Name of Drug Product: desloratadine 5 mg Tablets

Therapeutic Classification: Standard (S)

Date of Application: October 20, 1999

Date of Receipt: October 21, 1999

Our Reference Number: NDA 21-165

Unless we notify you within 60 days of our receipt date that the application is not sufficiently complete to permit a substantive review, this application will be filed under section 505(b) of the Act on December 20, 1999 in accordance with 21 CFR 314.101(a). If the application is filed, the primary user fee goal date will be August 21, 2000 and the secondary user fee goal date will be October 21, 2000.

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). If you have not already fulfilled the requirements of 21 CFR 314.55 (or 601.27), please submit your plans for pediatric drug development within 120 days from the date of this letter unless you believe a waiver is appropriate. Within 120 days of receipt of your pediatric drug development plan, we will notify you of the pediatric studies that are required under section 21 CFR 314.55.

If you believe that this drug qualifies for a waiver of the pediatric study requirement, you should submit a request for a waiver with supporting information and documentation in accordance with the provisions of 21 CFR 314.55 within 60 days from the date of this letter. We will notify you within 120 days of receipt of your response whether a waiver is granted. If a waiver is not granted, we will ask you to submit your pediatric drug development plans within 120 days from the date of denial of the waiver.

Pediatric studies conducted under the terms of section 505A of the Federal Food, Drug, and Cosmetic Act may result in additional marketing exclusivity for certain products (pediatric exclusivity). You should refer to the *Guidance for Industry on Qualifying for Pediatric Exclusivity* (available on our web site at www.fda.gov.cder/pediatric) for details. If you wish to qualify for pediatric exclusivity you should submit a "Proposed Pediatric Study Request" (PPSR) in addition to your plans for pediatric drug development described above. We recommend that you submit a Proposed Pediatric Study Request within 120 days from the date of this letter. If you are unable to meet this time frame but are interested in pediatric exclusivity, please notify the division in writing. FDA generally will not accept studies submitted to an NDA before issuance of a Written Request as responsive to a Written Request. Sponsors should obtain a Written Request before submitting pediatric studies to an NDA. If you do not submit a PPSR or indicate that you are interested in pediatric exclusivity, we will proceed with the pediatric drug development plan that you submit and notify you of the pediatric studies that are required under section 21 CFR 314.55. Please note that satisfaction of the requirements in 21 CFR 314.55 alone may not qualify you for pediatric exclusivity. FDA does not necessarily ask a sponsor to complete the same scope of studies to qualify for pediatric exclusivity as it does to fulfill the requirements of the pediatric rule.

Under 21 CFR 314.102(c) of the new drug regulations, you may request an informal conference with this Division (to be held approximately 90 days from the above receipt date) for a brief report on the status of the review but not on the application's ultimate approvability. Alternatively, you may choose to receive such a report by telephone.

Please cite the NDA number listed above at the top of the first page of any communications concerning this application. All communications concerning this NDA should be addressed as follows:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Pulmonary and Allergy Drug Products, HFD-570
Attention: Division Document Room
5600 Fishers Lane
Rockville, Maryland 20857

If you have any questions, call Mrs. Gretchen Trout, Project Manager, at (301) 827-1058.

Sincerely yours,

/S/

Cathie Schumaker, R.Ph.
Chief, Project Management Staff
Division of Pulmonary and Allergy Drug Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research