CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22-221

OTHER REVIEW(S)

REGULATORY PROJECT MANAGER LABELING REVIEW (PHYSICIAN LABELING RULE)

Division of Anti-Infective and Ophthalmology Products

Application Number: N 22-221

Name of Drug: Akten™ (lidocaine hydrochloride) Ophthalmic Gel, 3.5%)

Applicant: Akorn, Inc.

Material Reviewed:

Submission Date(s): June 29, 2007

Receipt Date(s): August 2, 2007

Submission Date of Structure Product Labeling (SPL): June 29, 2007

Type of Labeling Reviewed: PLR and SPL versions of the label

Background and Summary

This review provides a list of revisions for the proposed labeling that should be conveyed to the applicant. These comments are based on Title 21 of the Code of Federal Regulations (201.56 and 201.57), the preamble to the Final Rule, Guidance(s), and FDA recommendations to provide for labeling quality and consistency across review divisions. When a reference is not cited, consider these comments as recommendations only.

Review

The following labeling issues have been identified in the PLR proposed label:

1. In the **HIGHLIGHTS OF PRESCRIBING INFORMATION** section –

    a. Under **INDICATIONS AND USAGE** – an extra bullet should be removed.

    b. Under **CONTRAINDICATIONS** – an extra bullet should be removed.

The following labeling issues have been identified in the SPL proposed label:

1. In the **HIGHLIGHTS OF PRESCRIBING INFORMATION** section –

    a. The acronym "hcl" should be completely spelled out as "hydrochloride" after the trade name.

    b. Under **INDICATIONS AND USAGE** – an extra bullet should be removed.

    c. Under **CONTRAINDICATIONS** – an extra bullet should be removed.

Recommendations

The above listed recommendations will be conveyed to the sponsor via email and a copy of the email will be saved in the Division File System (DFS).

Jane A. Dean, RN, MSN
Regulatory Health Project Manager

Supervisory Comment/Concurrence:

Maureen Dillon-Parker
Chief, Project Management Staff

Drafted: JAD/April 9, 2008
Revised/Initialed:
Finalized:
Filename: \\cdsnas\daaodps1\Dean\NDAs\NDA22-221\PM_Label_Review_PLR.doc
CSO LABELING REVIEW OF PLR FORMAT

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

/s/

Jane Dean
4/22/2008 06:52:00 PM
CSO

Maureen Dillon-Parker
4/24/2008 04:16:03 PM
CSO
NDA 22-221/Labeling Review - AKTEN

Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Surveillance and Epidemiology

Date:	March 27, 2008
To:	Wiley Chambers, MD, Acting Director Division of Anti-Infective and Ophthalmology Products
Thru:	Kellie Taylor, PharmD, MPH, Team Leader Denise Toyer, PharmD, Deputy Director Division of Medication Error Prevention
From:	Judy Park, PharmD, Safety Evaluator Division of Medication Error Prevention
Subject:	Labeling Review
Drug Name(s):	Akten™ (Lidocaine Hydrochloride) Ophthalmic Gel 3.5%
Application Type/Number:	NDA 22-221
Applicant/Applicant:	Akorn, Inc.
OSE RCM #:	2007-1673

CONTENTS

EXECUTIVE SUMMARY

The results of the Label and Labeling Risk Assessment found that the presentation of information and design of the proposed container labels and carton labeling appears to be vulnerable to confusion that could lead to medication errors. DMETS believes the risks we have identified can be addressed and mitigated prior to drug approval, and provides recommendations in Section 5.2 that aim at reducing the risk of medication errors.

1 BACKGROUND

1.1 INTRODUCTION

This consult was written in response to a request from the Division of Anti-Infective and Ophthalmology Products to evaluate the container labels and carton labeling of Akten for its potential to contribute to medication errors. The proposed name, Akten, was reviewed without objection in OSE Review #2006-1673 dated March 3, 2008.

1.2 PRODUCT INFORMATION

Akten (Lidocaine Hydrochloride) is a topical, local anesthetic indicated for ocular surface anesthesia during ophthalmologic procedures. The recommended dose is 2 drops applied to the ocular surface in the area of the planned procedure. Akten is available as ophthalmic gel in a single strength of 3.5%, containing 35 mg/mL lidocaine hydrochloride. It is supplied for single-use in — plastic dropper bottles. b(4)

2 METHODS AND MATERIALS

This section describe the methods and materials used by DMETS medication error staff to conduct a label, labeling, and/or packaging risk assessment. The primary focus of the assessments is to identify and remedy potential sources of medication error prior to drug approval. DMETS defines a medication error as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer. [1]

The label and labeling of a drug product are the primary means by which practitioners and patients (depending on configuration) interact with the pharmaceutical product. The container labels and carton labeling communicate critical information including proprietary and established name, strength, form, container quantity, expiration, and so on. The insert labeling is intended to communicate to practitioners all information relevant to the approved uses of the drug, including the correct dosing and administration.

Given the critical role that the label and labeling has in the safe use of drug products, it is not surprising that 33 percent of medication errors reported to the USP-ISMP Medication Error Reporting Program may be attributed to the packaging and labeling of drug products, including 30 percent of fatal errors.[2]

---

[1] National Coordinating Council for Medication Error Reporting and Prevention. http://www.nccmerp.org/aboutMedErrors.html. Last accessed 10/11/2007.

[2] Institute of Medicine. Preventing Medication Errors. The National Academies Press: Washington DC. 2006. p275.

Because DMETS staff analyze reported misuse of drugs, DMETS staff are able to use this experience to identify potential errors with all medication similarly packaged, labeled or prescribed. DMETS uses FMEA and the principles of human factors to identify potential sources of error with the proposed product labels and insert labeling, and provided recommendations that aim at reducing the risk of medication errors.

For this product the Applicant submitted on June 29, 2007 the following labels for DMETS review (see Appendix A, B, C, D for images):

- Retail Container: 5 mL
- Sample Container: 5 mL
- Retail Carton: 5 mL
- Sample Carton: 5 mL

3 RESULTS

A review of the container labels and carton labeling identified several potential sources of medication error.

There is a triangular graphic near the 'A' of the proprietary name on the container label and carton labeling. The established name appears smaller in size and prominence than the dosage form and the proprietary name. The container label does not include the statement "Discard unused portion" as included on the carton labeling. There is no distinction between the professional sample and the retail labels

4 DISCUSSION

The results of the Label and Labeling Risk Assessment found that the presentation of information and design of the proposed container labels and carton labeling appears to be vulnerable to confusion that could lead to medication errors.

The triangular graphic is distracting and interferes with the readability of the proprietary name. Per 21 CFR 201.10(g)(2), the established name should be at least ½ the size of the proprietary name and have the prominence commensurate with the prominence of the proprietary name, taking into account all pertinent factors, including typography, layout, contrast, and other printing features. The statement "Discard unused portion" should be included consistently on the container label and carton labeling, especially since the carton labeling will likely be discarded. It is difficult to distinguish the professional sample and the retail from the current presentation of the labels because the statement "Sample Not for Sale" lacks prominence, especially since the net quantity is the same for both.

5 CONCLUSIONS AND RECOMMENDATIONS

The Label and Labeling Risk Assessment findings indicate that the presentation of information and design of the proposed carton and container labels introduces vulnerability to confusion that could lead to medication errors. DMETS believes the risks we have identified can be addressed and mitigated prior to drug approval, and provides recommendations in Section 5.2 that aim at reducing the risk of medication errors.

5.1 COMMENTS TO THE DIVISION

Based upon our assessment of the labels and labeling, DMETS has identified areas needed of improvement. We have provided recommendations in Section 5.2 and request this information be forwarded to the Applicant.

DMETS would appreciate feedback on the final outcome of this review. Please copy DMETS on any communication to the Applicant with regard to this review. We would be willing to meet with the Division for further discussion, if needed. If you have further questions or need clarifications, please contact Anne Crandall, Project Manager, at 301-796-2282.

5.2 COMMENTS TO THE APPLICANT

Overall, our Risk Assessment is limited by our current understanding of medication errors and causality. The successful application of Failure Modes and Effect Analysis depends upon the learning gained from a spontaneous reporting program. It is quite possible that our understanding of medication error causality would benefit from unreported medication errors; and, that this understanding could have enabled the Staff to identify vulnerability in the packaging and labeling that was not identified in this assessment. To help minimize this limitation in future assessments, we encourage the Applicant to provide the Agency with medication error reports involving their marketed drug products regardless of adverse event severity.

1. Remove the triangular graphic near the 'A' of the proprietary name.
2. Per 21 CFR 201.10(g)(2), ensure that the established name is the same font size as the dosage form and at least ½ the size of the proprietary name, and have the prominence commensurate with the prominence of the proprietary name, taking into account all pertinent factors, including typography, layout, contrast, and other printing features.
3. Include the statement, "Discard unused portion" on the container label.
4. Change the font color or increase the prominence of the statement "Sample Not for Sale" to distinguish the professional sample from the trade product.

2 Page(s) Withheld

_____ Trade Secret / Confidential (b4)

✓ Draft Labeling (b4)

_____ Draft Labeling (b5)

_____ Deliberative Process (b5)

Withheld Track Number: Other Review(s) - 1

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

/s/

Judy Park
3/27/2008 02:48:18 PM
DRUG SAFETY OFFICE REVIEWER

Kellie Taylor
3/27/2008 03:17:39 PM
DRUG SAFETY OFFICE REVIEWER

Denise Toyer
3/27/2008 03:25:21 PM
DRUG SAFETY OFFICE REVIEWER