CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22-030

PROPRIETARY NAME REVIEW(S)

Final
10/16/08

Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Surveillance and Epidemiology

Date:	October 15, 2008
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From:	Jinhee J. Lee, PharmD, Safety Evaluator Division of Medication Error Prevention and Analysis
Subject:	Final Proprietary Name, Label, and Labeling Review
Drug Name(s):	Toviaz (Fesoterodine Fumarate) Extended-release Tablets
Application Type/Number:	NDA # 22-030
Applicant/Applicant:	Pfizer, Inc. (Schwarz Pharma)
OSE RCM #:	2008-810

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

CONTENTS

EXECUTIVE SUMMARY

Toviaz, has some similarity to other proprietary and established drug names, but the findings of the Failure Modes and Effects Analysis (FMEA) indicates that the proposed name is not vulnerable to name confusion that could lead to medication errors. Thus, the Division of Medication Error Prevention and Analysis (DMEPA) has no objections to the use of the proprietary name, Toviaz for this product.

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 recommends that the name be resubmitted for review. Additionally, if the product approval is delayed beyond 90 days from the signature date of this review, the proposed name must be resubmitted for evaluation.

The results of the Label and Labeling Risk Assessment find the proposed container labels and labeling introduce vulnerabilities that could lead to medication errors. DMEPA's recommendations for label and labeling modifications are found in Section 5.2.

1 BACKGROUND

1.1 INTRODUCTION

This review was written in response to a request from the Division of Reproductive and Urologic Products (DRUP) to re-evaluate the product for its potential to contribute to medication errors. The proposed proprietary name, Toviaz, is evaluated to determine if the name could be potentially confused with other proprietary or established drug names. The container label, carton and insert labeling were submitted to DMEPA at the time of this review.

1.2 REGULATORY HISTORY

DMEPA reviewed the proposed name, Toviaz, previously with no objections to the name in OSE Review 2007-2078 (dated April 22, 2008). However, the container labels, carton and insert labeling were not submitted to DMEPA at the time of that review.

1.3 PRODUCT INFORMATION

Toviaz is the proposed name for Fesoterodine Fumarate Extended-release tablets. Fesoterodine fumarate is a competitive muscarinic receptor antagonist in an extended-release tablet formulation. Toviaz is proposed to be indicated for the treatment of overactive bladder with symptoms of urinary urgency, frequency, and/or urge incontinence.

The recommended starting dose is 4 mg once daily. Based upon individual response and tolerability, the dose may be increased to 8 mg once daily.

2 METHODS AND MATERIALS

This section describes the methods and materials used by the DMEPA staff conducting a proprietary name risk assessment (see 2.1 Proprietary Name Risk Assessment). The primary focus of the assessment is to identify and remedy potential sources of medication error prior to drug approval. DMEPA defines a medication error as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer. [1]

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

2.1 PROPRIETARY NAME RISK ASSESSMENT

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

For the proprietary name, Toviaz, the medication error staff of DMEPA 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 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.[2] FMEA is used to analyze whether the drug names identified with look- or sound-alike similarity to the proposed name could cause confusion that subsequently leads to medication errors in the clinical setting. DMEPA 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 consider 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, DMEPA considers the potential for confusion throughout the entire U.S. medication use process, including drug procurement, prescribing and ordering, dispensing, administration, and monitoring the impact of the medication.[3]

2.1.1 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 'T' when searching to identify potentially similar drug names, as 75% of the confused drug names reported by the USP-ISMP Medication Error Reporting Program involve pairs beginning with the same letter.[4][5]

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

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

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

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

To identify drug names that may look similar to Toviaz, 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 (six letters), upstrokes (one, capital letter 'T'), downstrokes (one, if "z" is scripted), cross-strokes (none), and dotted letters (one, 'i'). Additionally, several letters in Toviaz may be vulnerable to ambiguity when scripted, including the letter 'T' may appear as 'F', 'L', or 'Z'; lower case 'o' appear as a lower case 'a' or 'u'; and '-iaz' may appear as '-ior'. As such, the Staff should also consider these alternate appearances when identifying drug names that may look similar to Toviaz.

When searching to identify potential names that may sound similar to Toviaz, the Medication Error Staff search for names with similar number of syllables (3), stresses (to-VEE-az or TO-vee-az or to-vee-AZ), consonant sound pronunciation ("az" versus "as" or 'v' versus 'p' or 'b'), and placement of vowel and consonant sounds. In addition, several letters in Toviaz may be subject to misinterpretation when spoken, including the letter 'v' which may be interpreted as 'b', 'f', or 'p' and the letter 'z' may be misinterpreted as 's'. As such, the staff also considers these alternate pronunciations when identifying drug names that may sound similar to Toviaz. The Applicant's intended pronunciation of the proprietary name could not be expressly taken into consideration, as this was not provided with the proposed name submission.

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 (Toviaz), the established name (fesoterodine fumarate), proposed indication (treatment of overactive bladder with symptoms of urinary urgency, frequency, and/or urge continence), strength (4 mg, 8 mg), dose (4 mg daily, titrate up to 8 mg daily based on clinical response), frequency of administration (daily), route (oral) and dosage form of the product (tablet). Appendix A provides a more detailed listing of the product characteristics the medication error staff general 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 Databases and Information Sources

The proposed proprietary name, Toviaz, was provided to the medication error staff of DMEPA to conduct a search of the internet, several standard published drug product reference texts, and FDA databases to identify existing and proposed drug names that may sound-alike or look-alike to Toviaz 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 DMEPA to gather CDER professional opinions on the safety of the product and the proprietary name, Toviaz. Potential concerns regarding drug marketing and

promotion related to the proposed names are also discussed. This group is composed of the DMEPA 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 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.[6] When applying FMEA to assess the risk of a proposed proprietary name, DMEPA 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 Toviaz 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 Toviaz 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.

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

DMEPA 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. 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)].
3. FMEA identifies potential for confusion between the proposed proprietary name and other proprietary or established drug names, and demonstrates that medication errors are likely to result from the drug name confusion under the conditions of usual clinical practice.
4. The proposed proprietary name contains an USAN stem, particularly in a manner that is contradictory to the USAN Council's definition.
5. Medication error staff identify a potential source of medication error within the proposed proprietary name. The proprietary name may be misleading, or inadvertently introduce ambiguity and confusion that leads to errors. Such errors may not necessarily involve confusion between the proposed drug and another drug product.

In the event that 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 is awarded approval first has the right to the use the name, while DMEPA will recommend that the second product to reach approval seek an alternative name.

If none of these conditions are met, then DMEPA will not object to the use of the proprietary name. If any of these conditions are met, then DMEPA will object to the use of the proprietary 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 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, DMEPA contends that the threshold set for the Proprietary Name Risk Assessment is reasonable because proprietary drug name confusion is a predictable and preventable source of medication error that, in many instances, can be identified and remedied prior to approval to avoid patient harm.

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

If DMEPA 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. 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, and so DMEPA may be able to provide the Applicant with recommendations that reduce or eliminate the potential for error would render the proposed name acceptable.

2.2 LABEL AND LABELING RISK ASSESSMENT

This section describes the methods and materials used by the DMEPA medication error staff to conduct a label, labeling, and/or packaging risk assessment (see Section 3, Results). The primary focus of the assessments is to identify and remedy potential sources of medication errors prior to drug approval. DMEPA defines a medication error as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer. [7]

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 label 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 United States Pharmacopeia-Institute for Safe Medication Practices Medication Error Reporting Program may be attributed to the packaging and labeling of drug products, including 30 percent of fatal errors.[8]

Because the DMEPA staff analyzes reported misuse of drugs, the DMEPA staff is able to use this experience to identify potential errors with all medications 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 provide recommendations that aim at reducing the risk of medication errors.

DMEPA reviewed the following labels and labeling submitted by the Applicant on May 1, 2008. See Appendices G through P for pictures of the labels and labeling.

- Commercial Container Labels (30 tablet and 90 tablet)
- Sample Container Labels (7 tablet, 14 tablet, [redacted]
- Commercial Unit Dose Blister Labels (4 mg and 8 mg)
- Sample Dose Pack Blister Cards (4 mg and 8 mg)
- Commercial Unit Dose Pack Carton Labeling (100 tablet)
- [redacted]

b(4)

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

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

- Sample Carton Labelin [redacted] b(4)
- Sample Blister Carton Labeling
- Sample Blister Carton Labeling (Shelf display)
- [redacted]
- Package Insert Labeling (no image)

3 RESULTS

3.1 PROPRIETARY NAME RISK ASSESSMENT

3.1.1 Databases and Information Sources

The search of the internet and several standard published databases and information sources (see Section 6 References) identified a total of 23 names as having some similarity to the name Toviaz.

Sixteen of the 23 names were thought to look like Toviaz, which include: [redacted] Fortaz [redacted] Fovane, Lariam, Lovaza, Taztia [redacted] Tenex, Tiazac, Topex, Toriac, Torisel, Tovalt ODT, Trovan, and Zovirax. Two names ([redacted] and Toprol) were thought to sound like Toviaz. Five names (Tavist, Tobi, Tovalt, Triaz, and Zovia) were thought to look and sound similar to Toviaz. b(4)

A search of the United States Adopted Name (USAN) stem list on September 8, 2008 identified no USAN stems within the proposed name, Toviaz. As such, a total of 27 names were analyzed to determine if the drug names could be confused with Toviaz and if the drug name confusion would likely result in a medication error.

3.1.2 CDER Expert Panel Discussion

The Expert Panel reviewed the pool of names identified by the DMEPA staff (see section 3.1.1. above), and noted no additional names.

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 Safety Evaluator Risk Assessment of the Proposed Proprietary Name

Independent searches by the primary Safety Evaluator four additional names (Toviaz, Lovas, Lovina, and Kovia) thought to look similar to Toviaz and represent a potential source of drug name confusion.

Fifteen of the 27 names (Fovane, Lovaza, [redacted] Tiazac, Topex, Toriac, Tovalt and Tovalt ODT, Trovan, Zovirax, Toprol, Tavist, Tobi, Triaz, and Zovia) were identified in OSE # 2007-2078, dated April 22, 2008). Toviaz's product characteristics have not changed, and during the aforementioned analysis these names were determined not to pose a risk of confusion and error with Toviaz. Thus, these names were eliminated from further analysis. b(4)

Four of the 12 remaining names lacked orthographic and phonetic similarity (Appendix B). The remaining eight names were determined to have some orthographic similarity to Toviaz, and thus determined to present some risk for confusion. Failure modes and effects analysis was then applied to determine if the proposed name, Toviaz, could potentially be confused with any of the eight names and lead to medication error.

This analysis determined that the name similarity between Toviaz and the identified names was unlikely to result in medication errors for all eight products for reasons described/outlined in Appendices C through F.

3.2 LABEL AND LABELING RISK ASSESSMENT

Our analysis of the labels and labeling determined the following areas of vulnerability.

3.2.1 General Comments

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3.2.2 Commercial (30 tablet and 90 tablet) and Sample (7 tablet, 14 tablet Container Labels

See General Comments.

3.2.3 Unit Dose Blister Labels (4 mg and 8 mg)

3.2.4 Sample Dose Pack Blister Cards

b(4)

3.2.5 Commercial Unit Dose Carton Labeling (100 tablet)

See General Comments.

3.2.6 Sample Carton Labeling (30 tablet)

See General Comments.

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3.2.7 Sample Carton Labeling

b(4)

3.2.8 Sample Carton Labeling (Blister and

3.2.9

3.2.10 Insert Labeling

No comments.

4 DISCUSSION

4.1 PROPRIETARY NAME RISK ASSESSMENT

We analyzed 27 names for their similarity to the proposed name Toviaz. The findings of the FMEA indicate that the proposed name does not appear to be vulnerable to name confusion that could lead to medication errors with any of the names evaluated.

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 once the product is commercially marketed. However, DMEPA believes that these limitations are sufficiently minimized by the use of an Expert Panel.

4.2 LABEL AND LABELING RISK ASSESSMENT

Our Label and Labeling Risk Assessment noted several areas of needed improvement.

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1 Page(s) Withheld

_____ § 552(b)(4) Trade Secret / Confidential

X § 552(b)(4) Draft Labeling

_____ § 552(b)(5) Deliberative Process

1 Name Review

b(4)

5 CONCLUSIONS AND RECOMMENDATIONS

The Proprietary Name Risk Assessment findings indicate that the proposed name, Toviaz, is not vulnerable to name confusion that could lead to medication errors. As such, DMEPA does not object to the use of the proprietary name, Toviaz, for this product at this time. However, if **any** of the proposed product characteristics as stated in this review are altered prior to submission of the NDA or approval of the product, DMEPA rescinds this Risk Assessment finding. If the product approval is delayed beyond 90 days from the date of this review, the proposed name must be resubmitted for evaluation. If the product approval is delayed beyond 90 days from the date of this review, the proposed name must be resubmitted for evaluation.

The Label and Labeling Risk Assessment findings indicate that the presentation of information and design of the proposed container labels and carton labeling introduces vulnerability to confusion that could lead to medication errors. Specifically, DMEPA notes problems with the prominence, presentation, and consistency of information that is vital to the safe use of the product. DMEPA believes the risks we have identified can be addressed and mitigated prior to drug approval, and provides recommendations in Section 5.2 that aim at reducing the risk of medication errors.

5.1 COMMENTS TO THE DIVISION

DMEPA 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 DMEPA on any correspondence to the Applicant pertaining to this issue. If you have further questions or need clarifications, please contact Cherye Milburn, OSE Project Manager, at 301-796-2084.

b(4)

5.2 COMMENTS TO THE APPLICANT

5.2.1 Proprietary Name

DMEPA has no objections to the use of the proprietary name Toviaz for this product. If **any** of the proposed product characteristics as stated in this review are altered prior to approval of the product, DMEPA rescinds this Risk Assessment finding, and recommends that the name be resubmitted for review. If the product approval is delayed beyond 90 days from the date of this review, the proposed name must be resubmitted for evaluation.

5.2.2 Labels and Labeling

The Label and Labeling Risk Assessment findings indicate that the presentation of information and design of the proposed carton and container labels introduces vulnerability to confusion that could lead to

medication errors. DMEPA believes the risks we have identified can be addressed and mitigated prior to drug approval, and provides recommendations below that aim at reducing the risk of medication errors.

1. b(4)

The dosage form should appear with the same prominence as the established name per 21 CFR 201.10(g)(2). Revise accordingly the following labels and labeling:

- Commercial Container Labels (30 tablet and 90 tablet)
- Sample Container Labels (7 tablet, 14 tablet ;
- Commercial Unit Dose Carton Labeling (100 tablet)
- Sample Carton Labeling
- Sample Carton Labeling
- Sample Blister Carton Labeling
- Sample Blister Carton Labeling

b(4)

2. b(4)

Revise the following labels and labeling:

- Commercial Container Labels (30 tablet and 90 tablet)
- Sample Container Labels (7 tablet, 14 tablet,
- Commercial Unit Dose Carton Labeling (100 tablet)
- Sample Carton Labeling
- Sample Blister Carton Labeling
- Sample Blister Carton Labeling

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4. b(4)

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. DMEPA 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, DMEPA will consider the Applicant's intended pronunciation of the proprietary name. However, because the Applicant has little control

over how the name will be spoken in practice, DMEPA 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 Upstokes Downstrokes 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

Appendix B: Names that lack convincing orthographic and/or phonetic similarities

Name	Similarity to Toviaz
Taztia	Look
Topex	Look
Torisel	Look
Tolerak	Sound

Appendix C: Proprietary names used only in Foreign Countries

Proprietary Name	Similarity to Toviaz	Country
Toriac	Look	Belgium – active ingredient is loperamide HCl, however, this product is no longer actively marketed.
Lovas	Look	Thailand – active ingredient is amlodipine besilate. Venezuela – active ingredient is lovastatin, however, this product is no longer actively marketed here.
Lovina	Look	Germany – active ingredient is desogestrel and ethinyl estradiol, however, this product is no longer actively marketed.

Appendix D: Products whose proposed proprietary names were found unacceptable and/or withdrawn.

Name	Similarity to Toviaz	Status
[redacted]	Look	[redacted]
[redacted]	Look	

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Appendix E: Products with no numerical overlap in strength and dose.

Product name with potential for confusion	Similarity to Toviaz	Strength	Usual Dose
Toviaz (Fesoterodine Fumarate)		**4 mg, 8 mg**	**Usual dose: 4 mg to 8 mg per day**
Fortax (Ceftazidime)	Look	500 mg, 1 gm, 2 gm, and 6 gm injectable	1 gm intravenously/intramuscularly every 8 to 12 hours.
Lariam (Mefloquine HCl)	Look	250 mg tablet	Malaria Treatment: 1250 mg (5 tablets) to be given as a single oral dose. Malaria Prophylaxis: 250 mg once weekly.

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

Appendix F: Potential confusing name with numerical overlap in dose

Toviaz (Fesoterodine Fumarate)	**4 mg, 8 mg**	**Usual dose: 4 mg to 8 mg per day.**
Failure Mode: Name confusion	**Causes** **(could be multiple)**	**Effects**
Tenex (Guanfacine HCL)	Orthographic similarity - Both names begin with the letter 'T', have a cross stroke letter at the end ('x' versus 'z'), and have a similar number of letters (five versus six). Both have overlapping routes of administration (oral), dosage form (tablet), and frequency of administration (once daily).	Orthographic differences in the names minimize the likelihood of medication error in the usual practice setting. *Rationale:* When written, the names appear similar, however, the addition of another letter in the name Toviaz, and presence of the dotted letter 'i', helps to distinguish this Tenex from the proposed name, Toviaz. The strengths do not overlap, however, the doses are attainable since Tenex is available as a 1 mg and 2 mg tablet. Thus, a prescription for Toviaz 4 mg by mouth daily may be substituted with Tenex 2 mg – 2 tablets daily. However, despite this overlap in dosing, we believe the risk for medication error is minimized by the orthographic differences in the names.

Appendix G: Commercial Container Labels (30 tablet and 90 tablet)

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10 Page(s) Withheld

_____ § 552(b)(4) Trade Secret / Confidential

_X_ § 552(b)(4) Draft Labeling

_____ § 552(b)(5) Deliberative Process

2 Name Review

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/s/

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