CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

200175

PROPRIETARY NAME REVIEW(S)

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

Date:	June 10, 2010
To:	Norman Stockbridge, MD, Director Division of Cardiovascular and Renal Products
Through:	Melina Griffis RPh, Team Leader Denise Toyer, PharmD, Deputy Director Carol Holquist, RPh, Director Division of Medication Error Prevention and Analysis (DMEPA)
From:	Richard Abate, RPh, MS, Safety Evaluator Division of Medication Error Prevention and Analysis (DMEPA)
Subject:	Proprietary Name Review
Drug Name(s):	Tribenzor (Olmesartan Medoxomil, Amlodipine, and Hydrochlorothiazide) Tablets 20 mg/5 mg/12.5 mg, 40 mg/5 mg/12.5 mg, 40 mg/5 mg/25 mg, 40 mg/10 mg/12.5 mg, and 40 mg/10 mg/25 mg
Application Type/Number:	NDA 200175
Applicant/sponsor:	Daiichi-Sankyo
OSE RCM #:	2010-709

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EXECUTIVE SUMMARY

This review summarizes the Division of Medication Error Prevention and Analysis' risk assessment for the proposed proprietary name, Tribenzor (Olmesartan Medoximil, Amlodipine, and Hydrochlorothiazide) Tablets. Our evaluation identified no concerns from a safety and promotional perspective that would render the name unacceptable. Thus, DMEPA finds the proposed proprietary name, Tribenzor, acceptable for this product.

The proposed proprietary name, Tribenzor, must be re-reviewed 90 days before approval of the NDA. Additionally, if any of the proposed product characteristics as stated in this review are altered, DMEPA rescinds this finding and the name must be resubmitted for review. The conclusions upon re-review are subject to change.

1 BACKGROUND

1.1 INTRODUCTION

This review responds to a March 30, 2010 request from the Applicant, Daiichi Sankyo Pharma Development for an assessment of the proposed proprietary name, Tribenzor. The Applicant submitted an external study and a gap analysis in support of their proposed proprietary name.

The Applicant also submitted draft container labels and carton labeling which are evaluated under a separate review (OSE review # 2010-392).

1.2 REGULATORY HISTORY

The Applicant previously submitted the proposed proprietary name, (b) (4), for this product under IND 77651 which the Division of Medication Error Prevention and Analysis (DMEPA) objected to based on safety concerns. An alternative proposed proprietary name, (b) (4), was submitted on February 12, 2010 which was found promotional by the Division of Drug Marketing, Advertising, and Communications (DDMAC). However, the Applicant withdrew that proposed proprietary name March 22, 2010 prior to DMEPA sending the Applicant a letter.

1.3 PRODUCT INFORMATION

Tribenzor is a combination tablet containing Olmesartan Medoximil, Amlodipine, and Hydrochlorothiazide. The proposed indication for Tribenzor is hypertension, but not as a first line treatment. Tribenzor will be available as oral tablets in five strength presentations 20 mg/5 mg/12.5 mg, 40 mg/5 mg/12.5 mg, 40 mg/5 mg/25 mg, 40 mg/10 mg/12.5 mg, and 40 mg/10 mg/25 mg. The dose will be one tablet by mouth daily. The strength of the tablet prescribed will be determine by the doses of the individual components. The dose of individual ingredients may be adjusted in blood pressure control is inadequate. Tribenzor will be supplied in bottles of 30 and 90 tablets as well as in cartons containing 10 x 10 unit-dose blisters for institutional use. The Applicant also will distribute professional samples of seven tablets in bottles and blister cards. The product is stored at room temperature.

2 METHODS AND MATERIALS

Appendix A describes the general methods and materials used by DMEPA when conducting a proprietary name risk assessment for all proprietary names. Sections 2.1, 2.2, and 2.3 identify specific information associated with the methodology for the proposed proprietary name, Tribenzor.

2.1 SEARCH CRITERIA

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.[1,2]

To identify drug names that may look similar to Tribenzor, the DMEPA staff also considers the orthographic appearance of the name on lined and unlined orders. Specific attributes taken into consideration include the length of the name (nine letters), upstrokes (two, capital letter 'T' and lower case 'b'), down strokes (z, lower case), cross strokes (two, lower case 't' and 'z') and dotted (one, lower case 'i'). Additionally, several letters in Tribenzor may be vulnerable to ambiguity when scripted (See Appendix B). As a result, the DMEPA staff also considers these alternate appearances when identifying drug names that may look similar to Tribenzor.

When searching to identify potential names that may sound similar to Tribenzor, the DMEPA staff search for names with similar number of syllables (three), stresses (TRI-ben-zor, tri-BEN-zor, or tri-ben-ZOR), and placement of vowel and consonant sounds. (See Appendix B) The Applicant's intended pronunciation (Try-ben-zor) was also taken into consideration, as it was included in the Proprietary Name Review Request. Moreover, names are often mispronounced and/or spoken with regional accents and dialects, so other potential pronunciations of the name are considered.

2.2 PRESCRIPTION ANALYSIS STUDIES

In order to evaluate the potential for misinterpretation of the proposed proprietary name in handwriting and verbal communication of the name, the following inpatient medication order, outpatient and verbal prescription was communicated during the FDA prescription studies. (See Appendix for samples and results.)

2.3 EXTERNAL PROPRIETARY NAME RISK ASSESSMENT

For this product, the Applicant submitted an external evaluation of the proposed proprietary name. The Division of Medication Error Prevention and Analysis conducts an

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

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

independent analysis and evaluation of the data provided, and responds to the overall findings of the assessment. When the external proprietary name risk assessment identifies potentially confusing names that were not captured in DMEPA's database searches or in the Expert Panel Discussion, these names are included in the Safety Evaluator's Risk Assessment and analyzed independently by the Safety Evaluator to determine if the potentially confusing name could lead to medication errors in usual practice settings. After the Safety Evaluator has determined the overall risk associated with proposed name, the Safety Evaluator compares the findings of their overall risk assessment with the findings of the proprietary name risk assessment submitted by the Applicant. The Safety Evaluator then determines whether the Division's risk assessment concurs or differs with the findings. When the proprietary name risk assessments differ, the Division of Medication Error Prevention and Analysis provides a detailed explanation of these differences.

3 RESULTS

The names identified from DMEPA's methods as potential sources for name confusion with Tribenzor are listed below.

3.1 DATABASE AND INFORMATION SOURCES

The DMEPA searches of the databases and DMEPA's information sources yielded a total of 33 names as having some similarity to the name Tribenzor.

Thirty-two were thought to look like Tribenzor. These include: Doribax, Durezol, Fulvicin P/G, Tambocor, Taxotere, Tikosyn, Trasicor, Trecator, Trelstar, Tretinoin, Tribestan, Tri-biotic, Tri-biozene, Tricor, Triesence, Trilafon, Tri-Legest, Tri-Legest FE, Trileptal, Trilipix, Tri-luma, Tridione, Trisenox, Trituss ER, Trivaris, Tri-Vi-Flor, Trizivir, Trobicin, Tuberculin, Tubersol, Tubizid and Triban. The remaining name was thought to look and sound similar to Tribenzor: Tribenzor.

Additionally, DMEPA staff did not identify any United States Adopted Names (USAN) stems in the proposed proprietary name, as of May 7, 2010.

3.2 EXPERT PANEL DISCUSSION

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

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

3.3 PRESCRIPTION ANALYSIS STUDIES

A total of 52 practitioners responded to the prescription analysis study with no responses overlapping with an existing name. Ten of the participants interpreted the name correctly as "Tribenzor," in the written studies. The remainder of the written responses misinterpreted the drug name. In the verbal study, two respondents understood the spoken name correctly as "Tribenzor." The remaining responses were misspelled

phonetic variations of the proposed name, Tribenzor. See Appendix C for the complete listing of interpretations from the verbal and written prescription studies.

3.4 EXTERNAL STUDY

In the proposed name risk assessment submitted by Daiichi Sankyo Pharma Development, the Drug Safety Institute (DSI) concluded, "The results of the DSI research favorably support the use of TRIBENZOR as a proposed proprietary name..." for this product. DSI evaluated 39 names thought to have some potential for confusion with the name Tribenzor. DMEPA's primary Safety Evaluator found 22 of the 39 names lacked orthographic or phonetic similarity to Tribenzor and thus minimized the risk of potential confusion. Six of the remaining 17 names were identified by DMEPA in Section 3.1. These include: Tricor, Trileptal, Trisenox, Tri-Vi-Flor, Trizivir, and Trobicin. The remaining 11 names will be added to the Safety Evaluator's risk assessment. These names include: Albenza, Benzoin, Effexor, Terbenafine, Tetrabenazine, Tri-Chlor, Tricodene, Tridesilon, Tri-Levlen 28, Trinsicon, and Trivora 28.

In addition, DSI completed a gap analysis for the names of drug products approved by the Agency from March 1, 2009 to March 24, 2010. DMEPA's primary Safety Evaluator found only one of these names, Trelstar, had orthographic or phonetic similarity that required further follow-up. However, this name was already identified by DMEPA in Section 3.1.

3.5 COMMENTS FROM THE DIVISION OF CARDIOVASCULAR AND RENAL PRODUCTS (DCRP)

3.5.1 Initial Phase of Review

In response to an April 13, 2010 OSE e-mail, the Division of Cardiovascular and Renal Products (DCRP) indicated they had no comments and/or concerns with the proposed proprietary name at the initial phase of the name review.

3.5.2 Midpoint of Review

DMEPA notified the Division of Cardiovascular and Renal Products via e-mail that we have no concerns with the proposed proprietary name, Tribenzor, on May 20 2010. Per e-mail correspondence from the Division of Cardiovascular and Renal Products on May 20, 2010, they indicated that they had identified no other concerns with the proposed proprietary name, Tribenzor, for this NDA.

3.6 SAFETY EVALUATOR RISK ASSESSMENT

Independent searches by the primary Safety Evaluator resulted in two additional names which were thought to look or sound similar to Tribenzor and represent a potential source of drug name confusion.

The name, Tracleer, was identified to have look-alike similarities. The name, (b) (4), was identified to have sound-alike similarities. Thus, a total of 45 names were identified as a potential source of confusion.

However, the name, Tribenzor, was not considered further as it was identified as a licensed trademark to the Applicant and not associated with any other product. Thus, we evaluated a total of 44 names: two identified by the primary safety evaluator, 11 from External Study, and 31 identified in section 3.1 above.

4 DISCUSSION

The proposed name, Tribenzor, was evaluated from a safety and promotional perspective. Furthermore, input from pertinent disciplines involved with the review of this application was considered accordingly.

4.1 PROMOTIONAL ASSESSMENT

DDMAC had no concerns regarding the proposed proprietary name, Tribenzor, from a promotional perspective, and did not offer any additional comments relating to the proposed name. DMEPA and the Division of Cardiovascular and Renal Products concurred with the findings of DDMAC's promotional assessment of the proposed name.

4.2 SAFETY ASSESSMENT

DMEPA evaluated 44 names for their potential similarity to the proposed name, Tribenzor. No other aspects of the name were considered to be a source of potential error.

Failure mode and effects analysis (FMEA) was applied to determine if the proposed proprietary name could potentially be confused with the 44 names and lead to medication errors. This analysis determined that the name similarity between Tribenzor and all of the 44 identified names was unlikely to result in medication error for the reasons presented in Appendices D through G.

5 CONCLUSIONS AND RECOMMENDATIONS

We have completed our review of the proposed proprietary name, Tribenzor, and it is not promotional nor is it vulnerable to name confusion that could lead to medication errors. Thus, the Division of Medication Error Prevention and Analysis has no objections to the proprietary name, Tribenzor, at this time. Our analysis is consistent with the external risk assessment and gap analysis conducted by DSI that was provided by the Applicant. The Applicant will be notified by letter.

The proposed proprietary name, Tribenzor, must be re-reviewed 90 days before approval of the NDA. Additionally, if any of the proposed product characteristics as stated in this review are altered, DMEPA rescinds this finding and the name must be resubmitted for review. The conclusions upon re-review are subject to change.

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

If you have further questions or need clarifications, please contact Nina Ton, project manager, at 301-796-1648.

5.1 COMMENTS TO THE APPLICANT

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

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

If any of the proposed product characteristics as stated in your March 30, 2010 submission are altered, the proprietary name should be resubmitted for review.

6 REFERENCES

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

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

2. Phonetic and Orthographic Computer Analysis (POCA)

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

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

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

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

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

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

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

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

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

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

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

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

USPTO provides information regarding patent and trademarks.

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

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

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

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

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

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

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

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

13. USAN Stems (http://www.ama-assn.org/ama/pub/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.

14. Red Book Pharmacy's Fundamental Reference

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

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

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

16. Medical Abbreviations Book

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

APPENDICES

Appendix A:

FDA's Proprietary Name Risk Assessment considers the potential for confusion between the proposed proprietary name and the proprietary and established names of drug products existing in the marketplace and those pending IND, NDA, BLA, and ANDA products currently under review by the Center. DMEPA defines a medication error as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer. [3]

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

The Safety Evaluator assigned to the Proprietary Name Risk Assessment is responsible for considering the collective findings, and provides an overall risk assessment of the proposed proprietary name. DMEPA bases the overall risk assessment on the findings of a Failure Mode and Effects Analysis (FMEA) of the proprietary name, and focuses on the avoidance of medication errors.

FMEA is a systematic tool for evaluating a process and identifying where and how it might fail. [4] DMEPA uses FMEA to analyze whether the drug names identified with orthographic or phonetic similarity to the proposed proprietary name could cause confusion that subsequently leads to medication errors in the clinical setting. DMEPA uses the clinical expertise of its staff to anticipate the conditions of the clinical setting where the product is likely to be used based on the characteristics of the proposed product.

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

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

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

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

monitoring the impact of the medication.[5] DMEPA provides the product characteristics considered for this review in section one.

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

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

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

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

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

1. Database and Information Sources

DMEPA staff conducts searches of the internet, several standard published drug product reference texts, and FDA databases to identify existing and proposed drug names that may sound-alike or look-alike to the proposed proprietary name using the criteria outlined in Section 2.1. Section 6 provides a standard description of the databases used in the searches. To complement

the process, the DMEPA staff use a computerized method of identifying phonetic and orthographic similarity between medication names. The program, Phonetic and Orthographic Computer Analysis (POCA), uses complex algorithms to select a list of names from a database that have some similarity (phonetic, orthographic, or both) to the trademark being evaluated. Lastly, the DMEPA staff review the USAN stem list to determine if any USAN stems are present within the proprietary name. The individual findings of multiple safety evaluators are pooled and presented to the CDER Expert Panel.

2. CDER Expert Panel Discussion

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

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

3. FDA Prescription Analysis Studies

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

In order to evaluate the potential for misinterpretation of the proposed proprietary name in handwriting and verbal communication of the name, inpatient medication orders and/or outpatient prescriptions are written, each consisting of a combination of marketed and unapproved drug products, including the proposed name. These orders are optically scanned and one prescription is delivered to a random sample of the 123 participating health professionals via e-mail. In addition, a verbal prescription is recorded on voice mail. The voice mail messages are then sent to a random sample of the participating health professionals for their interpretations and review. After receiving either the written or verbal prescription orders, the participants send their interpretations of the orders via e-mail to DMEPA.

4. Comments from the OND review Division or Generic drugs

DMEPA requests the Office of New Drugs (OND) or Office of Generic Drugs (OGD) Regulatory Division responsible for the application for their comments or concerns with the proposed proprietary name and 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 DDMAC's decision on the name. The primary Safety Evaluator addresses any comments or concerns in the safety evaluator's assessment.

The OND or 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 concur/not concur with DMEPA's final decision.

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, conducts a Failure Mode and Effects Analysis, and provides an overall risk assessment of name confusion. Failure Mode and Effects Analysis (FMEA) is a systematic tool for evaluating a process and identifying where and how it might fail.[6] When applying FMEA to assess the risk of a proposed proprietary name, DMEPA seeks to evaluate the potential for a proposed proprietary name to be confused with another drug name because of name confusion and, thereby, cause errors to occur in the medication use system. FMEA capitalizes on the predictable and preventable nature of medication errors associated with drug name confusion. FMEA allows the Agency to identify the potential for medication errors due to orthographically or phonetically similar drug names prior to approval, where actions to overcome these issues are easier and more effective than remedies available in the post-approval phase.

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

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

> ***"Is the proposed proprietary name convincingly similar to another drug name, which may cause practitioners to become confused at any point in the usual practice setting?"***

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

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

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

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

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

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

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

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

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

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

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

If DMEPA objects to a proposed proprietary name on the basis that drug name confusion could lead to medication errors, the primary Safety Evaluator uses the FMEA process to identify strategies to reduce the risk of medication errors. DMEPA is likely to recommend that the Sponsor select an alternative proprietary name and submit the alternate name to the Agency for DMEPA to review. However, in rare instances FMEA may identify plausible strategies that could reduce the risk of medication error of the currently proposed name. In that instance, DMEPA may be able to provide the 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 Sponsor. However, the safety concerns set forth in criteria a through e are supported either by FDA regulation or by external healthcare authorities, including the Institute of Medicine (IOM), World Health Organization (WHO), 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 and called for regulatory authorities to address the issue prior to approval. Additionally, DMEPA contends that the threshold set for the Proprietary Name Risk Assessment is reasonable because proprietary drug name confusion is a predictable and a preventable source of medication error that, in many instances, the Agency and/or 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. . (See Section 4 for 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 primary Safety Evaluator uses the FMEA process to identify strategies to reduce the risk of medication errors. DMEPA is likely to recommend that the Sponsor select an alternative proprietary name and submit the alternate name to the Agency for DMEPA to review. However, in rare instances FMEA may identify plausible strategies that could reduce the risk of medication error of the currently proposed name. In that instance, DMEPA may be able to provide the 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.

Appendix B: Letters with possible orthographic or phonetic misinterpretation

Letters in Name, Tribenzor	Scripted may appear as	Spoken may be interpreted as
Capital 'T'	F, I, L, or Z	'D'
lower case 't'	r	'd'
lower case 'r'	n, s, t, or v	'w'
lower case 'i'	c, e, l	any vowel
lower case 'b' in combination with e "be'	h, k, 'le,' or 'li' 'lu'	'd,' 'p,' or 'v'
lower case 'e'	c, i, or l	any vowel
lower case 'n'	h, m, r, s, u, v, or x	'gn,' 'm' or 'mn'
lower case 'z'	c, e, g, n, m, q, r, s, v	'c,' 's,' or 'x'
lower case 'o'	a, c u, or v	any vowel

Appendix C: FDA Prescription Study Samples and Responses.

Tribenzor Study (conducted on April 4, 2010)

HANDWRITTEN REQUISITION MEDICATION ORDER	VERBAL PRESCRIPTION
Medication Order : Tubinsor 40mg/5mg/12.5mg PO daily	Tribenzor 40 mg/5 mg/12.5 mg by mouth daily.
Outpatient prescription: Tribenzor 40/5/12.5 # 90 1 tab Q day	

Rx Study Responses

Inpatient Medication Order	Outpatient Prescription	Voice Prescription
Lubinzar	Torbensor	Trivenzor
Fubinsor	Fibenzor	Tribenzor
Lubunzor	Tribenzor	Trivenzor
Lubinzar	Tribenzor	Tribensor
Lubinzar	Tribensor	Trivenzor
Lubinzor	Tribezror	Trivensor
Zubinzar	Tribenzor	TriBenZor
Lubinzar	Tribenzol	Tribenzor
Lulinzor?	Tribensor	Trivenzor
Tribenzor	Tribenzor	Trivensur
Lubinzor	Fribenror (or Tribenror?)	Trivensor
Lubinzor	Tribenzor	Trivenzor

Lubinzar	Tribenzor	Trivensor
Lubinsor	Torbensor	
Lubinzar	Tribenzor	
Zubingar	Tribenzor	
Lubinzor	Toibensor	
Lubinzar	tribensor	
	Tribensor	
	Tribensor	
	Tribenzor	

Appendix D: Proprietary names that lack convincing orthographic and/or phonetic similarities

Proprietary Name	Similarity to
Doribax	Look
Durezol***	Look
Taxotere	Look
Tricor	Look

Appendix E: Proprietary names not used in usual practice settings for the reasons described.

Proprietary Name	Active Ingredient	Similarity to Tribenzor	Failure preventions
Fulvicin P/G	Griseofulvin, microcrystalized	Look	This product was discontinued 2004. Marketing griseofulvin products are not of the same strengths of this product and doses are not achievable with the marketed oral tablet.
Trasicor	Oprenolol HCl	Look	This product was discontinued in 1995 with no generic equivalents available.
Triban	Trimethabenzamine HCl Suppository	Look	FDA took action against all products which marketed this unapproved formulation (suppository) of Trimethabenzamide HCL April 2006.
Trobicin	Spectinomycin HCl	Look	This product has been discontinued in the US with no generic equivalents.

Appendix F: Risk of name confusion minimized by preventions listed. (Potential contributing causes highlighted by *italics*)

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)	Failure Mode of name confusion prevented by the combination of stated product characteristics as well as orthographic and/or phonetic differences as described.
Tribenzor **(**Olmesartan Medoxomil, Amlodipine and Hydrochlorothiazide) tablets		20 mg/5 mg/12.5 mg, 40 mg/5 mg/12.5 mg, 40 mg/5 mg/25 mg, 40 mg/10 mg/ 12.5 mg, and 40 mg/10 mg/25 mg (three strengths, leading to the possible dropping of the units of measure from the strength)	One tablet by mouth daily.	
Albenza (Albendazole)	Look and Sound (DSI)	*200 mg tablet*	Two tablets (400 mg) by mouth twice daily	**Ortho graphic difference:** The beginning of each name appear different (Al vs. Tri) **Phonetic difference:** The first syllable in each name sounds different (Al- vs. Tri). **Strength:** Tribenzor is a three ingredient product requiring all three strengths for a complete prescription. Although the strength of Albenza is numerically similar with Tribenzor, the similarity is visual not phonetic (200 mg vs. 20 mg). Albenza is available in a single strength. **Frequency of use:** twice daily vs. daily.
Benzoin (Tincture of Benzoin)	Sound (DSI)	no strength Solution or Spray	Apply topically as needed as a skin protectant	**Phonetic difference:** The first syllable in Tribenzor, "Tri-" is not in Benzoin. **Strength:** Benzoin is commonly written without a strength. (Tinture of Benzoin or Benzoin Compound) Tribenzor is a three ingredient product requiring all three strengths for a complete prescription. **Dosage form and Route of administration:** Spray or solution applied topically vs. an oral tablet

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)	Failure Mode of name confusion prevented by the combination of stated product characteristics as well as orthographic and/or phonetic differences as described.
Tribenzor **(**Olmesartan Medoxomil, Amlodipine and Hydrochlorothiazide) tablets		20 mg/5 mg/12.5 mg, 40 mg/5 mg/12.5 mg, 40 mg/5 mg/25 mg, 40 mg/10 mg/ 12.5 mg, and 40 mg/10 mg/25 mg (three strengths, leading to the possible dropping of the units of measure from the strength)	One tablet by mouth daily.	
Terbenafine (established name for Lamisil)	Sound (DSI)	250 mg tablet, 125 mg and 187.5 mg granules (packets) 1 % cream, gel, and spray	*One tablet* (250 mg for adults) or one packet (125 mg or 187.5 mg for pediatrics) *by mouth daily.* Apply small amount or one spray topically to affected area once or twice daily.	**Phonetic difference:** Terbenafine contains an additional syllable at the end of the name "-fine." Tribenzor includes the 'zz' sound at the beginning of the third syllable. **Strength:** Tribenzor is a three ingredient product requiring all three strengths for a complete prescription. Terbenafine have numerically similar strengths (125 mg and 250 mg vs. 12.5 mg and 25 mg). However, the numeric similarity of the strengths occurs in the last (third) strength presented in Tribenzor's strengths.
Tetrabenazine (established name for Xenazine)	Look and Sound (DSI)	*12.5 mg and 25 mg tablets*	*One tablet by mouth* twice daily or three times daily	**Orthographic difference:** Tetrabenazine contains thirteen letters and appears longer when scripted. Tetrabenazine also includes a second 't' providing an additional upstroke as well as a cross stroke. **Phonetic difference:** Tetrabenazine includes five syllables compared to three in Tribenzor. **Strength:** Tribenzor is a three ingredient product requiring all three strengths for a complete prescription. The overlap in strength occurs in the last (third) strength presented in Tribenzor's strengths. Tetrabenazine is an orphan drug used for the treatment of chorea in patients with Huntington's Disease.

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)	Failure Mode of name confusion prevented by the combination of stated product characteristics as well as orthographic and/or phonetic differences as described.
Tribenzor **(**Olmesartan Medoxomil, Amlodipine and Hydrochlorothiazide) tablets		20 mg/5 mg/12.5 mg, 40 mg/5 mg/12.5 mg, 40 mg/5 mg/25 mg, 40 mg/10 mg/ 12.5 mg, and 40 mg/10 mg/25 mg (three strengths, leading to the possible dropping of the units of measure from the strength)	One tablet by mouth daily.	
Tikosyn (Dofetilide)	Look	125 mcg, 250 mcg, 500 mcg capsules	*One capsule by mouth* twice daily	**Orthographic difference:** Tribenzor has two additional letters providing added length to the name. **Strength:** Tribenzor is a three ingredient product requiring all three strengths for a complete prescription. The numeric similarity of the strengths occurs in the last (third) strength presented in Tribenzor's strengths. **Frequency of use:** twice daily vs. daily.
Tracleer (Bosentan)	Look	62.5 mg and *125 mg tablets*	*One tablet (125 mg*) by mouth twice daily. (Dose is titrated up to usual dose)	**Orthographic difference:** The 'z' in Tribenzor may provide a down stroke when scripted. Tribenzor also appears longer. **Strength:** Tribenzor is a three ingredient product requiring all three strengths for a complete prescription. Although one of the strengths of Tracleer is numerically similar with Tribenzor, the similarity occurs in the last of three strengths. **Frequency of use:** twice daily vs. daily

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)	Failure Mode of name confusion prevented by the combination of stated product characteristics as well as orthographic and/or phonetic differences as described.
Tribenzor **(**Olmesartan Medoxomil, Amlodipine and Hydrochlorothiazide) tablets		20 mg/5 mg/12.5 mg, 40 mg/5 mg/12.5 mg, 40 mg/5 mg/25 mg, 40 mg/10 mg/ 12.5 mg, and 40 mg/10 mg/25 mg (three strengths, leading to the possible dropping of the units of measure from the strength)	One tablet by mouth daily.	
Trecator (Ethionamide)	Look	250 mg *tablets*	15-20 mg/kg/day *by mouth as a single daily* or divided doses twice to four times daily to a maximum daily dose of 1000 mg.	**Orthographic difference:** The letters providing an upstroke in each name appear in differing positions. The 'z' in Tribenzor may provide a down stroke when scripted. **Strength:** Trecator is available in one strength which may be omitted during the procurement and prescribing steps of the medication use process. Tribenzor is a three ingredient product requiring all three strengths for a complete prescription. The numeric similarity of the strengths occurs in the last (third) strength presented in Tribenzor's strengths.
Trelstar (Triptorelin Pamoate)	Look	Depot - 3.75 mg LA- 11.25 mg 22.5 mg	Inject the contents of one vial intramuscularly Depot- every four weeks, LA- every 12 weeks or 22.5 mg every 24 weeks	**Orthographic difference:** Trelstar includes an addition upstroke provided by 't.' The 'z' in Tribenzor may provide a down stroke when scripted. **Strength:** Trelstar is available in three strengths which do not overlap with the strengths of Tribenzor. **Dosage form:** powder for injection in a vial vs. tablets. **Route of administration:** intramuscular vs. oral **Frequency of use:** single doses repeated at specific weekly intervals based on strength or modifier vs. daily. Trelstar is limited to use in a physicians office

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)	Failure Mode of name confusion prevented by the combination of stated product characteristics as well as orthographic and/or phonetic differences as described.
Tribenzor **(**Olmesartan Medoxomil, Amlodipine and Hydrochlorothiazide) tablets		20 mg/5 mg/12.5 mg, 40 mg/5 mg/12.5 mg, 40 mg/5 mg/25 mg, 40 mg/10 mg/ 12.5 mg, and 40 mg/10 mg/25 mg (three strengths, leading to the possible dropping of the units of measure from the strength)	One tablet by mouth daily.	
Tretinoin (also as a topical the established name for Renova, Retin-A, Altinac, Avita, and Atralin)	Look	*10 mg* oral capsules topical product creams 0.02%, 0.025%, 0.05% and 0.1%, topical Gels 0.01%, 0.025%, 0.04%, 0.05% and 0.1%	<u>Induction of remission of Acute myelogenous leukemia</u> 45 mg/m^2/day divided and given *by mouth* twice or three times daily. For an average patient, the BSA is 1.73 m^2. The daily dose is 80 mg or four capsules (*40 mg*) twice daily. <u>Treatment of acne and reduce appearance of wrinkles</u> Apply small amount to affected area of face *daily.*	**Orthographic difference:** The 't' providing the upstroke in the middle of Tretinoin also provides a cross stroke not in Tribenzor. **Strength:** Tribenzor is a three ingredient product requiring all three strengths for a complete prescription. The overlap of the strengths of the oral product (10 mg) occurs in the second strength presented in Tribenzor's strengths.
Tribestan (Tribulis trirestris) an herbal supplement	Look	500 mg *tablet*	*One* or two tablets by mouth three times daily with food.	**Orthographic difference:** Tribestan includes an addition upstroke provided by 't.' The 'z' in Tribenzor may provide a down stroke when scripted. **Strength:** Tribenzor is a three ingredient product requiring all three strengths for a complete prescription. . Tribestan is a direct to consumer marketed oral herbal supplement. A prescriber is unlikely to write for this product.

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)	Failure Mode of name confusion prevented by the combination of stated product characteristics as well as orthographic and/or phonetic differences as described.
Tribenzor **(**Olmesartan Medoxomil, Amlodipine and Hydrochlorothiazide) tablets		20 mg/5 mg/12.5 mg, 40 mg/5 mg/12.5 mg, 40 mg/5 mg/25 mg, 40 mg/10 mg/ 12.5 mg, and 40 mg/10 mg/25 mg (three strengths, leading to the possible dropping of the units of measure from the strength)	One tablet by mouth daily.	
Tri-biotic (Gramicidin, polymycin B and Neomycin) No longer marketed but products with the same dosage form and the same ingredients are currently marketed	Look	0.025 mg, 10,000 units and 1.75 mg/ml ophthalmic solution	One to two drops into affected eye every four hours.	**Orthographic difference:** Tri-biotic includes an addition upstroke provided by 't.' The 'z' in Tribenzor may provide a down stroke when scripted. **Strength:** Tribenzor is a three ingredient product requiring all three strengths for a complete prescription. Tri-biotic is a triple ingredient product with only one configuration thus the strength may be omitted when prescribing or ordering this product. **Dosage form and Route of administration:** Ophthalmic solution vs. oral tablet.
Tri-Chlor (Trichloroacetic Acid)	Look (DSI EPD)	80 %	Apply to genital warts and cover with suitable dressing for 5 to 6 days.	**Orthographic difference:** Tri-Chlor may include an additional upstroke provided by the 'l.' The 'z' in Tribenzor may provide a down stroke when scripted. **Strength:** Tri-Chlor is available in one strength which may be omitted during the procurement and prescribing steps of the medication use process. Tribenzor is a three ingredient product requiring all three strengths for a complete prescription. **Dosage form and route of administration:** Topical liquid to apply to warts under a dressing vs. an oral tablet.

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)	Failure Mode of name confusion prevented by the combination of stated product characteristics as well as orthographic and/or phonetic differences as described.
Tribenzor **(**Olmesartan Medoxomil, Amlodipine and Hydrochlorothiazide) tablets		20 mg/5 mg/12.5 mg, 40 mg/5 mg/12.5 mg, 40 mg/5 mg/25 mg, 40 mg/10 mg/ 12.5 mg, and 40 mg/10 mg/25 mg (three strengths, leading to the possible dropping of the units of measure from the strength)	One tablet by mouth daily.	
Tricodene with the modifiers Sugar Free (Dextromethorphan HBr and Chlorpeniramine Maleate) Pediatric DM (Guaifenesin and Dextromethorphan HBr GG/SE (Guaifenesin and Pseudoephedrine HCl) CF Cold Formula (Dextromethorphan HBr, Guaifenesin and Pseudoephedrine HCl) #1 (Pyrilamine Maleate and Codeine Phosphate)	Look and Sound (DSI's COPA)	10 mg/2 mg per 10 mL oral liquid 100 mg/10 mg per 5 mL oral liquid 100 mg/30 mg per 5 mL oral liquid 10 mg/100 mg/30 mg per 5 mL oral liquid 25 mg/16.4 mg per 10 mL	One to Four teaspoonfuls (5-20 mL) by mouth every six hours One to two teaspoonfuls (5-10 mL) by mouth every four hours. One to two teaspoonfuls (5-10 mL) by mouth every six hours. One to two teaspoonfuls (5-10 mL) by mouth every six hours. One to two teaspoonfuls (5-10 mL) by mouth every six hours.	**Orthographic difference:** The upstroke provided by the 'b' and 'd' appear in different locations. The 'z' in Tribenzor may provide a down stroke when scripted. Tricodene requires an additional modifier which adds length, **Phonetic difference:** The second and third syllables sound different (coh-deen vs. ben-zohr) **Dosage form:** oral liquid vs. oral tablet **Strength:** Tribenzor is a three ingredient product requiring all three strengths for a complete prescription. The Tricodene modifier distinguishes the appropriate product. Although Tricodene CF includes three ingredients and thus three strengths, the product will be identified by the modifier , CF, in clinical practice.
Tridesilon (Desonide) Discontinued product with generic equivalents currently marketed.	Look (DSI's COPA)	0.5% cream or ointment	Apply small amount topically twice to four times daily.	**Orthographic difference:** Tridesilon includes the letter 'l' providing an additional upstroke. The 'z' in Tribenzor may provide a down stroke when scripted. **Strength:** These products are a single strength which is often omitted during prescribing and procurement. Tribenzor is a three ingredient product requiring all three strengths for a complete prescription. **Dosage form and route of administration:** topical cream or ointment vs. oral tablet

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)	Failure Mode of name confusion prevented by the combination of stated product characteristics as well as orthographic and/or phonetic differences as described.
Tribenzor **(**Olmesartan Medoxomil, Amlodipine and Hydrochlorothiazide) tablets		20 mg/5 mg/12.5 mg, 40 mg/5 mg/12.5 mg, 40 mg/5 mg/25 mg, 40 mg/10 mg/ 12.5 mg, and 40 mg/10 mg/25 mg (three strengths, leading to the possible dropping of the units of measure from the strength)	One tablet by mouth daily.	
Tridione (Trimethadione)	Look	150 mg chewable tablet	Petit mal seizure not controlled by other medication Chew and swallow two to four tablets (300 mg- 600 mg) three times to four times daily.	**Orthographic Similarity:** The 'z' in Tribenzor may provide a down stroke when scripted. **Strength:** Tridione is available in one strength and it does not overlap with the strength of Tribenzor. Tribenzor is a three ingredient product requiring all three strengths for a complete prescription.
Trilafon (perphenazine) (Discontinued product but generic equivalents are currently marketed.)	Look	*2 mg, 4 mg*, 8 mg and 16 mg *tablets* and 16 mg/5 mL oral solution	One tablet (2 mg to 16 mg) *by mouth* twice, three times, or four times daily.	**Orthographic difference:** Trilafon includes an addition upstroke provided by 'f.' **Strength:** The beginning strength of Tribenzor may be numerically similar to Trilafon. However, Tribenzor is a three ingredient product requiring all three strengths for a complete prescription **Frequency of use:** twice, three times or four times daily vs. once daily.
Tri-Legest (norethindrone and ethinyl estradiol) Tri-Legest Fe (norethindrone, ethinyl estradiol and ferrous fumerate)	Look	Triphasic oral contraceptive 1 mg/0.02 mg, 1 mg/0.03 mg, and 1 mg/0.035 mg 1 mg/0.02 mg, 1 mg/0.03 mg, and 1 mg/0.035 mg and 75 mg	*One tablet by mouth daily.*	**Orthographic Difference:** Tri-Legest includes an addition upstroke provided by 't' at the end of the name. **Strength:** Tribenzor is a three ingredient product requiring all three strengths for a complete prescription. Tri-Legest may include a modifier "Fe" but the strength of Tri-legest is likely to be omitted as is it a triphasic oral contraceptive. Additionally, the strengths of these products differ from the strengths of Tribenzor.

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)	Failure Mode of name confusion prevented by the combination of stated product characteristics as well as orthographic and/or phonetic differences as described.
Tribenzor **(**Olmesartan Medoxomil, Amlodipine and Hydrochlorothiazide) tablets		20 mg/5 mg/12.5 mg, 40 mg/5 mg/12.5 mg, 40 mg/5 mg/25 mg, 40 mg/10 mg/ 12.5 mg, and 40 mg/10 mg/25 mg (three strengths, leading to the possible dropping of the units of measure from the strength)	One tablet by mouth daily.	
Trileptal (Oxcarbazepine)	Look	150 mg, 300 mg, and 600 mg *tablets*, and 60 mg/mL oral suspension	One tablet (300 mg) by mouth twice daily.	**Orthographic difference:** Tripleptal includes two additional upstrokes provided by the letters 't' and 'l.' **Strength:** The strengths of Trileptal do not overlap with the strengths of Tribenzor. Tribenzor is a three ingredient product requiring all three strengths for a complete prescription.
Tri-Levlen 28 (discontinued product with generic equivalents marketed) and Trivora 28 Ethinyl Estradiol and Levonorgesterol	Look and Sound (DSI's COPA)	0.03/0.05 mg (6 tablets), 0.04 mg/ 0.075 mg (5 tablets), 0.03 mg/0.125 mg (10 tablets)	*One tablet by mouth daily*	**Tri-Levlen orthographic difference:** Tri-Levlen includes a second 'l' providing an additional upstroke. The 'z' in Tribenzor may provide a down stroke when scripted. **Tri-Levlen phonetic differences**: The second and third syllables in each name sound different when spoken (lehv –lehn vs. behn-zohr), **Trivora orthographic difference:** Trivora includes no upstrokes or down strokes. Tribenzor includes the letter 'b' providing an upstroke and the letter 'z' may provide a down stroke when scripted. **Trivora phonetic difference:** the second and third syllables in each name sound different when spoken (voh-rah vs. behn-zohr). **Strength:** Although these products have multiple ingredients and strengths, these products have a single strength configuration which is often omitted during prescribing and procurement. Tribenzor is a three ingredient product requiring all three strengths for a complete prescription. Additionally, the strengths of these products differ from the strengths of Tribenzor.

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)	Failure Mode of name confusion prevented by the combination of stated product characteristics as well as orthographic and/or phonetic differences as described.
Tribenzor **(**Olmesartan Medoxomil, Amlodipine and Hydrochlorothiazide) tablets		20 mg/5 mg/12.5 mg, 40 mg/5 mg/12.5 mg, 40 mg/5 mg/25 mg, 40 mg/10 mg/ 12.5 mg, and 40 mg/10 mg/25 mg (three strengths, leading to the possible dropping of the units of measure from the strength)	One tablet by mouth daily.	
Trilipix (Fenofibric Acid)	Look	45 mg and 135 mg capsules	*One capsule by mouth daily*	**Orthographic difference:** Trilipix ends with an 'x' which provides a cross stoke. The letter grouping of 'en' following the b make Tribenzor appears longer when scripted. **Strength:** The strengths of Trilipix do not overlap with the strengths of Tribenzor. Tribenzor is a three ingredient product requiring all three strengths for a complete prescription.
Tri-Luma (Fluocinolone acetonide, hydroquinone, and tretinoin)	Look	0.01%/4%/0.05% cream	Apply a thin film topically to affected area *daily* at bed time.	**Orthographic difference:** Tribenzor has two additional letters providing added length to the name. The 'z' in Tribenzor may provide a down stroke when scripted. **Strength:** Tri-Luma contains three active ingredients in one product configuration. Therefore, the strength may be omitted and the prescription is still complete. Tribenzor is a three ingredient product requiring all three strengths for a complete prescription. **Dosage form and route of administration:** Cream administered topically vs. an oral tablet.
Trinsicon Ascorbic Acid (Vitamin C), Cyanocobalamin (Vitamin B12), Folic Acid (Vitamin B9), Ferrous Fumarate , Liver Stomach Concentrate (discontinued with similar products marketed)	Look (DSI's COPA)	75 mg/15 mcg/ 0.5 mg /110 mg/ 240mg capsule	*One capsule by mouth daily*	**Orthographic difference:** Trinsicon includes no letters providing an upstroke or down stroke. Tribenzor includes the letter 'b' providing an upstroke and the letter 'z' may provide a down stroke when scripted. **Strength:** These products have a single strength configuration which is often omitted during prescribing and procurement. Tribenzor is a three ingredient product requiring all three strengths for a complete prescription.

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)	Failure Mode of name confusion prevented by the combination of stated product characteristics as well as orthographic and/or phonetic differences as described.
Tribenzor **(**Olmesartan Medoxomil, Amlodipine and Hydrochlorothiazide) tablets		20 mg/5 mg/12.5 mg, 40 mg/5 mg/12.5 mg, 40 mg/5 mg/25 mg, 40 mg/10 mg/ 12.5 mg, and 40 mg/10 mg/25 mg (three strengths, leading to the possible dropping of the units of measure from the strength)	One tablet by mouth daily.	
Trisenox (Arsenic Trixode)	Look	10 mg/10 mL ampule	Infuse 0.015 mg/kg intravenously *daily.*	**Orthographic difference:** Tribenzor includes an upstroke proved by 'b.' Also, the 'z' in Tribenzor may provide a down stroke when scripted. **Strength:** Tribenzor is a three ingredient product requiring all three strengths for a complete prescription. **Dosage form and route of administration:** injection administered as an intravenous infusion vs. an oral tablet
Trituss ER Dextromethorphan HBr, Guaifenesin, and phenylephrine HCl	Look	30 mg/600 mg/10 mg *tablet*	*One* or two tablets by mouth every 12 hours.	**Orthographic Difference:** The 'z' in Tribenzor may provide a down stroke when scripted. The modifier 'ER' is likely to be separated for the root name, Trituss. **Strength:** Trituss ER contains three active ingredients in one single product configuration. Therefore, the strength may be omitted and the prescription is still complete. Tribenzor is a three ingredient product requiring all three strengths for a complete prescription. The strength of this product differs from the strengths of Tribenzor.

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)	Failure Mode of name confusion prevented by the combination of stated product characteristics as well as orthographic and/or phonetic differences as described.
Tribenzor **(**Olmesartan Medoxomil, Amlodipine and Hydrochlorothiazide) tablets		20 mg/5 mg/12.5 mg, 40 mg/5 mg/12.5 mg, 40 mg/5 mg/25 mg, 40 mg/10 mg/ 12.5 mg, and 40 mg/10 mg/25 mg (three strengths, leading to the possible dropping of the units of measure from the strength)	One tablet by mouth daily.	
Trivaris (Triamcinolone Acetonide)	Look	8 mg/0.1 mL syringe	Intravitreal- 1.4 mg one time Intramuscular- 60 mg one time. Intra-articular- 2.5-15 mg one time	**Orthographic difference:** Tribenzor includes an upstroke proved by 'b.' Also, the 'z' in Tribenzor may provide a down stroke when scripted. **Strength:** Trivaris is available in one strength which does not overlap with the strengths of Tribenzor. Tribenzor is a three ingredient product requiring all three strengths for a complete prescription. **Dosage form and route of administration:** injectable suspension to be administered intravitreal, intramuscular or intra-articular vs. an oral tablet. Trivaris is administered by a healthcare provider in a clinic or operating room setting.
Tri-Vi-Flor (Ascorbic acid, Cholecalciferaol, Vitamin A Palmitate, and Sodium Fluoride)	Look	35 mg/400 IU/ 1500 IU/0.55 mg/mL	One dropperful (1 mL) *by mouth daily.*	**Orthographic difference:** Tri-Vi-Flor may be written with hyphens adding length to the name and includes additional upstrokes provided by the 'l' and 'V,' if capitalized when scripted. **Strength:** Tri-Vi-Flor contains four active ingredients in one single product configuration. The strength is often omitted and the prescription is still complete. Tribenzor is a three ingredient product requiring all three strengths for a complete prescription. **Patient population:** Tri-Vi-Flor is a vitamin and fluoride supplement for young children. Tribenzor is for hypertensive adults.

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)	Failure Mode of name confusion prevented by the combination of stated product characteristics as well as orthographic and/or phonetic differences as described.
Tribenzor **(**Olmesartan Medoxomil, Amlodipine and Hydrochlorothiazide) tablets		20 mg/5 mg/12.5 mg, 40 mg/5 mg/12.5 mg, 40 mg/5 mg/25 mg, 40 mg/10 mg/ 12.5 mg, and 40 mg/10 mg/25 mg (three strengths, leading to the possible dropping of the units of measure from the strength)	One tablet by mouth daily.	
Trizivir (Abacavir, Lamivudine and Zidovudine)	Look	300 mg/150 mg/ 300 mg *tablets*	*One tablet* by mouth twice daily.	**Orthographic difference:** Tribenzor includes a 'b' providing an upstroke. **Strength:** Trizivir contains three active ingredients in one single product configuration. Therefore, the strength may be omitted and the prescription is still complete. Tribenzor is a three ingredient product requiring all three strengths for a complete prescription. Additionally, the strength of this product differs from the strengths of Tribenzor. **Frequency of use:** twice daily vs. daily.
Tuberculin (skin test) and Tubersol (Tuberculin Purified Protein Derivative)	Look	5,000 units/0.1 mL 1 mL and 5 mL vial 2 mL and 5 mL vial	0.1 mL (5000 units) intradermally one time.	**Tuberculin Orthographic difference:** Tuberculin includes the letter 'l' providing and additional upstroke. The 'z' in Tribenzor may provide a down stroke when scripted. **Tubersol Orthographic difference:** Tubersol includes the letter 'l' providing and additional upstroke at the end of the name . The 'z' in Tribenzor may provide a down stroke when scripted. **Strength:** These products are a single strength which is often omitted during prescribing and procurement. Tribenzor is a three ingredient product requiring all three strengths for a complete prescription. **Dose:** 0.1 mL vs. one tablet **Dosage form and route of administration:** injection administered intradermally vs. an oral tablet.

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)	Failure Mode of name confusion prevented by the combination of stated product characteristics as well as orthographic and/or phonetic differences as described.
Tribenzor **(**Olmesartan Medoxomil, Amlodipine and Hydrochlorothiazide) tablets		20 mg/5 mg/12.5 mg, 40 mg/5 mg/12.5 mg, 40 mg/5 mg/25 mg, 40 mg/10 mg/ 12.5 mg, and 40 mg/10 mg/25 mg (three strengths, leading to the possible dropping of the units of measure from the strength)	One tablet by mouth daily.	
Tubizid (Isoniazid) (discontinued product but product with the same active ingredient currently marketed	Look	300 mg delayed-release *tablet*	*One tablet by mouth daily*	**Orthographic difference:** Tubizid includes a 'd' at the end of the name providing an additional upstroke. **Strength:** Tubizid was available in one strength which does not overlap with the strengths of Tribenzor. Tribenzor is a three ingredient product requiring all three strengths for a complete prescription.

Appendix G: Risk of medication errors due to product confusion minimized by use in clinical practice for the reasons described.

Proposed name: **Tribenzor** **(**Olmesartan Medoxomil, Amlodipine and Hydrochlorothiazide) tablets	**Strength:** 20 mg/5 mg/12.5 mg, 40 mg/5 mg/12.5 mg, 40 mg/5 mg/25 mg, 40 mg/10 mg/ 12.5 mg, and 40 mg/10 mg/ 25 mg	**Usual dose:** One tablet by mouth daily.
Failure Mode: Name confusion	**Causes (could be multiple)**	**Prevention of Failure Mode;(name confusion)**
Tambocor (Flecanide Acetate) 50 mg, 100 mg, and 150 mg tablets One tablet (100 mg or 150 mg) by mouth twice daily.	Orthographic similarity: Both names begin and end with similar appearing letter groupings (Tamb- vs. Trib- and -cor vs. -zor), and both names have similar length when scripted (8 letters vs. 9 letters. Both products are available as an oral tablet. These products have numerically similar strengths (50 mg and 100 mg vs. the amlodipine strengths of 5 mg and 10 mg)	Use in clinical practice will minimize the risk of medication error. Rationale: Tribenzor may be scripted with a down stroke provided by the 'z' which does not appear in Tambocor. Tribenzor contains three active ingredients. All need to be specified for a complete prescription for this product. Tribenzor tablets are taken once a day. Tambocor contains only one active ingredient. Tambocor is taken twice daily. The numerically similar strengths appear as the second ingredient strength presented in Tribenzor likely making this similarity less a source of confusion. Tambocor must be initiated in an inpatient setting on a cardiac monitor and titrated from 100 mg twice daily to a maximum of 200 mg twice daily.
Tri Biozene (Bacitracin, Neomycin, Polymyxin B, and Pramoxine) topical cream Usual dose: Apply small amount to cut scrap our burn at dressing change.	Orthographic similarity: Both names begin with the same four letters (TRIB); the fifth letter appear similar when scripted (i vs. e); both names include the letter 'z' in the seventh position; and the names have a similar length (10 letters vs. 9 letters).	Use in clinical practice will minimize the risk of medication error. Rationale: Tribenzor contains three active ingredients, thus the strength of each active ingredient must be specified for a complete prescription for this product. Tribenzor tablets are taken by mouth once a day. Tri Benzene is a combination triple antibiotic with pain reliever in a topical cream available over-the counter as a first aid cream to be applied topically. The strengths of the active ingredients are not specified on the principle display panel of the product.

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

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-200175	ORIG-1	DAIICHI SANKYO INC	CS-8635 Combination of olmesartan medoxomil/amlodipine/hydrochlorothiazide

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/s/

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