

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

21-891

PROPRIETARY NAME REVIEW(S)

OTC Drug Labeling Review

Division of Over-The-Counter Drug Products (HFD-560)

Center for Drug Evaluation and Research • Food and Drug Administration

NDA Addendum Labeling Review

NDA # 21-891, S-000

Submission Date: 3/30/06

Review Date: 5/30/06

Applicant: Schering-Plough HealthCare Products
556 Morris Avenue
Summit, NJ 07901-1330
(908) 473-1784

Applicant's Representative: Mary Pierro
Regulatory Affairs Manager

Drug: Claritin Chewable Tablets; Grape Flavor
Loratadine Tablet (Chewable), 5 mg

Pharmacologic Category: Antihistamine

Submitted: Revised draft labeling and annotated specifications provided for:

- 2-count Sachet
- 5- and 10-count carton
- Bi-fold card and bi-fold card tray

Background:

On March 23, 2006, the Division of Medication Errors and Technical Support (DMETS) sent a memo to the Dr. Andrea Leonard-Segal, Director of the Division of Nonprescription Clinical Evaluation in the Office of Nonprescription Products, in response to the Division's request that DMETS review the sponsor's proprietary name for the proposed Children's Claritin (allergy) SKU.

Reviewer comment:

Based on the comments and recommendations included in the DMETS memo concerning the proprietary name and statement of identity that appear on the PDP of this product, addendum labeling review comments are as follows.

- a. Concur with DMETS comment that the proposed proprietary name for the product line is "Children's Claritin" and not "Children's ~~Allergy~~ Allergy". Accordingly, the sponsor must relocate the red flag statement "Allergy" that appears on the PDP of the 5- and 10-count SKU, 2-count sachet, and the bi-fold card and bi-fold card tray. This reviewer recommends that the red flag statement "Allergy" appear immediately below the statement of identity on the PDP.
- b. Concur with DMETSs comment that the term "chewable" should appear as part of the statement of identity wherever is it stated for this proposed product.

According to the review chemist, because the term "chewable" is not yet an official USP compendial dosage form, this term must appear in parenthesis after the word "tablet" as part of

the statement of identity for this proposed drug product. The revised established name must read as follows: "Loratadine Tablets (Chewable) 5 mg/ Antihistamine"

Recommendations:

Inform the sponsor to revise the 5- and 10-count carton, 2-count sachet, and the bi-fold card and bi-fold card tray labeling as follows:

1. Because the red flag "Allergy" is not considered part of the proprietary name for this SKU, the sponsor must relocate the term "Allergy" to appear immediately below the established name of this drug product on the PDP.
2. For accurate and complete labeling, the sponsor must revised the establish name for this SKU to read as follows: "Loratadine Tablets (Chewable) 5 mg/ Antihistamine"
3. Resubmit the 5- and 10-count carton, 2-count sachet, and the bi-fold card and bi-fold card tray labeling for Agency review and prior approval before submitting final printed labeling.

Cazemiro R. Martin
Reg. Review Chemist/IDS

Concur: Marina Chang, R.Ph.
Team Leader

**This is a representation of an electronic record that was signed electronically and
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/s/

Cazemiro Martin
5/30/2006 10:57:50 AM
INTERDISCIPLINARY

Marina Chang
5/30/2006 11:14:21 AM
INTERDISCIPLINARY

The recommended dose of Loratadine for children from 2 years to 6 years of age is 5 mg taken once daily, and the dose for children and adults 6 years of age and older is 10 mg taken once daily. Loratadine has an approved nonprescription drug monograph.

II. RISK ASSESSMENT:

The medication error staff of DMETS conducted a search of several standard published drug product reference texts^{1,2} as well as several FDA databases^{3,4} for existing drug names which sound-alike or look-alike to Children's Claritin to a degree where potential confusion between drug names could occur under the usual clinical practice settings. A search of the electronic online version of the U.S. Patent and Trademark Office's Text and Image Database was also conducted⁵. The Saegis⁶ Pharma-In-Use database was searched for drug names with potential for confusion. An expert panel discussion was conducted to review all findings from the searches. In addition, DMETS conducted three prescription analysis studies for each proposed name consisting of two written prescription studies (inpatient and outpatient) and one verbal prescription study, involving health care practitioners within FDA. This exercise was conducted to simulate the prescription ordering process in order to evaluate potential errors in handwriting and verbal communication of the name.

A. EXPERT PANEL DISCUSSION (EPD)

An Expert Panel discussion was held by DMETS to gather professional opinions on the safety of the proprietary name, Children's Claritin. Potential concerns regarding drug marketing and promotion related to the proposed name were also discussed. This group is composed of DMETS Medication Errors Prevention Staff and representation from the Division of Drug Marketing, Advertising, and Communications (DDMAC). The group relies on their clinical and other professional experiences and a number of standard references when making a decision on the acceptability of a proprietary name.

1. DDMAC has no objections to the tradename "Children's Claritin" from a promotional perspective.
2. The Expert Panel identified three proprietary names that were thought to have the potential for look-alike confusion with Children's Claritin. These products are listed in Table 2 (page 4), along with the dosage forms available and usual dosage.

¹ MICROMEDEX Integrated Index, 2006, MICROMEDEX, Inc., 6200 South Syracuse Way, Suite 300, Englewood, Colorado 80111-4740, which includes all products/databases within ChemKnowledge, DrugKnowledge, and RegsKnowledge Systems.

² Facts and Comparisons, online version, Facts and Comparisons, St. Louis, MO.

³ AMF Decision Support System [DSS], the Division of Medication Errors and Technical Support [DMETS] database of Proprietary name consultation requests, New Drug Approvals 98-06, and the electronic online version of the FDA Orange Book.

⁴ Phonetic and Orthographic Computer Analysis (POCA)

⁵ WWW location <http://www.uspto.gov/tmdb/index.html>.

⁶ Data provided by Thomson & Thomson's SAEGIS™ Online Service, available at www.thomson-thomson.com

Table 2: CHILDREN'S CLARITIN: Potential Sound-Alike/Look-Alike Names Identified by DMETS Expert Panel

Product Name	Dosage form(s), Established name	Usual adult dose	Other
Children's Claritin	Loratadine Chewable Tablets, 5 mg Oral Suspension, 5 mg/mL Syrup, 5 mg/mL Redi-Tabs (Orally Disintegrating Tablets), 5 mg	Children 2 years to 6 years of age: 5 mg orally once daily Children and Adults 6 years and over: 10 mg orally once daily	SA
Clarinetx Rx Only	Desloratadine Oral Syrup: 0.5 mg/mL Tablets: 5 mg Redi-Tabs (Orally Disintegrating Tablets): 2.5 mg	Adults including the elderly, adolescents, and children > 12 years: 5 mg once daily. Children 6—11 years: 2.5 mg once daily, administered as oral syrup. Children 1—5 years: 1.25 mg once daily, administered as oral syrup. Infants 6—11 months: 1 mg once daily, administered as oral syrup. Infants < 6 months: Not recommended.	LA
Claravis Rx Only	Isotretinoin Capsules: 10 mg, 20 mg, 40 mg	Adults and adolescents > 12 years: 0.5—1 mg/kg/day given in 2 divided doses for 15—20 weeks or until the total cyst count decreases by 70% if this occurs sooner than 15—20 weeks. Once daily dosing is not recommended.	LA
*Frequently used, not all-inclusive **LA (look-alike), SA (sound-alike)			

B. PRESCRIPTION ANALYSIS STUDIES

1. Methodology:

Three separate studies were conducted within the Centers of the FDA for the proposed proprietary names to determine the degree of confusion of Children's Claritin with marketed U.S. drug names (proprietary and established) due to similarity in visual appearance with handwritten prescriptions or verbal pronunciation of the drug name. The set of studies (i.e., inpatient, outpatient, and verbal study for each name) employed a total of 124 health care professionals (pharmacists, physicians, and nurses). This exercise was conducted in an attempt to simulate the prescription ordering process. An inpatient order and outpatient prescription were written, each consisting of a combination of marketed and unapproved drug products and a prescription for Children's Claritin (see page 5). These prescriptions were optically scanned and one prescription was delivered to a random sample of the participating health professionals via e-mail. In addition, the outpatient orders were recorded on voice mail. The voice mail messages were then sent to a random sample of the participating health professionals for their interpretations and review. After receiving either the written or verbal prescription orders, the participants sent their interpretations of the orders via e-mail to the medication error staff.

HANDWRITTEN PRESCRIPTION	VERBAL PRESCRIPTION
<p>Outpatient RX:</p> <p>Children's Claritin #20 chew 1 tablet</p>	<p>"Children's Claritin, dispense #20, chew 1 tablet daily..."</p>
<p>Inpatient RX:</p> <p>Children's Claritin - chew 1 tab QD</p>	

2. Results for Children's Claritin:

None of the interpretations of the proposed name overlap, sound similar, or look similar to any currently marketed U.S. product other than the current Children's Claritin product line. The majority of misinterpretations were misspelled/phonetic variations of the name, Children's Claritin. See Appendix A (page 7) for the complete listing of interpretations from the verbal and written studies.

C. ADVERSE EVENT REPORTING SYSTEM (AERS)

Since the name "Children's Claritin" is currently marketed, DMETS searched the FDA Adverse Event Reporting System (AERS) for medication errors associated with the currently marketed Children's Claritin products. The preferred terms "overdose", "accidental overdose", "pharmaceutical product complaint", "treatment noncompliance", "medication error", "Underdose", "accidental exposure", "intercepted medication error", "circumstance or information capable of leading to medication error", and "drug prescribing error" were used. The higher level terms "medication errors due to accidental exposures" and "maladministrations" were used. DMETS retrieved no reports of post-market confusion with the nomenclature, label, and labeling of Children's Claritin.

D. SAFETY EVALUATOR RISK ASSESSMENT

In reviewing the proprietary name Children's Claritin, the primary concerns identified from the Expert Panel related to look-alike and sound-alike confusion with Claravis, Clarinex, and the Children's Claritin product line. DMETS' search of the AERS database found no reports of confusion with the current Children's Claritin product line, Claravis, and Clarinex, so the names were not reviewed further for potential confusion as a result of visual or spoken similarity.

DMETS conducted prescription studies to simulate the prescription ordering process. In this case, there was no confirmation that the proposed name could be confused with any of the aforementioned names. The results of these studies show that the majority of misinterpretations were misspelled/phonetic variations of Children's Claritin.

A search of the AERS database retrieved no reports of post-market confusion with the nomenclature, label, and labeling of Children's Claritin. However, with the introduction of the chewable tablets to the product line, a potential source of confusion may be if the consumer is unaware that there are several formulations with different dosing recommendations that exist for children.

Additionally, the consumer may not be aware that Claritin Redi-Tabs (orally disintegrating tablets) are not the same product as the "chewable" tablets. Hence, it is possible that the two tablet formulations may be confused, which would result in the patient getting the wrong dose of Claritin. The proposed chewable tablet will be available as a 5 mg tablet with the usual dose of 5 mg once daily for ages 2-6 years and 10 mg once daily for age 6 years and up; whereas the Redi-Tabs are available as a 10 mg strength and the usual dose is 10 mg once daily for ages 6 years and up. DMETS is primarily concerned with the possibility of the 10 mg Redi-Tabs, intended for ages 6 years and older, being inadvertently administered instead of the 5 mg chewable tablet to a younger child by a parent/caregiver. However, one deterrent in this possible scenario is that the carton labeling for the Redi-Tabs only provides the dosing information for children over 6 years of age and recommends to "ask a doctor" for dosing instructions under 6 years old. Furthermore, both formulations state the intended age group on the principal display panel of the product. For example, "5 mg" is stated on the chewable tablets and "ages 6 years and older" is stated on the Redi-Tabs which may help to differentiate between the two tablet formulations. DMETS is not able to ascertain the clinical significance of a patient receiving the 10 mg dose rather than a 5 mg dose. Although, DMETS has no objections to the use of the proprietary name, Children's Claritin, for the chewable tablets, we recommend that educational measures be taken to emphasize the difference between the pediatric formulations and dosing recommendations for the different age groups. This plan should be executed before and after product launch.

III. LABELING, PACKAGING, AND SAFETY RELATED ISSUES

DMETS has reviewed the proposed container labels and carton labeling for Children's Claritin in an attempt to focus on safety issues to prevent possible medication errors. We have identified the following areas of possible improvement, which might minimize potential user error.

A. GENERAL COMMENTS

1. Post-marketing experience has shown when a new formulation of an existing drug product is launched, confusion and errors occur. DMETS recommends that the sponsor create and implement a plan for the education of healthcare professionals and consumers about the difference between the available Claritin pediatric formulations and dosing recommendations for the different age groups. This plan should be executed before and after product launch.
2. The front panel of the submitted labels and labeling is extremely busy with distracting graphics such as the bright and colorful display of balloons, clouds, tablet, and grapes in its layout. DMETS recommends removing these graphics or revising so that it is not more prominent than the drug names, established name, and strength.

3. The established name appears less than ½ the size of the proprietary name. Increase the prominence of the established name on all labels and labeling so that it is at least ½ the size of the proprietary name in accordance with 21 CFR 201.10(g)(2). Additionally, the white text font used on a fading blue background is difficult to read. Use contrasting color to increase readability.
4. The term “chewable” should appear following the established name on all labels and labeling.
5. The strength of the product (5 mg) is difficult to read with the white text on fading blue background. We recommend the use of contrasting color to increase readability. Additionally, the strength should be featured more prominently than the net quantity of the package size. Currently the net quantity (2 chewable tablets, 5 chewable tablets, or 10 chewable tablets) is bolded while the text of the actual strength appears smaller. Revise to increase visibility of the strength.

B. CARTON LABELING (2 count, 5 count, and 10 count packages)

1. See General Comments A1 through A5.
2. The term “New!” may appear on the carton labeling not to exceed a period of 6 months.

C. CONTAINER LABELS (Blister Version 1 and Blister Version 2)

1. See General Comments A1 through A5.
2. Each version of the blisters should be labeled with the strength per tablet (i.e., 5 mg per tablet or 5 mg/tablet) in addition to the lot number, expiration date, and number of tablets per blister. Revise accordingly.

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ON ORIGINAL**

Appendix A: Children's Claritin

Outpatient	Voice	Inpatient
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CHILDREN'S CLARITIN	Children's Claritin	Children's Claritin
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/s/

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5/23/2006 11:46:53 AM
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5/23/2006 12:17:07 PM
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CONSULTATION RESPONSE
DIVISION OF MEDICATION ERRORS AND TECHNICAL SUPPORT
OFFICE OF DRUG SAFETY
(DMETS; WO22, Mail Stop 4447)

DATE RECEIVED: January 9, 2006	DESIRED COMPLETION DATE: March 31, 2006	ODS CONSULT #: 06-0013
DOCUMENT DATE: August 2, 2005	PDUFA DATE: June 3, 2006	

TO: Andrea Leonard-Segal, M.D., Director
Division of Nonprescription Clinical Evaluation

THROUGH: Linda Kim-Jung, Pharm.D., Team Leader
Denise Toyer, Pharm.D., Deputy Director
Carol Holquist, R.Ph., Director
Division of Medication Errors and Technical Support

FROM: Laura L. Pincock, Pharm.D., Safety Evaluator
Division of Medication Errors and Technical Support

PRODUCT NAME: **Children's Claritin**
(Loratadine Tablets) Chewable
5 mg

NDA #: 21-891

NDA SPONSOR: Schering Plough Consumer Healthcare

RECOMMENDATIONS:

1. DMETS has no objections to use of the proprietary name, Children's Claritin, for the chewable tablet formulation. This is considered a final decision. However, if the approval of this application is delayed beyond 90 days from the signature date of this document, the name must be re-evaluated. A re-review of the name prior to NDA approval will rule out any objections based upon approvals of other proprietary and established names from the signature date of this document.
2. DMETS recommends implementation of the comments outlined in Section III of this review in order to minimize potential errors with the use of this product.
3. DDMAC finds the proprietary name "Children's Claritin" acceptable from a promotional perspective.

DMETS would appreciate feedback of the final outcome of this consult. We would be willing to meet with the Division for further discussion, if needed. If you have further questions or need clarifications, please contact Diane Smith, project manager, at 301-796-0538.