

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

21-891

CHEMISTRY REVIEW(S)

NDA 21-891

**Children's Claritin
(Loratadine Tablet) Chewable, 5 mg
Schering – Plough HealthCare Products
Division of Nonprescription Drug Products**

Tarun Mehta, M.Sc.

ONDQA Pre Approval Marketing Division II, Branch III



Chemistry Review Data Sheet

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CHEMISTRY REVIEW

Chemistry Review Data Sheet

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1. NDA #: 21-891
2. REVIEW #: 1
3. REVIEW DATE: 25-May-2006
4. REVIEWER: Tarun Mehta
5. PREVIOUS DOCUMENTS: None

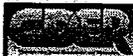
6. SUBMISSION(S) BEING REVIEWS:

<u>Submission(s) Reviewed</u>	<u>Document Date</u>
ORIGINAL	02-AUG-2005
AMENDMENT-2	27-JAN-2006
Meeting Minutes	16-FEB-2006
AMENDMENT-3	24-FEB-2006
AMENDMENT-6	14-MAR-2006
AMENDMENT-7	20-MAR-2006
AMENDMENT-9	03-MAY-2006
Telephone Con.	04-MAY-2006

7. NAME & ADDRESS OF APPLICANT:

Name: Schering-Plough HealthCare Products
Address: 3030 Jackson Ave
Memphis, TN 38151
Representative: Marry E. Williams, Associate Director Reg. Affairs
Telephone: 908-679-1952

8. DRUG PRODUCT NAME/CODE/TYPE:



CHEMISTRY REVIEW

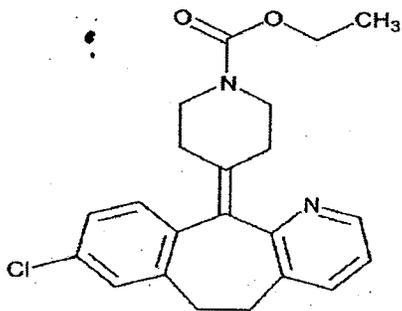


Chemistry Review Data Sheet

- a) Proprietary Name: Children's Claritin
b) Non-Proprietary Name (USAN): Loratadine Chewable Tablet
c) Code Name/# (ONDC only): NA
d) Chem. Type/Submission Priority (ONDC only):
• Chem. Type: 3
• Submission Priority: Standard
9. LEGAL BASIS FOR SUBMISSION: Not applicable
10. PHARMACOL. CATEGORY: Antihistamine
11. DOSAGE FORM: Chewable
12. STRENGTH/POTENCY: 5 mg
13. ROUTE OF ADMINISTRATION: Oral
14. Rx/OTC DISPENSED: Rx OTC
15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):
 SPOTS product – Form Completed
 Not a SPOTS product
16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA,
MOLECULAR WEIGHT:

Chemical Name: Loratadine, USP

Chemical Structure:



Molecular weight: 382.88

Molecular formula: $C_{22}H_{23}ClN_2O_2$

CHEMISTRY REVIEW

Chemistry Review Data Sheet

17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE ¹	STATUS ¹	DATE REVIEW COMPLETED	COMMENTS
6626	II	Schering-Plough Co. Rathdrum, Ireland	Loratadine drug substance	1	Adequate	14-APR-2006	Review for N 21-891 by Tarun Mehta
13032	II	Schering-Plough Co. Singapore	Loratadine drug substance	1	Adequate	14-APR-2006	Review for N 21-891 by Tarun Mehta
—	IV	—	—	3	Adequate	21-APR-2005	Reviewed for N 21-312
—	III	—	—	3	Adequate	06-JUN-2005	Review for N 20-145 by Raman Krishna
—	III	—	—	3	Adequate	11-JAN-2006	Review for NDA 21-058 by Dr. Tran, Soung.

¹ Action codes for DMF Table:

1 – DMF Reviewed.

Other codes indicate why the DMF is not review, as follows:

2 – Type I 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)

CHEMISTRY REVIEW

Chemistry Review Data Sheet

18. STATUS:

ONDQA:

CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
DMETS	Acceptable	5/23/06	Laura L. Pincock, Pharm.D.
EES	Acceptable (see attached end of this review, EES report)	5/24/06	Adams, Shawnte L

**APPEARS THIS WAY
ON ORIGINAL**

Chemistry Assessment Section

The Chemistry Review for NDA 21-891

The Executive Summary**I. Recommendations****A. Recommendation and Conclusion on Approvability**

From the Chemistry, Control, and Manufacturing standpoint, this NDA can be approved.

B. Recommendation on Phase 4 (Post-Marketing) Commitments

None

II. Summary of Chemistry Assessments**A. Description of the Drug Product(s) and Drug Substance(s)**

Children's Claritin 5mg is an OTC Chewable tablet and delivered 5mg of loratadine drug. Loratadine is marketed in three different dosage forms i.e. tablet, syrup and orally disintegrated tablet. Loratadine is used for the treatment of allergic rhinitis and chronic idiopathic urticaria. The dose for children 2 to 6 years of age is one tablet a day, the adult dose for 6 years and over is two 5mg tablets daily.

The drug product manufacture includes _____ procedure. Focus of formulation development was to achieve tablet with smooth chewable property and comparable hardness with pleasant taste. Drug product composition include compendial excipients. _____ is used as main (about % of tablet mass) _____ of drug product. There is no novel excipient used in formulation. Manufacturing process was finalized with _____ feasibility batches prior to the subject NDA stability batches.

The manufacturing process is controlled by in-process acceptance criteria, in-process specification and they are found to be adequate. Critical attributes such as tablet weight variation, hardness, and friability were monitored during the process.

Final drug product quality is monitored using detailed specification. Proposed finished product specifications such as tablet hardness, potency assay, dissolution and impurities

Individual specified known and unknown related substances are monitored according to ICH guideline at released as well as shelf life.

CHEMISTRY REVIEW TEMPLATE

Chemistry Assessment Section

The proposed container/closure system for the drug product is _____

Long-term stability data for up to 18 months on the drug product packaged in proposed _____ showed no significant change in drug quality. Data support the proposed expiration period of 24 months.

Schering Corporation, Ireland, manufactures Loratadine. The Chemistry, Manufacturing and Control information of the drug substance is described in Schering's DMF 6626 and 13032 and deemed adequate to support the NDA.

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

The recommended dosing schedule for CLARITIN 5mg Chewable tablets; children 2 to under 6 years of age, chew 1 tablet daily, not more than 1 tablet in 24 hours; adults and children 6 years and over, chew 2 tablets daily, not more than 2 tablets in 24 hours

The drug product storage condition is between 20-25°C (68 – 77°F).

C. Basis for Approvability

- Following submissions were reviewed for the NDA 21-891; Original submission, chemistry amendment-2, meeting minutes, amendment-3, amendment-6, amendment-7, and amendment-9 dated 27-JAN-2006, 16-FEB 2006, 24-FEB-2006, 14-MAR-2006, 20-MAR-2006, and 3-MAY -2006, respectively and they all provided satisfactory CMC information to assure the quality of the drug product.
- The final recommendations from the Office of Compliance for the drug product-manufacturing sites are **ACCEPTABLE** (see Attachment, page 53 of this NDA report).

III. Administrative

A. Reviewer's Signature: Electronically entered in the DFS

B. Endorsement Block:

Chemist Name/Date:	Tarun Mehta, M.Sc,
Branch Chief:	Moo-Jhong Rhee, Ph.D
Project Manager:	Elaine Abraham

Applicant submitted the following amendments during the review cycle:

- Stability Data , Amendment-2; 27-JAN-2006

Chemistry Assessment Section

- Meeting Minutes, 16-FEB-2006, justification for the limits of hardness ranges in stability specification.
- Section 3.2.P.5.4 (COA of Drug Substance Clinical Batches), Amendment-3; 24-FEB-2006
- Section 3.2.P.4.4 (COA of excipients); Amendment-6; 14-MAR-2006
- Hardness Testing Data on Children's Vitamin Tablets; Amendment-7; 20-MAR-2006
- Revised Released Dissolution Specification and commitment (Post approval) to revised shelf-life specification based on commercial batches results. (Amendment - 9, 03-May-2006)
- Telephone conference held on May 4, 2006 with applicant. Applicant commits to send dissolution sampling protocol for commercial batch. It will be submitted as post approval general corresponds.

**APPEARS THIS WAY
ON ORIGINAL**

50 Page(s) Withheld

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

 § 552(b)(4) Draft Labeling

 § 552(b)(5) Deliberative Process

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

/s/

Tarun Mehta
5/30/2006 12:28:43 PM
CHEMIST

Moo-Jhong Rhee
5/30/2006 04:01:49 PM
CHEMIST
Chief, Branch III