CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

201922Orig1s000

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--Final

Date:	February 8, 2012
Reviewer(s):	Lissa C. Owens, PharmD Division of Medication Error Prevention and Analysis
Team Leader	Lubna Merchant, M.S., PharmD Division of Medication Error Prevention and Analysis
Division Director	Carol Holquist, RPh Division of Medication Error Prevention and Analysis
Drug Name(s) and Strength(s):	Ximino (Minocycline Hydrochloride) Extended-release Capsules, 45 mg, 67.5 mg, 90 mg, 112.5 mg, and 135 mg
Application Type/Number:	NDA 201922
Applicant/sponsor:	Ranbaxy
OSE RCM #:	2011-3936

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

CONTENTS

1 INTRODUCTION

This re-assessment of the proposed proprietary name, Ximino is written in response to the anticipated approval of this NDA within 90 days from the date of this review. DMEPA found the proposed name, Ximino, acceptable in OSE Review RCM # 2011-2832 dated October 26, 2011.

2 METHODS AND DISCUSSION

For re-assessments of proposed proprietary names, DMEPA searches a standard set of databases and information sources (see section 4) to identify names with orthographic and phonetic similarity to the proposed name that have been approved since the previous OSE proprietary name review. For this review we used the same search criteria described in OSE Review RCM # 2011-2832. Since none of the proposed product characteristics were altered we did not re-evaluate previous names of concern. The searches of the databases yielded no new names, thought to look or sound similar to Ximino and represent a potential source of drug name confusion.

Additionally, DMEPA searched the USAN stem list to determine if the name contains any USAN stems as of the last USAN updates. The Safety Evaluator did not identify any United States Adopted Names (USAN) stems in the proposed proprietary name, as of February 2, 2012. The Office of Prescription Drug Promotion OPDP re-reviewed the proposed name on January 5, 2012 and had no concerns regarding the proposed name from a promotional perspective.

3 CONCLUSIONS

The re-evaluation of the proposed proprietary name, Ximino, did not identify any vulnerabilities that would result in medication errors with any additional names. Thus, DMEPA has no objection to the proprietary name, Ximino, for this product at this time.

DMEPA considers this a final review; however, if approval of the NDA is delayed beyond 90 days from the date of this review, Division of Dermatology and Dental Products should notify DMEPA because the proprietary name must be re-reviewed prior to the new approval date.

If you have further questions or need clarifications, please contact Janet Anderson, OSE project manager, at 301-796-0675.

4 REFERENCES

1. OSE Reviews

2011-2832, Proprietary Name Review for Ximino (Minocycline hydrochloride) Extended-release 45 mg, 67.5 mg, 90 mg, 112.5 mg, 135 mg Capsules, Owens, Lissa, October 26, 2011.

2. 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.

3. USAN Stems (http://www.ama-assn.org/ama/pub/physician-resources/medical-science/united-states-adopted-names-council/naming-guidelines/approved-stems.page?)

USAN Stems List contains all the recognized USAN stems.

4. Division of Medication Error Prevention and Analysis Proprietary Name Consultation Request

Compiled list of proposed proprietary names submitted to the Division of Medication Error Prevention and Analysis for review. The list is generated on a weekly basis from the Access database/tracking system.

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

/s/

LISSA C OWENS
02/09/2012

LUBNA A MERCHANT
02/09/2012

CAROL A HOLQUIST
02/09/2012

Department of Health and Human Services
Public Health Service
Food and Drug Administration
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Proprietary Name Review

Date:	October 26, 2011
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CONTENTS

1 INTRODUCTION

This review evaluates the proposed proprietary name, Ximino, 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.

1.1 REGULATORY HISTORY

Minocycline Extended-release Capsules is the subject of the 505 (b)(2) application originally submitted to the FDA on May 10, 2010 that references Solodyn Tablets (NDA 050808). However, the Application received a Refuse to File response on July 16, 2010 due to inadequate bioequivalence evaluation for safety and/or effectiveness of the product in patients under 200 pounds (91 kg) and due to missing Debarment Certification and Financial Disclosure forms. The Applicant resubmitted this Application (NDA 050808) to the FDA for review on February 4, 2011

1.2 PRODUCT INFORMATION

Minocycline Extended-release Capsules are a tetracycline antibiotic indicated to treat only inflammatory lesions of non-nodular moderate to severe acne vulgaris in patients 12 years of age and older. The product will contain the following strengths: 45 mg, 67.5 mg, 90 mg, 112.5 mg, and 135 mg. The recommended dosage of the product is approximately 1 mg/kg once daily for 12 weeks. The following table shows strength and body weight to achieve approximately 1 mg/kg:

Table 1: Dosing Table for Minocycline Hydrochloride Extended-release Capsules

Patient's weight (Kg)	Capsule Strength (mg)
45 kg to 55 kg	45 mg
56 kg to 74 kg	67.5 mg
75 kg to 96 kg	90 mg
97 kg to 125 kg	112.5 mg
126 kg to 136 kg	135 kg

The product will be supplied is bottles containing 30 tablets, 500 tablets, and in blister packs containing 10 tablets. Minocycline Extended-release Capsules should be stored between 20°C to 25°C (68°F to 77°F) and protected from light, moisture, and excessive heat.

Some of the proposed Minocycline Extended-release product's characteristics differ from the reference listed drug, Solodyn. The proposed product will be available in capsules whereas Solodyn is available in tablets. Additionally, although three of the products' strengths overlap (i.e., 45 mg, 90 mg, and 135 mg), the remaining strengths are different (i.e., 67.5 mg, 112.5 mg, and 135 mg vs 55 mg, 65 mg, 80 mg, 105 mg, and 115 mg). The remaining product characteristics are the same. Both products should be administered by the same route of administration (oral), same dose (1 capsule vs. 1 tablet), and same frequency (once daily). Additionally, both products contain a

recommended dosage of 1 mg/kg and should be administered for 12 weeks. Both products should be stored at the room temperature.

2 RESULTS

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

2.1 PROMOTIONAL ASSESSMENT

DDMAC determined the proposed name is acceptable from a promotional perspective. DMEPA and the Division of Dermatology and Dental Products concurred with the findings of DDMAC's promotional assessment of the proposed name.

2.2 SAFETY ASSESSMENT

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

2.2.1 United States Adopted Names (USAN) SEARCH

The United States Adopted Name (USAN) stem search conducted on October 11, 2011, identified that a USAN stem is not present in the proposed proprietary name.

2.2.2 Components of the Proposed Proprietary Name

The proposed name is comprised of a single word that does not contain components (e.g. medical abbreviation, dosage form, frequency of administration, etc) that can contribute to medication error.

2.2.3 Medication Error Data

Since the Reference Listed Drug, Solodyn and its generic products (i.e., Minocycline Extended-release Tablets) are currently marketed, DMEPA searched the FDA Adverse Event Reporting System (AERS) database to identify medication errors involving Solodyn and Minocycline Extended-release Tablets. The AERS search conducted on September 28, 2011 used the following search terms: active ingredient "Minocycline", trade name "Solodyn" and "Minocycline", and verbatim terms "Solod%" and "Mynocy%". The reaction terms used were the MedDRA High Level Group Terms (HLGT) "Medication Errors" and "Product Quality Issues". Since Solodyn was approved on May 8, 2006, the time frame of the search was limited to May 8, 2006 to June 7, 2011.

The reports were manually reviewed to determine if a medication error occurred. Duplicate reports were combined into cases. The cases that described a medication error were categorized by type of error. We reviewed the cases within each category to identify factors that contributed to the medication errors. Those cases that did not describe a medication error were excluded from further analysis. For cases describing a medication error, we reviewed the cases to identify factors that contributed to the errors. Reports excluded from the case series included those that did not describe a medication error, related to suicide attempt, adverse drug reactions, or did not describe confusion between Immediate-release Minocycline products (i.e., Minocin, Dynacin) and extended-release Minocycline products.

Following exclusions, no relevant cases remained.

2.2.4 FDA Name Simulation Studies

Forty-three practitioners responded to DMEPA's prescription studies. See Appendix C for the complete listing of interpretations from the verbal and written prescription studies.

2.2.5 Comments from Other Review Disciplines

In response to the OSE, August 19, 2011 e-mail, the Division of Dermatology and Dental Products (DDDP) did not forward any comments or concerns relating to the proposed name at the initial phase of the name review.

2.2.6 Failure Mode and Effects Analysis of Similar Names

Table 1 lists the names with orthographic, phonetic, or spelling similarity to the proposed proprietary name, Ximino (see Appendix B). These names were identified by the primary reviewer, the Expert Panel Discussion (EPD), and other review disciplines.

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

Look Similar		**Sound Similar**		**Look and Sound Similar**	
Name	***Source***	***Name***	***Source***	***Name***	***Source***
Ximinox-5	FDA	Zymine	FDA	NONE FOUND	
(b) (4)***	FDA				
Incivo***	FDA				
(b) (4)***	FDA				
(b) (4)***	FDA				
Xanax	FDA				
Xeomin	FDA				
Xerese	FDA				
Kinrix	FDA				
Kionex	FDA				
Kinevac	FDA				
Vimovo	FDA				
Viravan P	FDA				
Vumon	FDA				
Xeloda	FDA				
Vermox	FDA				

Our analysis of the 17 names contained in Table 1 considered the information obtained in the previous sections along with the product characteristics. We determined the seventeen names will not pose a risk for confusion as described in Appendix D and E.

DMEPA communicated these findings to the Division of Dermatology and Dental Products via e-mail on October 11, 2011. At that time we also requested additional information or concerns that could inform our review. Per e-mail correspondence from the Division of Dermatology and Dental Products, they stated no additional concerns with the proposed proprietary name, Ximino.

3 CONCLUSIONS

DMEPA concludes the proposed proprietary name is acceptable from both a promotional and safety perspective. The Applicant will be notified of this conclusion via letter.

3.1 COMMENTS TO THE APPLICANT

We have completed our review of the proposed proprietary name, Ximino, and have concluded that this name is acceptable at this time for this product.

However, 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

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

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.

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. ***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.

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 promotional and safety aspects of a proposed proprietary name. The promotional review of the proposed name is conducted by DDMAC. DDMAC 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. DDMAC 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. [1]

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

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

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 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.[2] The product characteristics considered for this review appears in Appendix B1 of this review.

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*
	Similar spelling	Identical prefix	• Names may appear similar

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

Look-alike		Identical infix Identical suffix Length of the name Overlapping product characteristics	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 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, 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 Division of Drug Marketing, Advertising, and Communications (DDMAC). 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 DDMAC'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.[3] 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 Appendix B1 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***

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

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 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.

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. 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 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.

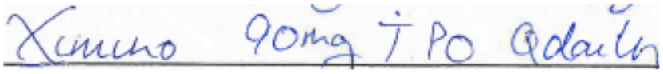
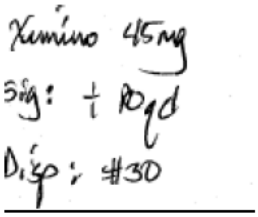
Furthermore, post-marketing experience has demonstrated that medication errors resulting from drug name confusion are notoriously difficult to rectify post-approval. Educational and other post-approval efforts are low-leverage strategies that have had limited effectiveness at alleviating medication errors 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 with Possible Orthographic or Phonetic Misinterpretation

Letters in Name, NAME	Scripted May Appear as	Spoken May Be Interpreted as
Capital 'X'	'd','f','K','P','t','U','V','Y'	KS','KZ','S',X'.'Z'
lower case 'i'	'g,'p','q','y'	'e'
lower case 'm'	'rn','nn','n','v','w','wi','vi','onc','z'	'n'
lower case 'n'	'm','u','x','r','h','s'	'dn','gn,'kn','mn','pn'
lower case 'o'	Any Vowel	'oh'

Appendix C: Prescription Simulation Samples and Results

Figure 1. Ximino Study (Conducted on *July* 14, 2011)

Handwritten Requisition Medication Order	Verbal Prescription
Medication Order:  	Ximino 45 mg #30 1 by mouth daily
Outpatient Prescription:  	

FDA Prescription Simulation Responses.

Study Name: Ximino

Total	19	10	14
INTERPRETATION	**INPATIENT**	**VOICE**	**OUTPATIENT**	**TOTAL**
SIMINO	0	0	1	1
XEMINO	0	0	2	2
XIMCHO	2	0	0	2
XIMCUO 90 MG	1	0	0	1

XIMINO	12	0	8	20
XIMINO 90 MG 1 PO QDAILY	1	0	0	1
XIMURO	1	0	0	1
XUMINO	0	0	3	3
XUNCHO	2	0	0	2
ZEMENO	0	1	0	1
ZEMINO	0	2	0	2
ZIMINO	0	7	0	7

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

Proprietary Name	Active Ingredient	Similarity to Ximino	Failure preventions
Ximinox-5	Minoxidil	Look	Product found on Google. Only sold in India. Not found in common drug references.
(b) (4) ***	Moxifloxacin Hydrochloride	Look	Secondary name for Moxeza (NDA 22428) approved November 19, 2010
Incivo***	Telaprevir	Look	DMEPA objection. Approved Incivek (NDA 201917) May 23, 2011
(b) (4) ***	Fentanyl	Look	Secondary name for Lazanda (NDA 22569) approved June 30, 2011
(b) (4) ***	Itraconazole	Look	Secondary name for Onmel (NDA 22484) approved April 28, 2010
Zymine	Triprolidine	Sound	Ximino has three syllables vs. Zymine which has two. Ximino ending stresses the 'o' sound vs. Zymine which does not

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.

Proposed name: **Ximino (Minocycline Hydrochloride)**	**Strength(s):** **45 mg, 67.5 mg, 90 mg, 112.5 mg, and 135 mg**	**Usual dose:** **Once Capsule by mouth daily**
Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion	**Causes (could be multiple)**	**Prevention of Failure Mode**
Xanax (Alprazolam) Tablets 0.25 mg, 0.5 mg, 1 mg, 2 mg Usual Dose 0.25 mg to 1 mg three times a day Maximum of 4 mg/day	Orthographic Both names begin with similar letter strings 'Xim' and 'Xan'	Orthographic Ximino has two dotted letters 'i' vs. Xanax which has none. The ending letter string 'ino' looks different when scripted than 'nax' Frequency of Administration Once a day vs. Three times a day Dose 45 mg to 135 mg vs. 0.25 mg to 2 mg Schedule Rx vs. CIV
Xeomin (IncobotuliniumtoxinA) Lyophilized Powder 50 Units and 100 units Usual Dose 1.25 Units to 120 Units depending on condition	Orthographic Both names begin with similar letter strings 'Xim' and 'Xeo'. Both names contain the letter string 'min'	Route of Administration Oral vs. Intramuscular Dosage Form Capsule vs. Injection Dose One capsule vs. XX Units

Xerese (Acyclovir and Hydrocortisone) Cream 5 %/1 % Usual Dose Apply to affected area five times a day	Orthographic Both names begin with similar letter strings 'Xim' and 'Xer'	Orthographic Ximino has two dotted letters 'i' vs. Xerese which has none Route of Administration Oral vs. Topical Dosage Form Capsule vs. Cream Frequency of Administration Once a day vs. Five times a day Strength Single vs. Multiple
Kinrix (Diptheria and Tetanus Toxoid and Acellular Pertussis adsorbed and inactivated poliovirus vaccine) Suspension Usual Dose One time dose	Orthographic Both names begin with similar letter strings 'Xim' and 'Kin'. Both names have two dotted letters 'i'	Route of Administration Oral vs. Intramuscular Dosage Form Capsule vs. Suspension for Injection Frequency of Administration Once a day vs. One time injection Storage Room Temperature vs. Refrigerator
Kionex (Sodium Polystyrene Sulfonate) Powder Usual Dose 15 grams one to four times a day	Orthographic Both names begin with similar letter strings 'Xim' and 'Kio'	Dosage Form Capsule vs. Powder Dose One Capsule vs. XX grams Strength Multiple vs. Single
Kinevac (Sincalide) lypholized powder 5 mcg Usual Dose 0.02 mcg/kg over a 30 to 60 sec interval	Orthographic Both names begin with similar letter strings 'Xim' and 'Kio'	Route of Administration Oral vs. Intravenous Dosage Form Capsule vs. Powder for Injection Dose One Capsule vs. XX mcg Strength Multiple vs. Single

Vimovo (Naproxen and Esomeprazole Magnesium) Tablet delayed release 375 mg/20 mg, 500 mg/20 mg <u>Usual Dose</u> One tablet twice a day	<u>Orthographic</u> Both names begin with similar letter strings 'Xim' and 'Vim' and end in similar looking ending strings 'no' and 'vo' <u>Route of Administration</u> Oral	<u>Frequency of Administration</u> Once a day vs. Twice a day <u>Strength</u> Since both have multiple strengths, the strength would have to be written on the prescription. There is no overlap in strength
Viravan P (Pseudoephedrine Hydrochloride and Pyrilamine Maleate) Liquid 30 mg/20 mg <u>Usual Dose</u> 5 ml to 10 ml every 6 hours	<u>Orthographic</u> Both names begin with similar letter strings 'Xi' and 'Vi'	<u>Frequency of Administration</u> Once a day vs. Four times a day <u>Dose</u> One Capsule vs. XX ml <u>Dosage Form</u> Capsule vs. Oral Liquid <u>Strength</u> Multiple vs. Single
Vumon (Teniposide) Injection 50 mg/5 ml <u>Usual Dose</u> 165 mg/m² twice weekly for 8 to 8 doses or 250 mg/m² weekly for 4 to 8 weeks	<u>Orthographic</u> Both names begin with similar letter strings 'Xim' and 'Vum'	<u>Route of Administration</u> Oral vs. Intravenous <u>Dose</u> One Capsule vs. XX mg or ml <u>Dosage Form</u> Capsule vs. Injection <u>Strength</u> Multiple vs. Single <u>Storage</u> Room Temperature vs. Refrigerator

Xeloda (Capecitabine) Tablet 150 mg and 500 mg Usual Dose 1250 mg/m² twice daily for two weeks	Route of Administration Oral	Orthographic Ximino has two dotted letters 'i' vs. Xeloda which has none. Ximino has no upstrokes vs. Xeloda which has two upstroke letters, 'l' and 'd' Frequency of Administration Once a day vs. Twice a day
Vermox (Mebendazole) 100 mg Tablet Usual Dose One tablet twice a day for three days	Orthographic Both names begin with similar letter strings 'Xim' and 'Ver'	Frequency of Administration Once a day vs. Twice a day Strength Multiple vs. Single

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

/s/

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