CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-563

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

Patent Information Pursuant to 21 CFR§314.59

RE: CLARINEX®(Brand of Desloratadine) Syrup for use in the treatment of allergic rhinitis and for use in the treatment of symptoms of chronic idiopathic urticaria in subjects 6 months to less than 2 years of age

Trade Name:	CLARINEX®
Active Ingredient:	Desloratadine
Strength:	0.5 mg/mL.
Dosage Form:	Syrup

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]pyridine, as the compound per se, the active ingredient in desloratadine syrup, 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 syrup 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-piperidyidene]-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 syrup and a method of treating allergy mammals by use of the active metabolite of desloratadine in the desloratadine syrup 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 Patient:	A method of treating allergic rhinitis in a human using desloratadine, the active ingredient in the desloratadine syrup product used for the indication for which approval is sought.
	Patent Owner:	Sepracor, Inc.

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., allergic rhinitis and chronic idiopathic urticaria, in a mammal using it, (b) that U.S. Patent No. 4,863,931 covers the desloratadine syrup 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, and (d) that U.S. Patent No. 5,595,997 covers a method of treating of allergic rhinitis in a human using desloratadine; and (e) that desloratadine is the active ingredient in the desloratadine syrup product used for the treatment of allergic rhinitis and chronic idiopathic urticaria, and (f) that the treatment of allergic rhinitis and chronic idiopathic urticaria are the indications for which approval is being sought.

The undersigned further declares that (a) approval of desloratadine syrup for the treatment of allergic rhinitis and chronic idiopathic urticaria in patients 6 months to less than 2 years of age 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; and 5,595,997 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 use in the desloratadine syrup product for the treatment of allergic rhinitis and chronic idiopathic urticaria in patients 6 months to less than 2 years of age.

PEDIATRIC EXCLUSIVITY DETERMINATION CHECKLIST

PART I - TO BE COMPLETED BY THE REVIEWING DIVISION.

Date of Written Request from FDA 06/06/00, 10/19/00, 12/05/00, and 05/07/01.
Application Written Request was made to: IND# 57, 960
Timeframe Noted in Written Request for Submission of Studies 12/17/02.
NDA# 21-563 Sponsor Schering Corporation Generic Name desloratadine Trade Name Clarinex
Strength .5 mg/ml Dosage Form/Route Syrup Date of Submission of Reports of Studies 12/04/02.
Pediatric Exclusivity Determination Due Date (60 or 90 days from date of submission of studies) 03/04/02.

Was a formal Written Request made for the pediatric studies submitted?	Y √	N ___
Were the studies submitted after the Written Request?	Y √	N ___
Were the reports submitted as a supplement, amendment to an NDA, or NDA?	Y √	N ___
Was the timeframe noted in the Written Request for submission of studies met?	Y √	N ___
If there was a written agreement, were the studies conducted according to the written agreement? OR If there was no written agreement, were the studies conducted in accord with good scientific principles?	Y √	N ___
Did the studies fairly respond to the Written Request?	Y √	N ___

SIGNED Richard A. Nicklas MD DATE 2/11/2003
(Reviewing Medical Officer)

Do not enter in DFS - FORWARD TO PEDIATRIC EXCLUSIVITY BOARD, HFD-960.

Pediatric Exclusivity ✓ **Granted** ___ **Denied**

Existing Patent or Exclusivity Protection:

NDA/Product #	Eligible Patents/Exclusivity	Current Expiration Date
SEE	ATTACHMENT	

SIGNED _____ DATE 2/12/03

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

Form Approved: OMB No. 0910-0297
Expiration Date: February 29, 2004.

USER FEE COVER SHEET

See Instructions on Reverse Side Before Completing This Form

A completed form must be signed and accompany each new drug or biologic product application and each new supplement. See exceptions on the reverse side. If payment is sent by U.S. mail or courier, please include a copy of this completed form with payment. Payment instructions and fee rates can be found on CDER's website: http://www.fda.gov/cder/pdufa/default.htm

1. APPLICANT'S NAME AND ADDRESS

Schering Corporation
2000 Galloping Hill Road
Kenilworth, NJ 07033

Attn: Joseph Lamendola

2. TELEPHONE NUMBER *(Include Area Code)*

(908) 740-2628

3. PRODUCT NAME

CLARINEX® (desloratadine) Syrup

4. BLA SUBMISSION TRACKING NUMBER (STN) / NDA NUMBER

NDA 21-563

5. DOES THIS APPLICATION REQUIRE CLINICAL DATA FOR APPROVAL?

[X] YES [ ] NO

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:

[X] THE REQUIRED CLINICAL DATA ARE CONTAINED IN THE APPLICATION.

[X] THE REQUIRED CLINICAL DATA ARE SUBMITTED BY REFERENCE TO:

NDA 21-300
(APPLICATION NO. CONTAINING THE DATA).

6. USER FEE I.D. NUMBER

4422

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

[ ] A LARGE VOLUME PARENTERAL DRUG PRODUCT APPROVED UNDER SECTION 505 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT BEFORE 9/1/92
(Self Explanatory)

[ ] A 505(b)(2) APPLICATION THAT DOES NOT REQUIRE A FEE
(See item 7, reverse side before checking box.)

[ ] 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.)

[ ] 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.)

[ ] THE APPLICATION IS SUBMITTED BY A STATE OR FEDERAL GOVERNMENT ENTITY FOR A DRUG THAT IS NOT DISTRIBUTED COMMERCIALLY
(Self Explanatory)

8. HAS A WAIVER OF AN APPLICATION FEE BEEN GRANTED FOR THIS APPLICATION?

[ ] YES [X] NO

(See Item 8, reverse side if answered YES)

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:

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

and

Food and Drug Administration
CDER, HFD-94
12420 Parklawn Drive, Room 3046
Rockville, MD 20852

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.

SIGNATURE OF AUTHORIZED COMPANY REPRESENTATIVE	TITLE	DATE
/for Joseph Lamendola, Ph.D.	Vice President Worldwide Regulatory Affairs	December 4, 2002

FORM FDA 3397 (3/01)

Created by: PSC Media Arts (301) 443-2454 EF

16. DEBARMENT CERTIFICATION

In accordance with 21 U.S.C. 335a(k) of the Food, Drug and Cosmetic Act, Schering Corporation certifies that, with respect to this application, it did not and will not use in any capacity the services of any persons debarred under subsections (a) or (b) of the Act.

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Food and Drug Administration

Form Approved: OMB No. 0910-0396
Expiration Date: 3/31/02

CERTIFICATION: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

TO BE COMPLETED BY APPLICANT

With respect to all covered clinical studies (or specific clinical studies listed below (if appropriate)) submitted in support of this application, I certify to one of the statements below as appropriate. I understand that this certification is made in compliance with 21 CFR part 54 and that for the purposes of this statement, a clinical investigator includes the spouse and each dependent child of the investigator as defined in 21 CFR 54.2(d).

Please mark the applicable checkbox.

— (1) As the sponsor of the submitted studies, I certify that I have not entered into any financial arrangement with the listed clinical investigators (enter names of clinical investigators below or attach list of names to this form) whereby the value of compensation to the investigator could be affected by the outcome of the study as defined in 21 CFR 54.2(a). I also certify that each listed clinical investigator required to disclose to the sponsor whether the investigator had a proprietary interest in this product or a significant equity in the sponsor as defined in 21 CFR 54.2(b) did not disclose any such interests. I further certify that no listed investigator was the recipient of significant payments of other sorts as defined in 21 CFR 54.2(f).

Clinical Investigators		
	See attached listing —	
	and —	

— (2) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that based on information obtained from the sponsor or from participating clinical investigators, the listed clinical investigators (attach list of names to this form) did not participate in any financial arrangement with the sponsor of a covered study whereby the value of compensation to the investigator for conducting the study could be affected by the outcome of the study (as defined in 21 CFR 54.2(a)); had no proprietary interest in this product or significant equity interest in the sponsor of the covered study (as defined in 21 CFR 54.2(b)); and was not the recipient of significant payments of other sorts (as defined in 21 CFR 54.2(f)).

— (3) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that I have acted with due diligence to obtain from the listed clinical investigators (attach list of names) or from the sponsor the information required under 54.4 and it was not possible to do so. The reason why this information could not be obtained is attached.

NAME	TITLE
Patricia Rohane, M.D.	Vice President Clinical Research-Allergy
FIRM/ORGANIZATION: Schering-Plough Research Institute	
SIGNATURE: Pa Rohane MD	DATE: Nov 6, 02

Paperwork Reduction Act Statement

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. Public reporting burden for this collection of information is estimated to average 1 hour per response, including time for reviewing instructions, searching existing data sources, gathering and maintaining the necessary data, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information to the address to the right:

Department of Health and Human Services
Food and Drug Administration
5600 Fishers Lane, Room 14C-03
Rockville, MD 20857

FORM FDA 3454 (3/99)

Created by Electronic Document Services/USDHHS: (301) 443-2454 EF

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Food and Drug Administration

Form Approved: OMB No. 0910-0396
Expiration Date: 3/31/02

DISCLOSURE: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

TO BE COMPLETED BY APPLICANT

The following information concerning [redacted], who participated as a clinical investigator in the submitted study [redacted], is submitted in accordance with 21 CFR part 54. The named individual has participated in financial arrangements or holds financial interests that are required to be disclosed as follows:

Name of clinical investigator

Name of clinical study

Please mark the applicable checkboxes.

/ any financial arrangement entered into between the sponsor of the covered study and the clinical investigator involved in the conduct of the covered study, whereby the value of the compensation to the clinical investigator for conducting the study could be influenced by the outcome of the study;

/ any significant payments of other sorts made on or after February 2, 1999 from the sponsor of the covered study such as a grant to fund ongoing research, compensation in the form of equipment, retainer for ongoing consultation, or honoraria;

/ any proprietary interest in the product tested in the covered study held by the clinical investigator;

/ any significant equity interest as defined in 21 CFR 54.2(b), held by the clinical investigator in the sponsor of the covered study.

Details of the individual's disclosable financial arrangements and interests are attached, along with a description of steps taken to minimize the potential bias of clinical study results by any of the disclosed arrangements or interests.

NAME	TITLE
Patricia Rohane, M.D.	Vice President Clinical Research-Allergy
FIRM/ORGANIZATION: Schering-Plough Research Institute	
SIGNATURE: Pa Rohane MD	DATE: Nov 6, 02

Paperwork Reduction Act Statement

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. Public reporting burden for this collection of information is estimated to average 4 hours per response, including time for reviewing instructions, searching existing data sources, gathering and maintaining the necessary data, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information to:

Department of Health and Human Services
Food and Drug Administration
5600 Fishers Lane, Room 14C-03
Rockville, MD 20857

FORM FDA 3455 (3/99) Created by Electronic Document Services/USDHHS: (301) EF

NDA/EFFICACY SUPPLEMENT ACTION PACKAGE CHECKLIST

Application Information			
NDA 21-563	Efficacy Supplement Type SE-	Supplement Number	
Drug: Clarinex (desloratadine) Syrup		Applicant: Schering Corporation	
RPM:Zeccola		HFD-570	Phone # 301-827-1058
Application Type: ( ) 505(b)(1) ( ) 505(b)(2)		Reference Listed Drug (NDA #, Drug name):	

❖ Application Classifications:	
• Review priority	( ) Standard (X) Priority
• Chem class (NDAs only)	3
• Other (e.g., orphan, OTC)	
❖ User Fee Goal Dates	June 3, 2003
❖ Special programs (indicate all that apply)	(X) None Subpart H ( ) 21 CFR 314.510 (accelerated approval) ( ) 21 CFR 314.520 (restricted distribution) ( ) Fast Track ( ) Rolling Review
❖ User Fee Information	
• User Fee	(X) Paid
• User Fee waiver	( ) Small business ( ) Public health ( ) Barrier-to-Innovation ( ) Other
• User Fee exception	( ) Orphan designation ( ) No-fee 505(b)(2) ( ) Other
❖ Application Integrity Policy (AIP)	
• Applicant is on the AIP	( ) Yes (X) No
• This application is on the AIP	( ) Yes (X) No
• Exception for review (Center Director's memo)	
• OC clearance for approval	
❖ Debarment certification: verified that qualifying language (e.g., willingly, knowingly) was not used in certification and certifications from foreign applicants are co-signed by U.S. agent.	(X) Verified
❖ Patent	
• Information: Verify that patent information was submitted	(X) Verified
• Patent certification [505(b)(2) applications]: Verify type of certifications submitted	21 CFR 314.50(i)(1)(*i*)(A) ( ) I ( ) II ( ) III ( ) IV 21 CFR 314.50(i)(1) ( ) (ii) ( ) (iii)
• For paragraph IV certification, verify that the applicant notified the patent holder(s) of their certification that the patent(s) is invalid, unenforceable, or will not be infringed (certification of notification and documentation of receipt of notice).	( ) Verified
❖ Exclusivity Summary (approvals only)	N/A deferred until AP action
❖ Administrative Reviews (Project Manager, ADRA) *(indicate date of each review)*	N/A deferred until AP action

N