CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-512

PHARMACOLOGY REVIEW(S)

PHARMACOLOGY/TOXICOLOGY COVER SHEET

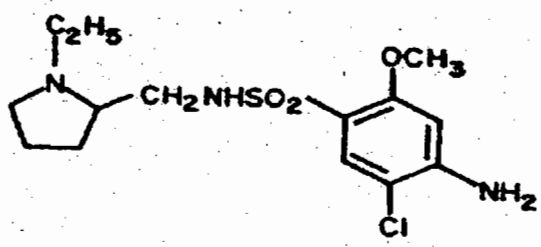
NDA number: 21-512
Review number: Original
Sequence number/date/type of submission: 6/28/02/Original
Information to sponsor: Yes ( ) No (X)
Sponsor and/or agent: Perrigo
515 Eastern Ave.
Allergan, Michigan 49010

Manufacturer for drug substance:
Perrigo
515 Eastern Ave.
Allergan, Michigan 49010

Reviewer name: Lawrence F. Sancilio, Ph.D.
Division name: Division of Allergy and Pulmonary Drug Products
HFD #: 570
Review completion date: 11/06/02

Drug:

Trade name: —
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: 76-301

Drug class: H_1 Receptor Antagonist

Indication: —

Clinical formulation: Tablet.

Ingredient	mg/tablet
Loratadine Lactose Monohydrate, NF Pregelatinized Starch,, NF Povidone, USP Magnesium Stearate, NF	/

The levels of all the excipients have been used in marketed products.

Route of administration: Oral.

Proposed use: —————

This NDA was submitted as a 505 (b)(2).

Executive Summary

I. Recommendations

A. Recommendation on Approvability
Recommend approval.

B. Recommendation for Nonclinical Studies
None.

C. Recommendations on Labeling
None, since this will be 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. 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: _____
Lawrence F. Sancilio, Ph.D.

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

TABLE OF CONTENTS - PHARMACOLOGY/TOXICOLOGY REVIEW

HARMACOLOGY/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.44

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 excipients in the proposed tablet are acceptable.

Recommendation: Approval of NDA 21-512.

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
4/16/03 02:27:05 PM
PHARMACOLOGIST

Joseph Sun
4/16/03 04:40:33 PM
PHARMACOLOGIST
I concur.