CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-952

CHEMISTRY REVIEW(S)

NDA 21-952

Claritin® Liqui-Gels™ Capsules
(Loratadine 10 mg)

Schering-Plough HealthCare Products

Division of Non-Prescription Clinical Evaluation
(HFD-560)

Gene W. Holbert, Ph.D.

Office of New Drug Quality Assessment
Division of Premarketing Assessment II

Table of Contents

Chemistry Review Data Sheet

1. NDA 21-952

2. REVIEW #: 1

3. REVIEW DATE: 13-NOV-2006

4. REVIEWER: Gene W. Holbert, Ph.D.

5. PREVIOUS DOCUMENTS:

Previous Documents	Document Date

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
Original	15-MAR-2006
Amendment (BC)	06-NOV-2006

7. NAME & ADDRESS OF APPLICANT:

Name:	Schering-Plough HealthCare Products
Address:	556 Morris Avenue Summit, NJ 07901-1330
Representative:	Doreen Frank, Director, Regulatory Affairs
Telephone:	(908) 473-1655

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name: Claritin Liqui-Gels Capsules
b) Non-Proprietary Name (USAN): Loratadine
c) Code Name/# (ONDQA only):
d) Chem. Type/Submission Priority (ONDQA only):

- Chem. Type: 3
- Submission Priority: S

9. LEGAL BASIS FOR SUBMISSION: 505 (b) (1)

10. PHARMACOL. CATEGORY: Antihistamine

11. DOSAGE FORM: Capsules, liquid filled Code: 606

12. STRENGTH/POTENCY: 10 mg

13. ROUTE OF ADMINISTRATION: Oral Code: 001

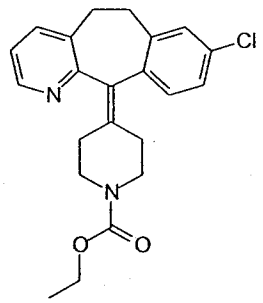
14. Rx/OTC DISPENSED: ___Rx __X__OTC

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:

Name: Ethyl 4-(8-chloro-5,6-dihydro-11*H*-benzo[5,6]cyclohepta[1,2-*b*]pyridine-11-ylidine)-1-piperidinecarboxylate



Molecular Formula: $C_{22}H_{23}ClN_2O_2$ Molecular Weight: 382.89 CAS: 79794-75-5

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17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	HOLDER	ITEM REFERENCED	CODE[1]	STATUS[2]	DATE REVIEW COMPLETED	COMMENTS
6626	Schering-Plough (Avondale)	Loratadine Drug Substance	3	Adequate	16-APR-2004 (Bart Ho, Ph.D.)	LOA Date: 10-OCT-2005
13032	Schering-Plough LTD (Singapore)	Loratadine Drug Substance	3	Adequate	16-APR-2004 (Bart Ho, Ph.D.)	LOA Date: 17-JAN-2006
18696	Cardinal Health	Loratadine Softgels (10 mg)	1	Adequate	19-OCT-2006 (G.W. Holbert, Ph.D.)	LOA Date: 30-AUG-2006
[redacted]			3	Adequate	04-APR-2002 (Jila Boal, Ph.D.)	LOA Date: 21-MAR-2005
			3	Adequate	22-MAY-2002 (Lorenzo Roca, Ph.D.)	LOA Date: 21-MAR-2005

b(4)

[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)

B. Other Documents:

DOCUMENT	APPLICATION NUMBER	DESCRIPTION
NDA	19-658	Claritin Tablet, 10 mg
NDA	21-891	Claritin Chewable Tablet, 5 mg
NDA	21-993	Claritin Reditabs, 5 mg, 12 h

18. STATUS:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Biometrics	N/A		
EES	Acceptable	05-OCT-2006	S. Ferguson
Pharm/Tox	N/A		
Biopharm	N/A		
OTC Drug Labeling	Tentatively adequate	16-AUG-2006	Cazemiro Martin
Methods Validation	N/A		
DDMAC	N/A		
EA	Categorical exclusion	16-SEP-2006	Gene W. Holbert
Microbiology	N/A		

The Chemistry Review for NDA 21-952

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

This product may be approved from a chemistry, manufacturing and controls perspective.

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

II. Summary of Chemistry Assessments

A. Description of the Drug Product and Drug Substance

Claritin® 10 mg LiquiGels™ Capsules are clear, blue liquid-filled soft gelatin capsules printed on one side with "C10" in white ink. Each capsule contains 10 mg of loratadine and the inactive ingredients caprylic/capric glycerides, FD&C blue #1, gelatin, glycerin, pharmaceutical ink, polysorbate 80, povidone, purified water and sorbitol.

The product is packaged in [redacted] blister film [redacted] with paper/aluminum foil lidding. Blister cards may be prepared in various count configurations and assembled in various quantities to create the finished product market presentations. Secondary packaging consists of a cardboard carton. b(4)

Claritin® 10 mg LiquiGels™ are manufactured by Cardinal Health. The manufacturing process consists of preparation of the capsule fill solution and manufacture of the [redacted] followed by a [redacted] process on specially designed equipment at Cardinal Health and described in Cardinal Health's DMF 18696. Raw material controls and manufacturing process controls are found in DMF 18696. b(4)

The drug product specification includes tests for Appearance, Loratadine Identity and Assay, Uniformity of Dosage Units, Fill Weight Variation, Related Substances, Specified and Unspecified Unknown Substances, Dissolution and Microbial Limits.

As amended, the application contains 18 months of long term stability data on 3 lots of product manufactured on a pilot scale by Cardinal Health. There were no significant changes in any of the lots stored at the long term, intermediate or accelerated condition. Based on this, a 24 month expiration date is granted when stored at 20-25°C (68-77°F) and protected from freezing.

Since this is an OTC product, there is no package insert. The labeling has been reviewed by the Division of Over-the-Counter Drug Products and found acceptable.

Loratadine, the drug substance, is a selective peripheral H_1-receptor antagonist with no significant effects on the central or autonomic nervous system and does not have the undesirable sedation and anticholinergic effects found with earlier antihistamines. Loratadine is currently marketed OTC in the U.S. in three monotherapy formulations, tablets, syrup and orally disintegrating tablets, and in two extended release formulations in combination with pseudoephedrine. Loratadine is marketed in over 100 countries worldwide either as prescription or over-the-counter drug products. There have been no product withdrawals in any country. Loratadine is manufactured by Schering-Plough in County Wicklow, Ireland (DMF 6626) or in Singapore (DMF 13032).

Information concerning the preparation of loratadine drug substance is contained in two Schering-Plough Drug Master Files, both of which have been reviewed several times and found adequate.

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

Claritin® 10 mg LiquiGels™ Capsules are indicated for temporary relief of symptoms of runny nose, itchy, watery eyes, sneezing and itching of the nose or throat, due to hay fever or other upper respiratory allergies. The dose for adults and children over 6 years of age is one capsule every 24 hours.

C. Basis for Approvability or Not-Approval Recommendation

Adequate controls for raw materials are in place. Manufacturing processes are robust and adequately controlled. Specifications are adequate to ensure the identity, strength, quality, purity and potency of the drug product. The container/closure system is adequate to protect the drug product. The product is stable over the proposed shelf life (24 months) when stored as labeled. Labeling is acceptable. Facilities inspections are complete and acceptable.

III. Administrative

A. Reviewer's Signature

Signed electronically in DFS

B. Endorsement Block

Gene W. Holbert, Ph.D./Date: 14-NOV-2006
Moo Jhong Rhee, Ph.D./Date: 29-NOV-2006

C. CC Block

Project Manager:	Elaine G. Abraham
ONDQA Project Manager:	Linda Mullins-Athey
Pharmaceutical Assessment Lead:	Shulin Ding
Biopharmaceutics:	Shinja Rhea Kim
Medical Officer:	Lolita Lopez
Pharmacologist:	Lawrence Sancilio
OND/ONP/DNRD:	Cazemiro Martin

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53 Page(s) Withheld

✓ Trade Secret / Confidential (b4)

_____ Draft Labeling (b4)

_____ Draft Labeling (b5)

_____ Deliberative Process (b5)

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/

Gene Holbert
11/29/2006 12:16:57 PM
CHEMIST

Moo-Jhong Rhee
11/29/2006 01:43:00 PM
CHEMIST
Chief, Branch III