

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER: 21-312

ADMINISTRATIVE DOCUMENTS

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

APPLICATION TO MARKET A NEW DRUG, BIOLOGIC,
OR AN ANTIBIOTIC DRUG FOR HUMAN USE

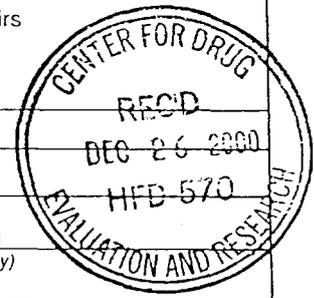
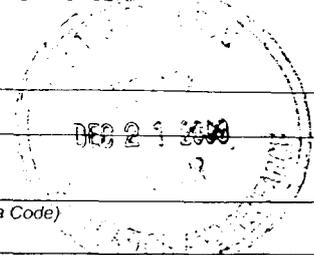
(Title 21, Code of Federal Regulations, 314 & 601)

Form Approved: OMB No. 0910-0338
Expiration Date: March 31, 2003
See OMB Statement on page 2.

FOR FDA USE ONLY
APPLICATION NUMBER: _____

APPLICANT INFORMATION

NAME OF APPLICANT Schering Corporation	DATE OF SUBMISSION December 20, 2000
TELEPHONE NO. (include Area Code) (908) 740-2628	FACSIMILE (FAX) Number (Include Area Code) (908) 740-2982
APPLICANT ADDRESS (Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued): 2000 Galloping Hill Road Kenilworth, New Jersey 07033	AUTHORIZED U.S. AGENT NAME & ADDRESS (Number, Street, City, State, ZIP Code, telephone & FAX number) IF APPLICABLE Joseph F. Lamendola, Ph.D. Vice President, U.S. Regulatory Affairs 2000 Galloping Hill Road Kenilworth, NJ 07033



PRODUCT DESCRIPTION

NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER, OR BIOLOGICS LICENSE APPLICATION NUMBER (if previously issued)		
ESTABLISHED NAME (e.g., Proper name, USP/USAN name) Desloratadine tablet	PROPRIETARY NAME (trade name) IF ANY CLARINEX™ (desloratadine) RediTabs® 5 mg	
CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME (if any) 8-chloro-6,11-dihydro-1-(4-piperidinylidene)-5H-benzo-[5,6]cyclohepta[1,2-b]pyridine	CODE NAME (if any) SCH 34117	
DOSEAGE FORM: Rapidly disintegrating tablet	STRENGTHS: 5 mg	ROUTE OF ADMINISTRATION: Oral administration
(PROPOSED) INDICATION(S) FOR USE: seasonal allergic rhinitis/chronic idiopathic urticaria		

APPLICATION INFORMATION

APPLICATION TYPE (check one)	<input checked="" type="checkbox"/> NEW DRUG APPLICATION (21 CFR 314.50)	<input type="checkbox"/> ABBREVIATED NEW DRUG APPLICATION (ANDA, 21 CFR 314.94)
	<input type="checkbox"/> BIOLOGICS LICENSE APPLICATION (21 CFR part 601)	
IF AN NDA, IDENTIFY THE APPROPRIATE TYPE	<input checked="" type="checkbox"/> 505 (b) (1)	<input type="checkbox"/> 505 (b) (2)
IF AN ANDA, OR 505(b)(2), IDENTIFY THE REFERENCE LISTED DRUG PRODUCT THAT IS THE BASIS FOR THE SUBMISSION	Name of Drug _____ Holder of Approved Application _____	
TYPE OF SUBMISSION (check one)	<input checked="" type="checkbox"/> ORIGINAL APPLICATION	<input type="checkbox"/> AMENDMENT TO A PENDING APPLICATION
	<input type="checkbox"/> PRESUBMISSION	<input type="checkbox"/> RESUBMISSION
	<input type="checkbox"/> ANNUAL REPORT	<input type="checkbox"/> ESTABLISHMENT DESCRIPTION SUPPLEMENT
	<input type="checkbox"/> LABELING SUPPLEMENT	<input type="checkbox"/> EFFICACY SUPPLEMENT
	<input type="checkbox"/> CHEMISTRY, MANUFACTURING, AND CONTROLS SUPPLEMENT	<input type="checkbox"/> OTHER
IF A SUBMISSION OR PARTIAL APPLICATION, PROVIDE LETTER DATE OF AGREEMENT TO PARTIAL SUBMISSION:		
IF A SUPPLEMENT, IDENTIFY THE APPROPRIATE CATEGORY	<input type="checkbox"/> CBE	<input type="checkbox"/> CBE-30
	<input type="checkbox"/> Prior Approval (PA)	
REASON FOR SUBMISSION		
PROPOSED MARKETING STATUS (check one)	<input checked="" type="checkbox"/> PRESCRIPTION PRODUCT (Rx)	<input type="checkbox"/> OVER THE COUNTER PRODUCT (OTC)
NUMBER OF VOLUMES SUBMITTED <u>10</u>	THIS APPLICATION IS <input type="checkbox"/> PAPER <input checked="" type="checkbox"/> PAPER AND ELECTRONIC <input type="checkbox"/> ELECTRONIC	
ESTABLISHMENT INFORMATION (Full establishment information should be provided in the body of the Application.) Provide locations of all manufacturing, packaging and control sites for drug substance and drug product (continuation sheets may be used if necessary). Include name, address, contact, telephone number, registration number (CFN), DMF number, and manufacturing steps and/or type of testing (e.g. Final dosage form, Stability/testing) conducted at the site. Please indicate whether the site is ready for inspection or, if not, when it will be ready.		
See attached		
Cross References (list related License Applications, INDs, NDAs, PMAs, 510(k)s, IDEs, BMFs, and DMFs referenced in the current application)		
DMF _____	DMF _____	DMF _____
NDA 21-165	NDA 21-297	NDA _____

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This application contains the following items: (Check all that apply)			Paper	Electronic
<input checked="" type="checkbox"/>	1. Index		<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
<input checked="" type="checkbox"/>	2. Labeling (check one)	<input checked="" type="checkbox"/> Draft Labeling <input type="checkbox"/> Final Printed Labeling	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
<input checked="" type="checkbox"/>	3. Summary (21 CFR 314.50 (c))		<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
<input checked="" type="checkbox"/>	4. Chemistry section		<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
<input checked="" type="checkbox"/>	A. Chemistry, manufacturing, and controls information (e.g. 21 CFR 314.50 (d) (1), 21 CFR 601.2)		<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
<input type="checkbox"/>	B. Samples (21 CFR 314.50 (e) (1), 21 CFR 601.2 (a)) (Submit only upon FDA's request)		<input type="checkbox"/>	<input type="checkbox"/>
<input checked="" type="checkbox"/>	C. Methods validation package (e.g. 21 CFR 314.50 (e) (2) (i), 21 CFR 601.2)		<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
<input checked="" type="checkbox"/>	5. Nonclinical pharmacology and toxicology section (e.g. 21 CFR 314.50 (d) (2), 21 CFR 601.2)		<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
<input checked="" type="checkbox"/>	6. Human pharmacokinetics and bioavailability section (e.g. 21 CFR 314.50 (d) (3), 21 CFR 601.2)		<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
<input type="checkbox"/>	7. Clinical Microbiology (e.g. 21 CFR 314.50 (d) (4))		<input type="checkbox"/>	<input type="checkbox"/>
<input checked="" type="checkbox"/>	8. Clinical data section (e.g. 21 CFR 314.50 (d) (5), 21 CFR 601.2)		<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
<input type="checkbox"/>	9. Safety update report (e.g. 21 CFR 314.50 (d) (5) (vi) (b), 21 CFR 601.2)		<input type="checkbox"/>	<input type="checkbox"/>
<input checked="" type="checkbox"/>	10. Statistical section (e.g. 21 CFR 314.50 (d) (6), 21 CFR 601.2)		<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
<input type="checkbox"/>	11. Case report tabulations (e.g. 21 CFR 314.50 (f) (1), 21 CFR 601.2)		<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	12. Case reports forms (e.g. 21 CFR 314.50 (f) (2), 21 CFR 601.2)		<input type="checkbox"/>	<input checked="" type="checkbox"/>
<input checked="" type="checkbox"/>	13. Patent information on any patent which claims the drug (21 U.S.C. 355 (b) or (c))		<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
<input type="checkbox"/>	14. A patent certification with respect to any patent which claims the drug (21 U.S.C. 355 (b) (2) or (j) (2) (A))		<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	15. Establishment description (21 CFR Part 600, if applicable)		<input type="checkbox"/>	<input type="checkbox"/>
<input checked="" type="checkbox"/>	16. Debarment certification (FD&C Act 306 (k) (1))		<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
<input checked="" type="checkbox"/>	17. Field copy certification (21 CFR 314.5 (k) (3))		<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
<input checked="" type="checkbox"/>	18. User Fee Cover Sheet (Form FDA 3397)		<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
<input checked="" type="checkbox"/>	19. Financial Information (21 CFR Part 54)		<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
<input checked="" type="checkbox"/>	20. OTHER (Specify) Pediatric Use, Exclusivity Statement		<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>

CERTIFICATION

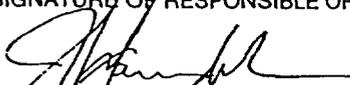
I agree to update this application with new safety information about the product that may reasonably affect the statement of contraindications, warnings, precautions, or adverse reactions in the draft labeling. I agree to submit safety update reports as provided for by regulation or as requested by FDA. If this application is approved, I agree to comply with all applicable laws and regulations that apply to approved applications, including, but not limited to the following:

1. Good manufacturing practice regulations in 21 CFR Parts 210 and 211, or applicable regulations, Parts 606, and/or 820.
2. Biological establishment standards in 21 CFR Part 600.
3. Labeling regulations in 21 CFR Part 201, 606, 610, 660 and/or 809.
4. In the case of a prescription drug or biological product, prescription drug advertising regulations in 21 CFR 202.
5. Regulations on making changes in application in FD&C Act Section 506A, 21 CFR 314.71, 314.72, 314.97, 314.99, and 601.12.
6. Regulations on Reports in 21 CFR 314.80, 314.81, 600.80 and 600.81.
7. Local, state and Federal environmental impact laws.

If this application applies to a drug product that FDA has proposed for scheduling under the Controlled Substances Act I agree not to market the product until the Drug Enforcement Administration makes a final scheduling decision.

The data and information in this submission have been reviewed and, to the best of my knowledge are certified to be true and accurate.

Warning: A willfully false statement is a criminal offense, U.S. Code, title 18, section 1001.

SIGNATURE OF RESPONSIBLE OFFICIAL OR AGENT  for Dr. Lamendola		TYPED NAME AND TITLE Joseph F. Lamendola, Ph.D. Vice President, U.S. Regulatory Affairs	DATE December 20, 2000
ADDRESS (Street, City, State, and ZIP Code) 2000 Galloping Hill Road, Kenilworth, NJ 07033		Telephone Number (908) 740-2628	

Public reporting burden for this collection of information is estimated to average 40 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Department of Health and Human Services
Food and Drug Administration
CBER, HFM-99
1401 Rockville Pike
Rockville, MD 20852-1448

An agency may not conduct or sponsor, and a Person is not required to respond to, a collection of information unless it displays a currently valid OMB Control Number

Establishment Information:

[]

Registration Number: —

Operations Conducted at the Site: []

Contact Person/Phone Number: []

Ready for Inspection: Yes

- 2. Schering Corporation
2000 Galloping Hill Road
Kenilworth, New Jersey 07033

CFN: 2210048

Operations Conducted at the Site: Secondary packaging operations and associated controls

Contact Person/Phone Number: Mr. Lawrence J. Casciano/
908-298-4653

Ready for Inspection: Yes

- 3. Schering Corporation
1011 Morris Avenue
Union, New Jersey 07083

CFN: 2211256

Operations Conducted at the Site: Release Testing/Stability Testing

Contact Person/Phone Number: Mr. Lawrence J. Casciano/
908-298-4653

Ready for Inspection: Yes

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4. Schering Corporation
13900 N.W. 57th Court
Miami Lakes, Florida 33014

CFN: 1010370

Operations Conducted at the Site: Secondary packaging operations and associated controls
Contact Person/Phone Number: Warren Meinschein
Manager QC Compliance
305-698-4711

Ready for Inspection: Yes

5. ScheringPlough (Avondale) Company
Rathdrum, County Wicklow
Ireland

CFN: FCIE 017

Operations Conducted at the Site: Drug Substance Manufacture, Packaging and Quality Control Operations
Contact Person/Phone Number: Mr. Stephen Barrett
353-404-46209

Ready for Inspection: Yes

6. Schering-Plough LTD, Singapore
Branch
50 Tuas Drive
Singapore 638408

Labeler Code Number: 64176

Operations Conducted at the Site: Drug Substance Manufacture, Packaging and Quality Control Operations

Contact Person/Phone Number: Dr. Patrick P. Yeung
65-869-8888

Ready for Inspection: Yes

Electronic Submission Information

Description Format (Electronic/Paper)

The following identifies the primary sections included in this submission. Each section has been identified with an "X" if presented in paper or electronically. If a section is not included in this application, it has been removed from this list.

Item	Description	Electronic	Paper
1	Index	X	X
2	Labeling	X	X
3	Application Summary	X	X
4	Chemistry	X	X
5	Nonclinical Pharmacology & Toxicology	X	X
6	Human Pharmacokinetics and Bioavailability	X	X
8	Clinical	X	X
10	Statistical	X*	X
12	Case Report Forms	X	
13	Patent Information	X	X
16	Debarment Certification	X	X
17	Field Copy Certification	X	X
18	User Fee Cover Sheet	X	X
19	Financial Information	X	X
20	Other	X	X

* This information is identical to Item 8.

Electronic Submission Summary

Media Type: CD-ROM / Diskette

Number of Media: 1 CD-ROM – Electronic Submission
1 CD-ROM – Supporting Clinical Data
1 Diskette – Labeling

File Formats: Portable Document Format (PDF)/Word 8.0/
SAS Transport Version 5 Format

Total Size: Electronic Submission – 102 MB
Supporting Clinical Data – 13.5 MB
Labeling – 145 KB

**APPEARS THIS WAY
ON ORIGINAL**

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USER FEE COVER SHEET

See Instructions on Reverse Side Before Completing This Form

1. APPLICANT'S NAME AND ADDRESS Schering Corporation 2000 Galloping Hill Road Kenilworth, NJ 07033 Attn: Joseph F. Lamendola, Ph.D.	3. PRODUCT NAME CLARINEX™ (desloratadine) RediTabs® 5 mg
2. TELEPHONE NUMBER (Include Area Code) (908) 740-2628	4. DOES THIS APPLICATION REQUIRE CLINICAL DATA FOR APPROVAL? IF YOUR RESPONSE IS "NO" AND THIS IS FOR A SUPPLEMENT, STOP HERE AND SIGN THIS FORM. IF RESPONSE IS "YES", CHECK THE APPROPRIATE RESPONSE BELOW: <input checked="" type="checkbox"/> THE REQUIRED CLINICAL DATA ARE CONTAINED IN THE APPLICATION. <input type="checkbox"/> THE REQUIRED CLINICAL DATA ARE SUBMITTED BY REFERENCE TO _____ (APPLICATION NO. CONTAINING THE DATA).
5. USER FEE I.D. NUMBER 4024	6. LICENSE NUMBER / NDA NUMBER N021312

7. IS THIS APPLICATION COVERED BY ANY OF THE FOLLOWING USER FEE EXCLUSIONS? IF SO, CHECK THE APPLICABLE EXCLUSION.

<input type="checkbox"/> A LARGE VOLUME PARENTERAL DRUG PRODUCT APPROVED UNDER SECTION 505 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT BEFORE 9/1/92 (Self Explanatory)	<input type="checkbox"/> A 505(b)(2) APPLICATION THAT DOES NOT REQUIRE A FEE (See item 7, reverse side before checking box.)
<input type="checkbox"/> THE APPLICATION QUALIFIES FOR THE ORPHAN EXCEPTION UNDER SECTION 736(a)(1)(E) of the Federal Food, Drug, and Cosmetic Act (See item 7, reverse side before checking box.)	<input type="checkbox"/> THE APPLICATION IS A PEDIATRIC SUPPLEMENT THAT QUALIFIES FOR THE EXCEPTION UNDER SECTION 736(a)(1)(F) of the Federal Food, Drug, and Cosmetic Act (See item 7, reverse side before checking box.)
<input type="checkbox"/> THE APPLICATION IS SUBMITTED BY A STATE OR FEDERAL GOVERNMENT ENTITY FOR A DRUG THAT IS NOT DISTRIBUTED COMMERCIALY (Self Explanatory)	

FOR BIOLOGICAL PRODUCTS ONLY

<input type="checkbox"/> WHOLE BLOOD OR BLOOD COMPONENT FOR TRANSFUSION	<input type="checkbox"/> A CRUDE ALLERGENIC EXTRACT PRODUCT
<input type="checkbox"/> AN APPLICATION FOR A BIOLOGICAL PRODUCT FOR FURTHER MANUFACTURING USE ONLY	<input type="checkbox"/> AN "IN VITRO" DIAGNOSTIC BIOLOGICAL PRODUCT LICENSED UNDER SECTION 351 OF THE PHS ACT
<input type="checkbox"/> BOVINE BLOOD PRODUCT FOR TOPICAL APPLICATION LICENSED BEFORE 9/1/92	

8. HAS A WAIVER OF AN APPLICATION FEE BEEN GRANTED FOR THIS APPLICATION? YES NO
(See reverse side if answered YES)

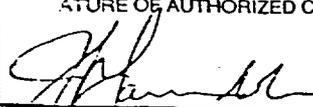
A completed form must be signed and accompany each new drug or biologic product application and each new supplement. If payment is sent by U.S. mail or courier, please include a copy of this completed form with payment.

Public reporting burden for this collection of information is estimated to average 30 minutes per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

DHHS, Reports Clearance Officer
Paperwork Reduction Project (0910-0297)
Hubert H. Humphrey Building, Room 531-H
200 Independence Avenue, S.W.
Washington, DC 20201

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

Please DO NOT RETURN this form to this address.

SIGNATURE OF AUTHORIZED COMPANY REPRESENTATIVE  /for Dr. Lamendola	TITLE Vice President U.S. Regulatory Affairs	DATE 12/20/00
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Debarment Certification

Schering Corporation hereby certifies that it did not and will not use in any capacity the services of any person debarred under section 306 of the Federal Food, Drug and Cosmetic Act in connection with this application.

**APPEARS THIS WAY
ON ORIGINAL**



SCHERING-PLOUGH RESEARCH INSTITUTE

Patent Information Pursuant to 21 CFR§314.59(Section 13)

RE: CLARINEX™ (Brand of Desloratadine) Reditabs® for use in the treatment of the symptoms of seasonal allergic rhinitis and chronic idiopathic urticaria in adults 12 years of age and older.

Trade Name: CLARINEX™
Active Ingredient: Desloratadine
Strength: 5 mg.
Dosage Form: Rapidly Disintegrating Tablet

Pursuant to the provisions of 21 CFR§ 314.53, we hereby supply the patent information for the captioned Schering Corporation NDA:

- 1A U.S. Patent No. 4,659,716
Expiration Date: April 21, 2004
Type of Patent: Desloratadine, 8-chloro-6,11-dihydro-11-(4-piperidylidene)-5H-benzo[5,6]cyclohepta[1,2-b]pyridine, as the compound per se, the active ingredient in desloratadine rapidly disintegrating tablets, pharmaceutical compositions containing it and methods of using it to treat allergic reactions in mammals.
Patent Owner: Schering Corporation.
- 1B U.S. Patent No. 4,863,931
Expiration Date: September 15, 2008
Type of Patent: A drug and a drug product patent covering among other things 8-chloro-11-fluoro- 6,11-dihydro-(4-piperidylidene)-5H-benzo[5,6]cyclohepta[1,2-b]pyridine, which is a by-product of the process of making desloratadine, which is the active ingredient in the desloratadine rapidly disintegrating tablet product used for the indications for which approval is sought.
Patent Owner: Schering Corporation
- 1C U.S. Patent No. 4,804,666
Expiration Date: February 14, 2006
Type of Patent: 3-Hydroxy-8-chloro-11-[4-piperidylidene]-6,11-dihydro-5H-benzo[5,6]cyclohepta [1,2-b]pyridine, which is an active

metabolite of desloratadine, as the compound per se which is the active ingredient in the desloratadine rapidly disintegrating tablet and a method of treating allergy mammals by use of the active metabolite of desloratadine in the desloratadine rapidly disintegrating tablet product used for the indication for which approval is sought.

Patent Owner: Schering Corporation

1D U.S. Patent No. 5,595,997

Expiration Date: December 30, 2014

Type of Patent: A method of treating allergic rhinitis in a human while avoiding the concomitant liability of adverse side-effects associated with administering non-sedating antihistamines by using desloratadine, the active ingredient in the desloratadine rapidly disintegrating tablet product for which approval is being sought.

Patent Owner: Sepracor, Inc.

1E U.S. Patent No. 6,100,274

Expiration Date: July 7, 2019

Type of Patent: Pharmaceutical compositions suitable for oral administration covering among other things an anti-allergic effective amount of desloratadine in a pharmaceutically acceptable carrier medium wherein the compositions contain less than about 1% by weight of N-formyl-desloratadine.

Patent Owner: Schering Corporation

The undersigned declares (a) that U.S. Patent No. 4,659,716 covers desloratadine, as the compound per se, pharmaceutical compositions containing it and a method of treating allergic reactions, e.g., seasonal allergic rhinitis and chronic idiopathic urticaria, in a mammal using it, (b) that U.S. Patent No. 4,863,931 covers the desloratadine rapidly disintegrating tablet product used for treating seasonal allergic rhinitis and chronic idiopathic urticaria, (c) that U.S. Patent No. 4,804,666 covers an active metabolite of desloratadine as the compound per se, and a method of treating allergy in a mammal using this active metabolite, (d) that U.S. Patent No. 5,595,997 covers a method for treating allergic rhinitis in a human using desloratadine, (e) that U.S. Patent No. 6,100,274 covers the pharmaceutical composition containing desloratadine used for the treatment of the symptoms of seasonal allergic rhinitis and chronic idiopathic urticaria, and (f) that desloratadine is the active ingredient in the desloratadine rapidly disintegrating tablet product used for the treatment of the symptoms of seasonal allergic rhinitis and chronic idiopathic urticaria, and (g) that the treatment of the

symptoms of seasonal allergic rhinitis and chronic idiopathic urticaria are the indications for which approval is being sought.

The undersigned further declares that (a) approval of desloratadine rapidly disintegrating tablets is being sought under section 505 of the Federal Food, Drug and Cosmetic Act, 21 USC§355, and that (b) a claim of patent infringement under one or more of U.S. Patent Nos. 4,659,716; 4,863,931; 4,804,666; 5,595,997 and 6,100,274 could reasonably be asserted if a person not licensed by the owner of each of the above-listed U.S. Patents engaged in the commercial manufacture, importation, use, sale or offer for sale of desloratadine for the treatment of seasonal allergic rhinitis and chronic idiopathic urticaria in adults 12 years of age and older.

**APPEARS THIS WAY
ON ORIGINAL**

Claim for Exclusivity (Section 20)

1. Pursuant to the provisions of Sections 505(c)(3)(D)(iii) and 505 (j)(4)(D)(iii) of the Food, Drug and Cosmetic Act (FDCA) and 21 CFR 314.108 (b)(4)(iv), the applicant claims three (3) years of exclusivity for its CLARINEX™ (Brand of Desloratadine) Reditabs, for use in the treatment of the symptoms of seasonal allergic rhinitis and for use in the treatment of symptoms of chronic idiopathic urticaria in patients 12 years of age and older.

2. The applicant certifies that to the best of the applicant's knowledge each of the clinical investigations included in the application meets the definition of "new clinical investigation" set forth in 21 CFR 314.108(a).

3. The applicant certifies that it has thoroughly searched the scientific literature through a computer-assisted search of the Scholar database, and Dialog database encompassing the subfiles MEDLINE, BIOSIS Previews, EMBASE and SciSearch, for English and non-English literature relating to desloratadine rapidly disintegrating tablets in humans, covering the period from 1/1/95 to 9/11/00.

4. To the best of the applicant's knowledge, there are no published studies in the scientific literature or publicly related reports of clinical investigations known to the applicant pertaining to desloratadine rapidly disintegrating tablets is complete and accurate, and in the opinion of the applicant, such published studies or publicly available information do not provide a sufficient basis for the approval of the use of desloratadine rapidly disintegrating tablets for the treatment of seasonal allergic rhinitis and chronic idiopathic urticaria without reference to the new information contained in the clinical trials in the application. The applicant's opinion that the studies or reports are insufficient is based on the following:

- The literature does not contain adequate characterization of the efficacy and safety profile of desloratadine use in the treatment of the symptoms of seasonal allergic rhinitis and for treatment of chronic idiopathic urticaria, which is established by the data from the new clinical studies conducted by the applicant under IND, ~~_____~~ and included in this application.

5. The applicant was the sponsor named in the Form FDA-1571 for IND ~~_____~~ under which the new clinical investigations were conducted.

**APPEARS THIS WAY
ON ORIGINAL**

CONSULTATION RESPONSE
Office of Post-Marketing Drug Risk Assessment
(OPDRA; HFD-400)

DATE RECEIVED: July 31, 2001	DUE DATE: October 1, 2001	OPDRA CONSULT #: 01-0171
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TO: Robert J. Meyer, M.D.
Director, Division of Pulmonary Drug Products
HFD-570

THROUGH: David Hilfiker, Project Manager
HFD-570

PRODUCT NAME: Clarinet RediTabs (desloratadine rapidly-disintegrating tablets) 5 mg NDA #: 21-312	MANUFACTURER: Schering Corporation
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SAFETY EVALUATOR: Alina R. Mahmud, R.Ph.

SUMMARY: In response to a consult from the Division of Pulmonary Drug Products (HFD-570), OPDRA reviewed the labeling and packaging of "Clarinet RediTabs" for possible interventions that may help minimize medication errors.

OPDRA RECOMMENDATION: OPDRA has made recommendations for labeling revisions to minimize potential errors with the use of this product.

**APPEARS THIS WAY
ON ORIGINAL**

Jerry Phillips, R.Ph.
Associate Director for Medication Error Prevention
Office of Post-Marketing Drug Risk Assessment
Phone: (301) 827-3246
Fax: (301) 480-8173

Martin Himmel, M.D.
Deputy Director
Office of Post-Marketing Drug Risk Assessment
Center for Drug Evaluation and Research
Food and Drug Administration

**Office of Post-Marketing Drug Risk Assessment
HFD-400; Rm 15B-32
Center for Drug Evaluation and Research**

DATE OF REVIEW: September 6, 2001
NDA: 21-312
NAME OF DRUG: Clarinex RediTabs (desloratadine rapidly-disintegrating tablets) 5 mg
NDA HOLDER: Schering Corporation

I. INTRODUCTION

This consult was written in response to a request from the Division Pulmonary Drug Products (HFD-570), for assessment of artwork of Clarinex RediTabs.

PRODUCT INFORMATION

Clarinex RediTabs contain the antihistamine desloratadine and is indicated for the relief of the nasal and non-nasal symptoms of seasonal allergic rhinitis and for the treatment of chronic idiopathic urticaria in patients 12 years of age and older. The recommended dose of Clarinex is one tablet once daily. Tablet disintegration occurs rapidly once Clarinex is placed on the tongue. Clarinex may be administered with or without water. Because the tablets are heat sensitive, it is to be taken immediately after opening the blister. Clarinex Reditabs will be available in unit-of-use blister packs of 4 (professional sample), ~~30~~ 30 count.

II. LABELING, PACKAGING, AND SAFETY RELATED ISSUES

In the review of the labeling and packaging, OPDRA has attempted to focus on safety issues relating to possible medication errors. We have identified some areas of possible improvement, in the interest of minimizing potential user errors.

A. Carton Label (Professional Sample)

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B. Carton Label (30-Tablets)

1. See comments 1 through 4 above.

[]

**APPEARS THIS WAY
ON ORIGINAL**

III. RECOMMENDATION:

OPDRA has recommended some labeling interventions that might minimize user error.

OPDRA would appreciate feedback of the final outcome of this consult. We would be willing to meet with the Division for further discussion, if needed. If you have further questions or need clarifications, please contact Sammie Beam at (301) 827-3231.

Alina R. Mahmud, RPh.
Safety Evaluator
Office of Post-Marketing Drug Risk Assessment

Concur:

Jerry Phillips, RPh
Associate Director for Medication Error Prevention
Office of Post-Marketing Drug Risk Assessment

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this page is the manifestation of the electronic signature.

/s/

Alina Mahmud
9/17/01 02:03:36 PM
PHARMACIST

Jerry Phillips
9/17/01 02:08:59 PM
DIRECTOR

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CONSULTATION RESPONSE
Office of Post-Marketing Drug Risk Assessment
(OPDRA; HFD-400)

DATE RECEIVED: April 2, 2001

DUE DATE:
May 25, 2001

OPDRA CONSULT #: 01-0087

TO: Robert Meyer, MD
Director, Division of Pulmonary Drug Products
HFD-570

THROUGH: Craig Bertha, Project Manager
HFD-570

PRODUCT NAME:
Clarinx

(desloratadine rapidly-disintegrating tablets)

DISTRIBUTOR: Schering Corporation

NDA #: 21-312

SAFETY EVALUATOR: Alina R. Mahmud, RPh.

SUMMARY: In response to a consult from the Division of Pulmonary Drug Products (HFD-570), OPDRA conducted a review to determine the look-alike similarity, in regards to the unit-of-use packaging, between Clarinx Reditabs and Claritin Reditabs. In addition, OPDRA was asked to review the appropriateness of the dosage form descriptor "rapidly-disintegrating tablets".

OPDRA RECOMMENDATION: OPDRA has no objections to the appearance of the proposed dosage unit for "Clarinx". In addition, OPDRA recommends using "orally disintegrating tablets" as a dosage form descriptor.

**APPEARS THIS WAY
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Carol Holquist for Jerry Phillips, R.Ph.
Associate Director for Medication Error Prevention
Office of Post-Marketing Drug Risk Assessment
Phone: (301) 827-3242
Fax: (301) 480-8173

Martin Himmel, M.D.
Deputy Director
Office of Post-Marketing Drug Risk Assessment
Center for Drug Evaluation and Research
Food and Drug Administration

Office of Post-Marketing Drug Risk Assessment
HFD-400; Rm. 15B03
Center for Drug Evaluation and Research

PROPRIETARY NAME REVIEW

DATE OF REVIEW: April 23, 2001
NDA NUMBER: 21-312
NAME OF DRUG: Clarinex Reditabs
(desloratadine rapidly-disintegrating tablets)
NDA HOLDER: Schering Corporation

I. INTRODUCTION

This consult was written in response to a request from the Division of Pulmonary Drug Products (HFD-570) regarding potential dosage unit similarity between Clarinex Reditabs and Claritin Reditabs. In addition, the division requested a review of the appropriateness of the dosage form descriptor "rapidly-disintegrating tablet" since "orally disintegrating tablet" is widely used to describe similar dosage forms.

Schering first received approval for NDA 20-704 on December 23, 1996 for loratadine rapidly-disintegrating tablets, under the proprietary name CLARITIN REDITABS. CLARITIN REDITABS is packaged in unit-of-use blister packs with a transparent — cover. The white tablet, which is visible through the — cover, contains an impression of the letter "C".

NDA 21-312 for CLARINEX REDITABS, desloratadine rapidly-disintegrating tablets, is still pending approval. Although, CLARINEX REDITABS is packaged in a unit-of-use blister pack as well, the tablet is covered with opaque foil and is therefore not visible. The tablet is large and pink and contains a smaller impression of the letter "C" within a circle.

II. SAFETY EVALUATOR RISK ASSESSMENT

In reviewing tablet samples provided for Clarinex Reditabs and the Claritin Reditabs, many differences were noted. The aluminum foil cover for the Clarinex Reditabs is distinctly different than the Claritin Reditabs, which has the transparent cover. The size of the tablet varies as well; The Clarinex Reditab is larger than the Claritin Reditab. The tablet is also distinctly different in color; Clarinex Reditab is white and Claritin Reditab is pink in color. In addition, the size of the impressed "C" is much smaller on the Clarinex Reditab than the Claritin Reditabs' impression. The tablets appear distinctly different and therefore comply with 21 CFR 206.10(a), which states that "...it is clearly marked or imprinted with a code imprint that, in conjunction with the

product's size, shape, and color, permits the unique identification of the drug product and the manufacturer or distributor of the product." It is difficult to determine, from the samples provided, how the commercially available label will appear. Therefore, we recommend that the unit-of-use label and labeling appear distinctly different for each product with the use of contrasting colors or some other means. The use of colors to differentiate certain aspects of the label can facilitate the practitioner in selecting the correct product.

In regards to the dosage form descriptor, OPDRA contacted Dan Boring, FDA's representative on the USAN council and the USP Labeling and Nomenclature Committee. Dan Boring stated that the dosage form descriptor "orally disintegrating tablet" has not been officially adopted by the USP. However, it has been discussed with USP and will likely be adopted sometime in the near future. Therefore, OPDRA strongly recommends the usage of "orally disintegrating tablet" as a dosage form descriptor given that this may be accepted as an official descriptor and would be consistent with other approved applications.

III. RECOMMENDATIONS

OPDRA has no objections to the appearance of the proposed dosage unit for "Clarinex". In addition, OPDRA recommends using "orally disintegrating tablets" as a dosage form descriptor.

OPDRA would appreciate feedback of the final outcome of this consult (e.g., copy of revised labels/labeling). We are willing to meet with the Division for further discussion as well. If you have any questions concerning this review, please contact Sammie Beam, R.Ph. at 301-827-3231.

Alina R. Mahmud, R.Ph.
Safety Evaluator
Office of Postmarketing Drug Risk Assessment (OPDRA)

Concur:

Jerry Phillips, R.Ph.
Associate Director for Medication Error Prevention
Office of Postmarketing Drug Risk Assessment (OPDRA)

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/s/

Alina Mahmud
5/22/01 10:31:38 AM
PHARMACIST

Carol Holquist
5/22/01 11:04:24 AM
PHARMACIST

Martin Himmel
5/23/01 01:20:14 PM
MEDICAL OFFICER

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REQUEST FOR CONSULTATION

TO: *Division/Office*: HFD-400/OPDRA/Assoc. Director for Medication
Error Prevention

FROM: HFD-570/DPADP/CBertha

DATE:
March 15, 2001

IND NO.:

NDA NO.:
21-312

TYPE OF DOCUMENT:
CMC Original Submission

DATE OF DOCUMENT:
December 21, 2000

NAME OF DRUG:
Clarinet Reditabs

PRIORITY CONSIDERATION:
standard

CLASSIFICATION OF DRUG:
1S

DESIRED COMPLETION DATE:
May 15, 2001

NAME OF FIRM: Schering Corporation

REASON FOR REQUEST

I. GENERAL

- | | | |
|--|--|---|
| <input type="checkbox"/> NEW PROTOCOL
<input type="checkbox"/> PROGRESS REPORT
<input type="checkbox"/> NEW CORRESPONDENCE
<input type="checkbox"/> DRUG ADVERTISING
<input type="checkbox"/> ADVERSE REACTION REPORT
<input type="checkbox"/> MANUFACTURING CHANGE/ADDITION
<input type="checkbox"/> MEETING PLANNED BY | <input type="checkbox"/> PRE-NDA MEETING
<input type="checkbox"/> END OF PHASE II MEETING
<input type="checkbox"/> RESUBMISSION
<input type="checkbox"/> SAFETY/EFFICACY
<input type="checkbox"/> PAPER NDA
<input type="checkbox"/> CONTROL SUPPLEMENT | <input type="checkbox"/> RESPONSE TO DEFICIENCY LETTER
<input type="checkbox"/> FINAL PRINTED LABELING
<input type="checkbox"/> LABELING REVISION
<input type="checkbox"/> ORIGINAL NEW CORRESPONDENCE
<input type="checkbox"/> FORMULATIVE REVIEW
<input checked="" type="checkbox"/> OTHER (SPECIFY BELOW):
Tradename Consult |
|--|--|---|

II. BIOMETRICS

STATISTICAL EVALUATION BRANCH

STATISTICAL APPLICATION BRANCH

- TYPE A OR B NDA REVIEW
 END OF PHASE II MEETING
 CONTROLLED STUDIES
 PROTOCOL REVIEW
 OTHER:

- CHEMISTRY REVIEW
 PHARMACOLOGY
 BIOPHARMACEUTICS
 OTHER:

III. BIOPHARMACEUTICS

- | | |
|---|--|
| <input type="checkbox"/> DISSOLUTION
<input type="checkbox"/> BIOAVAILABILITY STUDIES
<input type="checkbox"/> PHASE IV STUDIES | <input type="checkbox"/> DEFICIENCY LETTER RESPONSE
<input type="checkbox"/> PROTOCOL-BIOPHARMACEUTICS
<input type="checkbox"/> IN-VIVO WAIVER REQUEST |
|---|--|

IV. DRUG EXPERIENCE

- | | |
|--|---|
| <input type="checkbox"/> PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL
<input type="checkbox"/> DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES
<input type="checkbox"/> CASE REPORTS OF SPECIFIC REACTIONS (List below)
<input type="checkbox"/> COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP | <input type="checkbox"/> REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY
<input type="checkbox"/> SUMMARY OF ADVERSE EXPERIENCE
<input type="checkbox"/> POISON RISK ANALYSIS |
|--|---|

V. SCIENTIFIC INVESTIGATIONS

CLINICAL

PRECLINICAL

COMMENTS/SPECIAL INSTRUCTIONS: Please comment: 1). The acceptability of the fact that Schering's new Clarinet Reditabs (desloratadine rapidly-disintegrating tablets) of N21-312 have the same style "C" embossed onto the dosage unit as the approved Claritin Reditabs (loratadine rapidly-disintegrating tablets) of N20-704 (color, size, and shape appear distinct, however). 2). The acceptability of "rapidly-disintegrating tablet" as the dosage form descriptor. We are aware that in other divisions drug products with this dosage form have been approved with the description of "orally disintegrating tablet." It would be advantageous for consistency if an official position was taken on what the dosage form descriptor should be. Note that these dosage units disperse readily in the presence of water. Please find a sample of the dosage form of each enclosed (Clarinet Reditabs, N21312 and Claritin Reditabs, N20704, approved 12/23/96).

cc: Original NDA 21-312
HFD-570/Div. Files
HFD-570/GTrout, RNicklaus, Bertha

SIGNATURE OF REQUESTER:

METHOD OF DELIVERY (Check one):

MAIL HAND

SIGNATURE OF RECEIVER:

SIGNATURE OF DELIVERER:

/s/

Guiragos Poochikian
3/21/01 11:02:12 AM

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Review

Electronic submission of the Final Draft Label received June 26, 2002. A visual line-by-line comparison with the most recently approved label found that this version contained all items agreed to as of this date as indicated in the attached facsimile to Schering.

Conclusions

All appropriate changes have been implemented as discussed above.

Anthony M. Zeccola
Regulatory Management Officer

**APPEARS THIS WAY
ON ORIGINAL**



NDA 21-312

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: Clarinex (desloratadine) Reditabs 5 mg

Review Priority Classification: Standard (S)

Date of Application: December 20, 2000

Date of Receipt: December 21, 2000

Our Reference Number: NDA 21-312

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 February 19, 2001 in accordance with 21 CFR 314.101(a). If the application is filed, the primary user fee goal date will be October 21, 2001 and the secondary user fee goal date will be December 21, 2001.

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 approximately 120 days of receipt of your pediatric drug development plan, we will review your plan and notify you of its adequacy.

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 make a determination whether to grant or deny a request for a waiver of pediatric studies during the review of the application. In no case, however, will the determination be made later than the date action is taken on the

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application. 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 review your pediatric drug development plan and notify you of its adequacy. 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.

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:

U.S. Postal/Courier/Overnight Mail:

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 me at (301) 827-1058.

Sincerely yours,

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

REST POSSIBLE COPY

/s/

Gretchen Trout
1/3/01 02:04:51 PM

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