CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-996

PROPRIETARY NAME REVIEW(S)

CONSULTATION RESPONSE

DIVISION OF MEDICATION ERRORS AND TECHNICAL SUPPORT
OFFICE OF EPIDEMIOLOGY AND SURVEILLANCE
(DMETS; WO 22, STOP: 4447)

DATE RECEIVED: June 1, 2006 **DATE OF DOCUMENT:** May 24, 2006	**DESIRED COMPLETION DATE:** September 1, 2006 **PDUFA DATE:** December 1, 2006	**OSE REVIEW #:** 06-0096-1

TO: Janice Soreth, MD
Director, Division of Anti-Infective and Ophthalmology Products, HFD-520

THROUGH: Alina Mahmud, RPh., MS, Team Leader
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Division of Medication Errors and Technical Support, HFD-420

FROM: Linda M. Wisniewski, RN, Safety Evaluator
Division of Medication Errors and Technical Support, HFD-420

PRODUCT NAME:	**NDA SPONSOR: Alimera Sciences, Inc.**
Alaway (Ketotifen Fumarate Ophthalmic Solution) 0.025% **NDA#: 21-996**	

RECOMMENDATIONS:

1. DMETS has no objections to the use of the proprietary name, Alaway from a safety perspective, but believes the name is promotional. It implies that all symptoms of allergies will be gone. 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 will rule out any objections based upon approval of other proprietary or established names from the signature date of this document.
2. DMETS recommends implementation of the label and labeling revisions outlined in section III of this review to minimize potential errors with the use of this product.
3. DDMAC is unable to provide comments on the proposed trade name "Alaway," as this is an over-the-counter drug product.

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.

Division of Medication Errors and Technical Support (DMETS)
Office of Surveillance and Epidemiology
WO 22, STOP: 4447
Center for Drug Evaluation and Research

PROPRIETARY NAME REVIEW

DATE OF REVIEW: June 22, 2006

NDA#: 21-996

NAME OF DRUG: **Alaway**
(Ketotifen Fumarate Ophthalmic Solution)
0.025%

NDA HOLDER: Alimera Sciences, Inc.

I. INTRODUCTION:

This consult was written in response to a request from the Division of Anti-Infective and Ophthalmology Products (HFD-520), for assessment of the proprietary name, Alaway, regarding potential name confusion with other proprietary or established drug names. The sponsor has submitted a 505(b)(2) application to switch Zaditor from Rx to over-the-counter status. DMETS previously reviewed the proposed name, — for this NDA, and found it unacceptable in ODS Consult# 05-0096, dated May 31, 2006, due to potential similarity to the currently marketed product of the same name, —. Draft container labels, carton and insert labeling were provided for review and comment at this time.

PRODUCT INFORMATION

Alaway is an ophthalmic solution containing 0.025% ketotifen fumarate. It is antihistamine and allergy response preventer. It is an over-the-counter product used for the temporary prevention and relief of itchy eyes due to allergies caused by ragweed, pollen, grass, animal dander, and hair. The dosing regimen is one drop in the affected eye(s) twice daily. It will be supplied as a sterile solution in 10 mL containers.

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] for existing drug names which sound-alike or look-alike to Alaway 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 conducted[4]. The Saegis[5] Pharma-In-Use database was

[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], Drugs@FDA, the Division of Medication Errors and Technical Support [DMETS] database of Proprietary name consultation requests, and the electronic online version of the FDA Orange Book.

[4] WWW location http://www.uspto.gov/tmdb/index.html.

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 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 Alaway. 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 is unable to provide comments on the proposed trade name "Alaway," as this is an over-the-counter drug product.

2. The Expert Panel identified two proprietary names that were thought to have the potential for confusion with Alaway from a safety perspective. These products are listed in Table 1 (see below), along with the dosage forms available and usual dosage.

Table 1: Potential Sound-Alike/Look-Alike Names Identified by DMETS Expert Panel

Product Name	Dosage form(s), Established name	Usual adult dose*	Other**
Alaway	Ketotifen Fumarate Ophthalmic Solution	One drop in the affected eye twice daily.	NA
Alamag	Aluminum Hydroxide/Magnesium Hydroxide Oral Suspension: 225 mg/200 mg	Oral Suspension: 5 mL to 20 mL four times a day with a maximum OTC dose of 80 mL/day.	LA
	Chewable Tablets: 300 mg/150 mg	Tablets: one to four tablets orally as needed, up to 16 tablets a day.	
Alamag Plus	Aluminum Hydroxide/Magnesium Hydroxide/Simethicone Oral Suspension: 225 mg/200 mg/25 mg	10 ml to 20 mL between meals, at bedtime, or as directed by a physician.	
	Chewable Tablets: 200 mg/200 mg/25 mg	Two to four tablets orally between meals, at bedtime, or as directed by a physician.	

*Frequently used, not all-inclusive.
**L/A (look-alike)

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

B. PRESCRIPTION ANALYSIS STUDIES

1. Methodology:

Three separate studies were conducted within the Centers of the FDA for the proposed proprietary name to determine the degree of confusion of Alaway 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. These studies employed a total of 122 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 prescriptions were written, each consisting of a combination of marketed and unapproved drug products and a prescription for Alaway (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
Outpatient RX: Alaway 0.025% #1 Instill 1 drop into affected eye(s) bid	Alaway 0.025% Dispense #1 1 drop into affected eye twice daily.
Inpatient Rx: Alaway 0.025% Instill 1 drop into affected eye bid	

2. Results:

None of the interpretations of the proposed name overlap, sound similar, or look similar to any currently marketed U.S. product. See Appendix A for the complete listing of interpretations from the verbal and written studies.

C. SAFETY EVALUATOR RISK ASSESSMENT

In reviewing the proprietary name, the primary concerns relating to look-alike confusion with Alaway are Alamag and Alamag Plus.

DMETS also 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. However, negative findings are not predicative as to what may occur once the drug is widely prescribed, as these studies have limitations primarily due to a small sample size. The majority of misinterpretations were misspelled/phonetic variations of the proposed name, Alaway.

Alamag and Alamag Plus were identified as names with potential look-alike similarities to Alaway. The Alamag product line consists of Alamag and Alamag Plus. For the purposes of this review, only the name Alamag will be evaluated since there is the possibility that the modifier, Plus, could be omitted resulting in an order for Alamag. Alamag is indicated in the treatment of gastrointestinal conditions such as heartburn, dyspepsia, and sour stomach, associated with gastrointestinal gas.

The orthographic similarities of this name pair stem from the beginning same three letters (Ala) and ending letters (way vs. mag) that may look similar when scripted. These similarities are a result of letters that each have three loops/humps (w vs. m) followed by letters that look similar when scripted (ay vs. ag). Despite some orthographic similarities, there are some differentiating product characteristics that may help to minimize confusion involving this name pair. They include dose (one drop vs. 5 mL to 20 mL and one to four tablets), frequency of administration (twice daily vs. four times a day as needed), strength (0.025% vs. 225 mg/200 mg, 300 mg/150 mg), route of administration (ophthalmic vs. oral), and dosage form (ophthalmic solution vs. oral suspension and chewable tablets). However, Alaway is supplied in one strength and has one dosing regimen, which means this information may be omitted from an order. Prescriptions could be written with a general direction of use, such as 'use as directed'. Despite this, an order for Alamag would most likely include, at a minimum, the dosage form, strength, dose, and frequency of administration because Alamag is supplied in multiple dosage forms and has multiple dosing regimens. This additional information would help to differentiate these two products when ordered.

Although DMETS has no objections to the use of the proprietary name, Alaway from a safety perspective, we believe that the name is promotional. It implies that all symptoms of allergies will be gone.

Alamag
Alaway

III. LABELING, PACKAGING, AND SAFETY RELATED ISSUES

In the review of the container labels, carton and insert labeling of Alaway, DMETS focused on safety issues relating to possible medication errors. DMETS has identified the following areas of improvement, which might minimize potential user error.

A. GENERAL COMMENTS

1. The proprietary name appears in a scripted font which is difficult to read and large in size. Additionally, the established name and strength are miniscule in comparison. Revise so that the established name and strength has a commensurate prominence as the proprietary name.

2. In the Directions section, revise the statement 'put 1 drop in the affected eye(s) twice daily' to include the appropriate dosing interval, for example, 'put 1 drop in the affected eye(s) twice daily, at least 8 hours apart, at least 12 hours apart, etc.'. Additionally, the side panel is too small to incorporate these directions; therefore, we recommend that the directions for use be relocated to the back panel.

B. CONTAINER LABEL

1. See GENERAL COMMENTS A1 and A2.

2. Relocate the established name and dosage form to follow the proprietary name and increase the prominence.

3. Revise the wording '*Directions*' to read 'Directions for use".

4. Include the appropriate age group in the directions for use: 'Adults and children 3 years and older: put 1 drop in the affected eye(s) twice daily' and revise to include time between dosing.

C. CARTON LABELING

1. See GENERAL COMMENTS A1, A2 and comment B3.

2.

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6.

7.

APPEARS THIS WAY
ON ORIGINAL

[6] www.m-w.com (accessed 07/02/06).

Appendix A:

OSE Review 06-0096-1 Alaway

Verbal	Inpatient Written	Outpatient Written
Alloway	Alawarz	Alaway
Alloway	Alaway	Alaway
Aloay	Alaway	Alaway
Aloway	Alaway	Alaway
Aloway	Alaway	Alaway
Aluvale	Alaway	Ataway
	Alaway	Ataway
	Alaway	Ataway
	Alaway	Haway
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/s/

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9/1/2006 08:09:58 AM
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Also signing for Carol Holquist, Director DMETS, in her absence