CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

203415Orig1s000

PROPRIETARY NAME REVIEW(S)

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

Proprietary Name Review

Date:	July 31, 2012
Reviewer:	Kimberly DeFronzo, RPh, MS, MBA Division of Medication Error Prevention and Analysis
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Drug Name and Strength (s):	Xtandi (Enzalutamide) Capsules 40 mg
Application Type/Number:	NDA 203415
Applicant:	Medivation, Inc.
OSE RCM #:	2012-1215

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

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1 INTRODUCTION

This review evaluates the proposed proprietary name, Xtandi, 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

On October 26, 2011, the Applicant submitted a request for proprietary name review for (b) (4). However, on December 16, 2011, the Applicant submitted a withdrawal of that request citing (b) (4) has been rejected by the European review body, and submitted a new name request for (b) (4) with the alternative name of Xtandi under IND 074563. On March 22, 2012, the Applicant submitted another withdrawal for the (b) (4) name review request citing "their commercial group prefers the alternative name Xtandi over the name (b) (4) as supported by their market research". Consequently, on May 22, 2012, the Applicant submitted a request for review of the proposed proprietary name Xtandi, under NDA 203415.

1.2 PRODUCT INFORMATION

The following product information is provided in the May 22, 2012 proprietary name submission.

- Active Ingredient: Enzalutamide
- Indication of Use: For the treatment of patients with castration-resistant prostate cancer who have received docetaxel (b) (4)
- Route of Administration: Oral
- Dosage Form: Capsules
- Strength: 40 mg
- Dose and Frequency: 160 mg or 4 capsules once daily with or without food. No dose adjustment is necessary in the elderly. No formal renal or hepatic impairment study has been completed.
- How Supplied: As white to off-white oblong soft gelatin capsules imprinted in black ink with MDV in bottles of 120 capsules.
- Storage: Store capsules at controlled room temperature 20°C-25°C (68°F-77°F) with excursions to 15°C-30°C (59°F-86°F) permitted.
- Container and Closure Systems: Drug product will be packaged and supplied in 300-cc, (b) (4) high density polyethylene (HDPE) bottles (b) (4) closures lined with induction seals.

2 RESULTS

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

2.1 PROMOTIONAL ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined the proposed name is acceptable from a promotional perspective. DMEPA and the Division of Oncology Products 1 (DOP1) concurred with the findings of OPDP's promotional assessment of the proposed name.

2.2 SAFETY ASSESSMENT

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

2.2.1 United States Adopted Names (USAN) SEARCH

The May 31, 2012 search of the United States Adopted Name (USAN) stems did not identify that a USAN stem is present in the proposed proprietary name.

2.2.2 Components of the Proposed Proprietary Name

The Applicant indicated in their submission that the proposed name, Xtandi, was "invented of made-up words without meaning that makes reference to androgens which bind to the androgen receptor to fuel prostate cancer growth". We find this "androgen" reference to the name acceptable since it is in line with the pharmacologic class of this drug as an androgen receptor signaling inhibitor.

The proprietary name is comprised of a single word that ends in the letter 'i'. DMEPA has considered the possibility of the ending letter 'i' in the name Xtandi being confused with the number '1' in scripted handwriting resulting in a written prescription for 'Xtandi 40 mg' to appear as 'Xtand 140 mg' with '140 mg' being misinterpreted as the product's strength or dose. However, the risk of strength confusion is mitigated by the fact that this product is a single strength product and the expression of the strength is often omitted on written prescriptions for single strength products. Furthermore, in the event that the strength is expressed but misinterpreted as '140 mg', the misinterpretation will be realized at the point of dispensing and questioned since this product is only available as a 40 mg strength capsule. Similarly, any possible confusion resulting from the '140 mg' being misinterpreted as the dose would also be mitigated since the healthcare professional involved would question this dose since it is not an obtainable dose with 40 mg strength capsules. The interventions required in these scenarios will provide the healthcare professional with an opportunity for clarification and corrective action.

2.2.3 FDA Name Simulation Studies

Twenty eight practitioners participated in DMEPA's prescription studies. The interpretations did not overlap with or appear or sound similar to any currently marketed products. All 8 participants in the written "Outpatient" study group interpreted the name Xtandi correctly. However, only 5 (out of 9) participants in the written "Inpatient" study group correctly identified the proposed proprietary name as Xtandi. The remaining participants in this "written" group misinterpreted the letter "i" as "r" and the letter "n" as "r". None of the 11 participants in the verbal or "Voice" study group correctly identified the proposed proprietary name as Xtandi. The participants in this "verbal" group misinterpreted the sound from the

letter "X" as "Z" or "S" and the vowel sound from letter "i" as "y". See Appendix C for the complete listing of interpretations from the verbal and written prescription studies.

2.2.4 Comments from Other Review Disciplines

In response to the OSE's May 31, 2012 e-mail, DOP1 did not forward any comments or concerns relating to the proposed name at the initial phase of the proprietary name review.

2.2.5 Failure Mode and Effects Analysis of Similar Names

Appendix B lists possible orthographic and phonetic misinterpretations of the letters appearing in the proposed proprietary name, Xtandi. Table 1 lists the names with orthographic, phonetic, or spelling similarity to the proposed proprietary name, Xtandi identified by the primary reviewer, the Expert Panel Discussion (EPD), and other review disciplines. Table 1 also includes the names identified from the FDA Prescription Simulation and/or by (b) (4) not identified by DMEPA and requires further evaluation.

Table 1: Collective List of Potentially Similar Names (DMEPA, EPD, Other Disciplines, FDA Name Simulation Studies, and External Name Study)

Look Similar		Look Similar		Look and Sound Similar	
Name	***Source***	***Name***	***Source***	***Name***	***Source***
Xtend-Life	FDA	Xpand	FDA	Xtandi	FDA
Extina	FDA	Xtend	FDA		
Xalkori	FDA	Stendra	FDA		
K-Tab	FDA	V-Tann	FDA		
Xanax	External	X-Viate	FDA		
Xologel	External	Vfend	FDA		
Extraneal	External	(b) (4)	FDA		
Sinequan	External	Plendil	FDA		
Toviaz	External	(b) (4)	FDA		
Zantac	External	Xalatan	FDA, External		

Our analysis of the 21 names contained in Table 1 considered the information obtained in the previous sections along with their product characteristics. We determined all 21 names will not pose a risk for confusion as described in Appendices D and E.

2.2.7 Communication of DMEPA's Final Decision to Other Disciplines

DMEPA communicated our findings to the DOP1 via e-mail on July 27, 2012. At that time we also requested additional information or concerns that could inform our review. Per e-mail correspondence from DOP1 on July 31, 2012, they stated having no additional concerns with the proposed proprietary name, Xtandi.

3 CONCLUSIONS

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

If you have further questions or need clarifications, please contact Frances Fahnbulleh, OSE Project Manager, at 301-796-0942.

3.1 COMMENTS TO THE APPLICANT

We have completed our review of the proposed proprietary name, Xtandi, and have concluded that this name is acceptable. However, if any of the proposed product characteristics as stated in your May 21, 2012, submission are altered, DMEPA rescinds this finding and the name must be resubmitted for review.

Additionally, the proposed proprietary name must be re-reviewed 90 days prior to approval of the NDA. The conclusions upon re-review are subject to change.

4 REFERENCES

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

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

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

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

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

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

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

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

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

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

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

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

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

   USPTO provides information regarding patent and trademarks.

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

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

9. ***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.

10. ***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.

11. ***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.

12. ***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.

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

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

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

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

15. ***Medical Abbreviations Book***

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

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

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

17. Walgreens (www.walgreens.com)

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

18. Rx List (www.rxlist.com)

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

19. Dogpile (www.dogpile.com)

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

APPENDICES

Appendix A

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

The safety assessment is conducted by DMEPA. DMEPA staff search a standard set of databases and information sources to identify names that are similar in pronunciation, spelling, and orthographically similar when scripted to the proposed proprietary name. Additionally, we consider inclusion of USAN stems or other characteristics that when incorporated into a proprietary name may cause or contribute to medication errors (i.e., dosing interval, dosage form/route of administration, medical or product name abbreviations, names that include or suggest the composition of the drug product, etc.). DMEPA defines a medication error as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer.

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

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

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

Typical product characteristics considered when identifying drug names that could potentially be confused with the proposed proprietary name include, but are not limited to; established name of the proposed product, proposed indication of use, dosage form, route of administration, strength, unit of measure, dosage units, recommended dose, typical quantity or

volume, frequency of administration, product packaging, storage conditions, patient population, and prescriber population. DMEPA considers how these product characteristics may or may not be present in communicating a product name throughout the medication use system. Because drug name confusion can occur at any point in the 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.[1] 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 Applicant's intended pronunciation of the proprietary name. However, DMEPA also considers a variety of pronunciations that could occur in the English language because the Applicant 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).

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

<u>Table 1.</u> Criteria Used to Identify Drug Names that Look- or Sound-Similar to a Proposed Proprietary Name.

Type of Similarity	**Considerations when Searching the Databases**		
	Potential Causes of Drug Name Similarity	*Attributes Examined to Identify Similar Drug Names*	*Potential Effects*
Look-alike	Similar spelling	Identical prefix Identical infix Identical suffix Length of the name Overlapping product characteristics	Names may appear similar in print or electronic media and lead to drug name confusion in printed or electronic communication Names may look similar when scripted and lead to drug name confusion in written communication
	Orthographic similarity	Similar spelling Length of the name/ Similar shape Upstrokes Down strokes Cross-strokes Dotted letters Ambiguity introduced by scripting letters Overlapping product 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 (OPDP). We also consider input from other review disciplines (OND, ONDQA/OBP). The Expert Panel also discusses potential concerns regarding drug marketing and promotion related to the proposed names.

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

3. FDA Prescription Simulation Studies

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

orthographic or phonetic vulnerability of the proposed name to be misinterpreted by healthcare practitioners.

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

4. Comments from Other Review Disciplines

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

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

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

5. Safety Evaluator Risk Assessment of the Proposed Proprietary Name

The primary Safety Evaluator applies his/her individual expertise gained from evaluating medication errors reported to FDA, considers all aspects of the name that may be misleading or confusing, conducts a Failure Mode and Effects Analysis, and provides an overall decision on acceptability dependent on their risk assessment of name confusion. Failure Mode and Effects Analysis (FMEA) is a systematic tool for evaluating a process and identifying where and how it might fail.[2] 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.

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

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

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

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

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

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

If DMEPA objects to a proposed proprietary name on the basis that drug name confusion could lead to medication errors, the primary Safety Evaluator uses the FMEA process to identify strategies to reduce the risk of medication errors. DMEPA generally recommends that the Applicant 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 Applicant 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 Applicant 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. Applicants have undertaken

higher-leverage strategies, such as drug name changes, in the past but at great financial cost to the Applicant and at the expense of the public welfare, not to mention the Agency's credibility as the authority responsible for approving the error-prone proprietary name. Moreover, even after Applicants' 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, Xtandi	Scripted May Appear as	Spoken May Be Interpreted as
Capital 'X'	Z, S, P, K, U, V, Y, d, f, t	Z, S, KS, KZ
lower case 't'	r, f, x, A	d
lowercase 'a'	el, ci, cl, d, o, u	any vowel
lower case 'n'	r, m, u, x, h, s	dn, gn, kn, mn, pn
lower case 'd'	cl, ci	b, t
lower case 'i'	a, c, e, l, r	y, any vowel

Appendix C: **Prescription Simulation Samples and Results**

Figure 1. Xtandi (Conducted on May 31, 2012)

Handwritten Medication Order	Verbal Prescription
Medication Order: Xtandi 160mg PO QD	Xtandi Take 4 po qd Disp#120
Outpatient Prescription: Patient _____ Date _____ Address _____ ℞ Xtandi #120 4 caps po daily MEDWATCH 1-800-FDA-1088 Refill(s): _____ Dr. _____ DEA No. _____ Address _____ Telephone _____	

Study Name: Xtandi

As of Date 6/26/2012

84 People Received Study

28 People Responded

INPATIENT	VOICE	OUTPATIENT
XTANDI (5)	SATANDY (1)	XTANDI (7)
XTANDIR (1)	ZATANDY (3)	XTANDI 4 CAPS PO QD (1)
XTANDR (1)	ZETANDI (1)	
XTARDI (1)	ZETANDY (1)	
XTARIDI (1)	ZITANDI (1)	
	ZITANDY (2)	
	ZYTANDI (1)	
	ZYTANDY (1)	

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 Xtandi	Failure preventions
Xtend-Life	5-HTP (5-hydroxytryptophan)/ Alpha Lipoic Acid/ Betaine HCl/ Choline Bitartrate/ DMAE (dimethylaminoethanol)/ Huperzine A/ Phosphatidyl Choline (as lecithin)/ Phosphatidyl Serine (phosphatidyl-L-serine)/ Quercetin/ Resveratrol/ SAMe (S-adenosylmethionine)/ Vinpocetine/ Acetyl L-Carnitine/ L-Carnosine/ L-Carnitine Tartrate/ L-Glutamine/ L-Histidine/ L-Taurine/ L-Threonine/ L-Tyrosine/ L-Valine/ Amylase/ Bromelain/ Biotin/ Folic Acid/ Inositol Hexaphosphate/ Piperine/ Selenium/ Vitamin B6/ Vitamin D (D3, as cholecalciferol)/ Bacopin/ Bilberry/ Blueberry/ Chamomile/ Dandelion root/ Ginkgo Biloba/ Gotu Kola/ Green Tea/ Hawthorn berry/ Hops/ Passion Flower/ Pomegranate/ Grape seed/ Rhodiola Rosea/ Rosemary/ Schizandra/ Siberian Ginseng/ Silymarin (milk thistle)/ Yucca root	Look	The pair have sufficient orthographic differences
Extina	Ketoconazole	Look	The pair have sufficient orthographic differences
Xalkori	Crizotinib	Look	The pair have sufficient orthographic differences
Xologel	Ketoconazole	Look	The pair have sufficient orthographic differences
Extraneal	Icodextrin	Look	The pair have sufficient orthographic differences
Sinequan	Doxepin	Look	The pair have sufficient orthographic differences
Toviaz	Fesoterodine	Look	The pair have sufficient orthographic differences

Proprietary Name	Active Ingredient	Similarity to Xtandi	Failure preventions
Zantac	Ranitidine	Look	The pair have sufficient orthographic differences
K-Tab	Potassium Chloride	Look	The pair have sufficient orthographic differences
Xtandi	Enzalutamide	Look & Sound	Subject of this review

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.

Xtandi (Enzalutamide) Capsule 40 mg 160 mg or 4 capsules once daily (max daily dose 160 mg)	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion Causes (could be multiple)	Prevention of Failure Mode: In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names
Xtend (Vit B6 as pyridoxine HCl, Electrolyte Blend of trisodium citrate dihydrate, potassium chloride, and sodium chloride, L-Leucine, L-Glutamine, L-Isoleucine, L-Valine, Citrulline Malate) Powder for oral use (no strength) Usual Dose: As a dietary supplement, mix one serving (one level scoop) of Scivation Xtend per 8 ounces of water. Stir or shake and consume during exercise on training days, or throughout the day on non-training days.	**Orthographic similarity** -Both names begin with same letter 'X' followed by similarly shaped letter string 'tand' and 'tend' -Both names have similar length with 5 vs. 6 letters **Product characteristic similarity** -Strength: Xtandi is a single strength product so the strength may be omitted on a prescription and Xtend does not have a strength designation -Frequency: Both products may be administered once daily -Route of administration: Both products are administered orally	**Orthographic differences** -Xtend lacks the ending dotted letter 'i' found in Xtandi **Product characteristic differences** -Dose: no overlap and not achievable -Unit of measure: mg vs. scoop -Setting of use: Xtend is a specialized dietary supplement mostly used by body builders and is unlikely to be prescribed on a prescription or be dispensed in a pharmacy
Xpand (Creatine Ethyl Ester Maleate, R-gene Alpha-Ketoglutarate (A-AKG), amino acid Alpha-Ketoglutarate (Glut-AKG), Betaine Anhydrous, Glycocyamine, L-Citrulline, Taurine, Cinnulin PF®, Aqueous Cinnamon Extract) Caplets (no strength) Usual Dose: As a dietary supplement, take 4 caplets with an 8 oz. glass of water	**Orthographic similarity** -Both names begin with same letter 'X' and contain same letter string 'and' -Both names have similar length with 5 vs. 6 letters **Product characteristic similarity** -Strength: Xtandi is a single strength product so the strength may be omitted on a prescription and Xpand does not have a	**Orthographic differences** -Xpand has a downstroke letter 'p' not found in Xtandi -Xtandi has an upstroke/crosstroke letter 't' not found in Xpand -Xpand lacks the ending dotted letter 'i' found in Xtandi

Xtandi (Enzalutamide) Capsule 40 mg 160 mg or 4 capsules once daily (max daily dose 160 mg)	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion Causes (could be multiple)	Prevention of Failure Mode: In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names
two times daily. Pre-Workout: Take 4 caplets 45-60 minutes before your workout. Post-Workout: Take 4 caplets 15-45 minutes after your workout. Non-Workout Days: Take 4 caplets once in the morning on an empty stomach and 4 caplets 1/2 hour prior to lunch.	strength designation -Dose: overlapping dose when written as take "4 caps" -Dosage form: Both products may be ordered as "caps" -Route of administration: Both products are administered orally -Frequency: Both products may be administered once daily	**Product characteristic differences** -Setting of use: Xpand is a specialized dietary supplement mostly used by body builders and is unlikely to be prescribed on a prescription or be dispensed in a pharmacy
Vfend (Voriconazole) Tablet, Oral Suspension, Injection 50 mg and 200 mg Tablets 40 mg/mL Oral Suspension 200 mg/vial Powder For Injection Usual Dose: Loading dose: 6 mg/kg every 12 hours intravenously for the first 24 hours Maintenance dose: 3-4 mg/kg every 12 hours intravenously or 200 mg every 12 hours orally. Patients who weigh 40 kg or more should receive an oral maintenance dose of 200 mg every 12 hours. Adult patients who weigh less than 40 kg should receive an oral maintenance dose of 100 mg every 12 hours.	**Orthographic similarity** -Both names begin with similar letter 'X vs. V', contain an upstroke letter ('t' vs. 'f'), same upstroke letter 'd' towards the end of the names, and similar letter string 'an' vs. 'en' in the middle of the names -Both names have similar length with 5 vs. 6 letters **Product characteristic similarity** -Dose: overlapping dose if both Xtandi and Vfend are prescribed as 'take 4' (since maintenance dose of Vfend 200 mg can be achieved by taking '4' tablets of the 50 mg strength) -Strength: overlap with 40 mg vs. 40 mg/mL if the strength is noted or since both Xtandi and Vfend oral suspension products	**Orthographic differences** -Vfend lacks the ending dotted letter 'i' found in Xtandi **Product characteristic differences** -Dose: overlapping scenario depicted under "Product characteristic similarity" is rare since it is unlikely that a prescriber would select 4 of the 50 mg strength tablets for a 200 mg dose when 200 mg strength tablets are available. The 50 mg strength tablets would more likely be selected for the 100 mg dosing schedule in adult patients who weight less than 40 kg. -Setting of use: Although a prescription for Xtandi may

Xtandi (Enzalutamide) Capsule 40 mg 160 mg or 4 capsules once daily (max daily dose 160 mg)	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion Causes (could be multiple)	Prevention of Failure Mode: In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names
	are single strength products, the strength may be omitted on a prescription -Route of administration: Both products can be administered orally	be simply written as "Xtandi 160 mg daily or Xtandi take 4 daily" due to its single strength characteristic, a prescription for Vfend may include the dosage form and/or strength for the tablets (since the tablet formulation is available in two strengths). This additional information will provide an opportunity for product differentiation.
Xalatan (Latanoprost) Ophthalmic Solution 0.005% Usual dose: One drop (1.5 µg) in the affected eye(s) once daily in the evening	**Orthographic similarity** -Both names begin with same letter 'X', contain same crosstroke letter 't' and upstroke letter 'l' vs. 'd', with same letter string 'an' -Both names have similar length with 7 vs. 6 letters **Product characteristic similarity** -Strength: Both products are single strength products so strength may be omitted on a prescription -Frequency: Both products may be administered once daily	**Orthographic differences** -The positions of the upstroke letters are different in the two names -Xalatan has an extra letter 'a' between the beginning letter 'X' and the upstroke letter 'l vs. t' **Product characteristic differences** -Dose: no overlap and not achievable
Stendra (Avanafil) 50 mg, 100 mg, 200 mg tablets Usual Dose: 100 mg once per day orally as needed approximately 30 minutes before	**Orthographic similarity** -Both names begin with similar letter 'X vs. S', followed by the same crosstroke letter 't', and contain similarly shaped letter string 'end' vs. 'and'	**Orthographic differences** -Stendra has a different ending from Xtandi due to the letter string 'ra' vs. 'i'

Xtandi (Enzalutamide) Capsule 40 mg 160 mg or 4 capsules once daily (max daily dose 160 mg)	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion Causes (could be multiple)	Prevention of Failure Mode: In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names
sexual activity (dose may be increased to a maximum dose of 200 mg or decreased to 50 mg)	-Both names have similar length with 7 vs. 6 letters **Product characteristic similarity** -Frequency: Both products may be administered once daily -Route of administration: Both products are orally administered -Dosage form: Both are solid dosage forms (tablet vs. capsule)	**Product characteristic differences** -Dose: no overlap and not achievable -Strength: Xtandi is a single strength product so strength may be omitted on a prescription but Stendra is a multiple strength product that must be specified
X-Viate (Urea) 40% Cream Usual Dose: Apply a small amount of medicine to the affected area daily. Keep dry and occlusive for 3-7 days. Cleanse, debride and reapply if necessary.	**Orthographic similarity** -Both names begin with same letter 'X', contain same crosstroke letter 't', and end with similar letter 'i' vs. 'e' -Both names have same length with 6 letters **Product characteristic similarity** -Strength: Both products are single strength product so strength may be omitted on a prescription or numerical overlap with '40' mg and '40'% if strength is expressed -Frequency: Both products may be written as "daily"	**Orthographic differences** -X-Viate lacks the upstroke letter 'd' present in Xtandi -The infix of the two names are different with 'viat' vs. 'tand' **Product characteristic differences** -Dose: no overlap and not achievable -Administration: X-Viate has special administration instructions vs. Xtandi is simply to take 4 caps once daily
V-Tann (Phenylephrine Tannate, Pyrilamine Tannate) 12.5mg/5mL & 30mg/5mL oral suspension	**Orthographic similarity** -Both names begin with similar letter 'X vs. V', followed by the same crosstroke letter 't', and same letter string 'an'	**Orthographic differences** -Xtandi has a different ending from V-Tann due to the letter string 'di' vs. 'n'

Xtandi (Enzalutamide) Capsule 40 mg 160 mg or 4 capsules once daily (max daily dose 160 mg)	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion Causes (could be multiple)	Prevention of Failure Mode: In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names
25mg & 30mg Chewable tablet Usual Dose: 1-2 tablets orally every 12 hours or 2.5 ml to 10 ml orally every 12 hours depending on age Note: V-Tann has been discontinued since 3/31/2008.	-Both names have similar length with 5 vs. 6 letters **Product characteristic similarity** -Strength: Both products are single strength products (since each formulation of V-Tann has only one strength) so strength may be omitted on a prescription -Route of administration: Both products are orally administered -Dosage form: Both are solid dosage forms (tablet vs. capsule)	**Product characteristic differences** -Dose: no overlap and not achievable
Plendil (Felodipine) 2.5 mg, 5 mg, 10 mg Tablets Usual Dose: 5 mg once a day (decreased to 2.5 mg or increased to 10 mg once a day at intervals of not less than 2 weeks(range is 2.5−10 mg once daily)	**Orthographic similarity** -Both names begin with similar letter 'X vs. P', followed by similar upstroke letter 't' vs. 'l', and similar letter string 'andi' vs. 'endi' -Both names have similar length with 7 vs. 6 letters **Product characteristic similarity** -Route of administration: Both products are orally administered -Frequency: Both products are administered once daily -Dosage form: Both are solid dosage forms (tablet vs. capsule)	**Orthographic differences** -Plendil ends with an extra upstroke letter 'l' not present in Xtandi **Product characteristic differences** -Dose: no overlap and not achievable -Strength: Xtandi is a single strength product so strength may be omitted on a prescription but Plendil is a multiple strength product that must be specified
Xanax (alprazolam) Tablet	**Orthographic similarity** -Both names begin with same letter 'X' and contain same letter	**Orthographic differences** -Xanax lacks the two upstroke letters 't' and 'd'

Xtandi (Enzalutamide) Capsule 40 mg 160 mg or 4 capsules once daily (max daily dose 160 mg)	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion Causes (could be multiple)	Prevention of Failure Mode: In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names
0.25 mg, 0.5 mg, 1 mg, 2 mg Usual Dose: 0.25 to 0.5 mg given three times daily (up to 10 mg/day) depending on condition	string 'an' -Both names have similar length with 5 vs. 6 letters **Product characteristic similarity** -Route of administration: Both products are orally administered -Dosage form: Both are solid dosage forms (tablet vs. capsule)	found in Xtandi -Xanax ends in the crosstroke letter 'x' not found in Xtandi **Product characteristic differences** -Dose: no overlap and not achievable -Strength: Xtandi is a single strength product so strength may be omitted on a prescription but Xanax is a multiple strength product that must be specified -Frequency: once vs. three times daily
(b) (4)		

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Xtandi (Enzalutamide) Capsule 40 mg 160 mg or 4 capsules once daily (max daily dose 160 mg)	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion Causes (could be multiple)	Prevention of Failure Mode: In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names

(b) (4)

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