CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:
22-134

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

Date:	July 20, 2010
To:	Wiley Chambers, MD, Acting Director Division of Anti-infective and Ophthalmology Division
Thru:	Melina Griffis, RPh, Team Leader Denise Toyer, PharmD, Deputy Director Carol Holquist, RPh, Director Division of Medication Error Prevention and Analysis (DMEPA)
From:	Anne Crandall, PharmD, Safety Evaluator Division of Medication Error Prevention and Analysis (DMEPA)
Subject:	Proprietary Name Review
Drug Name(s):	Lastacaft (Alcaftadine) Ophthalmic Solution, 0.25%
Application Type/Number:	NDA # 022134
Sponsor:	Vistakon Pharmaceuticals, L.L.C.
OSE RCM #:	2010-1494

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

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EXECUTIVE SUMMARY

This review summarizes the analysis of the proposed proprietary name Lastacaft for Alcaftadine Ophthalmic Solution. Our evaluation did not identify concerns that would render the name unacceptable based on the product characteristics and safety profile known at the time of this review. Thus DEMPA finds the proposed propriety name, Lastacaft, acceptable for this product. DMEPA considers this a final review, however, if approval of the NDA is delayed beyond 90 days from the date of this review, the proposed proprietary name, Lastacaft, must be re-evaluated.

Additionally, if any of the proposed product characteristics as stated in this review are altered, DMEPA rescinds this finding and the name must be resubmitted for review. The conclusions upon re-review are subject to change.

1 BACKGROUND

1.1 INTRODUCTION

This review is in response to a request from Vistakon dated July 8, 2010 to evaluate the proposed proprietary name, Lastacaft, for its potential to contribute to medication errors. The proprietary name, Lastacaft, was evaluated to determine if the name could be potentially confused with other proprietary or established drug names. A previously proposed proprietary name for this product, (b) (4) was found unacceptable (OSE review # 2009-1810) due to orthographic similarity to Xalatan. Three additional names, (b) (4) and (b) (4) were submitted for review. These names were subsequently withdrawn by the Applicant due to preliminary safety concerns associated with all three names. The Applicant submitted container labels and carton labeling for review in a previous submission, which have been reviewed under separate cover (OSE Review #2009-1813).

1.2 PRODUCT INFORMATION

Lastacaft (Alcaftadine) is a H_1, H_2, and H_4 histamine receptor antagonist indicated for the prevention of itching associated with allergic conjunctivitis. The recommended dose of Lastacaft is one drop in each eye once daily. Lastacaft is available as a single strength (0.25%) and is packaged in 5 mL bottles which will contain either 1 mL or 3 mL.

2 METHODS AND MATERIALS

Appendix A describes the general methods and materials used by the Division of Medication Error Prevention and Analysis (DMEPA) when conducting a proprietary name risk assessment for all proprietary names. Sections 2.1, 2.2, and 2.3 identify specific information associated with the methodology for the proposed proprietary name, Lastacaft.

2.1 SEARCH CRITERIA

For this review, particular consideration was given to drug names beginning with the letter 'L' 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.[1,2]

To identify drug names that may look similar to 'Lastacaft', the DMEPA staff also considers the orthographic appearance of the name on lined and unlined orders. Specific attributes taken into consideration include the

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

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

length of the name (nine letters), upstrokes (four, capital letter 'L' and lower case letters 'l', 'f' and 't'), downstrokes (one, 'f' when scripted), and cross-strokes (three, lower case letters 't', 'f' and 't'). Additionally, several letters in Lastacaft may be vulnerable to ambiguity when scripted (see Appendix B). As a result, the DMEPA staff also considers these alternate appearances when identifying drug names that may look similar to Lastacaft.

When searching to identify potential names that may sound similar to Lastacaft, the DMEPA staff searches for names with similar number of syllables (three), stresses (LAS-ta-caft, las-TA-caft, or las-ta-CAFT), and placement of vowel and consonant sounds. Additionally, the DMEPA staff considers that pronunciation of parts of the name can vary (See Appendix B). Furthermore, names are often mispronounced and/or spoken with regional accents and dialects, so other potential pronunciations of the name are considered.

2.2 FDA PRESCRIPTION ANALYSIS STUDIES

Due to the impending PDUFA date of July 29, 2010 sufficient time was not available to conduct the Prescription Studies.

3 RESULTS

3.1 DATABASE AND INFORMATION SOURCES

The DMEPA Safety Evaluator searches yielded a total of nine names as having some similarity to the name Lastacaft.

Eight of the ten names (Labetalol (b) (4) Zafirlukast, Zostavax, Laronidase, Latanoprost, Lunesta, Gastrografin, and Lacrisert) were thought to look like Lastacaft by the DMEPA Safety Evaluators. The remaining name (Lactocal-F) was thought look and sound similar to Lastacaft by the DMEPA Safety Evaluators.

A search of the United States Adopted Name stem list on July 13, 2010 did not identify any United States Adopted Names (USAN) stem within the proposed name, Lastacaft.

3.2 EXPERT PANEL DISCUSSION

The Expert Panel reviewed the pool of names identified by DMEPA Safety Evaluators (See Section 3.1 above) and no noted additional names thought to have orthographic or phonetic similarity to Lastacaft.

DDMAC had no concerns regarding the proposed name from a promotional perspective.

3.3 FDA PRESCRIPTION ANALYSIS STUDIES

Due to the impending PDUFA date of July 29, 2010 sufficient time was not available to conduct the Prescription Studies.

3.4 SAFETY EVALUATOR RISK ASSESSMENT

Independent searches by the primary Safety Evaluator identified ten additional names, Cortastat, Carteolol, Calfactant, Calcitriol, Cilostazol, Levalbuterol, Lamictal, Nasacort, Carlesta, and Capastat thought to look similar to Lastacaft. Thus, a total of 20 names were identified as names with some similarity to Lastacaft.

As such, a total of 20 names were further analyzed to determine if the drug names could be confused with Lastacaft and if the drug name confusion would likely result in a medication error in the usual practice setting. Failure Mode and Effects Analysis was then applied to determine if the proposed name, Lastacaft, could potentially be confused with any of the 20 names and lead to medication errors.

3.5 COMMENTS FROM THE DIVISION OF ANTI-INFECTIVE AND OPHTHALMOLOGY PRODUCTS (DAIOP)

3.5.1 Initial Phase of Review

During a meeting held on July 14, 2010 with DAIOP, DAIOP did not state any comments or concerns related to the proposed proprietary name that would preclude the name's approvability.

3.5.2 Midpoint Review

On July 19, 2010 DMEPA notified the Division of Anti-Infective and Ophthalmology Products via e-mail that we had no objections to the proposed proprietary name, Lastacaft. Per email correspondence from DAIOP, the Division did not forward any concerns or comments with regards to the name analysis.

4 DISCUSSION

Lastacaft is the proposed proprietary name for Alcaftadine Ophthalmic Solution. This proposed name was evaluated from a safety and promotional perspective based on the product characteristics provided by Vistakon. We sought input from pertinent disciplines involved with the review of this application and considered it accordingly.

4.1 PROMOTIONAL ASSESSMENT

DDMAC found the proposed proprietary name acceptable from a promotional perspective, and did not offer any additional comments relating to the proposed name. DMEPA and the Division of Anti-infective and Ophthalmology Products concurred with the findings of DDMAC's promotional assessment of the proposed name.

4.2 SAFETY ASSESSMENT

DMEPA identified and evaluated 20 names for their potential similarity to the proposed name, Lastacaft. No other aspects of the name were identified as additional sources of error.

Failure Mode and Effects Analysis was applied to determine if the proposed name, Lastacaft, could potentially be confused with the 20 names and lead to medication errors. This analysis determined that the name similarity between Lastacaft and the identified names was unlikely to result in medication errors with any of the 20 products identified for the reasons presented in Appendix C.

5 CONCLUSIONS AND RECOMMENDATIONS

The Proprietary Name Risk Assessment findings indicate that the proposed name, Lastacaft, is not vulnerable to name confusion that could lead to medication errors, nor is it considered promotional. Thus the Division of Medication Error Prevention and Analysis (DMEPA) has no objection to the proposed proprietary name, Lastacaft, for this product at this time.

However, 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 the name must be resubmitted for review. In the event that our Risk Assessment finding is rescinded, the evaluation of the name on resubmission is independent of the previous Risk Assessment, and as such, the conclusions on re-review of the name are subject to change. Furthermore, if the approval of this application is delayed beyond 90 days from the signature date of this review, the proposed name must be resubmitted for evaluation.

We are willing to meet with the Division for further discussion, if needed. If you have further questions or need clarifications, please contact Brantley Dorch, OSE Project Manager at 301-796-0150.

5.1 COMMENTS TO THE APPLICANT

We have completed our review of the proposed proprietary name, Lastacaft, and have concluded that the name is acceptable.

The proposed proprietary name, Lastacaft, will need to be re-reviewed 90 days prior to the approval of the NDA. If we find the name unacceptable following the re-review, we will notify you.

If any of the proposed product characteristics are altered prior to approval of the marketing application, the proprietary name should be resubmitted for review. The conclusions upon re-review are subject to change.

6 REFERENCES

1. Micromedex Integrated Index (*http://csi.micromedex.com****)***

Micromedex contains a variety of databases covering pharmacology, therapeutics, toxicology and diagnostics.

2. Phonetic and Orthographic Computer Analysis (POCA)

POCA is a database which was created for the Division of Medication Error Prevention and Analysis, FDA. As part of the name similarity assessment, proposed names are evaluated via a phonetic/orthographic algorithm. The proposed proprietary name is converted into its phonemic representation before it runs through the phonetic algorithm. Likewise, an orthographic algorithm exists which operates in a similar fashion.

3. Drug Facts and Comparisons, online version, St. Louis, MO (*http://factsandcomparisons.com****)***

Drug Facts and Comparisons is a compendium organized by therapeutic course; it contains monographs on prescription and OTC drugs, with charts comparing similar products.

4. FDA Document Archiving, Reporting & Regulatory Tracking System [DARRTS]

DARRTS is a government database used to organize Applicant and Sponsor submissions as well as to store and organize assignments, reviews, and communications from the review divisions.

5. Division of Medication Errors Prevention and Analysis proprietary name consultation requests

This is a list of proposed and pending names that is generated by the Division of Medication Error Prevention and Analysis from the Access database/tracking system.

6. Drugs@FDA (*http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm****)***

Drugs@FDA contains most of the drug products approved since 1939. The majority of labels, approval letters, reviews, and other information are available for drug products approved from 1998 to the present. Drugs@FDA contains official information about FDA approved brand name, generic drugs, therapeutic biological products, prescription and over-the-counter human drugs and discontinued drugs and “Chemical Type 6” approvals.

7. Electronic online version of the FDA Orange Book *(http://www.fda.gov/cder/ob/default.htm)*

The FDA Orange Book provides a compilation of approved drug products with therapeutic equivalence evaluations.

8. U.S. Patent and Trademark Office (*http://www.uspto.gov****)***

USPTO provides information regarding patent and trademarks.

9. Clinical Pharmacology Online (www.clinicalpharmacology-ip.com)

Clinical Pharmacology contains full monographs for the most common drugs in clinical use, plus mini monographs covering investigational, less common, combination, nutraceutical and nutritional products. It also provides a keyword search engine.

10. Data provided by Thomson & Thomson's SAEGIS ™ Online Service, available at (www.thomson-thomson.com)

The Pharma In-Use Search database contains over 400,000 unique pharmaceutical trademarks and trade names that are used in about 50 countries worldwide. The data is provided under license by IMS HEALTH.

11. Natural Medicines Comprehensive Databases (www.naturaldatabase.com)

Natural Medicines contains up-to-date clinical data on the natural medicines, herbal medicines, and dietary supplements used in the western world.

12. Stat!Ref (www.statref.com)

Stat!Ref contains full-text information from approximately 30 texts; it includes tables and references. Among the database titles are: Handbook of Adverse Drug Interactions, Rudolphs Pediatrics, Basic Clinical Pharmacology, and Dictionary of Medical Acronyms Abbreviations.

13. USAN Stems (http://www.ama-assn.org/ama/pub/category/4782.html)

USAN Stems List contains all the recognized USAN stems.

14. Red Book Pharmacy's Fundamental Reference

Red Book contains prices and product information for prescription, over-the-counter drugs, medical devices, and accessories.

15. Lexi-Comp (www.lexi.com)

Lexi-Comp is a web-based searchable version of the Drug Information Handbook.

16. Medical Abbreviations Book

Medical Abbreviations Book contains commonly used medical abbreviations and their definitions

APPENDICES

Appendix A:

FDA's Proprietary Name Risk Assessment considers the potential for confusion between the proposed proprietary name and the proprietary and established names of drug products existing in the marketplace and those pending IND, NDA, BLA, and ANDA products currently under review by the Center. 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. 3

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

For the proposed proprietary name, DMEPA staff search a standard set of databases and information sources to identify names with orthographic and phonetic similarity and hold a Center for Drug Evaluation and Research (CDER) Expert Panel discussion to gather professional opinions on the safety of the proposed proprietary name. DMEPA staff also conducts internal CDER prescription analysis studies. When provided, DMEPA considers external prescription analysis study results and incorporate 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. DMEPA bases the overall risk assessment on the findings of a Failure Mode and Effects Analysis (FMEA) of the proprietary name, and focuses on the avoidance of medication errors.

FMEA is a systematic tool for evaluating a process and identifying where and how it might fail. 4 DMEPA uses FMEA to analyze whether the drug names identified with orthographic or phonetic similarity to the proposed proprietary name could cause confusion that subsequently leads to medication errors in the clinical setting. DMEPA uses the clinical expertise of its staff to anticipate the conditions of the clinical setting where the product is likely to be used 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. Accordingly, the DMEPA staff considers the product characteristics associated with the proposed drug throughout the risk assessment because 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 proprietary name include, but are not limited to; established name of the proposed product, proposed indication of use, 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, DMEPA staff 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.[5] DMEPA provides the product characteristics considered for this review in section one.

The Division of Medication Error Prevention and Analysis considers the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted. DMEPA also compares the spelling of the proposed proprietary name with the proprietary and established name of existing and proposed drug products because similarly in spelled names may have greater likelihood to sound similar to one another when spoken or look similar to one another when scripted. DMEPA staff also examines the orthographic appearance of the proposed name using a number of different handwriting samples. Handwritten communication of drug names has a long-standing association with drug name confusion. Handwriting can cause similarly and even dissimilarly spelled drug name pairs to appear very similar to one another. The similar appearance of drug names when scripted has led to medication errors. The DMEPA staff applies expertise gained from root-cause analysis of such medication errors to identify sources of ambiguity within the name that could be introduced when scripting (e.g.,"T" may look like "F," lower case 'a' looks like a lower case 'u,' etc). Additionally, other orthographic attributes that determine the overall appearance of the drug name when scripted (see Table 1 below for details). In addition, the DMEPA staff compares the pronunciation of the proposed proprietary name with the pronunciation of other drug names because

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

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

verbal communication of medication names is common in clinical settings. If provided, DMEPA will consider the Applicant's intended pronunciation of the proprietary name. However, DMEPA also considers a variety of pronunciations that could occur in the English language because the Applicant has little control over how the name will be spoken in clinical practice.

Table 1. Criteria used to identify drug names that look- or sound-similar to a proposed proprietary name.

Type of similarity	**Considerations when searching the databases**		
	Potential causes of drug name similarity	*Attributes examined to identify similar drug names*	*Potential Effects*
Look-alike	Similar spelling	Identical prefix Identical infix Identical suffix Length of the name Overlapping product characteristics	• Names may appear similar in print or electronic media and lead to drug name confusion in printed or electronic communication • Names may look similar when scripted and lead to drug name confusion in written communication
	Orthographic similarity	Similar spelling Length of the name Upstrokes Down strokes Cross-stokes Dotted letters Ambiguity introduced by scripting letters Overlapping product characteristics	• Names may look similar when scripted, and lead to drug name confusion in written communication
Sound-alike	Phonetic similarity	Identical prefix Identical infix Identical suffix Number of syllables Stresses Placement of vowel sounds Placement of consonant sounds Overlapping product characteristics	• Names may sound similar when pronounced and lead to drug name confusion in verbal communication

Lastly, the DMEPA staff also considers the potential for the proposed proprietary name to inadvertently function as a source of error for reasons other than name confusion. Post-marketing experience has demonstrated that proprietary names (or components of the proprietary name) can be a source of error in a variety of ways. Consequently, DMEPA considers and evaluates these broader safety implications of the name throughout this assessment and the medication error staff provides additional comments related to the safety of the proposed proprietary name or product based on professional experience with medication errors.

1. Database and Information Sources

DMEPA staff conducts searches 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 the proposed proprietary name using the criteria outlined in Section 2.1. Section 6 provides a standard description of the databases used in the searches. To complement the process, the DMEPA staff use 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 DMEPA staff review the USAN stem list to determine if any USAN stems are present within the proprietary name. The individual findings of multiple safety evaluators are pooled and presented to the CDER Expert Panel.

2. CDER Expert Panel Discussion

DMEPA conducts an Expert Panel Discussion to gather CDER professional opinions on the safety of the proposed product and the proposed proprietary name. The Expert Panel is composed of Division of Medication Errors Prevention (DMEPA) staff and representatives from the Division of Drug Marketing, Advertising, and Communications (DDMAC). The Expert Panel also discusses potential concerns regarding drug marketing and promotion related to the proposed names.

The primary Safety Evaluator presents the pooled results of the DMEPA staff 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 primary Safety Evaluator to supplement the pooled results, or general advice to consider when reviewing the proposed proprietary name.

3. 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 the proposed proprietary name 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. The studies employ healthcare professionals (pharmacists, physicians, and nurses), and attempts to simulate the prescription ordering process. The primary Safety Evaluator uses the results to identify orthographic or phonetic vulnerability of the proposed name to be misinterpreted by healthcare practitioners.

In order to evaluate the potential for misinterpretation of the proposed proprietary name in handwriting and verbal communication of the name, inpatient medication orders and/or outpatient prescriptions are written, each consisting of a combination of marketed and unapproved drug products, including the proposed name. These orders are optically scanned and one prescription is delivered to a random sample of the 123 participating health professionals via e-mail. In addition, a verbal prescription is 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 DMEPA.

4. Safety Evaluator Risk Assessment of the Proposed Proprietary Name

The primary Safety Evaluator applies his/her individual expertise gained from evaluating medication errors reported to FDA, conducts a Failure Mode and Effects Analysis, and provides an overall risk assessment 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, DMEPA seeks to evaluate the potential for a proposed proprietary name to be confused with another drug name because of name confusion and, thereby, 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 orthographically or phonetically similar 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 an FMEA of the proposed name, the primary Safety Evaluator must analyze the use of the product at all points in the medication use system. Because the proposed product is has not been marketed, the primary Safety Evaluator anticipates the use of the product in the usual practice settings by considering the clinical and product characteristics listed in Section one. 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 to all of the names gathered from the above searches, Expert Panel Discussion, and prescription studies, external studies, and identifies potential failure modes by asking:

> ***"Is the proposed proprietary name convincingly 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 the proposed proprietary name 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 posses similarity that would cause confusion at any point in the medication use system, thus the name is eliminated from further review.

In the second stage of the Risk Assessment, the primary Safety Evaluator evaluates all potential failure modes 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 not ultimately be a source of medication errors in the usual practice setting, the primary Safety Evaluator eliminates the name 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 the use of an alternate proprietary name.

DMEPA will object to the use of proposed proprietary name when the primary Safety Evaluator identifies one or more of the following conditions in the Risk Assessment:

a. 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 PROPRIETARY name or otherwise [21 U.S.C 321(n); See also 21 U.S.C. 352(a) & (n)].
b. DMEPA 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)].

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

c. FMEA identifies the potential for confusion between the proposed proprietary name and other proprietary or established drug name(s), and demonstrates that medication errors are likely to result from the drug name confusion under the conditions of usual clinical practice.
d. The proposed proprietary name contains an USAN (United States Adopted Names) stem.
e. DMEPA identifies a potential source of medication error within the proposed proprietary name. For example, 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.

If DMEPA objects to a proposed proprietary name on the basis that drug name confusion could lead to medication errors, the primary Safety Evaluator uses the FMEA process to identify strategies to reduce the risk of medication errors. DMEPA is likely to recommend that the Applicant select an alternative proprietary name and submit the alternate name to the Agency for DMEPA to review. However, in rare instances FMEA may identify plausible strategies that could reduce the risk of medication error of the currently proposed name. In that instance, DMEPA may be able to provide the Applicant with recommendations that reduce or eliminate the potential for error and, thereby, would render the proposed name acceptable.

In the event that DMEPA objects to the use of the proposed proprietary name, based upon the potential for confusion with another proposed (but not yet approved) proprietary name, DMEPA will provide a contingency objection based on the date of approval. Whichever product, the Agency approves first has the right to use the proprietary name, while DMEPA will recommend that the second product to reach approval seek an alternative name.

The threshold set for objection to the proposed proprietary name may seem low to the Applicant. However, the safety concerns set forth in criteria a through e are supported either by FDA regulation or by external healthcare authorities, including the Institute of Medicine (IOM), World Health Organization (WHO), Joint Commission on Accreditation of Hospitals (JCOAH), and the Institute for Safe Medication Practices (ISMP). These organizations have examined medication errors resulting from look- or sound-alike drug names and called for regulatory authorities to address the issue prior to approval. Additionally, DMEPA contends that the threshold set for the Proprietary Name Risk Assessment is reasonable because proprietary drug name confusion is a predictable and a preventable source of medication error that, in many instances, the Agency and/or Applicant can identify and rectify prior to approval to avoid patient harm.

Furthermore, post-marketing experience has demonstrated that medication errors resulting from drug name confusion are notoriously difficult to rectify post-approval. Educational and other post-approval efforts are low-leverage strategies that have had limited effectiveness at alleviating medication errors involving drug name confusion. Applicants have undertaken higher-leverage strategies, such as drug name changes, 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 approving the error-prone proprietary name. Moreover, even after Applicants' have changed a product's proprietary name in the post-approval phase, it is difficult to eradicate the original proprietary name from practitioners' vocabulary, and as a result, the Agency has continued to receive reports of drug name confusion long after a name change in some instances. Therefore, DMEPA believes 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 Section 4 for limitations of the process).

Appendix B: Letters with possible orthographic or phonetic misinterpretation

Letters in Name, Lastacaft	Scripted may appear as	Spoken may be interpreted as
Capital ‘L’	‘C’, ‘V’, ‘Z’, ‘h’, ‘b’	
Lower case ‘a’	‘e’, ‘o’	
Lower case ‘s’	‘r’, ‘n’	“z”, “c”
Lower case ‘t’	‘f’, ‘l’	“d”
Lower case ‘a	‘e’, ‘o’	
Lower case ‘c	‘e’	“k”, “ck”
Lower case ‘a’	‘e’, ‘o’	
Lower case ‘f’	‘t’, ‘l’	
Lower case ‘t’	‘f’, ‘l’	“d”

Appendix C: Name confusion is prevented by the combination of stated product characteristics and/or orthographic differences

Product name with potential for confusion	**Similarity to Lastacaft**	**Strength**	**Usual Dosage and administration**	**Name confusion is prevented by the stated product characteristics and/or orthographic differences as described**
Lastacaft (Alcaftadine)		**0.25% Ophthalmic solution**	**Instill 1 drop in each eye once daily**	
Capastat (Capreomycin sulfate)	Orthographic	1 g/10 mL lyophilized powder for injection	10 to 15 mg/kg/day intravenous or intramuscular once daily for 5 to 7 days a week. Can reduce to 2 to 3 times per week after 2 to 4 months	*Orthographic differences* - Lastacaft has four upstrokes vs. Capastat has three upstrokes - Lastacaft has one potential downstroke as the second to last letter vs. Capastat has a downstroke as the third letter - Lastacaft has two consecutive upstrokes as the last two letters vs. Capastat has a letter in between the two upstrokes, making the names appear visually different *Product characteristics* - Route of administration (ophthalmic vs. intravenous) - Dose (1 drop vs. weight based regimen, average 1000 mg per dose)
Carlesta (Dimethicone and Zinc)	Orthographic	2% topical ointment	Apply liberally to skin that will be exposed to sun	*Orthographic differences* - Lastacaft has four upstrokes vs. Carlesta has three upstrokes - Lastacaft has three cross-strokes vs. Carlesta has one cross-stroke -Lastacaft ends with two consecutive upstrokes vs. Carlesta does not end with an upstroke which increases the visual difference *Product characteristics* - Dose (1 drop vs. Apply liberally) Dosage form (solution vs. ointment)

Product name with potential for confusion	Similarity to Lastacaft	Strength	Usual Dosage and administration	Name confusion is prevented by the stated product characteristics and/or orthographic differences as described
Lastacaft (Alcaftadine)		**0.25% Ophthalmic solution**	**Instill 1 drop in each eye once daily**	
Nasacort (Triamcinolone)	Orthographic	55 mcg/acuation; 16.5 g bottle	1 – 2 sprays in each nostril once daily	*Orthographic differences* - 'L' in Lastacaft does not appear similar to 'N' in Nasacort scripted - Lastacaft contains three cross-strokes vs. Nasacort contains one cross-stroke - Lastacaft contains four upstrokes vs. Nasacort has two *Product characteristics* - Dose (drop vs. spray) - Route of administration (ophthalmic vs. nasal)
Lamictal (Levetiracetam)	Orthographic	25 mg, 100 mg, 150 mg, 200 mg	Titrate up to goal of 100 mg to 500 mg per day in one dose or equally divided doses	*Orthographic differences* - Lastacaft contains four upstrokes vs. Lamictal contains 3 upstrokes - Lastacaft has three cross-strokes vs. Lamictal has one cross-stroke - Lastacaft has nine letters vs Lamictal has seven letters making it appear shorter *Product characteristics* - Route of adminsitration (ophthalmic vs. oral) - Dose (drop vs. tablet) - Strength (single strength vs. multiple strengths, must be specified on prescription)

Product name with potential for confusion	Similarity to Lastacaft	Strength	Usual Dosage and administration	Name confusion is prevented by the stated product characteristics and/or orthographic differences as described
Lastacaft (Alcaftadine)		**0.25% Ophthalmic solution**	**Instill 1 drop in each eye once daily**	
Levalbuterol	Orthographic	0.31 mg/3 mL, 0.63 mg/3 mL, 1.25 mg/3 mL, 1.25 mg/0.5 mL	0.31 mg – 1.25 mg nebulized three times daily	*Orthographic differences* - Lastacaft ends with two consecutive upstrokes vs. Levalbuterol ends with one upstroke - Lastacaft contains nine letters vs. Levalbuterol has 12 letters - Lastacaft has three cross-strokes vs. Levalbuterol has one cross-stroke *Product characteristics* - Route of adminstration (ophthalmic vs. oral inhalation) - Dose (drop vs. ampule) - Strength (single strength, 0.25% vs. various strengths, 0.31 mg, 0.63 mg, 1.25 mg)
Lunesta (Eszopiclone)	Orthographic	1 mg, 2 mg, 3 mg oral tablet	1 mg to 3 mg immediately before bedtime	*Orthographic differences* - Lastacaft contains nine letters vs. Lunesta has seven letters which makes the name look shorter - Lastacaft contains 3 cross-strokes vs. Lunesta has one cross-stroke - Lastacaft has four upstrokes vs. Lunesta has two upstrokes *Product characteristics* - Route of adminstration (ophthalmic vs. oral) - Strength (single strength, 0.25% vs. various strengths, 1 mg, 2 mg, 3 mg) - Dose (drop vs. tablet)

Product name with potential for confusion	Similarity to Lastacaft	Strength	Usual Dosage and administration	Name confusion is prevented by the stated product characteristics and/or orthographic differences as described
Lastacaft (Alcaftadine)		**0.25% Ophthalmic solution**	**Instill 1 drop in each eye once daily**	
Lacrisert (hydroxypropyl cellulose)	Orthographic	5 mg ophthalmic insert; 60 inserts and applicator per box	One insert in each eye once daily	*Orthographic differences* - Lastacaft contains four upstrokes vs. Lacrisert has two – Lastacaft has three cross-strokes vs. Lacrisert has one - Lastacaft ends with two consecutive upstrokes and cross-strokes vs. Lacrisert ends with one upstroke and cross-stroke *Product characteristics* - Dosage form (solution vs. insert)
Laronidase	Orthographic	2.9 mg/5 mL injection solution	Titration dose: 10 mcg/kg/hour may be incrementaly increased every 15 minutes for first hour Maintenance dose: 0.58 mg/kg intravenous infusion once per week	*Orthographic differences* - Lastacaft contains four upstrokes vs. Laronidase has two - Lastacaft has three cross-strokes vs. Laronidase has none *Product characteristics* - Strength (single, 0.25% vs. weight based regimen ranging from 5 mg to 100 mg) Route of administration (ophthalmic vs. intravenous) Frequency of administration (every day vs. once a week)

Product name with potential for confusion	Similarity to Lastacaft	Strength	Usual Dosage and administration	Name confusion is prevented by the stated product characteristics and/or orthographic differences as described
Lastacaft (Alcaftadine)		**0.25% Ophthalmic solution**	**Instill 1 drop in each eye once daily**	
Latanoprost	Orthographic	0.005% ophthalmic solution	One drop in the affected eye once daily in the evening	*Orthographic differences* - Lastacaft has nine letters vs. Latanoprost has 11 letters which makes it appear longer - Lastacaft has one possible downstroke, depending on how 'f' is scripted, as the second to last letter vs. Latanoprost has a down stroke in the middle of the name - Lastacaft has three cross-strokes vs. Latanoprost has two – Lastacaft has two letters between the first two upstrokes vs. Latanoprost has one letter between the first two upstrokes
Zafirlukast	Orthographic	10 mg, 20 mg oral tablet	10 mg to 20 mg by mouth twice daily	*Orthographic differences* - Lastacaft has two consecutive upstrokes and cross-strokes as the last letters vs. Zafirlukast has one upstroke and cross-stroke - Lastacaft has two letters between the first two upstrokes vs. Zafirlukast has one letter between the first upstrokes *Product characteristics* - strength (single strength, 0.25% vs. 10 mg or 20 mg) - Route of administration (ophthalmic vs. oral) - Dosage form (solution vs. tablet)

Product name with potential for confusion	Similarity to Lastacaft	Strength	Usual Dosage and administration	Name confusion is prevented by the stated product characteristics and/or orthographic differences as described
Lastacaft (Alcaftadine)		**0.25% Ophthalmic solution**	**Instill 1 drop in each eye once daily**	
Cilostazol	Orthographic	50 mg, 100 mg oral tablet	50 mg to 100 mg by mouth twice daily	*Orthographic differences* - Lastacaft has three cross-strokes vs. Cilostazol has one cross-stroke - Lastacaft has two consecutive upstrokes at the end of the name vs. Cilostazol has only one *Product characteristics* - Strength (single strength vs. 50 mg, 100 mg) - Route of administration (ophthalmic vs. oral) - Dosage form (solution vs. tablet)
Calcitriol (1a,25 Dihydroxy-cholecalciferol)	Orthographic	0.25 mcg, 0.5 mcg oral capsule, 1mcg/mL oral solution 1 mcg/mL, 2 mcg/mL intravenous injection	0.25 mcg to 0.5 mcg by mouth once daily 0.5 mcg to 2 mcg intravenously three times a week	*Orthographic differences* - Lastacaft has three cross-strokes vs. Calcitriol has one cross-stroke - Lastacaft ends with two consecutive upstrokes and cross-strokes vs. Calcitriol ends with one up-stroke and no cross-stroke *Product differences* - Route of administration (ophthalmic vs. oral or intravenous) - Dose (drop vs. capsule or vial)

Product name with potential for confusion	Similarity to Lastacaft	Strength	Usual Dosage and administration	Name confusion is prevented by the stated product characteristics and/or orthographic differences as described
Lastacaft (Alcaftadine)		**0.25% Ophthalmic solution**	**Instill 1 drop in each eye once daily**	
Calfactant	Orthographic	35 mg phospholipids per mL; 6 mL vial	3 mL/kg intrathecally every 12 hours for a total of up to 3 doses as soon as possible after birth	*Orthographic differences* - Lastacaft is nine letters vs. Calfactant is 11 letters, making it appear longer - Lastacaft has four upstrokes vs. Calfactant has five upstrokes *Product characteristics* - Route of administration (ophthalmic vs. intrathecal) - Dose (drop vs. mL/kg) - Frequency (once daily vs. every 12 hours for 3 doses)
Carteolol	Orthographic	1% ophthalmic solution	1 drop in the affected eye(s) twice daily	*Orthographic differences* - Lastacaft has three cross-strokes vs. Carteolol has one cross-stroke - Lastacaft ends with two consecutive cross-strokes vs. Carteolol does not end with a cross-stroke - The last upstrokes of Lastacaft are situated next to one another vs. Carteolol has one letter in between the upstrokes *Product characteristics* - Frequency of administration (once daily vs. twice daily)

Product name with potential for confusion	Similarity to Lastacaft	Strength	Usual Dosage and administration	Name confusion is prevented by the stated product characteristics and/or orthographic differences as described
Lastacaft (Alcaftadine)		**0.25% Ophthalmic solution**	**Instill 1 drop in each eye once daily**	
Labetalol	Orthographic	100 mg, 200 mg, 300 mg oral tablets, 5 mg/mL injection	200 mg to 1200 mg by mouth twice daily 20 mg slow intravenous injection over 2 minutes, 40 mg to 80 mg at 10 minute intervals or 50 mg to 200 mg at 2 mg/minute	*Orthographic differences* - Lastacaft has three cross-strokes vs. Labetalol has one cross-stroke - Lastacaft ends with two consecutive cross-strokes vs. Labetalol ends with no cross-strokes - The last upstrokes of Lastacaft are situated next to one another vs. Labetalol has one letter in between the upstrokes *Product characteristics* - Strength (single strength, 0.25% vs. 100 mg, 200 mg, 300 mg or 20 mg to 80 mg) - Route of administration (ophthalmic vs. oral or intravenous)
Lustra-Ultra (Hydroquinone)	Orthographic	4% topical cream	Apply sparingly to affected area twice daily	*Orthographic differences* - Lastacaft is nine letters vs. Lustra-Ultra is 11 letters - Lastacaft ends with two upstrokes and cross-strokes vs. Lustra-Ultra does not end with either upstrokes or cross-strokes *Product characteristics* - Frequency of administration (once daily vs. twice daily) - Application site (eyes vs. affected area) - Dosage form (solution vs. cream) - Dose (drop vs. small amount or sparingly)

Product name with potential for confusion	Similarity to Lastacaft	Strength	Usual Dosage and administration	Name confusion is prevented by the stated product characteristics and/or orthographic differences as described
Lastacaft (Alcaftadine)		**0.25% Ophthalmic solution**	**Instill 1 drop in each eye once daily**	
Zostavax (Zoster vaccine live)	Orthographic	19,400 PFU of varicella-zoster live virus	Single dose administered subcutaneously once	*Orthographic differences* - Lastacaft has four upstrokes vs. Zostavax has two upstrokes - Lastacaft ends with two upstrokes and cross-strokes vs. Zostavax ends with no cross-strokes or upstrokes *Product differences* - Route of administration (ophthalmic vs. subcutaneous) - Frequency of administration (every day vs. once) - Setting of use (clinic, must be administered by health care professional vs. self administration at home)
Cortastat (Dexamethasone)	Orthographic	4 mg/mL; 5 mL	1 mg to 9 mg per day, up to 40 mg every 4 to 6 hours, 2-6 mg/kg as single intravenous injection, can be given intramuscular, intravenous push or intravenous infusion	*Orthographic differences* - Lastacaft has three letters between the second and third upstrokes vs. Cortastat has two letters giving the name a different shape *Product differences* - Strength (single strength vs. strength varies with indication, 1 mg up to 600 mg - Route of administration (ophthalmic vs. intramuscular or intravenous)

Product name with potential for confusion	Similarity to Lastacaft	Strength	Usual Dosage and administration	Name confusion is prevented by the stated product characteristics and/or orthographic differences as described
Lastacaft (Alcaftadine)		**0.25% Ophthalmic solution**	**Instill 1 drop in each eye once daily**	
Lactocal-F (Multivitamin)	Orthographic and Phonetic	1 mg folate, 65 mg Iron, multivitamin	One tablet daily as directed	*Orthographic differences* - Lastcaft has three cross-strokes vs. Lactocal has one - Lastacaft has four upstrokes vs. Lactocal has three - Lastacaft ends with two consecutive upstrokes and cross-strokes vs. Lastocal ends with one upstroke *Product differences* - Dose (drop vs. tablet) - Route (ophthalmic vs. oral)
Gastrografin (Diatrizoate meglumine and Diatrizoate sodium)	Orthographic	660 mg/100 mg/mL oral or rectal solution; 30 mL and 120 mL bottles	Adult oral dose: 30 mL to 90 mL by mouth or 25 mL of Gastrografin in one liter of tap water prior to procedure Pediatric oral dose: 30 mL to 60 mL by mouth prior to procedure, can be diluted as 1:1 Enema: 240 mL of Gastrografin diluted in 1,000 mL of tap water	*Orthographic differences* - Lastacaft is nine letters vs. Gastrografin is 12 letters which makes it appear longer - Lastacaft has one possible down-stroke, depending on how 'f' is scripted vs. Gastrografin has one down-stroke and another possible down-stroke - Lastacaft ends with two consecutive upstrokes and cross-strokes vs. Gastrografin does not end with either an upstroke or a cross-stroke *Product characteristics* - Route of administration (ophthalmic vs. oral or rectal) - Dose (1 drop vs. 25 mL to 240 mL)

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

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22134	ORIG-1	VISTAKON PHARMACEUTICALS LLC	ALCAFTADINE OPHTHALMIC SOLUTION O.25%

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

/s/

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