CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22-369

PROPRIETARY NAME REVIEW(S)

Department of Health and Human Services

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Center for Drug Evaluation and Research

Office of Surveillance and Epidemiology

Date:	November 19, 2008
To:	Wiley Chambers, MD, Acting Director Division of Anti-infective and Ophthalmologic Products
Thru:	Kellie Taylor, PharmD, MPH, Team Leader Carol Holquist, R.Ph., Director Division of Medication Error Prevention and Analysis
From:	Melina Griffis, R.Ph., Safety Evaluator Division of Medication Error Prevention and Analysis
Subject:	Proprietary Name, Packaging, Label and Labeling Review
Drug Name(s):	Latisse (Bimatoprost Solution) 0.03%
Application Type/Number:	NDA 22-369
Applicant/sponsor:	Allergan
OSE RCM #:	2008-1144

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EXECUTIVE SUMMARY

The results of the Proprietary Name Risk Assessment found that the proposed name, Latisse, is not vulnerable to name confusion that could lead to medication errors. Thus, the Division of Medication Error Prevention and Analysis does not object to the use of the proprietary name, Latisse, for this product.

If **any** of the proposed product characteristics as stated in this review are altered prior to approval of the product, we rescind this Risk Assessment finding, and recommend that the name be resubmitted for review.

Furthermore, this name must be re-evaluated upon submission of the NDA and approximately 90 days prior to the expected action date of the NDA. A re-review of the name prior to NDA approval will rule out any objections based upon approval of other proprietary or established names from the signature date of this document.

However, we note our concerns about the potential for this product to be administered via the ophthalmic route instead of topically and have provided comments in section 5.1 of this review.

1 BACKGROUND

1.1 INTRODUCTION

This review is in response to a request from the Division of Anti-infective and Ophthalmologic Products for assessment of the proprietary name, Latisse, regarding potential name confusion with other proprietary or established drug names. The proposed product design, container label, and insert labeling were provided by the sponsor for our evaluation.

1.2 PRODUCT INFORMATION

Latisse (bimatoprost solution) is a pending NDA with an anticipated action date of December 27, 2008. Latisse is a synthetic prostaglandin structural analog indicated to improve the prominence of natural eyelashes as measured by increases in growth (length), fullness (thickness), and darkness (intensity). The recommended dose is one application nightly directly to the skin of the upper eyelid margin at the base of the eyelashes for each eye. It is supplied in a 5 mL bottle containing 3 mL of 0.03% bimatoprost solution. The applicators are packaged as two single use sterile disposable applicators and are supplied in a box of 60 total applicators. The instructions for use are to apply 1drop to the disposable applicator and brush cautiously along the skin of the upper eyelid margin at the base of the eyelashes. Patients are instructed not to apply to the lower eyelid and to blot any excess solution with a tissue.

Bimatoprost solution is also marketed under the proprietary name Lumigan® as an ophthalmic solution indicated in the treatment of open angle glaucoma or ocular hypertension.

2 METHODS AND MATERIALS

This section consists of methods and materials used by medication error staff conducting a proprietary name risk assessment (see 2.1 Proprietary Name Risk Assessment). The primary focus for this 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]

2.1 PROPRIETARY NAME RISK ASSESSMENT

FDA's Proprietary Name Risk Assessment considers the potential for confusion between the proposed proprietary name, Latisse, 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 CDER.

For the proprietary name, Latisse, the medication error staff of the Division of Medication Error Prevention and Analysis 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 held an CDER Expert Panel discussion to gather professional opinions on the safety of the proposed proprietary name (see 2.1.1.2). The Division 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 (see detail 2.1.4).

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 2.1.4). 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. [1] 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.[2]

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

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

2.1.1 Search Criteria

The Medication Error Staff consider 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 '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.[3,4]

To identify drug names that may look similar to Latisse, the Staff also consider the other orthographic appearance of the name on lined and unlined orders. Specific attributes taken into consideration include the length of the name (seven), upstrokes (two, capital letter 'L', lower case 't'), downstokes (none), cross-strokes (t), and dotted letters ('i'). Additionally, several letters in Latisse may be vulnerable to ambiguity when scripted, including the letter 'L' may appear as 'Z', 'C' or 'F'; lower case 'a' may appear as a lower case 'o' or 'e' and lower case 't' may appear as 'b'. As such, the Staff also considers these alternate appearances when identifying drug names that may look similar to Latisse.

When searching to identify potential names that may sound similar to Latisse, the Medication Error Staff search for names with similar number of syllables (two), stresses (LAH-tise or la-TISE), and placement of vowel and consonant sounds. The sponsor's intended pronunciation of the proprietary name could not be expressly taken into consideration, as this was not provided with the proposed name submission.

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 (Latisse), the established name (bimatoprost solution), proposed indication (improve the prominence of natural eyelashes), strength (0.03%), dose (one applicator), frequency of administration (nightly), route (topical) and dosage form of the product (solution). Appendix A provides a more detailed listing of the product characteristics the Medication Error Staff generally take into consideration.

Lastly, the Medication Error Staff also consider the potential for the proposed 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. As such, these broader safety implications of the name are considered and evaluated throughout this assessment and the Medication Error Staff provide 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, Latisse, was 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

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

[4] Kondrack, G and Dorr, B. Automatic Identification of Confusable Drug Names. Artifical Inteligence in Medicine (2005)

names that may sound-alike or look-alike to Latisse 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 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 Medication Error Staff review 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.

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, Latisse. 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 Medication Errors Prevention Staff and representatives from the Division of Drug Marketing, Advertising, and Communications (DDMAC).

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 CDER 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 Latisse 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 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 to be misinterpreted by healthcare practitioners.

In order to evaluate the potential for misinterpretation of Latisse 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 one prescription is delivered to a random sample of 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 the medication error staff.

Figure 1. 0813 Study (conducted on August 13, 2008)

HANDWRITTEN PRESCRIPITON AND MEDICATION ORDER	VERBAL PRESCRIPTION
Inpatient Medication Order: Latisse Apply once to upper eyelid hs	Latisse #1 Apply to upper eyelid at bedtime
Outpatient Prescription Order: Latisse #1 apply once to upper eyelid at bedtime	

2.1.3 Safety Evaluator Risk Assessment of the Proposed Proprietary Name

Based on the criteria set forth in Section 2.1.1, the Safety Evaluator Risk Assessment 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.[5] When applying FMEA to assess the risk of a proposed proprietary name, the Division of Medication Error Prevention and Analysis seeks 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 then remedies available in the post-approval phase.

In order to perform an 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 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 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 Latisse convincingly similar to another drug name, which may cause practitioners to become confused at any point in the usual

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

practice setting?" An affirmative answer indicates a failure mode and represents a potential for Latisse 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 and the name is eliminated from further review.

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 the 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 name and another drug product.

In the event that the Division of Medication Error Prevention and Analysis objects to the use of the proposed proprietary name, based upon the potential for confusion with another proposed (but not yet approved) proprietary name, the Division 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 the Division will recommend that the second product to reach approval seek an alternative name.

If none of these conditions are met, then the Division of Medication Error Prevention and Analysis will not object to the use of the proprietary name. If any of these conditions are met, then the

Division 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; however, the safety concerns set forth in criteria 1 through 5 are supported either by FDA Regulation or by external healthcare authorities, including the IOM, WHO, JCAHO, and ISMP, 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 Sponsor, 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 Sponsor'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, the Division of Medication Error Prevention and Analysis 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 limitations of the process).

If the Division of Medication Error Prevention and Analysis 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 Sponsor 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 the Division of Medication Error Prevention and Analysis may be able to provide the Sponsor with recommendations that reduce or eliminate the potential for error would render the proposed name acceptable.

2.2 PACKAGING, LABEL AND LABELING RISK ASSESSMENT

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

Given the critical role that the label and labeling has in the safe use of drug products, it is not surprising that 33 percent of medication errors reported to the USP-ISMP Medication Error Reporting Program may be attributed to the packaging and labeling of drug products, including 30 percent of fatal errors.[6]

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

Because our 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. DMEPA uses FMEA and the principles of human factors to identify potential sources of error with the proposed product labels and insert labeling, and provided recommendations that aim at reducing the risk of medication errors.

For this product the Sponsor submitted the following labels and insert labeling for our review (see Appendix K and L for images):

- Carton Labels (sterile applicators and 3 mL solution bottle)
- Container Labels (sterile applicators and 3 mL solution bottle)
- Package Insert (images not included)

In addition, a product sample, containing the bottle and applicator packaging, was provided for our review.

3 RESULTS

3.1 PROPRIETARY NAME RISK ASSESSMENT

3.1.1 Database and Information Sources

Our search of the internet, several standard published databases and information sources (see Section 7 References) identified 16 names as having some similarity to the name Latisse: Codituss DM, Lactase, Alesse, Lantus, Lotensin, Lutera, Catarase, Lactrase, Latis, Patanase, Lotemax, Lotronex, Lotrimin, Laten, Lidex, and Letairis.

Fourteen of the 16 names were thought to look like Latisse (Codituss DM, Lactase, Alesse, Lantus, Lotensin, Lutera, Catarase, Lactrase, Latis, Patanase, Lotemax, Lotronex, Lotrimin, Laten) and one name (Letairis) was thought to look and sound similar to Latisse. One name (Lidex) was thought to sound like Latisse.

No USAN stems were identified in Latisse as of August 18, 2008.

3.1.2 CDER Expert Panel Discussion

The Expert Panel reviewed the pool of names identified by the Division of Medication Error Prevention and Analysis staff (see section 3.1.1. above), but did not identify any additional names with similarity to Latisse.

DDMAC had no concerns regarding the proposed name from a promotional perspective, and did not offer any additional comments relating to the proposed name.

3.1.3 CDER Prescription Analysis Studies

A total of 31 practitioners responded, but none of the responses overlapped with any existing or proposed drug names. About 87% of the participants (n=26) interpreted the name correctly as "Latisse," with correct interpretation occurring more frequently in the written studies. The remainder of the responses misinterpreted the drug name. The majority of misinterpretations occurred in the phonetic prescription study, 4 respondents misinterpreted 'Latisse' as 'Latise' or 'Latese'. In the written prescription studies, the letter 'a' was misinterpreted as o by one respondent. See Appendix A for the complete listing of interpretations from the verbal and written prescription studies.

3.1.4 Safety Evaluator Risk Assessment

Independent searches by the primary Safety Evaluator identified one additional name thought to look similar to Latisse [redacted] As such, a total of 17 names were analyzed to determine if the drug names could be confused with Latisse and if the drug name confusion would likely result in a medication error. b(4)

All of the identified names were determined to have some orthographic and/or phonetic similarity to Latisse, and thus determined to present some risk for confusion. Failure mode and effects analysis (FMEA) was then applied to determine if the proposed name, Latisse, could potentially be confused with any of the 17 names and lead to medication error.

This analysis determined that the name similarity between Latisse and the identified names was unlikely to result in medication errors for all 17 product names for the reasons described in Appendices C through J.

Bimatoprost Solution 0.03% is also marketed under the proprietary name Lumigan and is intended for administration into the eye for the reduction of elevated intraocular pressure in patients with glaucoma or ocular hypertension. As such, the approval of Latisse would create a dual trade name for this active ingredient. DMEPA considered the risks associated with this nomenclature strategy.

3.2 PACKAGING, LABEL AND LABELING RISK ASSESSMENT

Review of the container labels, carton labeling, package insert and proposed product packaging identified several potential sources of medication error.

3.2.1 General Comment

The product is packaged in two components; one 5 mL bottle containing 3 mL of bimatoprost solution and shaped identical to ophthalmic products and one box containing 60 sterile disposable applicators.

The applicators consist of a thin plastic stick with an angled brush on one end.

3.2.2 Retail Container Labels and Carton Labeling

A graphic depicting an eyelash is located in close proximity to the proprietary name.

The proprietary name Latisse is prominently displayed on the carton label for the sterile applicators.

The 3 mL eye drop container label does not contain the statement 'For topical use only'.

4 DISCUSSION

4.1 PROPRIETARY NAME RISK ASSESSMENT

The results of the Proprietary Name Risk Assessment found that the proposed name, Latisse, has some similarity to other proprietary drug names, but the findings of the FMEA indicates that the proposed name does not appear to be vulnerable to name confusion that could lead to medication errors.

Bimatoprost Solution 0.03% is also marketed by the same manufacturer under the proprietary name Lumigan and is intended for administration into the eye for the reduction of elevated intraocular pressure in patients with glaucoma or ocular hypertension. As such, the approval of Latisse would create a dual trade name for this established name.

The introduction of a second bimatoprost solution with a different proprietary name could lead to inadvertent use of both products concurrently. Our Division's postmarketing surveillance of medication errors reveals that overdoses of medication occur when a prescriber, unfamiliar with all proprietary names of a medication, prescribes a medication to the patient who is already receiving the same medication under a different proprietary name for possibly a different indication. In these situations, the patient may receive an overdose, thus potentially leading to an adverse event.

Although such risks apply in this case, we acknowledge that the use of a different proprietary name would likely help minimize medication errors associated with the wrong route of administration since Lumigan is intended for administration into the eye and Latisse is for topical use only.

The findings of the Proprietary Name Risk Assessment are based upon current understanding of factors that contribute to medication errors involving name confusion. Although we believe the findings of the Risk Assessment to be robust, our findings do have limitations. First, because our assessment involves a limited number of practitioners, it is possible that the analysis did not identify a potentially confusing name. Also, there is some possibility that our Risk Assessment failed to consider a circumstance in which confusion could arise. However, the Division of Medication Error Prevention and Analysis believes that these limitations are sufficiently minimized by the use of an Expert Panel, the CDER Prescription Studies that involved 123 CDER practitioners, and, in this case, the data submitted by the Sponsor from an independent proprietary name risk assessment firm, which included the responses of frontline practitioners.

However, our risk assessment also faces limitations beyond the control of the Agency. First, our risk assessment is based on current health care practices and drug product characteristics, future changes to either could increase the vulnerability of the proposed name to confusion. Since these changes cannot be predicted for or accounted by the current Proprietary Name Risk Assessment process, such changes limit our findings. To help counterbalance this impact, the Division of Medication Error Prevention and Analysis recommends that the proprietary name be re-submitted for review when the NDA is filed and 90 days prior to the goal date.

4.2 PACKAGING, LABEL AND LABELING RISK ASSESSMENT

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

4.2.1 General Comment

The proposed packaging of Latisse as presented could lead to administration of the product into the eye either by direct application or inadvertent exposure. The bimatoprost solution supplied in a 3 ml eye drop container has an inherent risk of patients administering the product directly into the eye since the packaging is similar to most ophthalmic products. Additionally, there would be an increased risk of administration of Latisse in the eye if the applicators which are in a separate container were to be separated from the solution bottle. In previous discussions with the review division we were informed that an alternate packaging configuration for Latisse is not feasible due to sterility concerns associated with the product.

4.2.2 Retail Container Labels and Carton Labeling

The graphic depicting an eyelash is located in close proximity to the proprietary name and is distracting. It is recommended that it be located to another section of the label away from the proprietary name.

The proprietary name Latisse is displayed on the carton label for the sterile applicators. This is misleading and could lead patients to think that the applicators contain active drug. It is recommended that the labeling for the applicators display the Latisse name less prominently or avoid the name altogether and only state that the applicators contained are for use with Latisse.

The immediate container label for the 3 mL bottle does not bear the statement 'For topical use only'. It is recommended that this or a similar statement be added to help prevent administration of Latisse directly into the eye.

5 CONCLUSIONS AND RECOMMENDATIONS

The Proprietary Name Risk Assessment findings indicate that the proposed name, Latisse, is not vulnerable to name confusion that could lead to medication errors. As such, the Division of Medication Error Prevention and Analysis does not object to the use of the proprietary name, Latisse, for this product at this time.

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

5.1 COMMENTS TO THE DIVISION

The Division of Medication Errors Prevention 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 sponsor with regard to this review. If you have further questions or need clarifications, please contact Cheryl Campbell, project manager, at 301-796-0723.

1. The Division of Medication Error Prevention and Analysis has no objection to the use of the proprietary name Latisse for this product. If **any** of the proposed product characteristics as stated in this review are altered prior to approval of the product, we rescind this Risk Assessment finding, and recommend that the name be resubmitted for review. If the product approval is delayed beyond 90 day from the date of this review, the proposed name must be resubmitted for evaluation.
2. The proposed packaging of Latisse as presented could lead to administration of the product into the eye either by direct application or inadvertent exposure. The bimatoprost solution supplied in a 3 mL eye drop container has an inherent risk of patients administering the product directly into the eye since the packaging is similar to most ophthalmic products. Additionally, there would be an increased risk of administration of Latisse in the eye if the applicators which are in a separate container were to be separated from the solution bottle. In previous discussions with your Division we acknowledge that an alternate packaging configuration for Latisse is not feasible due to sterility concerns associated with the product.

5.2 COMMENTS TO THE APPLICANT

5.2.1.1 Proprietary Name

The Division of Medication Error Prevention and Analysis has no objections to the use of the proprietary name Latisse for this product.

5.2.1.2 Retail Container Labels and Carton Labeling

1. The graphic depicting an eyelash is located in close proximity to the proprietary name and is distracting. It should be relocated to another section of the label away from the proprietary name.
2. The proprietary name Latisse is prominently displayed on the carton label for the sterile applicators. This is misleading and could lead patients to think that the applicators contain active drug. The labeling for the applicators should be revised to state that the applicators contained are for use with Latisse.
3. The immediate container label for the 3 mL bottle does not bear the statement 'For topical use only'. This or a similar statement should be added to help minimize the risk of administrating Latisse directly into the eye.

6 REFERENCES

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

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

2. Phonetic and Orthographic Computer Analysis (POCA)

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. This is a database which was created for the Division of Medication Error Prevention and Analysis, FDA.

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

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

4. AMF Decision Support System [DSS]

DSS is a government database used to track individual submissions and assignments in 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)*

Provides a compilation of approved drug products with therapeutic equivalence evaluations.

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

Provides information regarding patent and trademarks.

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

Contains full monographs for the most common drugs in clinical use, plus mini monographs covering investigational, less common, combination, nutraceutical and nutritional products. 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)*

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)*

Contains full-text information from approximately 30 texts. 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)*

List contains all the recognized USAN stems.

14. ***Red Book Pharmacy's Fundamental Reference***

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

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

A web-based searchable version of the Drug Information Handbook.

16. ***Medical Abbreviations Book***

Contains commonly used medical abbreviations and their definitions.

APPENDICES

Appendix A:

The medication error staff consider the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted. The Division of Medication Error Prevention and Analysis also compare the spelling of the proposed proprietary name with the proprietary and established name of existing and proposed drug products because similarly spelled names may have greater likelihood to sound similar to one another when spoken or look similar to one another when scripted. The Medication Error Staff also examine 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* dissimilarly spelled drug name pairs to appear very similar to one another and the similar appearance of drug names when scripted has lead to medication errors. The medication error staff apply their expertise gained from root-cause analysis of such medication errors to identify sources of ambiguity within the name that could be introduced when scripting (i.e. "T" may look like "F," lower case 'a' looks like a lower case 'u,' etc), along with other orthographic attributes that determine the overall appearance of the drug name when scripted (see detail in Table 1 below). Additionally, since verbal communication of medication names is common in clinical settings, the Medication Error Staff compare the pronunciation of the proposed proprietary name with the pronunciation of other drug names. If provided, the Division of Medication Error Prevention and Analysis will consider the Sponsor's intended pronunciation of the proprietary name. However, because the Sponsor has little control over how the name will be spoken in practice, the Division of Medication Error Prevention and Analysis also considers a variety of pronunciations that could occur in the English language.

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 Downstrokes	• Names may look similar when scripted, and lead to drug name confusion in written communication

		Cross-stokes Dotted letters Ambiguity introduced by scripting letters Overlapping product characteristics	
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

Appendix B:

CDER Prescription Study Responses- Latisse Study

Inpatient Medication Order	Voice Prescription	Outpatient Prescription Order
Latisse	Latisse	Latisse
Latisse	Latise	Latisse
Latisse	Latisse	Latisse
Latisse	Latese	Latisse
Latisse	Latisse	Latisse
Latisse	Latise	Latisse
Latisse	Latisse	Latisse
Lotisse	Latise	Latisse
Latisse		
Latisse		
Latisse		
Latisse		
Latisse		

Latisse		
Latisse		

Appendix C: Names lacking convincing orthographic and/or phonetic similarities with Latisse

Proprietary Name	Similarity to Latisse
Codituss DM	Look Alike
Patanase	Look Alike

Appendix D: Names of products withdrawn from the market

Proprietary Name	Status	Date
Catarase (chymotrypsin)	NDA Withdrawn (no longer available in brand or generic formulations)	June 1, 1993

Appendix E: Proprietary names Safety Evaluator unable to locate in any pharmaceutical databases

Proprietary Name	Similarity to Latisse	Status of product name
Laten	Look alike	Listed in Martindale's, however, unable to locate in any other drug database

Appendix F: Unapproved Proposed Proprietary name

Proposed Proprietary Name	Status
[redacted] (not recommended for use by DMEPA; OSE review 04-0195)	NDA approved under the proprietary name [redacted]

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Appendix G: Names of products not considered to be pharmaceutical products

Proprietary Name	Product Type
Latis	Spinal implants for use in spinal surgery

Appendix H: Products with no overlap in strength and usual dosage

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)
Latisse (bimatoprost solution)		0.03%	Apply topically to each upper eyelid margin nightly
Lotronex (alosetron Hcl)	Look Alike	0.5 mg and 1 mg tablets	0.5 mg to 1 mg twice daily
Letairis (ambrisentan)	Look and sound alike	5 mg and 10 mg tablets	5 mg to 10 mg once daily
Lactase (gastroentestianl enzymes)	Look alike	3,000 and 9,000 FCCU tablets	Dose individualized according to patient need and response
Lotensin (benazepril)	Look alike	5 mg, 10 mg, 20 mg, and 40 mg tablets	20 mg to 40 mg daily given in 1-2 doses
Lactrase (gastroentestianl enzymes)	Look alike	250 mg tablets	Dose individualized according to patient need and response
Lotrimin (clotrimazole)	Look alike	1 % solution, cream or lotion 10 mg troche lozenge 100 mg and 200 mg vaginal tablet 1% and 2% vaginal cream	Individualized according to indication and formulation used
Lidex (fluocinonide)	Sound Alike	0.05 % solution, ointment, gel or cream	Apply to the affected area two to four times daily

Appendix I: Products with overlap in single strength availability but have multiple differentiating product characteristics

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)
Latisse (bimatoprost solution)		0.03%	Apply topically to each upper eyelid margin nightly
Lutera (ethinyl estradiol/levonorgestrel)	Look Alike	0.02 mg/0.1 mg tablets	Take one tablet daily for birth control
Alesse (ethinyl estradiol/levonorgestrel)	Look alike	0.02 mg/0.1 mg tablets	Take one tablet daily for birth control
Lantus (insulin glargine)	Look alike	100 units/mL	Individualized based on patient response and need

Appendix J: Potential confusing name with overlap in single strength availability

Latisse (bimatoprost solution)	0.03 %	Apply topically to each upper eyelid margin nightly
Failure Mode: Name confusion	**Causes (could be multiple)**	**Effects**
Lotemax (loteprednol etabonate suspension) 0.5% ophthalmic drops 2.5 mL 5 mL 10 mL 15 mL	Orthographic similarity (names both have 'L' and 't' in the same position; names are same in length) Both products available in single strength only and used either in the eye or applied topically to upper eyelid	Orthographic differences in the suffix of the name along with differences in product characteristics minimize the likelihood of medication error in the usual practice setting. Rationale: Lotemax is an ophthalmic corticosteroid recommended to be use four times daily in contrast with Latisse which is once daily. Additionally, Lotemax is available in 4 different size bottles while Latisse is only comes in a 3 mL size. Orthographic differences are introduced by the dotted letter 'i' in Latisse and the crossstroke 'x' in Lotemax. Additionally, the double 'ss' in Latisse further distinguishes the names. With the exception of the first and third letters, these names differ in the remaining letters.

2 Page(s) Withheld

_____ Trade Secret / Confidential (b4)

X Draft Labeling (b4)

_____ Draft Labeling (b5)

_____ Deliberative Process (b5)

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