CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-563

CHEMISTRY REVIEW(S)

NDA 21-563

Clarinex® (desloratadine) Syrup

Schering Corporation

Prasad Peri
Division of New Drug Chemistry II
Office of New Drug Chemistry

Division of Pulmonary and Allergy Drug Products

Table of Contents

Chemistry Review Data Sheet

1. NDA 21-563

2. REVIEW #: 1

3. REVIEW DATE: 07-May, 2003

4. REVIEWER: Prasad Peri

5. PREVIOUS DOCUMENTS:

Previous Documents	Document Date
Original	4-December 2002

6. SUBMISSION(S) BEING REVIEWED:

Original	4-December 2002

7. NAME & ADDRESS OF APPLICANT:

Name:	Schering Corporation
Address:	2000 Galloping Hill Road, Kenilworth, NJ 07033
Representative:	Joseph F. Lamendola, Ph.D. Vice President, Worldwide Regulatory Affairs
Telephone:	(908) 740 2628

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name: Clarinex® (desloratadine) Syrup
b) Non-Proprietary Name (USAN): Desloratadine
c) Code Name/# (ONDC only): N/A
d) Chem. Type/Submission Priority (ONDC only):

- Chem. Type: 3
- Submission Priority: P

9. LEGAL BASIS FOR SUBMISSION: N/A

10. PHARMACOL. CATEGORY: Peripheral H_1-receptor antagonist

11. DOSAGE FORM: Syrup

12. STRENGTH/POTENCY: 0.5 mg/mL

13. ROUTE OF ADMINISTRATION: Oral

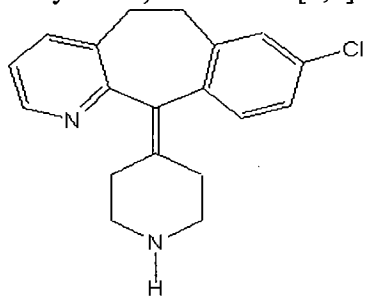
14. Rx/OTC DISPENSED: _X_ Rx ___ OTC

15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):
_____SPOTS product – Form Completed

___X___Not a SPOTS product

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

8-Chloro-6,11-dihydro-11-(4-piperdinylidene)-5*H*-benzo-[5,6]cyclohepta[1,2-b]pyridine



Molecular Formula: $C_{19}H_{19}ClN_2$
Molecular Weight: 310.8

Chemistry Review Data Sheet

17. RELATED/SUPPORTING DOCUMENTS:

A. Supporting DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE[1]	STATUS[2]	DATE REVIEW COMPLETED	COMMENTS[3]
[redacted]	III	[redacted]	[redacted]	3	Adequate*	11/5/99	D. Klein for [redacted] See CR1*
[redacted]	III	[redacted]	[redacted]	3	Adequate	11/5/98	C. Bertha for reformulated Claritin Syrup N20-641. See CR1
[redacted]	III	[redacted]	[redacted]	3	Adequate	4/30/96	C. Bertha for [redacted] for Claritin syrup. See CR1
[redacted]	IV	[redacted]	[redacted]	3	Adequate	1/11/01	K. Swiss for this NDA. See CR1
[redacted]	II	[redacted]	[redacted]	3	Adequate	1/11/01	K. Swiss for this NDA. See CR1
[redacted]	III	[redacted]	[redacted]	3	Adequate	1/23/01	K. Swiss for this NDA. See CR1
[redacted]	III	[redacted]	[redacted]	3	Adequate	1/23/01	K. Swiss for this NDA. See CR1
[redacted]	III	[redacted]	[redacted]	3	Adequate	1/11/01	K. Swiss for this NDA. See CR1
[redacted]	II	[redacted]	[redacted]	3	Withdrawn from NDA on 5/22/01	N/A	K. Swiss for this NDA. See CR1

* An update on the DMF reviews will be provided once NDA 21-300 CMC review is updated.

[1] Action codes for DMF Table:
1 – DMF Reviewed.
Other codes indicate why the DMF was not reviewed, as follows:
2 –Type 1 DMF
3 – Reviewed previously and no revision since last review
4 – Sufficient information in application
5 – Authority to reference not granted
6 – DMF not available
7 – Other (explain under "Comments")

[2] Adequate, Inadequate, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)
[3] Include reference to location in most recent CMC review

B. Other Supporting Documents:

Doc #	OWNER	ITEM REFERENCED	STATUS	DATE REVIEW COMPLETED	COMMENTS
NDA 21300	Schering	All CMC information	AE	18-October-2001	Chemistry DR Comments sent in letter dated Nov. 09, 2001. These comments have not been responded to yet.

Chemistry Review Data Sheet

18. CMC-RELATED REVIEWS:

CONSULTS	SUBJECT	DATE FORWARDED	STATUS/ REVIEWER	COMMENTS
Biometrics	All of this information is referenced in NDA21-300. All items are reviewed there.			
EES				
Pharm/Tox				
Biopharm				
LNC				
Methods Validation				
OPDRA				
EA				
Microbiology				

The Chemistry Review for NDA 21-563

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

Approvable from a CMC standpoint. CMC deficiencies listed for NDA 21-300 should be adequately responded to, before approval of this application. A Discipline Review deficiency letter for NDA 21-300, was sent to the applicant on Nov. 9, 2001. No response has been provided for this letter by the applicant as of today.

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable

None indicated so far.

II. Summary of Chemistry Assessments

A. Description of the Drug Product(s) and Drug Substance(s)

The following comments are imported from the CMC review of NDA 21-300 (Clarinex (desloratadine) Syrup. CMC information for this NDA is referenced to NDA 21-300. Establishment Evaluation System (EES) comments have been updated to reflect the current status.

Drug Substance

1). Schering references NDA 21-165 in total for desloratadine drug substance. Currently NDA (21-165) is approvable pending a satisfactory EER of the drug product-manufacturing site.

2). The drug substance manufacturing sites provided in NDA 21-165 are Schering Avondale ——— and Singapore : ——— . Schering Singapore ———) site has been withdrawn from the NDA in an amendment dated May 22, 2001.

3). An EER was sent on January 2, 2003 and is currently unacceptable for all Schering US sites. The Avondale (Ireland) drug substance manufacturing site has an acceptable OC recommendation on Jan 15, 2003 (based on profile).

Executive Summary Section

Drug Product

1). An EER was sent on January 2, 2003. The drug product manufacturing sites are currently under withhold status. An inspection is scheduled from May 19th to June 3 2003.

2). Drug product is an —— syrup dosage form, clear orange in color, presented in three container-closures: ¾ ounce amber glass —— bottle, 4 ounce amber glass —— bottle, and a 16 ounce amber glass —— bottle.

3). Schering provides — drug product batch with 24 month stability data and, — batches with 18 month stability data, all manufactured at 1/10 scale. Also provided are —— commercial scale batches (5500 L) with 6-9 months stability data.

4). The ¾ ounce amber glass —— bottle under accelerated stability conditions provides the highest drug product degradants after 6 months. The degradation data should be closely monitored in each review cycle for the ¾ ounce container-closure system. The applicant was asked to take appropriate action to reduce the degradants occurring in the ¾ oz bottle. The applicant has suggested that the degradants are higher here since the headspace to fill ratio is the highest for this presentation. Initial (5 week) experimental results support this theory and updated results will be needed to make a full assessment.

5). The biobatch is batch number IRQ-98-13M1 drug substance and batch number 75882-024B drug product.

6). Schering provides — batches of drug product with stability and release data from the Avondale drug substance manufacture. An additional drug product batch with stability and release data is provided with drug substance manufactured from Singapore.

7). An updated method validation package is being requested to pursue validation of the methods by the FDA labs. Similarly SAS transport files for the results obtained at 30°C/60% RH have been requested.

8). A Biometrics consult will be requested to evaluate the applicant proposed 24 months shelf life for the syrup once 30°C/60% RH stability data (in the SAS transport format) on a CD ROM are obtained from the applicant.

B. Description of How the Drug Product is Intended to be Used

The drug product is to be administered orally for patients 6 months to 2 years. NDA 21-300 is for patients 2 years and above.

C. Basis for Approvability or Not-Approval Recommendation

The application is approvable from a CMC perspective. A Discipline Review deficiency letter for NDA 21-300, was sent to the applicant on Nov. 9, 2001. No response has been provided for this letter by the applicant as of today.

III. Administrative

A. Reviewer's Signature

B. Endorsement Block

Chemist Name/Date: Same date as draft review
Chemistry Team Leader Name/Date
Project Manager Name/Date

C. CC Block

2 Page(s) Withheld

✓ § 552(b)(4) Trade Secret / Confidential

_____ § 552(b)(5) Deliberative Process

_____ § 552(b)(5) Draft Labeling

Withheld Track Number: Chemistry-1

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Prasad Peri
5/8/03 10:52:24 AM
CHEMIST

Guiragos Poochikian
5/8/03 04:12:11 PM
CHEMIST