

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

50-819

OTHER REVIEW(S)



**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: October 10, 2008

To: Susan Walker, MD, Director
Division of Dermatology and Dental Products

Through: Deveonne Hamilton-Stokes, RN, BSN, Acting Team Leader
Denise Toyer, PharmD, Deputy Director
Carol A. Holquist, RPh, Director
Division of Medication Error Prevention and Analysis

From: Jibril Abdus-Samad, PharmD, Safety Evaluator
Division of Medication Error Prevention and Analysis

Subject: Label and Labeling Review

Drug Name: Acanya (Clindamycin Phosphate and Benzoyl Peroxide) Gel
1.2% and 2.5%

Application Type/Number: NDA # 50-819

Applicant: Dow Pharmaceutical Sciences, Inc

OSE RCM #: 2008-1598

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EXECUTIVE SUMMARY

The Division of Medication Error Prevention and Analysis (DMEPA) reviewed the revised container label and carton labeling and noted that the facial graphic, although not as prominent as the previous version, interferes with the readability of the established name and strength. The graphic appears in white and the print on the label is also white. This decrease in color contrast hinders the readability of the name. The Division of Medication Error Prevention and Analysis believes the risks we have identified can be addressed and mitigated prior to drug approval, and provides recommendations in Section 6.2 that aim to reduce the risk of medication errors.

1 BACKGROUND

1.1 INTRODUCTION

This review was written in response to the Division of Dermatology and Dental Product's request to evaluate the Applicant's response to DMEPA's comments on the container label and carton labeling for Acanya, removal of the descriptor "," from the proprietary name, and identify any outstanding areas of concern from a medication errors perspective.

b(4)

1.2 REGULATORY HISTORY

The primary name, Gel, was found to be unacceptable (OSE Review 2008-211, dated June 3, 2008) due to vulnerability to name confusion that could lead to medication errors with Elocon, Cleocin T, and Ala-Quin. The proposed labels and labeling were evaluated in the aforementioned mentioned review.

b(4)

The secondary name, Acanya Gel was found unacceptable (OSE Review 2008-215, dated September 26, 2008) based upon the Office of New Drug Quality Assessment analysis that the descriptor "" is inappropriate for this dosage form. The Division of Medication Error Prevention and Analysis (DMEPA) did not object to the use of the proprietary name "Acanya".

b(4)

1.3 PRODUCT INFORMATION

Acanya is a combination topical gel containing clindamycin 1.2% and benzoyl peroxide 2.5%. Acanya is indicated for the treatment of acne vulgaris in patients 12 years of age or older. The gel should be applied once daily or as directed by physician. Acanya will require admixture by the pharmacist with the final product dispensed in a 50 gram jar.

2 METHODS AND MATERIALS

This section describes the methods and materials used by DMEPA medication error staff to conduct a label, labeling, and/or packaging risk assessment (see section 3 Results). The primary focus of the assessments is to identify and remedy potential sources of medication errors prior to drug approval. DMEPA 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

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

label and carton labeling communicate critical information including proprietary and established name, strength, form, container quantity, expiration, and so on.

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

Because the Division of Medication Error Prevention and Analysis staff analyze reported misuse of drugs, we are able to use this experience to identify potential errors with all medication similarly packaged, labeled or prescribed. The overall risk assessment is based on the findings of a Failure Mode and Effects Analysis (FMEA) of the label and labeling, and is focused on the avoidance of medication errors. FMEA is a systematic tool for evaluating a process and identifying where and how it might fail. The Division of Medication Error Prevention and Analysis uses FMEA and the principles of human factors to identify potential sources of error with the proposed product labels and insert labeling, and provides recommendations that aim at reducing the risk of medication errors.

On September 29, 2008, the Applicant submitted the following labels (see Appendices A through D):

- Container Labels (Trade and Professional Sample)
- Clindamycin Vial Label
- Carton Labeling

DMEPA compared the revised labels to the previously proposed labels reviewed in OSE Review 2008-211, dated June 3, 2008, to identify any outstanding areas of concern from a medication errors perspective.

3 RESULTS

The revised labels are generally consistent with DMEPA's requests forwarded to the Applicant regarding the container labels and carton labeling. However, one revision is inconsistent with the requests, and represents an area of concern from a medication errors perspective. In OSE Review 2008-211, dated June 3, 2008, DMEPA requested the Applicant to:

Delete the graphic of the face to increase the available label area to increase the size of text and inclusion of other important information.

DMEPA notes that the face image remains on the principle display panel and detracts from the established name and strength of the product. The revised face image is not as bright as the previously proposed container label and thus not as prominent. However, the placement of the image is superimposed with the established name thus interfering with the readability.

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

4 DISCUSSION

With respect to the trade container label, an outstanding area of concern involves the use of the graphic face image on the principle display panel. The contrast between the image and the established name does not provide sufficient contrast with the white colored text, thus decreasing the clarity of the text. We note that on the trade container lid label, carton labeling, and professional sample container lid label; the face image does not overlap with the established name and strength. It would be beneficial if the principle display panel could be revised so that the words are not washed out by the graphic. This could be accomplished by removing the image or reducing it in size, or revising the color of the text to provide a greater color contrast.

Figure 1: Trade Container Label

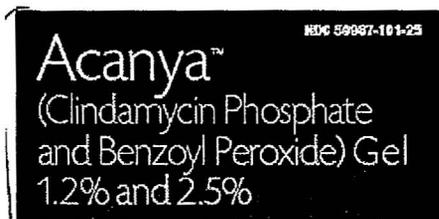
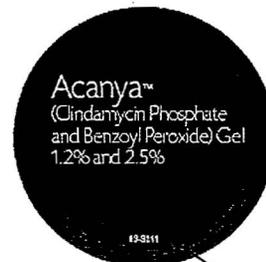


Figure 2: Trade Container Lid Label



5 CONCLUSIONS

The Label and Labeling Risk Assessment findings indicate that the presentation of the face graphic decreases the readability of the established name and strength. The Division of Medication Error Prevention and Analysis believes the risks we have identified can be addressed and mitigated prior to drug approval, and provides recommendations in Section 6.2 that aim to reduce the risk of medication errors.

6 RECOMMENDATIONS

6.1 COMMENTS TO THE DIVISION

The Division of Medication Error Prevention and Analysis would appreciate feedback on the final outcome of this review. We would be willing to meet with the Division for further discussion, if needed. Please copy us on any communication to the Applicant with regard to this review. If you have further questions or need clarifications, please contact Janet Anderson, OSE Project Manager, at 301-796-0675.

6.2 COMMENTS TO THE APPLICANT

Based upon DMEPA's assessment of the labels and labeling, they have identified the following area of needed improvement on the trade container label:

- On the trade container label, delete or minimize the graphic of the face to increase readability of the established name and strength. If you choose to minimize the face graphic, you should ensure the graphic does not obscure the proprietary name, established name, and strength. An example of the latter alternative can be found on the trade

container lid label (see Figure 2). Alternatively, you may also consider revising the font color of the text to provide a greater color contrast.

Figure 1: Trade Container Label

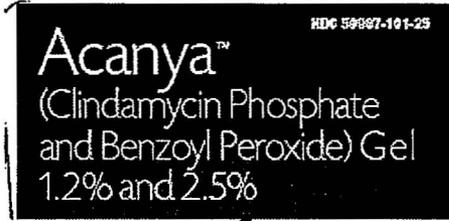
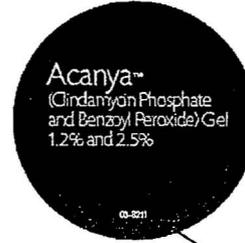


Figure 2: Trade Container Lid Label



APPENDICES

Appendix A: Trade Container Label

0 1 1 2 7 0

Acanya[®]
(Cindamycin Phosphate
and Benzoyl Peroxide) Gel
1.2% and 2.5%

IND 02043-01-01

FOR EXTERNAL USE ONLY
Use 55 grams for (after washing)

ONLY

Use 55 grams to apply once daily as directed by physician. See package insert.
Precautions: For an immediate effect, avoid contact with eyes and mucous
membranes. May stain colored fabric or hair.

Each 55 gram of Acanya[®] Gel, as dispensed, contains 50 mg (9%) cindamycin in
phosphate and 0.5 g (1.0%) benzoyl peroxide in a base of water, alcohol,
polyvinylpyrrolidone, polyethylene glycol, and purified water.
Use by date listed and store as specified on white Traveler's Kit Separately Sold.
Store at room temperature up to 25°C (77°F). Do not freeze.

Prior to dispensing, store at room temperature up to 25°C (77°F). Do not
freeze. When returning, seal the cindamycin phosphate and benzoyl peroxide
to the best of your ability and return to the manufacturer for recycling.

Discard if you have a reaction after applying. Discontinue use if you have a
rash or a severe allergic reaction. Store at room temperature up to 25°C (77°F).
Do not freeze.

See bottom of jar for lot Use by:

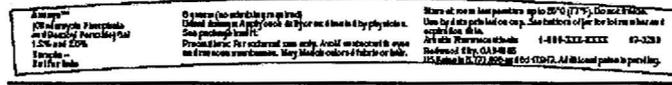
Dist. by: Amul's Pharmaceuticals, Inc., 600 E. 10th St., Erie, PA 16501
Mfg. by: Schering-Plough Pharmaceuticals Ltd., Kenilworth, NJ 07033 03-2014

Trade Container Lid Label

Acanya[®]
(Cindamycin Phosphate
and Benzoyl Peroxide) Gel
1.2% and 2.5%

03-2014

Appendix B: Professional Sample Container Label



Professional Sample Container Lid Label



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

/s/

Deveonne Hamilton-Stokes
10/10/2008 11:07:33 AM
DRUG SAFETY OFFICE REVIEWER

Denise Toyer
10/15/2008 04:56:16 PM
DRUG SAFETY OFFICE REVIEWER

Carol Holquist
10/15/2008 05:55:10 PM
DRUG SAFETY OFFICE REVIEWER

NDA REGULATORY FILING REVIEW
(Including Memo of Filing Meeting)

NDA # 50-819 Supplement # N/A Efficacy Supplement Type SE- N/A

Proprietary Name: _____

Established Name: 1.2 % clindamycin phosphate, 2.5% benzoyl peroxide
Strengths:

b(4)

Applicant: Dow Pharmaceutical Sciences, Inc.
Agent for Applicant (if applicable): N/A

Date of Application: December 21, 2007
Date of Receipt: December 26, 2007
Date clock started after UN: N/A
Date of Filing Meeting: February 13, 2008
Filing Date: 2/24/08

Action Goal Date (optional):

User Fee Goal Date: October 26, 2008
Actual Goal Date: October 24, 2008

Indication(s) requested: Acne Vulgaris

Type of Original NDA: (b)(1) (b)(2)
AND (if applicable)
Type of Supplement: (b)(1) (b)(2)

NOTE:

(1) If you have questions about whether the application is a 505(b)(1) or 505(b)(2) application, see Appendix A. A supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2). If the application or efficacy supplement is a (b)(2), complete Appendix B.

Review Classification: S P
Resubmission after withdrawal? Resubmission after refuse to file?
Chemical Classification: (1,2,3 etc.) 5
Other (orphan, OTC, etc.) N/A

Form 3397 (User Fee Cover Sheet) submitted: YES NO

User Fee Status: Paid Exempt (orphan, government)
Waived (e.g., small business, public health)

NOTE: If the NDA is a 505(b)(2) application, and the applicant did not pay a fee in reliance on the 505(b)(2) exemption (see box 7 on the User Fee Cover Sheet), confirm that a user fee is not required by contacting the User Fee staff in the Office of Regulatory Policy. The applicant is required to pay a user fee if: (1) the product described in the 505(b)(2) application is a new molecular entity or (2) the applicant claims a new indication for a use that has not been approved under section 505(b). Examples of a new indication for a use include a new indication, a new dosing regime, a new patient population, and an Rx-to-OTC switch. The best way to determine if the applicant is claiming a new indication for a use is to compare the applicant's proposed labeling to labeling that has already been approved for the product described in the application. Highlight the differences between the proposed and approved labeling. If you need assistance in determining if the applicant is claiming a new indication for a use, please contact the User Fee staff.

- Is there any 5-year or 3-year exclusivity on this active moiety in any approved (b)(1) or (b)(2) application? YES NO
If yes, explain:

Note: If the drug under review is a 505(b)(2), this issue will be addressed in detail in appendix B.

- Does another drug have orphan drug exclusivity for the same indication? YES NO

- If yes, is the drug considered to be the same drug according to the orphan drug definition of sameness [21 CFR 316.3(b)(13)]? YES NO

If yes, consult the Director, Division of Regulatory Policy II, Office of Regulatory Policy (HFD-007).

- Is the application affected by the Application Integrity Policy (AIP)? YES NO
If yes, explain:

- If yes, has OC/DMPQ been notified of the submission? YES NO

- Does the submission contain an accurate comprehensive index? YES NO
If no, explain:

- Was form 356h included with an authorized signature? YES NO
If foreign applicant, both the applicant and the U.S. agent must sign.

- Submission complete as required under 21 CFR 314.50? YES NO
If no, explain:

- Answer 1, 2, or 3 below (do not include electronic content of labeling as an partial electronic submission).

1. This application is a paper NDA YES

2. This application is an eNDA or combined paper + eNDA YES
This application is: All electronic Combined paper + eNDA
This application is in: NDA format CTD format
Combined NDA and CTD formats

Does the eNDA, follow the guidance?
(<http://www.fda.gov/cder/guidance/2353fnl.pdf>) YES NO

If an eNDA, all forms and certifications must be in paper and require a signature.

If combined paper + eNDA, which parts of the application were submitted in electronic format?

Additional comments:

3. This application is an eCTD NDA. YES
If an eCTD NDA, all forms and certifications must either be in paper and signed or be electronically signed.

Additional comments:

- Patent information submitted on form FDA 3542a? YES NO
- Exclusivity requested? YES, 3 Years NO
NOTE: An applicant can receive exclusivity without requesting it; therefore, requesting exclusivity is not required.
- Correctly worded Debarment Certification included with authorized signature? YES NO
If foreign applicant, both the applicant and the U.S. Agent must sign the certification.
NOTE: Debarment Certification should use wording in FD&C Act section 306(k)(1) i.e., "[Name of applicant] hereby certifies that it did not and will not use in any capacity the services of any person debarred under section 306 of the Federal Food, Drug, and Cosmetic Act in connection with this application." Applicant may not use wording such as "To the best of my knowledge . . ."
- Are the required pediatric assessment studies and/or deferral/partial waiver/full waiver of pediatric studies (or request for deferral/partial waiver/full waiver of pediatric studies) included? YES NO
- If the submission contains a request for deferral, partial waiver, or full waiver of studies, does the application contain the certification required under FD&C Act sections 505B(a)(3)(B) and (4)(A) and (B)? YES NO
- Is this submission a partial or complete response to a pediatric Written Request? YES NO
If yes, contact PMHT in the OND-IO
- Financial Disclosure forms included with authorized signature? YES NO
(Forms 3454 and/or 3455 must be included and must be signed by the APPLICANT, not an agent.)
NOTE: Financial disclosure is required for bioequivalence studies that are the basis for approval.
- Field Copy Certification (that it is a true copy of the CMC technical section) YES NO
- PDUFA and Action Goal dates correct in tracking system? YES NO
If not, have the document room staff correct them immediately. These are the dates EES uses for calculating inspection dates.
- Drug name and applicant name correct in COMIS? If not, have the Document Room make the corrections. Ask the Doc Rm to add the established name to COMIS for the supporting IND if it is not already entered.
- List referenced IND numbers: IND 41,733
- Are the trade, established/proper, and applicant names correct in COMIS? YES NO
If no, have the Document Room make the corrections.
- End-of-Phase 2 Meeting(s)? Date(s) September 18, 2006 NO
If yes, distribute minutes before filing meeting.
- Pre-NDA Meeting(s)? Date(s) November 27, 2007 NO
If yes, distribute minutes before filing meeting.

- Any SPA agreements? Date(s) _____ NO
If yes, distribute letter and/or relevant minutes before filing meeting.

Project Management

- If Rx, was electronic Content of Labeling submitted in SPL format? YES NO
If no, request in 74-day letter.
- If Rx, for all new NDAs/efficacy supplements submitted on or after 6/30/06:
Was the PI submitted in PLR format? YES NO

If no, explain. Was a waiver or deferral requested before the application was received or in the submission? If before, what is the status of the request:
- If Rx, all labeling (PI, PPI, MedGuide, carton and immediate container labels) has been consulted to DDMAC? YES NO
- If Rx, trade name (and all labeling) consulted to OSE/DMETS? YES NO
- If Rx, MedGuide and/or PPI (plus PI) consulted to ODE/DSRCS?
N/A YES NO
- Risk Management Plan consulted to OSE/IO? N/A YES NO
- If a drug with abuse potential, was an Abuse Liability Assessment, including a proposal for scheduling submitted? NA YES NO

If Rx-to-OTC Switch or OTC application: N/A

- Proprietary name, all OTC labeling/packaging, and current approved PI consulted to OSE/DMETS? YES NO
- If the application was received by a clinical review division, has DNPCE been notified of the OTC switch application? Or, if received by DNPCE, has the clinical review division been notified? YES NO

Clinical: N/A

- If a controlled substance, has a consult been sent to the Controlled Substance Staff? YES NO

Chemistry

- Did applicant request categorical exclusion for environmental assessment? YES NO
If no, did applicant submit a complete environmental assessment? YES NO
If EA submitted, consulted to EA officer, OPS? YES NO
- Establishment Evaluation Request (EER) submitted to DMPQ? YES NO
- If a parenteral product, consulted to Microbiology Team? YES NO