CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-375

PHARMACOLOGY REVIEW

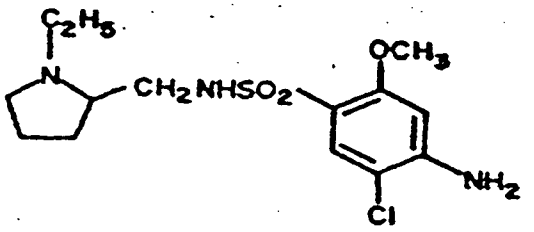
PHARMACOLOGY/TOXICOLOGY COVER SHEET

NDA number: 21-375
Review number: Original
Sequence number/date/type of submission: 8/23/01/Original
Information to sponsor: Yes ( ) No (X)
Sponsor and/or agent: Whitehall-Robins
Five Giralda Farms
Madison, NJ 07940
Manufacturer for drug substance: [redacted]

Reviewer name: Lawrence F. Sancilio
Division name: Division of Allergy and Pulmonary Drug Products
HFD #: 570
Review completion date: 6/12/02

Drug:

Trade name: Alevert and Dimetapp Allergy.
Generic name: Loratadine
Code name: Sch29851
Chemical name: Ethyl 4-(8-chloro-5,6-dihydro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11ylidene)-1-piperidinecarboxylate
CAS registry number: 79794-75-5
Mole file number: Unknown
Molecular formula/molecular weight: $C_{22}H_{23}ClN_2O_2$/382.89
Structure:



Relevant ANDA/DMFs: ANDA75822/DMFs [redacted]

Drug class: H_1 Receptor Antagonist

Indication: Treatment of the symptoms of allergic rhinitis.

Clinical formulation: [redacted] oral disintegrating tablet.

Ingredient	mg/tablet
Loratadine	10
Mannitol, USP	
Microcrystalline Cellulose, NF	
Crospovidone	
Aspartame, NF	
Sodium Bicarbonate, NF	
Citric acid,	
Magnesium Stearate, NF	
Colloidal Silicon Dioxide, NF	
Natural and Artificial Flavor.	

The levels of all the excipients and flavoring agents are at acceptable levels.

Route of administration: Oral; this tablet dissolves in the mouth.

Proposed use: As an over the counter (OTC) product to treat the symptoms due to seasonal allergic rhinitis in adults and in children aged 6 years and older at a daily oral dose of 10 mg.

This NDA is a 505(b)(2) application. Reference is made to ANDA 75,822 submitted by ESI Lederle for a prescription version of this same product.

Executive Summary

I. Recommendations

A. Recommendation on Approvability
Recommend approval.

B. Recommendation for Nonclinical Studies
None.

C. Recommendations on Labeling
None, since this is an over the counter product (OTC) which requires no preclinical data in the label.

II. Summary of Nonclinical Findings

A. Brief Overview of Nonclinical Findings
Loratadine is an approved prescription drug. Reference has been made to its profile in ANDA 75,822. There are no safety issues for potential adverse effects.

B. Pharmacologic Activity
Loratadine is a potent and selective H_1 receptor antagonist.

C. Nonclinical Safety Issues Relevant to Clinical Use
None.

III. Administrative

A. Reviewer signature: /S/
Lawrence F. Sancilio, Ph.D.

B. Supervisor signature: Concurrence - /S/
Ching-Long Joseph Sun, Ph.D.
Non-Concurrence - _____
(see memo attached)

C. cc: list:

TABLE OF CONTENTS - PHARMACOLOGY/TOXICOLOGY REVIEW

PHARMACOLOGY/TOXICOLOGY REVIEW

I. PHARMACOLOGY: NA.

Primary pharmacodynamics: NA.

Mechanism of action: NA.

Drug activity related to proposed indication: NA.

Secondary pharmacodynamics: NA.

Pharmacology summary: NA.

Pharmacology conclusions: NA.

II. SAFETY PHARMACOLOGY: NA.

Neurological effects: NA.

Cardiovascular effects: NA.

Pulmonary effects: NA.

Renal effects: NA.

Gastrointestinal effects: NA.

Abuse liability: NA.

Other: NA.

Safety pharmacology summary: NA.

Safety pharmacology conclusions: NA.

III. PHARMACOKINETICS/TOXICOKINETICS: NA.

PK parameters: NA.

Absorption: NA.

Distribution: NA.

Metabolism: NA.

Excretion: NA.

Other studies: NA.

PK/TK summary: NA.

PK/TK conclusions: NA.

IV. GENERAL TOXICOLOGY: NA.

Summary of individual study findings: NA.

Toxicology summary: NA.

Toxicology conclusions: NA.

V. GENETIC TOXICOLOGY: NA.

Summary of individual study findings: NA.

Genetic toxicology summary: NA.

Genetic toxicology conclusions: NA.

Labeling recommendations: NA.

VI. CARCINOGENICITY: NA.

Summary of individual study findings: NA.

Carcinogenicity summary: NA.

Carcinogenicity conclusions: NA.

Labeling Recommendations: NA.

Addendum/appendix listing: NA.

VII. REPRODUCTIVE AND DEVELOPMENTAL TOXICOLOGY: NA.

Summary of individual study findings: NA.

Reproductive and developmental toxicology summary: NA.

Reproductive and developmental toxicology conclusions: NA.

Labeling recommendations: NA.

VIII. SPECIAL TOXICOLOGY STUDIES: NA.

Summary of individual study findings: NA

IX. DETAILED CONCLUSIONS AND RECOMMENDATIONS: NA

Conclusions: Loratadine is a potent orally active and selective H_1 receptor antagonist.
From a preclinical standpoint, there are no safety or toxicity issues that would prevent loratadine from being an OTC product. The levels of the excipient components of the proposed tablet are acceptable.

Recommendation: Approval of NDA 21-375.

Labeling with basis for findings: None.

X. APPENDIX/ATTACHMENTS: NA

Addendum to review: NA.

Other relevant materials (Studies not reviewed, appended consults, etc.): NA.

Any compliance issues: NA.

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

/s/

Lawrence Sancilio
6/12/02 04:28:01 PM
PHARMACOLOGIST

Joseph Sun
6/13/02 11:59:55 AM
PHARMACOLOGIST
I concur.