CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

50-802

PROPRIETARY NAME REVIEW(S)

CONSULTATION RESPONSE

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

DATE RECEIVED: September 6, 2006 DATE OF DOCUMENT: May 6, 2006	DESIRED COMPLETION DATE: October 23, 2006 PDUFA DATE: November 8, 2006	OSE REVIEW #: 2006-197

TO: Susan Walker, MD
Director, Division of Dermatology and Dental Products
HFD-540

THROUGH: Nora Roselle, PharmD., Team Leader
Denise Toyer, PharmD., Deputy Director
Carol Holquist, RPh., Director
Division of Medication Errors and Technical Support, HFD-420

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

PRODUCT NAME: **Ziana**
(Clindamycin Phosphate and Tretinoin Gel)
1.2% and 0.025%

NDA#: 50-802

NDA SPONSOR: Dow Pharmaceutical Sciences

RECOMMENDATIONS:

1. DMETS has no objections to the use of the proprietary name Ziana. 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. DDMAC finds the proprietary name, Ziana, acceptable from a promotional perspective.

3. DMETS recommends implementation of the label and labeling revision outlined in section III of this review to minimize potential errors with the use of this 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
HFD: 420, WO 22, Mailstop: 4447
Center for Drug Evaluation and Research

PROPRIETARY NAME, LABEL and LABELING REVIEW

DATE OF REVIEW: September 21, 2006

NDA#: 50-802

NAME OF DRUG: Ziana
(Clindamycin Phosphate and Tretinoin Gel)
1.2% and 0.025%

NDA HOLDER: Dow Pharmaceutical Sciences, Inc.

*****NOTE: This review contains proprietary and confidential information that should not be released to the public.*****

I. INTRODUCTION:

This consult was written in response to a request from the Division of Dermatology and Dental Products (HFD-540), for assessment of the proprietary name, "Ziana", regarding potential name confusion with other proprietary or established drug names. DMETS previously reviewed the name ClinRa Gel for this product under NDA# 21-739 in ODS Consult # 04-0135, dated October 5, 2004, and it was found unacceptable at that time. DMETS also reviewed the name [redacted] for this product under NDA# 50-802, b(4) dated December 8, 2004, and it was found unacceptable at that time. NDA# 21-739 was administratively converted to NDA# 50-802 because it is a 505B2 application listing the active ingredients as the reference listed drugs. Container labels, carton and insert labeling were provided for review and comment.

PRODUCT INFORMATION

Ziana is a topical gel containing 1.2% clindamycin phosphate and 0.025% tretinoin and is indicated for the treatment of [redacted] acne vulgaris. For patients b(4) 12 years of age or older, Ziana is applied to the face once-daily at bedtime. The entire face, excluding the mouth, eyes and lips should be treated. Ziana is supplied in tubes containing 30 g and 60 g.

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 Ziana 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[5]. The Saegis[6] 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 consisting of two written prescription studies (inpatient and outpatient) and one verbal prescription study, involving health care practitioners within the 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 Ziana. 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 proposed proprietary name, Ziana, from a promotional perspective.

2. The Expert Panel identified seventeen proprietary names that were thought to have the potential for confusion with Ziana. Of the seventeen names identified, DMETS found that five names warranted further evaluation based on look-alike, sound-alike, and product characteristics (see Table 1 on page 4). Upon further review, it was determined that the remaining twelve names are either no longer marketed and have no generics available, lacked convincing look-alike/sound-alike similarities with Ziana, in addition to differentiating product characteristics such as product strength, indication for use, frequency of administration, route of administration, and/or dosage formulation. Thus, the following names will not be discussed further in this review: CeeNu, Lialda, Revia, Renova, Tiazac, Vaniqa, Viagra, Xanax, Ziagen, Zinc, Zone-A, Yasmin,

---

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

Product Name	Dosage form(s), Established name	Usual adult dose*	Other**
Ziana	Clindamycin Phosphate and Tretinoin Gel 1.25% and 0.025%	Apply to entire face once daily at bedtime.	NA
Sarna Anti-Itch Sarna Ultra Sarna Sensitive Anti-itch	Pramoxine Hydrochloride Lotion 1% and Cream 1%	Apply externally to the affected area 3 to 4 times a day.	LA
Senna-Gen Senna-Concentrate Senna	Sennosides Tablets: 8.6 mg Syrup:	2-4 tablets once or twice a day, not to exceed 4 tablets twice a day.	LA/SA
Zenvia***	Dextromethorphan Hydrobromide and Quinidine Sulfate Capsules		LA
Ziac	Bisoprolol Fumarate/Hydrochlorothiazide Tablets 2.5 mg/6.25 mg, 5 mg/6.25 mg, and 10 mg/6.25 mg	2.5 mg/6.25 mg to 10 mg/6.25 mg once daily.	LA
Zovia 1/35E-21 Zovia 1/35E-28 Zovia 1/50E-21 Zovia 1/50E-21	Ethinyl Estradiol; Ethynodiol Diacetate Tablets 0.035 mg/1 mg and 0.05 mg/1 mg	One tablet daily.	LA

*Frequently used, not all-inclusive. **L/A (look-alike), S/A (sound-alike)
***NOTE: **This review contains proprietary and confidential information that should not be released to the public.**

b(4)

b(4)

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 Ziana 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 125 health care professionals (pharmacists, physicians, and nurses). This exercise was conducted in an attempt to simulate the prescription ordering process. An inpatient order and an outpatient prescription were written, each consisting of a combination of marketed and unapproved drug products and a prescription for Ziana (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
Inpatient RX: ~~Ziana apply pea-sized amt to affected area qhs~~ Outpatient RX: Ziana #1 tube apply a pea-sized amt. to the affected area qhs	Ziana #1 Tube Apply a pea-sized amount to the affected area qhs.

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, Ziana, the primary concerns relating to look-alike and sound-alike confusion with Ziana are Zenvia***, Sarna, and Senna.

Additionally, 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. However, negative findings are not predicative as 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.

1. Zenvia*** was identified as a name that has the potential to look similar to Ziana when scripted. Zenvia*** is a name that is currently under review by the Agency under NDA# [redacted] and is indicated for the treatment of pseudobulbar affect. b(4)

The orthographic similarity stems from the beginning and ending letters that may look similar when scripted (Zi vs. Ze and ana vs. via). Zenvia*** contains an additional letter (n) which contributes to a lengthier appearance which may help to differentiate these two names when written. Although both products can be administered once daily and are available in one strength, there are some differentiating product characteristics, such as, dose ([redacted] or one capsule vs. sufficient amount), route of administration (oral vs. topical), and dosage form (capsule vs. gel). The lengthier orthographic appearance of Zenvia will help to differentiate these two products when ordered.

Zenvia
Ziana

NOTE: This review contains proprietary and confidential information that should not be released to the public.

2. Sarna was identified as a name that may look similar to Ziana when written. The Sarna product line includes Sarna Anti-Itch, Sarna Ultra, and Sarna Sensitive Anti-Itch. Sarna is indicated in the treatment of the itch and pain due to minor burns, abrasions and other irritated skin conditions.

Both Sarna and Ziana contain letters that may look similar when scripted (Z vs. S and ana vs. rana). Additionally, each name contains five letters which contributes to a similar length and orthographic presentation. Both products are topical products (gel vs. cream and lotion) and are supplied in one strength (1.2%/0.025% vs. 1%). However, they do differ with respect to frequency of administration (once daily vs. three or four times daily). Additionally, prescriptions are not usually seen for over-the-counter products.

Despite the difference in frequency of administration, it is not uncommon for topical products to be ordered with a general direction of 'use as directed'. However, the fact that the name of each product in the Sarna product line includes a modifier, which must be identified prior to dispensing, will help to differentiate these products when ordered. Despite the orthographic similarities and potential for similar prescribing practices, the modifiers associated with the name Sarna decrease the potential for confusion involving these two names.

Sarna
Ziana

3. Senna was identified as a name that has the potential to look similar to Ziana when scripted. Senna is indicated in the treatment of occasional constipation. The Senna product line includes the products Senna, Senna-Gen, and Senna-Concentrate. However, only the product Senna will be evaluated.

Both names contain letters that may look similar when scripted (Zi vs. Se and ana vs. nna). Additionally, they both contain five letters which contributes further to a similar orthographic appearance. Ziana and Senna differ with respect to strength (1%/0.025% vs. [redacted] dosage form (topical gel vs. syrup), frequency of administration (once daily vs. twice daily), and route of administration (topical vs. oral). Although order for topical products, such as Ziana, may be written 'Use as directed', orally administered liquid products, such as Senna, would most likely include a volume (mL or tsp) to be administered since the dose range is based on the age of the patient. This additional information will help to differentiate these two products when written. b(4)

Senna
Ziana

4. Ziac was identified as a name that has the potential to look similar to Ziana. Ziac is indicated for the treatment of hypertension.

Both Ziac and Ziana begin with the same three letters (Zia). However, Ziac contains a total of four letters, whereas, Ziana contains five letters, which provides a lengthier orthographic appearance to Ziana. There are some differentiating product characteristics, such as dose (sufficient amount vs. 2.5 mg/6.25 mg to 20 mg/6.25 mg), strength (1%/0.025% vs. 2.5 mg/6.25 mg, 5 mg/6.25 mg, and 10 mg/6.25 mg), route of administration (topical vs. oral), and dosage form (topical gel vs. tablet). The lengthier

orthographic appearance of Ziana in addition to the differentiating product characteristics will help to minimize errors involving these two products.

Zia
Ziana

5. Zovia was identified as a name that has the potential to look similar to Ziana. Zovia is an oral contraceptive that is indicated in the treatment of pregnancy.

Both names contain five letters, three of which are the same (Zia). These similarities contribute to a similar orthographic appearance of each name. There are some differentiating product characteristics, such as, dose (sufficient amount vs. 0.035 mg/1 mg and 0.05 mg/1 mg), strength (1%/0.025% vs. 0.035 mg/1 mg and 0.05 mg/1 mg), and dosage form (topical gel vs. tablet). Although either product may be ordered with a general direction of 'use as directed', Zovia, which is supplied in two different strengths would need to have a strength included in the order prior to dispensing. Thus, despite the potential for some orthographic similarities, the different strengths of Zovia will help to differentiate these two products when ordered.

Zovia
Ziana

Appears This Way
On Original

III. LABELING, PACKAGING, AND SAFETY RELATED ISSUES

In the review of the container labels, carton and insert labeling of Ziana, DMETS has attempted to focus 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. In the current presentation, the yellow and blue swirl graphic is the most prominent information on the principal display panel. The proprietary name, established name, and strength should be the most prominent information. Delete or decrease the size of the blue and yellow swirl graphic.

2. In the current presentation the background yellow swirl bisects the proprietary and established names and directions. This swirl interferes with the readability of this important information. Thus, we request you delete the yellow background swirl.

3. The dosage form should be presented in conjunction with the active ingredient, revise the presentation of the dosage form to appear directly after the active ingredients (i.e. outside the parentheses or inside). This will allow the strength to be presented on a line by itself.

B. CONTAINER LABEL (30 g and 60 g)

1. See GENERAL COMMENTS A1 through A3.

2. DMETS notes that the Usual Dosage states to: ' [redacted] whereas, the package insert DOSAGE AND ADMINISTRATION section, General Dosing Information subsection, states to [redacted] and the package insert, PATIENT COUNSELING INFORMATION Section states to [redacted] This information is inconsistent and may lead to confusion among health care practitioners and patients alike. Revise for accuracy and consistency. b(4)

C. CONTAINER LABEL (Professional Sample)

See GENERAL COMMENTS A1 through A3.

D. CARTON LABELING (30 g and 60 g)

See GENERAL COMMENTS A1 through A3 and comment B2.

E. CARTON LABELING (Professional Sample-12 count)

1. See GENERAL COMMENTS A1 through A3 and comment B2.

2. Delete the statement " [redacted] as this does not pertain to the professional samples. If this statement is not deleted it should be qualified to say 'Commercially available in 30 g and 60 g tubes'. b(4)

3. Relocate the statement 'Contains 12 sample tubes. Each tube contains 2g' so that it appears above the statement 'Sample – Not for Sale'.

F. INSERT LABELING

1. DMETS notes that the Usual Dosage statement on the container label and carton labeling are inconsistent with the directions stated elsewhere in the insert labeling. For example, (1) the container and carton states to: '[redacted], (2) the professional labeling, dosing and administration section says [redacted] and (3) the PATIENT COUNSELING INFORMATION Section states to '[redacted] and the PATIENT INSTRUCTIONS Leaflet states [redacted]. This information is inconsistent and may lead to confusion among health care practitioners and patients alike as to how much of the medication to use. Revise for accuracy and consistency. b(4)

2. The DOSAGE AND ADMINISTRATION Section, General Dosing Information subsection states "[redacted] however, the PATIENT INSTRUCTIONS Leaflet, HOW TO USE ZIANA GEL section states '[redacted] and the WHAT TO EXPECT WITH YOUR NEW TREATMENT section states '[redacted] The duration of therapy is presented in three different lengths of time (4 weeks, 7 weeks, and 12 weeks) which may be confusing to patients. Revise the wording for consistency and accuracy. b(4)

G. PATIENT INSTRUCTIONS LEAFLET

See comments F1 and F2.

Appears This Way
On Original

1. Appendix A:

Inpatient Written	Outpatient Written	Verbal
Vienna	Ziana	Ziana
Xeana	Ziana	Ziana
Zeanna	Ziana	Ziana
Ziana	Ziana	Ziana
Zianna	Ziana	Ziana
Ziena	Ziana	Ziana
Zienna	Ziana	Ziana
	Ziana	Ziana
	Ziana	Ziana
	Ziana	
	Ziana	
	Ziania	
	Ziaria	

Appears This Way
On Original

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

/s/

Linda Wisniewski
10/12/2006 08:09:59 AM
DRUG SAFETY OFFICE REVIEWER

Denise Toyer
10/12/2006 08:42:14 AM
DRUG SAFETY OFFICE REVIEWER
Also signing for Carol Holquist, DMETS Director, in her absence

Appears This Way
On Original