CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

204768Orig1s000

PROPRIETARY NAME REVIEW(S)

Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Surveillance and Epidemiology
Office of Medication Error Prevention and Risk Management

Proprietary Name Review

Date:	January 3, 2014
Reviewer:	James Schlick, RPh, MBA Division of Medication Error Prevention and Analysis
Team Leader:	Irene Z. Chan, PharmD, BCPS Division of Medication Error Prevention and Analysis
Drug Name and Strength:	Tivorbex (Indomethacin) Capsules 20 mg or 40 mg
Application Type/Number:	NDA 204768
Applicant:	Iroko Pharmaceuticals, LLC
OSE RCM #:	2013-2393

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

CONTENTS

1 INTRODUCTION

This review evaluates the proposed proprietary name, Tivorbex, from a safety and promotional perspective. The sources and methods used to evaluate the proposed name are outlined in the reference section and Appendix A respectively. This is the second proprietary name to be reviewed under this Application. The first proprietary name, (b) (4) was withdrawn by the Applicant on September 4, 2013 after DMEPA informed the Applicant (b) (4)

1.1 PRODUCT INFORMATION

The following product information is provided in the October 18, 2013 proprietary name submission.

- Active Ingredient: Indomethacin
- Indication of Use: acute pain
- Route of administration: oral
- Dosage form: Capsules
- Strengths: 20 mg, 40 mg
- Dose and Frequency: 20 mg three times daily, 40 mg twice daily to three times daily
- How Supplied: bottles of 30 and 90 (b) (4)
- Storage: (b) (4)
- Container and Closure systems: Capsules will be packaged in white HDPE bottles (60 cc) (b) (4) other bottle sizes and different numbers of capsules may also be used

2 RESULTS

The following sections provide information obtained and considered in the overall evaluation of the proposed proprietary name.

2.1 PROMOTIONAL ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined the proposed name is acceptable from a promotional perspective. DMEPA and the Division of Anesthesia, Analgesia, and Addiction Products (DAAAP) concurred with the findings of OPDP's promotional assessment of the proposed name.

2.2 SAFETY ASSESSMENT

The following aspects were considered in the safety evaluation of the name.

2.2.1 United States Adopted Names (USAN) SEARCH

There is no USAN stem present in the proposed proprietary name.[1]

[1] USAN stem list searched November 22, 2013.

2.2.2 Components of the Proposed Proprietary Name

The Applicant stated that the prefix, 'Ti', represents the anti-inflammatory properties of this drug product. The prefix, infix, and suffix do not contain any component that is misleading or can contribute to a medication error.

2.2.3 FDA Name Simulation Studies

Sixty-one practitioners participated in DMEPA's prescription studies. The interpretations did not overlap with any currently marketed products nor did the misinterpretations sound or look similar to any currently marketed products or any products in the pipeline. In the voice prescription, participants misinterpreted the letter 'T' as the letters 'D' and 'K', the letter 'i' was misinterpreted as the letter 'e', and the letter 'b' was misinterpreted as the letter 'v' and vice versa.

In the written prescription studies, the letter 'T' was misinterpreted as the letters 'J', 'F', and 'L' and the letters 'o' and 'b' were misinterpreted as the letters 'a' and 'f' respectively. We have considered these variations in our look-alike and sound-alike searches and analysis (see Appendix B). Appendix C contains the results from the verbal and written prescription studies.

2.2.4 Comments from Other Review Disciplines at Initial Review

In response to the OSE, October 31, 2013 e-mail, the Division of Anesthesia, Analgesia, and Addiction Products (DAAAP) did not forward any comments or concerns relating to the proposed proprietary name at the initial phase of the review.

2.2.5 Failure Mode and Effects Analysis of Similar Names

The potential letter and letter string variations listed in Appendix B were used to search for names with possible orthographic and phonetic similarity to the proposed proprietary name, Tivorbex (see Table 1).

Our analysis of the 23 names contained in Table 1 determined none pose a risk for confusion with Tivorbex as described in Appendices D through E.

Table 1: Collective List of Potentially Similar Names (DMEPA, EPD, Other Disciplines)

Look Similar (n=17)					
Name	***Source***	***Name***	***Source***	***Name***	***Source***
Teveten	FDA	Subutex	FDA	Tivicay	FDA
Casodex	FDA	Fiberlax	FDA	Tirosint***	FDA
Trivora	FDA	Livolex	FDA	Zevalin	FDA
Triatex	FDA	Tinactin	FDA	Tenormin	FDA
(b) (4) ***	FDA	(b) (4) ***	FDA	(b) (4) ***	FDA
Zorvolex	FDA	Tamoxifen	FDA		

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Table 1: Collective List of Potentially Similar Names (DMEPA, EPD, Other Disciplines)					
Sound Similar (n=1)					
Name	***Source***	***Name***	***Source***	***Name***	***Source***
Terbinex	FDA				
Look and Sound Similar (n=5)					
Name	***Source***	***Name***	***Source***	***Name***	***Source***
Tobradex	FDA	(b) (4) ***	FDA	Tivorbex***	FDA
Tobrex	FDA	Vortex	FDA		

2.2.6 Communication of DMEPA's Analysis at Midpoint of Review

DMEPA communicated our findings to the Division of Anesthesia, Analgesia, and Addiction Products (DAAAP) via e-mail on December 30, 2013. At that time we also requested additional information or concerns that could inform our review. Per e-mail correspondence from the Division of Anesthesia, Analgesia, and Addiction Products on January 2, 2014, they stated no additional concerns with the proposed proprietary name, Tivorbex.

3 CONCLUSIONS

The proposed proprietary name is acceptable from both a promotional and safety perspective.

If you have further questions or need clarifications, please contact Lisa Skarupa, OSE project manager, at 301-796-2219.

3.1 COMMENTS TO THE APPLICANT

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

If any of the proposed product characteristics as stated in your October 18, 2013 submission are altered, the name must be resubmitted for review.

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4 REFERENCES

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

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

2. ***Phonetic and Orthographic Computer Analysis (POCA)***

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

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

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

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

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

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

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

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

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

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

   USPTO provides information regarding patent and trademarks.

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

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

9. ***Natural Medicines Comprehensive Databases (****www.naturaldatabase.com****)***

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

10. ***Access Medicine (www.accessmedicine.com)***

    Access Medicine® from McGraw-Hill contains full-text information from approximately 60 titles; it includes tables and references. Among the titles are: Harrison's Principles of Internal Medicine, Basic & Clinical Pharmacology, and Goodman and Gilman's The Pharmacologic Basis of Therapeutics.

11. ***USAN Stems (http://www.ama-assn.org/ama/pub/about-ama/our-people/coalitions-consortiums/united-states-adopted-names-council/naming-guidelines/approved-stems.shtml)***

    USAN Stems List contains all the recognized USAN stems.

12. ***Red Book (www.thomsonhc.com/home/dispatch)***

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

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

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

14. ***Medical Abbreviations (www.medilexicon.com)***

    Medical Abbreviations dictionary contains commonly used medical abbreviations and their definitions.

15. ***CVS/Pharmacy (www.CVS.com)***

    This database contains commonly used over the counter products not usually identified in other databases.

16. ***Walgreens (www.walgreens.com)***

    This database contains commonly used over the counter products not usually identified in other databases.

17. ***Rx List (www.rxlist.com)***

    RxList is an online medical resource dedicated to offering detailed and current pharmaceutical information on brand and generic drugs.

18. ***Dogpile (www.dogpile.com)***

    Dogpile is a Metasearch engine that searches multiple search engines including Google, Yahoo! and Bing, and returns the most relevant results to the search.

19. ***Natural Standard (http://www.naturalstandard.com)***

    Natural Standard is a resource that aggregates and synthesizes data on complementary and alternative medicine.

APPENDICES

Appendix A

FDA's Proprietary Name Risk Assessment considers the promotional and safety aspects of a proposed proprietary name. The promotional review of the proposed name is conducted by OPDP. OPDP evaluates proposed proprietary names to determine if they are overly fanciful, so as to misleadingly imply unique effectiveness or composition, as well as to assess whether they contribute to overstatement of product efficacy, minimization of risk, broadening of product indications, or making of unsubstantiated superiority claims. OPDP provides their opinion to DMEPA for consideration in the overall acceptability of the proposed proprietary name.

The safety assessment is conducted by DMEPA. DMEPA staff search a standard set of databases and information sources to identify names that are similar in pronunciation, spelling, and orthographically similar when scripted to the proposed proprietary name. Additionally, we consider inclusion of USAN stems or other characteristics that when incorporated into a proprietary name may cause or contribute to medication errors (i.e., dosing interval, dosage form/route of administration, medical or product name abbreviations, names that include or suggest the composition of the drug product, etc.). 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.[2]

Following the preliminary screening of the proposed proprietary name, DMEPA gathers to discuss their professional opinions on the safety of the proposed proprietary name. This meeting is commonly referred to the Center for Drug Evaluation and Research (CDER) Expert Panel discussion. DMEPA also considers other aspects of the name that may be misleading from a safety perspective. DMEPA staff conducts a prescription simulation studies using FDA health care professionals. When provided, DMEPA considers external proprietary name studies conducted by or for the Applicant/Sponsor and incorporates the findings of these studies into the overall risk assessment.

The DMEPA primary reviewer assigned to evaluate the proposed proprietary name is responsible for considering the collective findings, and provides an overall risk assessment of the proposed proprietary name. DMEPA bases the overall risk assessment on the findings of a Failure Mode and Effects Analysis (FMEA) of the proprietary name and misleading nature of the proposed proprietary name with a focus on the avoidance of medication errors.

DMEPA uses the clinical expertise of its staff to anticipate the conditions of the clinical setting where the product is likely to be used based on the characteristics of the proposed product. DMEPA considers the product characteristics associated with the proposed product throughout the risk assessment because the product characteristics of the proposed may provide a context for communication of the drug name and ultimately determine the use of the product in the *usual* clinical practice setting.

Typical product characteristics considered when identifying drug names that could potentially be confused with the proposed proprietary name include, but are not limited to; established name of the proposed product, proposed indication of use, dosage form, route of administration, strength, unit of measure, dosage units, recommended dose, typical quantity or volume, frequency of administration, product packaging, storage conditions, patient population, and prescriber population. DMEPA considers how these product characteristics may or may not be present in communicating a product name throughout the medication use system. Because drug name confusion can occur at any point in the

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

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]

The DMEPA considers the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted. DMEPA compares the proposed proprietary name with the proprietary and established name of existing and proposed drug products and names currently under review at the FDA. DMEPA compares the pronunciation of the proposed proprietary name with the pronunciation of other drug names because verbal communication of medication names is common in clinical settings. DMEPA examines the phonetic similarity using patterns of speech. If provided, DMEPA will consider the Sponsor's intended pronunciation of the proprietary name. However, DMEPA also considers a variety of pronunciations that could occur in the English language because the Sponsor has little control over how the name will be spoken in clinical practice. The orthographic appearance of the proposed name is evaluated using a number of different handwriting samples. DMEPA applies expertise gained from root-cause analysis of postmarketing medication errors to identify sources of ambiguity within the name that could be introduced when scripting (e.g.,"T" may look like "F," lower case 'a' looks like a lower case 'u,' etc). Additionally, other orthographic attributes that determine the overall appearance of the drug name when scripted (see Table 1 below for details).

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/Similar shape Upstrokes Down strokes Cross-strokes Dotted letters Ambiguity introduced by scripting letters Overlapping product	• Names may look similar when scripted, and lead to drug name confusion in written communication

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

		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

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

1. Database and Information Sources

DMEPA searches the internet, several standard published drug product reference texts, and FDA databases to identify existing and proposed drug names that may sound-alike or look-alike to the proposed proprietary name. A standard description of the databases used in the searches is provided in the reference section of this review. To complement the process, the DMEPA uses a computerized method of identifying phonetic and orthographic similarity between medication names. The program, Phonetic and Orthographic Computer Analysis (POCA), uses complex algorithms to select a list of names from a database that have some similarity (phonetic, orthographic, or both) to the trademark being evaluated. Lastly, DMEPA reviews the USAN stem list to determine if any USAN stems are present within the proprietary name. The individual findings of multiple safety evaluators are pooled and presented to the CDER Expert Panel. DMEPA also evaluates if there are characteristics included in the composition that may render the name unacceptable from a safety perspective (abbreviation, dosing interval, etc.).

2. Expert Panel Discussion

DMEPA gathers gather CDER professional opinions on the safety of the proposed product and discussed the proposed proprietary name (Expert Panel Discussion). The Expert Panel is composed of Division of Medication Errors Prevention (DMEPA) staff and representatives from the Office of Prescription Drug Promotion (OPDP). We also consider input from other review disciplines (OND, ONDQA/OBP). The Expert Panel also discusses potential concerns regarding drug marketing and promotion related to the proposed names.

The primary Safety Evaluator presents the pooled results of the database and information searches to the Expert Panel for consideration. Based on the clinical and professional experiences of the Expert Panel members, the Panel may recommend additional names, additional searches by the primary Safety Evaluator to supplement the pooled results, or general advice to consider when reviewing the proposed

proprietary name.

3. FDA Prescription Simulation Studies

Three separate studies are conducted within the Centers of the FDA for the proposed proprietary name to determine the degree of confusion of the proposed proprietary name with marketed U.S. drug names (proprietary and established) due to similarity in visual appearance with handwritten prescriptions or verbal pronunciation of the drug name. The studies employ healthcare professionals (pharmacists, physicians, and nurses), and attempts to simulate the prescription ordering process. The primary Safety Evaluator uses the results to identify orthographic or phonetic vulnerability of the proposed name to be misinterpreted by healthcare practitioners.

In order to evaluate the potential for misinterpretation of the proposed proprietary name in handwriting and verbal communication of the name, inpatient medication orders and/or outpatient prescriptions are written, each consisting of a combination of marketed and unapproved drug products, including the proposed name. These orders are optically scanned and one prescription is delivered to a random sample of 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 record their interpretations of the orders which are recorded electronically.

4. Comments from Other Review Disciplines

DMEPA requests the Office of New Drugs (OND) and/or Office of Generic Drugs (OGD), ONDQA or OBP for their comments or concerns with the proposed proprietary name, ask for any clinical issues that may impact the DMEPA review during the initial phase of the name review. Additionally, when applicable, at the same time DMEPA requests concurrence/non-concurrence with OPDP's decision on the name. The primary Safety Evaluator addresses any comments or concerns in the safety evaluator's assessment.

The OND/OGD Regulatory Division is contacted a second time following our analysis of the proposed proprietary name. At this point, DMEPA conveys their decision to accept or reject the name. The OND or OGD Regulatory Division is requested to provide any further information that might inform DMEPA's final decision on the proposed name.

Additionally, other review disciplines opinions such as ONDQA or OBP may be considered depending on the proposed proprietary name.

5. Safety Evaluator Risk Assessment of the Proposed Proprietary Name

The primary Safety Evaluator applies his/her individual expertise gained from evaluating medication errors reported to FDA, considers all aspects of the name that may be misleading or confusing, conducts a Failure Mode and Effects Analysis, and provides an overall decision on acceptability dependent on their risk assessment of name confusion. Failure Mode and Effects Analysis (FMEA) is a systematic tool for evaluating a process and identifying where and how it might fail.[4] When applying FMEA to assess the risk of a proposed proprietary name, DMEPA seeks to evaluate the potential for a proposed proprietary name to be confused with another drug name because of name confusion and, thereby, cause errors to occur in the medication use system. FMEA capitalizes on the predictable and preventable nature of medication errors associated with drug name confusion. FMEA allows the Agency to identify the potential for medication errors due to orthographically or phonetically similar drug names prior to

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

approval, where actions to overcome these issues are easier and more effective than remedies available in the post-approval phase.

In order to perform an FMEA of the proposed name, the primary Safety Evaluator must analyze the use of the product at all points in the medication use system. Because the proposed product is has not been marketed, the primary Safety Evaluator anticipates the use of the product in the usual practice settings by considering the clinical and product characteristics listed in Section 1.2 of this review. The Safety Evaluator then analyzes the proposed proprietary name in the context of the usual practice setting and works to identify potential failure modes and the effects associated with the failure modes.

In the initial stage of the Risk Assessment, the Safety Evaluator compares the proposed proprietary name to all of the names gathered from the above searches, Expert Panel Discussion, and prescription studies, external studies, and identifies potential failure modes by asking:

> ***"Is the proposed proprietary name convincingly similar to another drug name, which may cause practitioners to become confused at any point in the usual practice setting? And are there any components of the name that may function as a source of error beyond sound/look-alike?"***

An affirmative answer indicates a failure mode and represents a potential for the proposed proprietary name to be confused with another proprietary or established drug name because of look- or sound-alike similarity or because of some other component of the name. If the answer to the question is no, the Safety Evaluator is not convinced that the names poses similarity that would cause confusion at any point in the medication use system, thus the name is eliminated from further review.

In the second stage of the Risk Assessment, the primary Safety Evaluator evaluates all potential failure modes to determine the likely *effect* of the drug name confusion, by asking:

> ***"Could the confusion of the drug names conceivably result in medication errors in the usual practice setting?"***

The answer to this question is a central component of the Safety Evaluator's overall risk assessment of the proprietary name. If the Safety Evaluator determines through FMEA that the name similarity would not ultimately be a source of medication errors in the usual practice setting, the primary Safety Evaluator eliminates the name from further analysis. However, if the Safety Evaluator determines through FMEA that the name similarity could ultimately cause medication errors in the usual practice setting, the Safety Evaluator will then recommend the use of an alternate proprietary name.

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

a. OPDP finds the proposed proprietary name misleading from a promotional perspective, and the Review Division concurs with OPDP's findings. The Federal Food, Drug, and Cosmetic Act provides that labeling or advertising can misbrand a product if misleading representations are made or suggested by statement, word, design, device, or any combination thereof, whether through a PROPRIETARY name or otherwise [21 U.S.C 321(n); See also 21 U.S.C. 352(a) & (n)].

b. DMEPA identifies that the proposed proprietary name is misleading because of similarity in spelling or pronunciation to another proprietary or established name of a different drug or ingredient [CFR 201.10.(C)(5)].

c. FMEA identifies the potential for confusion between the proposed proprietary name and other proprietary or established drug name(s), and demonstrates that medication errors are likely to result from the drug name confusion under the conditions of usual clinical practice.

d. The proposed proprietary name contains an USAN (United States Adopted Names) stem.

e. DMEPA identifies a potential source of medication error within the proposed proprietary name. For example, the proprietary name may be misleading or, inadvertently, introduce ambiguity and confusion that leads to errors. Such errors may not necessarily involve confusion between the proposed drug and another drug product but involve a naming characteristic that when incorporated into a proprietary name, may be confusing, misleading, cause or contribute to medication errors.

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

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

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

Furthermore, post-marketing experience has demonstrated that medication errors resulting from drug name confusion are notoriously difficult to rectify post-approval. Educational and other post-approval efforts are low-leverage strategies that have had limited effectiveness at alleviating medication errors involving drug name confusion. Sponsors have undertaken higher-leverage strategies, such as drug name changes, 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 approving the error-prone proprietary name. Moreover, even after Sponsors' have changed a product's proprietary name in the post-approval phase, it is difficult to eradicate the original proprietary name from practitioners' vocabulary, and as a result, the Agency has continued to receive reports of drug name confusion long after a name change in some instances. Therefore, DMEPA believes that post-approval efforts at reducing name confusion errors should be reserved for those cases in which the potential for name confusion could not be predicted prior to approval.

Appendix B: Letters and Letter Strings with Possible Orthographic or Phonetic Misinterpretation

Letters in Name Tivorbex	Scripted May Appear as	Spoken May Be Interpreted as
Capital 'T'	F, Z, J,I, L, S, D	D, K
Lower case ‘t’	r, f, x, A, l	d
Lower case 'i'	e, l,r	y,e
Lower case 'v'	r,s,n,u	f,b
Lower case 'o'	a, c,e, u	Oh, Any Vowel
Lower case ‘r’	s, n, e, ,v	
Lower case 'b'	l, h, k , f	p, v, d
Lower case 'e'	a, i, l, o, u,p	Any Vowel
Lower case ‘x’	a, d, skinny f, k, n, p, r, t, v, y	ks, kz, s, z, d, ts
Letter strings in Name Tivorbex	**Scripted May Appear as**	**Spoken May Be Interpreted as**
ti	h, n, r	
iv	w	

Appendix C: Prescription Simulation Samples and Results

Figure 1. Tivorbex Study (Conducted on November 22, 2013)

Handwritten Requisition Medication Order	Verbal Prescription
Medication Order: Tivorbex 40mg orally twice daily	Tivorbex 20 mg One po TID Disp# 90
Outpatient Prescription: Tivorbex 20 mg 1 PO TID #90	

FDA Prescription Simulation Responses (Aggregate 1 Rx Studies Report)

192 People Received Study
61 People Responded

Study Name: Tivorbex

Total	22	22	17	
INTERPRETATION	**OUTPATIENT**	**VOICE**	**INPATIENT**	**TOTAL**
DEBORBEX	0	3	0	3
DEBORBVEX	0	1	0	1
DEBVORVEX	0	1	0	1
DEPORVEX	0	1	0	1
DEVORBIX 20MG	0	1	0	1
DEVORVEX	0	1	0	1
DIBORVEX	0	1	0	1
DIVORBEX	0	3	0	3
EVORBEX	0	1	0	1
FIVORBEX	1	0	1	2
JIVORBEX	2	0	0	2
KEBORBEX	0	1	0	1
KEFORVAX	0	1	0	1
KIBORBEX	0	1	0	1
LIVORBEX	0	0	2	2
TEDORBEX	0	1	0	1
TEEFORVEX	0	1	0	1
TEPORBEX	0	1	0	1
TIAVORBEX	1	0	0	1
TIBORBEX	0	2	0	2
TIORBEX	1	0	0	1
TIVARBEX	0	0	5	5
TIVARFEX	0	0	1	1
TIVORBECS	0	1	0	1
TIVORBEX	15	0	6	21
TIVORFEX	0	0	2	2
TIVORVEX	1	0	0	1
TRIVORBEX	1	0	0	1

Appendix D: Proprietary names not likely to be confused or not used in usual practice settings for the reasons described**.**

No.	Proprietary Name	Active Ingredient	Similarity to Tivorbex	Failure preventions
1.	Casodex	Bicalutamide	Orthographic	The name pair has sufficient orthographic differences
2.	Tirosint***	Levothyroxine	Orthographic	The name pair has sufficient orthographic differences
3.	Trivora	Levonorgestrel/ Ethinyl Estradiol	Orthographic	The name pair has sufficient orthographic differences
4.	(b) (4)			
5.	Tivorbex***	Indomethacin	Orthographic and Phonetic	Name that is the subject of this review
6.	Livolex	Injectable iron and multivitamins	Orthographic	Name identified in Red Book Database. Unable to find product characteristics in other databases. The product was discontinued in 1995 per Red Book database.
7.	(b) (4)			
8.				

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

Appendix E: Risk of medication errors due to product confusion minimized by dissimilarity of the names and/ or use in clinical practice for the reasons described.

No.	**Proposed name: Tivorbex (Indomethacin)** **Dosage Form: Capsules** **Strengths:** **20 mg and 40 mg** **Usual Dose:** **20 mg orally three times daily** **40 mg two to three times daily**	**Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion** **Causes (could be multiple)**	**Prevention of Failure Mode** **In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names**
1.	Teveten (Eprosartan) Tablets 400 mg and 600 mg Usual Dose: 600 mg orally once daily or 400 mg orally once or twice daily	Orthographic: The letter string 'Tev' is similar to the letter string 'Tiv'. Both names contain an upstroke in similar positions ('t' vs. 'b') followed by the letter 'e'. Route of Administration: Both products are taken orally Dose: Both products can be prescribed as 'take 1'. Strength: The 40 mg Tivorbex strength is numerically similar to the 400 mg Teveten strength Frequency of Administration: Both products can be taken twice daily	Orthographic: The letter string 'or' preceding the upstroke letter 'b' in Tivorbex does not look similar to the 'e' preceding the upstroke letter 't' in Teveten. The cross stroke in the letter 't' provides orthographic differentiation with the letter 'b'. In addition, the letter 'b' has a rounded shape at the base of the letter where the letter 't' does not.
2.	Subutex (Buprenorphine) Sublingual Tablets 2 mg and 8 mg Discontinued but generic equivalents exist Usual Dose: 4 mg to 24 mg sublingually once daily. Dose is titrated in increments/decrements of 2 mg to achieve the desired maintenance dose	Orthographic: The letter 'S' and the letter 'T' can appear similar when scripted. Both names have upstroke letters in similar positions followed by the letter string 'ex'. Dose: Both products can be prescribed as 'take 1' or 'take 2'.	Orthographic: The name Subutex has an upstroke letter in the third position where Tivorbex does not; thus, making the shape of the names appear different. The cross stroke in the letter 't' provides orthographic differentiation with the letter 'b'. In addition, the letter 'b' has a rounded shape at the base of the letter where the letter 't' does not.

No.	Proposed name: Tivorbex (Indomethacin) Dosage Form: Capsules Strengths: 20 mg and 40 mg Usual Dose: 20 mg orally three times daily 40 mg two to three times daily	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion Causes (could be multiple)	Prevention of Failure Mode In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names
3.	Tivicay (Dolutegravir) Tablets 50 mg Usual Dose: 50 mg orally once or twice daily	Orthographic: Both names begin with the letter string 'Tiv'. The letter 'y' in Tivicay can appear similar to the letter 'x' in Tivorbex if the downstroke in the letter 'y' is not prominent. Route of Administration: Both products are taken orally Dose: Both products can be prescribed as 'take 1'. Frequency of Administration: Both products can be taken twice daily	Orthographic: The letter string 'orb' in Tivorbex does not appear similar to letter string 'ica' in Tivicay. Strength: Tivorbex has multiple strengths that would need to be indicated on the prescription. There is no overlap or numerical similarity in strength between the two products.
4.	Fiberlax (Calcium Polycarbophil) Chewable Tablets 500 mg Usual Dose: 1000 mg with 8 ounces of water four times daily; not to exceed 6 grams/day	Orthographic: The letter string 'Fi' can appear similar to the letter string 'Ti' when scripted. The letter string 'erlax' can appear similar to the letter string 'orbex' when scripted. Route of Administration: Both products are taken orally Dose: Both products can be prescribed as 'take 2'.	Orthographic: The name Fiberlax has an upstroke letter in the third position where Tivorbex does not; thus, making the shape of the names appear different. Strength: Tivorbex has multiple strengths that would need to be indicated on the prescription. There is no overlap or numerical similarity in strength

No.	Proposed name: Tivorbex (Indomethacin) Dosage Form: Capsules Strengths: 20 mg and 40 mg Usual Dose: 20 mg orally three times daily 40 mg two to three times daily	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion Causes (could be multiple)	Prevention of Failure Mode In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names
5.	Zevalin (Ibritumomab) Injection 3.2 mg/2 mL Usual Dose: 0.3 to 0.4 mCi/kg based in platelet count within 4 hours after rituximab infusion on days 7, 8, and 9.	Orthographic: The letter string 'Zeva' can appear similar to the letter string 'Tivo' when scripted. The letter string 'lin' can appear similar to the letter string 'bex' when scripted. Dose: There is overlap in dose (40 mg vs. 40 mCi based on weight)	Orthographic: The additional letter 'r' in Tivorbex prior to the upstroke letter 'b' makes the first part of the name Tivorbex appear longer than the first part of Zevalin prior to the upstroke letter 'l'. Setting of Use: Zevalin is prepared only in a radiopharmacy whereas Tivorbex is not prepared in a radiopharmacy. Thus, a prescription for these two products is unlikely to cause confusion. Frequency of Administration: After rituximab on days 7,8, and 9 vs. twice or three times daily

No.	Proposed name: Tivorbex (Indomethacin) Dosage Form: Capsules Strengths: 20 mg and 40 mg Usual Dose: 20 mg orally three times daily 40 mg two to three times daily	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion Causes (could be multiple)	Prevention of Failure Mode In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names
6.	Triatex (Triamcinolone) Topical Cream 0.025% 0.1% 0.5% Usual Dose: Apply a thin film to the affected area 2 to 4 times daily	Orthographic: Both names begin with the letter 'T' and both names end with the letter string 'ex'. Both names contain an upstroke letter near the end of the name giving them a similar shape. Frequency of Administration: Both products can be taken twice daily	Orthographic: The additional letter 'r' in Tivorbex prior to the upstroke letter 'b' makes the first part of the name Tivorbex appear longer than the first part of Triatex prior to the upstroke letter 't'. The cross stroke in the letter 't' provides orthographic differentiation with the letter 'b'. In addition, the letter 'b' has a rounded shape at the base of the letter where the letter 't' does not. Dose: Apply a thin film vs. 1 or 2 capsules (20 mg or 40 mg) Strength: Both products have multiple strengths that would need to be indicated on the prescription. There is no overlap or numerical similarity in strength

No.	Proposed name: Tivorbex (Indomethacin) Dosage Form: Capsules Strengths: 20 mg and 40 mg Usual Dose: 20 mg orally three times daily 40 mg two to three times daily	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion Causes (could be multiple)	Prevention of Failure Mode In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names
7.	Tinactin (Tolnaftate) Topical Cream – 1% Topical Powder – 1% Topical Spray – 1% Usual Dose: Apply to affected area twice daily for 2 to 4 weeks	Orthographic: The letter string 'Tinac' can appear similar to the letter string 'Tivor' when scripted. Both names have an upstroke letter in the same position. The letter string 'in' can appear similar to the letter string 'ex'. Frequency of Administration: Both products can be taken twice daily	Orthographic: The cross stroke in the letter 't' in the sixth position provides orthographic differentiation with the letter 'b'. In addition, the letter 'b' has a rounded shape at the base of the letter where the letter 't' does not. Dose: Apply a thin layer to the affected area vs. 1 or 2 capsules Strength: Tivorbex has multiple strengths that would need to be indicated on the prescription. There is no overlap or numerical similarity in strength
8.	Tenormin (Atenolol) Tablets 25 mg, 50 mg, 100 mg Usual Dose: 1 tablet once daily	Orthographic: The letter string 'Tenor' can appear similar to the letter string 'Tivor' when scripted. The letter string 'in' can appear similar to the letter string 'ex'. Route of Administration: Both products are taken orally Dose: Both products can be prescribed as 'take 1'.	Orthographic: Tivorbex has an upstroke letter 'b' in the name where Tenormin does not; thus, giving the names different shapes. Strength: Both products have multiple strengths that would need to be indicated on the prescription. There is no overlap or numerical similarity in strength.

No.	Proposed name: Tivorbex (Indomethacin) Dosage Form: Capsules Strengths: 20 mg and 40 mg Usual Dose: 20 mg orally three times daily 40 mg two to three times daily	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion Causes (could be multiple)	Prevention of Failure Mode In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names
9.	(b) (4)		
10.	Zorvolex (Diclofenac) Capsules 18 mg and 35 mg Usual Dose: One tablet orally three times daily	Orthographic: The letter 'Z' can appear similar to the letter 'T' when scripted. The letter string 'lex' can look similar to the letter string 'bex' when scripted. Dosage Form: Both products are oral capsules Therapeutic Class: Both products are in the same therapeutic class Dose: Both products can be prescribed as 'take 1'. Frequency of Administration: Both products can be taken three times daily	Strength: Both products have multiple strengths that would need to be indicated on the prescription. There is no overlap or numerical similarity in strength between the two products.

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No.	Proposed name: Tivorbex (Indomethacin) Dosage Form: Capsules Strengths: 20 mg and 40 mg Usual Dose: 20 mg orally three times daily 40 mg two to three times daily	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion Causes (could be multiple)	Prevention of Failure Mode In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names
11.	Tamoxifen Tablets 10 mg and 20 mg Usual Dose: 20 mg to 40 mg orally once or twice daily	Orthographic: Both names begin with the letter 'T' and the letter string 'fen' can look similar to the letter string 'bex' when scripted. Both names have the letter 'o' in fourth position. Route of Administration: Both products are taken orally Dose and Strength: There is overlap with dose and strength (20 mg) Frequency of Administration: Both products can be taken twice daily	Orthographic: The letter string 'am' does not appear similar to the letter string 'iv' when scripted. The additional letter 'x' in Tamoxifen helps to make the name appear longer before the upstroke letter 'f' compared to the letter string before the upstroke letter 'b' in Tivorbex.
12.	Vortex (Sodium Fluoride) Toothpaste (0.20%) Usual Dose: Brush after meals or at least twice daily	Orthographic: The letter string 'vortex' is similar to the letter string 'vorbex'. Phonetic: The letter string 'vortex' is similar to the letter string 'vorbex'. Frequency of Administration: Both products can be used twice daily	Orthographic: The letter string 'Ti' in Tivorbex makes the name longer compared to the name Vortex when scripted. The cross stroke in the letter 't' provides orthographic differentiation with the letter 'b'. In addition, the letter 'b' has a rounded shape at the base of the letter where the letter 't' does not. Phonetic: The letter string 'Ti' provides an additional syllable compared to the name Vortex. The letter 't' in Vortex does not sound similar to the letter 'b' in Tivorbex. Strength: Tivorbex has multiple strengths that would need to be indicated on the prescription. There is no overlap or numerical similarity in strength between the two products.

No.	Proposed name: Tivorbex (Indomethacin) Dosage Form: Capsules Strengths: 20 mg and 40 mg Usual Dose: 20 mg orally three times daily 40 mg two to three times daily	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion Causes (could be multiple)	Prevention of Failure Mode In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names
13.	Terbinex (Terbinafine) Tablets 250 mg Usual Dose: 1 tablet orally once daily for 6 to 12 weeks	Phonetic: The letter strings 'Te' and 'Ti' sound similar when scripted. Both names end with the letter string 'ex'. Route of Administration: Both products are taken orally Dose: Both products can be prescribed as 'take 1'.	Phonetic: The letter string 'rbin' does not sound similar to the letter string 'vorb'. Strength: Tivorbex has multiple strengths that would need to be indicated on the prescription. There is no overlap or numerical similarity in strength between the two products.
14.	Tobradex (Tobramycin and Dexamethasone) Ophthalmic ointment and suspension Ointment – 0.3%/0.1% Suspension – 0.3%/0.1% Usual Dose: Ointment – Apply ½ inch ribbon to the conjunctival sac 3 to 4 four times daily Suspension – Apply 1 to 2 drops to the conjunctival sac every 4 to 6 hours	Orthographic: Both names begin with the letter 'T' and both names end with the same letter string 'ex'. Both names have similar shaped letters ('a' vs' 'o' in the fifth and fourth position respectively. Phonetic: Both names begin with the letter 'T' and both names end with similar sounding letter strings (dex vs. bex). Both names have three syllables.	Orthographic: Tobradex has an additional upstroke letter 'b' in the third position that provides a different shape compared to Tivorbex. The letter 'o' in Tobradex does not look similar to the letter 'i' in Tivorbex. The letter 'd' in Tobradex has a rounded shape on the left side of the upstroke where the letter 'b' has a rounded shape on the right side of the upstroke. Phonetic: The letter string 'obra' does not sound similar to the letter string 'ivor'. Strength: Tivorbex has multiple strengths that would need to be indicated on the prescription. There is no overlap or numerical similarity in strength between the two products.

No.	Proposed name: Tivorbex (Indomethacin) Dosage Form: Capsules Strengths: 20 mg and 40 mg Usual Dose: 20 mg orally three times daily 40 mg two to three times daily	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion Causes (could be multiple)	Prevention of Failure Mode In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names
15.	Tobrex (Tobramycin) Ophthalmic ointment and suspension Ointment – 0.3% Suspension – 0.3% Usual Dose: Ointment – Apply ½ inch ribbon to the affected eye 3 to 4 four times daily Suspension – Apply 1 to 2 drops to the affected eye every 4 to 6 hours	Orthographic: Both names begin with the letter 'T' and both names end with similar letter strings ('brex' vs. 'dex'). Phonetic: Both names begin with the letter 'T' and both names end with similar letter strings ('brex' vs. 'dex').	Orthographic: The name Tivorbex has 8 letters in the name where Tobrex has 6 letters; thus, the name Tivorbex appears longer when scripted. Phonetic: The name Tobrex has two syllables where the name Tivorbex has three syllables when spoken. Strength: Tivorbex has multiple strengths that would need to be indicated on the prescription. There is no overlap or numerical similarity in strength between the two products.

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/s/

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01/03/2014

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