

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

50-819

PROPRIETARY NAME 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**

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Subject: Proprietary Name Review

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

Application Type/Number: NDA # 50-819

Applicant: Dow Pharmaceutical Sciences, Inc

OSE RCM #: 2008-215

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

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EXECUTIVE SUMMARY

The Proprietary Name Risk Assessment findings indicate that the proposed name, Acanya _____ Gel, does not appear to be vulnerable to name confusion that could lead to medication errors. However, based upon ONDQA's analysis that the descriptor " _____ " is inappropriate for this dosage form, we object to the name, Acanya _____ Gel. Conversely, the Division of Medication Error Prevention and Analysis (DMEPA) does not object to the use of the proprietary name Acanya Gel.

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If the product approval is delayed beyond 90 days from the signature date of this review, the proposed name must be resubmitted for evaluation. Additionally, if any of the proposed product characteristics as stated in this review are altered prior to approval of the product, DMEPA rescinds this Risk Assessment finding, and recommends that the name be resubmitted for review.

1 BACKGROUND

1.1 INTRODUCTION

This review was written in response to a request from the Division of Dermatology and Dental Products for assessment of the proposed proprietary name, Acanya _____ Gel, regarding potential name confusion with other proprietary or established drug names.

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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 above mentioned review.

1.3 PRODUCT INFORMATION

Acanya _____ Gel is a combination topical gel containing clindamycin 1.2 % and benzoyl peroxide 2.5%. Acanya _____ Gel 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 _____ Gel will require admixture by the pharmacist with the final product dispensed in a 50 gram jar.

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2 METHODS AND MATERIALS

This section describes the methods and materials used by the Division of Medication Error Prevention and Analysis (DMEPA) staff conducting a proprietary name risk assessment (see 2.1 Proprietary Name Risk Assessment). The primary focus of the assessment is to identify and remedy potential sources of medication error prior to drug approval. The Division of Medication Error Prevention and Analysis 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

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

2.1 PROPRIETARY NAME RISK ASSESSMENT

FDA's Proprietary Name Risk Assessment considers the potential for confusion between the proposed proprietary name, Acanya _____, Gel, and the proprietary and established names of drug products existing in the marketplace and those pending IND, NDA, and ANDA products currently under review by the Agency. Since we believe that practitioners may order this product as "Acanya" (i.e. without including the "_____ Gel" portion of the name), the same name risk assessment was conducted for Acanya.

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For the proprietary name, Acanya _____, Gel, and the root name, Acanya or Acanya Gel, we search a standard set of databases and information sources to identify names with orthographic and phonetic similarity (see Sections 2.1.1 for detail) and hold a CDER Expert Panel discussion to gather professional opinions on the safety of the proposed proprietary name (see 2.1.1.2). The Division of Medication Error Prevention and Analysis also conducts internal CDER prescription analysis studies (see 2.1.2), and, when provided, external prescription analysis studies results are considered and incorporated into the overall risk assessment.

The Safety Evaluator assigned to the Proprietary Name Risk Assessment is responsible for considering the collective findings, and provides an overall risk assessment of the proposed proprietary name (see detail 2.1.3). The overall risk assessment is based on the findings of a Failure Modes and Effects Analysis (FMEA) of the proprietary name, 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.² FMEA is used to analyze whether the drug names identified with look- or sound-alike similarity to the proposed name could cause confusion that subsequently leads to medication errors in the clinical setting. The Division of Medication Error Prevention and Analysis uses the clinical expertise of the medication error staff to anticipate the conditions of the clinical setting that the product is likely to be used in based on the characteristics of the proposed product.

In addition, the product characteristics provide the context for the verbal and written communication of the drug names and can interact with the orthographic and phonetic attributes of the names to increase the risk of confusion when there is overlap, or, in some instances, decrease the risk of confusion by helping to differentiate the products through dissimilarity. As such, the staff considers the product characteristics associated with the proposed drug throughout the risk assessment, since the product characteristics of the proposed may provide a context for communication of the drug name and ultimately determine the use of the product in the usual clinical practice setting.

Typical product characteristics considered when identifying drug names that could potentially be confused with the proposed drug name include, but are not limited to established name of the proposed product, the proposed indication, dosage form, route of administration, strength, unit of measure, dosage units, recommended dose, typical quantity or volume, frequency of administration, product packaging, storage conditions, patient population, and prescriber population. Because drug name confusion can occur at any point in the medication use process, the Division of Medication Error Prevention and Analysis considers the potential for confusion throughout the entire U.S. medication use process, including drug procurement, prescribing and ordering, dispensing, administration, and monitoring the impact of the medication.³

² Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

³ Institute of Medicine. Preventing Medication Errors. The National Academies Press: Washington DC. 2006.

2.1.1 Search Criteria

The medication error staff considers the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted as outlined in Appendix A.

For this review, particular consideration was given to drug names beginning with the letter 'A' when searching to identify potentially similar drug names, as 75% of the confused drug names reported by the USP-ISMP Medication Error Reporting Program involve pairs beginning with the same letter.^{4,5}

To identify drug names that may look similar to Acanya/Acanya Gel/Acanya Gel, the Staff also consider the orthographic appearance of the name on lined and unlined orders. Specific attributes taken into consideration include the length of the name (sixteen letters), shape of the name, upstrokes (4, two capital letters 'A', capital letter 'G', lowercase 'l'), downstrokes (2, lowercase 'y' and lowercase 'q'), cross-strokes (2, two capital letters 'A'), and dotted letters (none). Additionally, several letters in Acanya Gel may be vulnerable to ambiguity when scripted, including the letter 'A' may appear as 'e', 'o', 'u', 'c', 'ce', or 'ci'; lower case 'c' may appear as a lower case 'a'; lower case 'n' may appear as a lower case 'm', 'u', 'x', 'r', 'h' or 's'; lowercase 'y' appear as lowercase 'u' or 'g'; lowercase 'q' may appear as lower case 'g'; lowercase 'u' may appear as lower case 'a', 'e', 'i', 'o', 'y', 're', or 'n'; lower case 'e' may appear as 'a', 'i', 'o', 'u', or 'l'; lowercase 'o' may appear as a lowercase 'a', 'e', 'i', or 'u'; lowercase 's' may appear as a lowercase 'n' or 'g'; capital 'G' may appear as capital 'S'; lowercase 'g' may appear as a lowercase '8', 'j', or 'q'; and lowercase 'l' may appear as a lower case 'e' or 'b'

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When searching to identify potential names that may sound similar to Acanya/Acanya Gel/Acanya Gel, the medication error staff search for names with similar number of syllables (three for Acanya, four for Acanya Gel, and seven for Acanya Gel), stresses (a-CAN-ya or A-can-ya; GEL), and placement of vowel and consonant sounds. In addition, several letters in Acanya Gel may be subject to interpretation when spoken, including the letter "A" which may be interpreted as 'E' or 'I' and the letter combination '-can-' may be interpreted as 'can' or 'con'. As such, the staff also considers these alternate pronunciations when identifying drug names that may sound similar to Acanya/Acanya Gel/Acanya Gel. The Applicant's intended pronunciation of the proprietary name could not be expressly taken into consideration, as this was not provided with the proposed name submission.

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The Staff also consider the product characteristics associated with the proposed drug throughout the identification of similar drug names, since the product characteristics of the proposed drug ultimately determine the use of the product in the clinical practice setting. For this review, the medication error staff were provided with the following information about the proposed product: the proposed proprietary name (Acanya Gel), the established name (clindamycin phosphate and benzoyl peroxide), proposed indication (treatment of acne vulgaris), strength (1.2%/2.5%), frequency of administration (once daily or as directed by physician), route (topically) and dosage form of the product (gel). Appendix A provides a more detailed listing of the product characteristics the medication error staff generally takes into consideration.

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Lastly, the medication error staff also considers the potential for the proposed name to inadvertently function as a source of error for reasons other than name confusion. Post-marketing

⁴ Institute for Safe Medication Practices. Confused Drug name List (1996-2006). Available at <http://www.ismp.org/Tools/confuseddrugnames.pdf>

⁵ Kondrack, G and Dorr, B. Automatic Identification of Confusable Drug Names. Artificial Intelligence in Medicine (2005)

experience has demonstrated that proprietary names (or components of the proprietary name) can be a source of error in a variety of ways. As such, these broader safety implications of the name are considered and evaluated throughout this assessment and the medication error staff provides additional comments related to the safety of the proposed name or product based on their professional experience with medication errors.

2.1.1.1 Database and Information Sources

The proposed proprietary name, Acanya ~~_____~~ Gel, and the root name, Acanya or Acanya Gel, were provided to the medication error staff of the Division of Medication Error Prevention and Analysis to conduct a search of the internet, several standard published drug product reference texts, and FDA databases to identify existing and proposed drug names that may sound-alike or look-alike to Acanya/Acanya Gel/Acanya ~~_____~~ Gel using the criteria outlined in 2.1.1. A standard description of the databases used in the searches is provided in Section 7. To complement the process, the medication error staff uses a computerized method of identifying phonetic and orthographic similarity between medication names. The program, Phonetic and Orthographic Computer Analysis (POCA), uses complex algorithms to select a list of names from a database that have some similarity (phonetic, orthographic, or both) to the trademark being evaluated. Lastly, the medication error staff reviews the USAN stem list to determine if any USAN stems are present within the proprietary name. The findings of the individual Safety Evaluators were then pooled and presented to the Expert Panel.

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2.1.1.2 CDER Expert Panel Discussion

An Expert Panel Discussion is held by the Division of Medication Error Prevention and Analysis to gather CDER professional opinions on the safety of the product and the proprietary name, Acanya ~~_____~~ Gel. Potential concerns regarding drug marketing and promotion related to the proposed names are also discussed. This group is composed of the Division of Medication Error Prevention and Analysis Staff and representatives from the Division of Drug Marketing, Advertising, and Communications (DDMAC).

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The pooled results of the medication error staff were presented to the Expert Panel for consideration. Based on the clinical and professional experiences of the Expert Panel members, the Panel may recommend the addition of names, additional searches by the Safety Evaluator to supplement the pooled results, or general advice to consider when reviewing the proposed proprietary name.

2.1.2 FDA Prescription Analysis Studies

Three separate studies are conducted within the Centers of the FDA for the proposed proprietary name to determine the degree of confusion of Acanya ~~_____~~ Gel 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/modifier. The studies employ a total of 123 healthcare professionals (pharmacists, physicians, and nurses), and attempts to simulate the prescription ordering process. The results are used by the Safety Evaluator to identify any orthographic or phonetic vulnerability of the proposed name/modifier/suffix to be misinterpreted by healthcare practitioners.

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In order to evaluate the potential for misinterpretation of Acanya ~~_____~~ Gel in handwriting and verbal communication of the name, inpatient medication orders and outpatient prescriptions are written, each consisting of a combination of marketed and unapproved drug products, including the proposed name. These prescriptions are optically scanned and delivered to a random sample of 123 participating health professionals via e-mail. In addition, verbal prescriptions are recorded on voice mail. The voice mail messages are 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 send their interpretations of the orders via e-mail to the medication error staff.

Figure 1. Acanya ~~_____~~ Gel Study (conducted on March 19, 2008)

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HANDWRITTEN PRESCRIPTION AND MEDICATION ORDER	VERBAL PRESCRIPTION
<p><u>Outpatient Prescription:</u></p> <p><i>Acanya 50g</i></p> <p><i>Apply to affected areas daily</i></p>	<p>Acanya</p> <p>50 gm</p> <p>Apply to the affected areas daily</p>
<p><u>Inpatient Medication Order :</u></p> <p><i>Acanya AAA qdaily</i></p>	

2.1.3 Comments from the Office of New Drug Quality Assessment (ONDQA)

The chemist assigned to this application was asked if “~~_____~~ Gel” is an accurate dosage form designation for this product.

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2.1.4 Safety Evaluator Risk Assessment of the Proposed Proprietary Name

Based on the criteria set forth in Section 2.1.1, the Safety Evaluator applies their individual expertise gained from evaluating medication errors reported to FDA to conduct a Failure Modes and Effects Analysis and provide an overall risk of name confusion. Failure Mode and Effects Analysis (FMEA) is a systematic tool for evaluating a process and identifying where and how it might fail.⁶ When applying FMEA to assess the risk of a proposed proprietary name, we seek to evaluate the potential for a proposed name to be confused with another drug name as a result of the name confusion and cause errors to occur in the medication use system. FMEA capitalizes on the predictable and preventable nature of medication errors associated with drug name confusion. FMEA allows the Agency to identify the potential for medication errors due to look- or sound-alike drug names prior to approval, where actions to overcome these issues are easier and more effective than remedies available in the post-approval phase.

In order to perform a FMEA of the proposed name, the Safety Evaluator must analyze the use of the product at all points in the medication use system. Because the proposed product is not yet

⁶ Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

marketed, the Safety Evaluator anticipates the use of the product in the usual practice settings by considering the clinical and product characteristics listed in Appendix A. The Safety Evaluator then analyzes the proposed proprietary name in the context of the usual practice setting and works to identify potential failure modes and the effects associated with the failure modes.

In the initial stage of the Risk Assessment, the Safety Evaluator compares the proposed proprietary name and prefix/suffix to all of the names gathered from the above searches, expert panel evaluation, and studies, and identifies potential failure modes by asking: "Is the name Acanya/Acanya Gel/Acanya _____ Gel convincing similar to another drug name, which may cause practitioners to become confused at any point in the usual practice setting?" An affirmative answer indicates a failure mode and represents a potential for Acanya/Acanya Gel/Acanya _____ Gel to be confused with another proprietary or established drug name because of look- or sound-alike similarity. If the answer to the question is no, the Safety Evaluator is not convinced that the names possess similarity that would cause confusion at any point in the medication use system and the name is eliminated from further review. b(4)

In the second stage of the Risk Assessment, all potential failure modes are evaluated to determine the likely *effect* of the drug name confusion, by asking "Could the confusion of the drug names conceivably result in medication errors in the usual practice setting?" The answer to this question is a central component of the Safety Evaluator's overall risk assessment of the proprietary name. If the Safety Evaluator determines through FMEA that the name similarity would ultimately not be a source of medication errors in the usual practice setting, the name is eliminated from further analysis. However, if the Safety Evaluator determines through FMEA that the name similarity could ultimately cause medication errors in the usual practice setting, the Safety Evaluator will then recommend that an alternate proprietary name be used. In rare instances, the FMEA findings may provide other risk-reduction strategies, such as product reformulation to avoid an overlap in strength or an alternate modifier designation may be recommended as a means of reducing the risk of medication errors resulting from drug name confusion.

The Division of Medication Error Prevention and Analysis will object to the use of proposed proprietary name when one or more of the following conditions are identified in the Safety Evaluator's Risk Assessment:

1. DDMAC finds the proposed proprietary name misleading from a promotional perspective, and the review Division concurs with DDMAC's findings. The Federal Food, Drug, and Cosmetic Act provides that labeling or advertising can misbrand a product if misleading representations are made or suggested by statement, word, design, device, or any combination thereof, whether through a trade name or otherwise. [21 U.S.C 321(n); see also 21 U.S.C. 352(a) & (n)].
2. The Division of Medication Error Prevention and Analysis identifies that the proposed proprietary name is misleading because of similarity in spelling or pronunciation to another proprietary or established name of a different drug or ingredient [CFR 201.10.(C)(5)].
3. FMEA identifies potential for confusion between the proposed proprietary name and other proprietary or established drug names, and demonstrates that medication errors are likely to result from the drug name confusion under the conditions of usual clinical practice.
4. The proposed proprietary name contains an USAN stem, particularly in a manner that is contradictory to the USAN Council's definition.

5. Medication error staff identify a potential source of medication error within the proposed proprietary name. The proprietary name may be misleading, or inadvertently introduce ambiguity and confusion that leads to errors. Such errors may not necessarily involve confusion between the proposed drug and another drug product.

In the event that the Division of Medication Error Prevention and Analysis object to the use of the proposed proprietary name, based upon the potential for confusion with another proposed (but not yet approved) proprietary name, we will provide a contingency objection based on the date of approval: whichever product is awarded approval first has the right to the use the name, while we will recommend that the second product to reach approval seek an alternative name.

If none of these conditions are met, then we will not object to the use of the proprietary name. If any of these conditions are met, then we will object to the use of the proprietary name. The threshold set for objection to the proposed proprietary name may seem low to the Sponsor/Applicant; however, the safety concerns set forth in criteria 1 through 5 are supported either by FDA Regulation or by external healthcare authorities, including the Institute of Medicine, World Health Organization, Joint Commission, and Institute for Safe Medication Practices, which have examined medication errors resulting from look- or sound-alike drug names and called for Regulatory Authorities to address the issue prior to approval.

Furthermore, the Division of Medication Error Prevention and Analysis contends that the threshold set for the Proprietary Name Risk Assessment is reasonable because proprietary drug name confusion is a predictable and preventable source of medication error that, in many instances, can be identified and remedied prior to approval to avoid patient harm.

Additionally, post-marketing experience has demonstrated that medication errors resulting from drug name confusion are notoriously difficult to remedy post-approval. Educational efforts and so on are low-leverage strategies that have proven to have limited effectiveness at alleviating the medication errors involving drug name confusion. Higher-leverage strategies, such as drug name changes, have been undertaken in the past; but at great financial cost to the Applicant, and at the expense of the public welfare, not to mention the Agency's credibility as the authority responsible for the approving the error-prone proprietary name. Moreover, even after Applicant's have changed a product's proprietary name in the post-approval phase, it is difficult to eradicate the original proprietary name from practitioner's vocabulary, and as such, the Agency has continued to receive reports of drug name confusion long after a name change in some instances. Therefore, we believe that post-approval efforts at reducing name confusion errors should be reserved for those cases in which the potential for name confusion could not be predicted prior to approval (see limitations of the process in Section 4).

If the Division of Medication Error Prevention and Analysis staff objects to a proposed proprietary name on the basis that drug name confusion could lead to medication errors, the FMEA process is used to identify strategies to reduce the risk of medication errors. The Division of Medication Error Prevention and Analysis is likely to recommend that the Applicant select an alternative proprietary name and submit the alternate name to the Agency for the Division of Medication Error Prevention and Analysis to review. However, in rare instances FMEA may identify plausible strategies that could reduce the risk of medication error of the currently proposed name, and so we may be able to provide the Applicant with recommendations that reduce or eliminate the potential for error would render the proposed name acceptable.