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RESEARCH**

APPLICATION NUMBER:
022497Orig1s000

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: September 6, 2011

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Drug Name(s) and Strengths: Forfivo XL (Bupropion HCl Extended-release Tablets),
450 mg

Application Type/Number: NDA 022497

Sponsor: IntelGenx Corp

OSE RCM #: 2011-1816

*** 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, Forfivo XL, 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

This application, Forfivo XL (Bupropion Extended-release Tablets) NDA 022497, is a 505(b)(2) application. The reference listed drug is Wellbutrin XL 150 mg tablets. The Division of Medication Error Prevention and Analysis (DMEPA) previously reviewed this proposed proprietary name, Forfivo XL, and found it acceptable in OSE Review # 2009-2072. This review took into consideration an external name assessment conducted by a third party vendor, Drug Safety Institute. DMEPA's findings were conveyed to the Applicant at the time, Cary Pharmaceuticals, via letter. However, the Division of Psychiatry Products (DPP) issued a Complete Response on February 3, 2010 secondary to safety issues around the fact the product had significant changes to the pharmacokinetic profile when taken with food.

The current Applicant, IntelGenx Corp, revised the formulation and resubmitted the application May 13, 2011. Subsequently, the Applicant resubmitted the proposed proprietary name, Forfivo XL, for evaluation June 9, 2011.

1.2 PRODUCT INFORMATION

The following product characteristics were obtained from Request for Proprietary Name Review submitted June 9, 2011.

Established name: Bupropion Extended-release Tablets

Indication: Treatment of Major Depressive Disorder

Route: Oral

Dosage Form: Extended-release Tablet

Strength: 450 mg

Dose: One tablet (450 mg) by mouth daily

How supplied: 30 count bottles

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 Psychiatry Products concurred with the findings of DDMAC's promotional assessment of the proposed name.

2.2 SAFETY ASSESSMENT

The following sections are considered in the overall safety evaluation of the proposed name, Forfivo XL.

2.2.1 United States Adopted Names (USAN) SEARCH

The United States Adopted Name (USAN) stem search conducted on August 16, 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 includes the use of the modifier ‘XL’ which is used to indicate that this product is an extended-release tablet. Although there are no other formulations of Forfivo currently marketed, there are multiple extended-release formulations of Bupropion HCl. As noted in OSE review # 2009-2072, it is important that the modifier ‘XL’ helps to identify the once-daily dosing of this product and is consistent with the other currently marketed once-daily formulations of Bupropion. Thus, we find the use of the modifier ‘XL’ acceptable for this product.

2.2.4 FDA Name Simulation Studies

Thirty four practitioners participated in DMEPA’s prescription studies. See Appendix D for the complete listing of interpretations from the verbal and written prescription studies. Of note, two respondents omitted the modifier, XL in their interpretation of the proposed proprietary name, one written and one verbal, although it was included in all samples. Twelve respondents interpreted the written samples correctly as “Forfivo XL”. No respondents misinterpreted the lower case ‘f;’ however, both writing samples include a down stroke.

2.2.5 Comments from Other Review Disciplines

In response to the OSE, June 3, 2011 e-mail, the DPP stated they had no 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

Appendix B lists possible orthographic and phonetic misinterpretations of the letters appearing in Forfivo XL. Table 1 lists the names with orthographic, phonetic, or spelling similarity to the proposed proprietary name, Forfivo XL. These names were identified by the primary reviewer, the Expert Panel Discussion (EPD), or other review disciplines.

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

Look Similar				Look and Sound Similar	
Name	Source	Name	Source	Name	Source
Cardura XL	FDA	Pentasa	FDA	Forfivo	FDA

Factive	FDA	Pexeva	FDA	Forfivo XL	FDA
Fastin	FDA	Procardia XL	FDA		
Fazaclo	FDA	Taztia XT	FDA		
Fentora	FDA	Terfonyl	FDA		
Focalin XR	FDA	Tirofiban	FDA		
Folbic	FDA	Toprol XL	FDA		
Foltrin	FDA	Toradol	FDA		
Foradil	FDA	Torisel	FDA		
Forane	FDA	Fora V20	FDA		
Fortesta	FDA	Fora V10	FDA		
Fosfree	FDA	(b) (4)	FDA		
Fosrenol	FDA	Fertinex	FDA		
Fusilev	FDA	Fibro XL	FDA		

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

DMEPA communicated these midpoint review findings to the Division of Psychiatry Product via e-mail on August 31, 2011. At that time we requested DPP provide any information or concerns that could inform our review. Per e-mail correspondence from the DPP September 5, 2011, they stated no additional concerns with the proposed proprietary name, Forfivo XL.

3 CONCLUSIONS

DMEPA concludes the proposed proprietary name is acceptable from both a promotional and safety perspective. 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.

If you have further questions or need clarifications, please contact Sandra Griffith, OSE project manager, at 301-796-2445

3.1 COMMENTS TO THE APPLICANT

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

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

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		
	<i>Potential Causes of Drug Name Similarity</i>	<i>Attributes Examined to Identify Similar Drug Names</i>	<i>Potential Effects</i>
	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 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 possess 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.

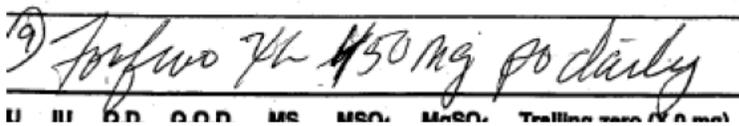
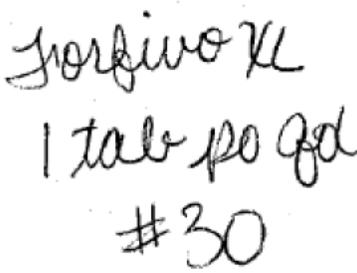
Furthermore, post-marketing experience has demonstrated that medication errors resulting from drug name confusion are notoriously difficult to rectify post-approval. Educational and other post-approval efforts are low-leverage strategies that have had limited effectiveness at alleviating medication errors 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, Forfivo XL	Scripted May Appear as	Spoken May Be Interpreted as
Capital 'F'	P or T	'Pf,' 'Ph' or 'V'
lower case 'f'	b, p, or t	'pf,' 'ph' or 'v'
lower case 'o'	a, c u, or v	any vowel
lower case 'r'	n, s, t, or v	'w'
lower case 'i'	c, e, or l	any vowel
lower case 'v'	n, o, r, or u	'b' or 'f'
Capital 'X'	K, V, Y	
Capital 'L'	Z, S or T	

Appendix C: Prescription Simulation Samples and Results

Figure 1. Forfivo XL (Conducted on June 3, 2011)

Handwritten Requisition Medication Order	Verbal Prescription
<p>Medication Order:</p>  <p>U II DD ODD MS MSO MSO Trailing zero (V 0 mg)</p>	<p>Forfivo XL Take one tab po qd dispense number thirty.</p>
<p>Outpatient Prescription:</p> 	

FDA Prescription Simulation Responses.

INPATIENT	STRENGTH	VOICE	STRENGTH	OUTPATIENT	STRENGTH
FORFIVO XL	450mg	FORFEVAL XL		FORFINO XL 1 PO QD #30	
FORFIVO XL	450 mg.	FORFEVO XL	1 tablet	FORFIVO	
FORFIVO XL	450 mg	FORFEVO XL	1 tab	FORFIVO XL	
FORFIVO XL	450mg	FORFEVO XL	none	FORFIVO XL	
FORFRUO XL	450 mg	FORFEVO XL		FORFIVO XL	
FORFRUO XL	450 mg	FORFEVO XL	one tab	FORFIVO XL	
FORFRVO XL	450 mg	FORFIVO		FORFIVO XL	
FORFUO XL	450 mg	FORFIVO XL		FORFIVO XL	
FORFUO XL	450 mg	PHORFEVO XL		FORFIVO XL	
FORFUVO XL	450 mg			FORFIVO-XL	
FORFWO XL	450 mg				
FORFWO XL	450mg				
FORVLUVO XL	450 mg				
TORFUR XL	450mg				
TORFUVO XL	450mg				

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 Forfivo or Forfivo XL	Failure preventions
Cardura XL	Doxazosin Mesylate	Look	Lacks sufficient orthographic similarity
Fazacllo	Clozapine	Look	Lacks sufficient orthographic similarity and has a restricted distribution system which requires patients, prescribers and pharmacists to be registered to use, prescribe and dispense medication, respectively.
Fertinex	Urofollitropin	Look	Discontinued product with no generic equivalents marketed.
Folbic	pyridoxine, cyanocobolamin, and folic acid	Look	Lacks sufficient orthographic similarity
Foltrin	Ascorbic acid, cyanocobolamin, folic acid, ferrous fumarate, liver stomach concentrate	Look	Lacks sufficient orthographic similarity
FORA V10	Glucose monitoring systems	Look	This is a glucose monitoring system that includes the monitoring device and the device-specific glucose test strips. Thus, a prescription needs to specify item is to be dispensed to be complete.
FORA V20	Glucose monitoring system	Look	This is a glucose monitoring system that includes the monitoring device and the device-specific glucose test strips. Thus, a prescription needs to specify item is to be dispensed to be complete.
Foradil	Formoterol Fumarate	Look	Lacks sufficient orthographic similarity
Forane	Isoflurane	Look	Lacks orthographic similarity and is limited to use in the Operating Room setting by a healthcare provider (anesthesiologist or nurse anesthetist)
Forfivo	Bupropion HCl	Look and sound	Identified in listed databases only as the product in this NDA.
Forfivo XL	Bupropion HCL	Look and Sound	Identified in listed databases only as the product in this NDA.
Fortigel***	Testosterone	Look	A proposed proprietary name that was withdrawn by the Applicant. The product was approved with the proprietary name, (b) (4)
Procardia XL	Nifedipine	Look	Lacks sufficient orthographic similarity
Terfonyl	Trisulfapyrimidines	Look	Discontinued product with no generic equivalents marketed.
Tirofiban	active moiety in Aggrastat	Look	Lacks sufficient orthographic similarity

Toradol	Ketorolac Tromethamine	Look	Lacks sufficient orthographic similarity
Torisel	Temsirolimus	Look	Lacks sufficient orthographic similarity

Appendix E: The evaluation of the failure modes leading to medication errors due to product name confusion during use in clinical practice.

Proposed name: Forfivo XL (Bupropion HCL extended-release tablets) Strength: 450 mg tablet Usual dose: One tablet by mouth daily.	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of name confusion	Other failures to consider with this product: <ul style="list-style-type: none"> <i>This product has a single strength presentation. Therefore, the strength may be omitted from a prescription or an order request but still results in sufficient information to dispense or procure the medication.</i> <i>The proprietary name includes the modifier 'XL' and no immediate release "Forfivo" exists. Therefore, the modifier is not necessary and may be omitted from a prescription or an order request but still results in sufficient information to dispense or procure the medication.</i>
	Causes (could be multiple)	Prevention of Failure Mode:
Factive (Gemafloxacin Mesylate) 320 mg tablet Usual dose: One tablet by mouth daily.	Orthographic similarity to Forfivo: Both names include seven letter and have similar length when scripted, Both names begin with the same letter (F) and include a letter in the center of the name that provides an upstroke and a cross stroke (t vs. f). Both products are oral tablets with a single strength presentation and are taken once daily.	Orthographic difference may be provided by the letter 'f' in Forfivo which may be scripted with a down stroke. Additionally, the modifier "XL" when scripted provides added length to the name, if included. Factive is an oral antibiotic which has a short duration of use of five or seven days depending on the infection site. Forfivo XL is a chronic medication for Major Depressive Disorder which takes several weeks of use to see an effect. For these products to be confused, a total of three failures have to occur simultaneously, 1) misinterpretation of the name most likely when the letter 'f' is written without a down stroke. 2) the modifier is omitted, which did occur in the Rx study and 3) the dose written without the numeric strength (450 mg). The Rx Studies completed by DSI included the 'f' written without a down stroke, the omission of the modifier and no numeric dose. No respondents misinterpreted these samples as an existing. Preliminary drug use data suggest that a strength is included in prescriptions for Bupropion containing medications and the strengths do not overlap nor are they achievable.

<p>Proposed name: Forfivo XL (Bupropion HCL extended-release tablets) Strength: 450 mg tablet Usual dose: One tablet by mouth daily.</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of name confusion</p>	<p>Other failures to consider with this product:</p> <ul style="list-style-type: none"> • <i>This product has a single strength presentation. Therefore, the strength may be omitted from a prescription or an order request but still results in sufficient information to dispense or procure the medication.</i> • <i>The proprietary name includes the modifier 'XL' and no immediate release "Forfivo" exists. Therefore, the modifier is not necessary and may be omitted from a prescription or an order request but still results in sufficient information to dispense or procure the medication.</i>
	<p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode:</p>
<p>Fastin (Phentermine Hydrochloride) 15 mg and 30 mg capsules Usual dose: one capsule by mouth daily. <i>Discontinued product with generic equivalents available. Preliminary drug use data suggest the name continues to be used in clinical practice.</i></p>	<p>Orthographic similarity to Forfivo: Both names begin with the same letter (F) and include a letter in the center of the name that provides an upstroke and a cross stroke (t vs. f). Both are oral solid dosage forms (capsules vs. extended-release tablets) that are taken once daily.</p>	<p>Orthographic difference stems from the fact that Forfivo has an additional letter and appears longer when scripted. The letter 'f' in Forfivo may provide a down stroke when scripted. Additionally, the modifier "XL" when scripted provides additional length to the name, if included. Fastin was available in two strength presentations and thus a strength is necessary for a complete prescription or to order this product. Forfivo XL has one strength presentation (450 mg) which is not similar to those of Fastin.</p>

<p>Proposed name: Forfivo XL (Bupropion HCL extended-release tablets) Strength: 450 mg tablet Usual dose: One tablet by mouth daily.</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of name confusion</p>	<p>Other failures to consider with this product:</p> <ul style="list-style-type: none"> <i>This product has a single strength presentation. Therefore, the strength may be omitted from a prescription or an order request but still results in sufficient information to dispense or procure the medication.</i> <i>The proprietary name includes the modifier 'XL' and no immediate release "Forfivo" exists. Therefore, the modifier is not necessary and may be omitted from a prescription or an order request but still results in sufficient information to dispense or procure the medication.</i>
	<p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode:</p>
<p>Fentora (Fentanyl citrate) 100 mcg, 200 mcg, 300 mcg, 400 mcg, 600 mcg, and 800 mcg buccal tablets Usual dose; One tablet placed in the buccal pouch of the mouth every four hours as needed,</p>	<p>Orthographic similarity to Forfivo: Both names include seven letter and have similar length when scripted, Both names begin with the same letter (F) and include a letter in the center of the name that provides an upstroke and a cross stroke (t vs. f). The products are similar dosage forms (Buccal tablets vs. extended-release tablets)</p>	<p>Orthographic difference may be provided by the letter 'f' in Forfivo which may be scripted with a down stroke. Additionally, the modifier "XL" when scripted provides added length to the name, if included. Fentora is available in six strength presentations and is administered every four hours as needed. A strength is necessary for a complete prescription or to order this product. Forfivo XL has one strength presentation (450 mg) which is not similar to those of Fentora. In addition, Forfivo XL is taken once daily routinely and not as needed.</p>

Proposed name: Forfivo XL (Bupropion HCL extended-release tablets) Strength: 450 mg tablet Usual dose: One tablet by mouth daily.	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of name confusion	Other failures to consider with this product: <ul style="list-style-type: none"> • <i>This product has a single strength presentation. Therefore, the strength may be omitted from a prescription or an order request but still results in sufficient information to dispense or procure the medication.</i> • <i>The proprietary name includes the modifier 'XL' and no immediate release "Forfivo" exists. Therefore, the modifier is not necessary and may be omitted from a prescription or an order request but still results in sufficient information to dispense or procure the medication.</i>
	Causes (could be multiple)	Prevention of Failure Mode:
Fibro XL (Psyllium) 675 mg capsule Usual dose: Seven capsules by mouth once daily.	Orthographic similarity to Forfivo XL: Both names begin with the same letter (F), include the same modifier (XL), and include a letter providing an upstroke in the center (b vs. f). Both are oral solid dosage forms (capsules vs. extended-release tablets) taken once daily. Both have a single strength presentation.	Orthographic differences stem from the fact that Forfivo XL includes a total of nine letters and appears longer when scripted. Additionally, the letter 'f' in Forfivo XL may provide a down stroke when scripted. Fibro XL is an over-the counter nutritional supplement with a dose of seven capsules. Additionally, the preliminary drug use data suggest minimal usage in clinical practice. Noted product is listed in Redbook but could only find to purchase on the company website as a Direct to Consumer product. Forfivo XL has a dose of one tablet (450 mg).

Proposed name: Forfivo XL (Bupropion HCL extended-release tablets) Strength: 450 mg tablet Usual dose: One tablet by mouth daily.	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of name confusion	Other failures to consider with this product: <ul style="list-style-type: none"> • <i>This product has a single strength presentation. Therefore, the strength may be omitted from a prescription or an order request but still results in sufficient information to dispense or procure the medication.</i> • <i>The proprietary name includes the modifier 'XL' and no immediate release "Forfivo" exists. Therefore, the modifier is not necessary and may be omitted from a prescription or an order request but still results in sufficient information to dispense or procure the medication.</i>
	Causes (could be multiple)	Prevention of Failure Mode:
<p>Focalin XR (Dexamethylphenidate HCl) 5 mg, 10 mg, 15 mg, 20 mg, 25 mg, 30 mg, 35 mg, and 40 mg capsules Usual dose: One capsule by mouth daily.</p>	<p>Orthographic similarity to Forfivo XL: Both names include nine letters and have a similar length when scripted, begin with the same two letters (Fo-), include a letter near the center of the name that provides an upstroke (l vs. f) and include a similar modifier (XR vs. XL).</p> <p>Both are oral solid dosage forms (capsule vs. extended-release tablets) taken once daily.</p>	<p>Orthographic difference stems from the fact that Forfivo XL includes the letter 'f' in Forfivo XL which may provide a down stroke or a cross stroke when scripted. Additionally, Forfivo XL includes two letters separating the Capital 'F' from the lower case f and three letters following the lower case 'f,' while Focalin XR which includes three letters separating the Capital 'F' from the letter 'l' and two letters following the letter 'l.'</p> <p>Focalin XR is available in eight strength presentations and thus a strength is necessary for a complete prescription or to order this product.</p> <p>Forfivo XL has one strength presentation (450 mg) which is not similar to those of Focalin XR.</p>

Proposed name: Forfivo XL (Bupropion HCL extended-release tablets) Strength: 450 mg tablet Usual dose: One tablet by mouth daily.	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of name confusion	Other failures to consider with this product: <ul style="list-style-type: none"> <i>This product has a single strength presentation. Therefore, the strength may be omitted from a prescription or an order request but still results in sufficient information to dispense or procure the medication.</i> <i>The proprietary name includes the modifier 'XL' and no immediate release "Forfivo" exists. Therefore, the modifier is not necessary and may be omitted from a prescription or an order request but still results in sufficient information to dispense or procure the medication.</i>
	Causes (could be multiple)	Prevention of Failure Mode:
<p>Fortesta (Testosterone) gel 10 mg per actuation Usual dose: Four actuations (40 mg) applied topically once daily. (Dose ranges from one actuation or 10 mg to seven actuations or 70 mg)</p>	<p>Orthographic similarity to Forfivo XL: Both names have similar length, begin with the same two letters (Fo-), include a letter near the center of the name that provides an upstroke (l vs. f) and the second to last letter provides a cross stroke (X vs. t).</p> <p>Both products have a single strength presentation and are administered once daily.</p>	<p>Orthographic difference stems from the fact that Forfivo XL includes the letter 'f' in Forfivo XL which may provide a down stroke when scripted. In addition, the modifier, XL, includes two letters providing upstrokes at the end of the name.</p> <p>Fortesta is a topically applied gel packaged in a can that requires pumping to dispense the product. The cans are packaged in cartons contain one, two or three cans.</p> <p>Forfivo XL is an oral tablet packaged in bottles containing 30 tablets.</p>

Proposed name: Forfivo XL (Bupropion HCL extended-release tablets) Strength: 450 mg tablet Usual dose: One tablet by mouth daily.	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of name confusion	Other failures to consider with this product: <ul style="list-style-type: none"> • <i>This product has a single strength presentation. Therefore, the strength may be omitted from a prescription or an order request but still results in sufficient information to dispense or procure the medication.</i> • <i>The proprietary name includes the modifier 'XL' and no immediate release "Forfivo" exists. Therefore, the modifier is not necessary and may be omitted from a prescription or an order request but still results in sufficient information to dispense or procure the medication.</i>
	Causes (could be multiple)	Prevention of Failure Mode:
<p>Fosfree (multivitamin and mineral supplement) Usual dose: Two tablets by mouth at bedtime.</p>	<p>Orthographic similarity to Forfivo: Both names include seven letters and have a similar length when scripted, begin with the same two letters (Fo-), and include the letter 'f' in the center.</p> <p>Both are oral tablets with a single strength presentation, taken once daily.</p>	<p>Orthographic difference may be provided by the modifier, XL, provides added length to the name, Forfivo XL when scripted.</p> <p>Fosfree is a nutritional supplement which is dosed as two tablets to be taken at bedtime (qhs). Preliminary drug use data suggest minimal use of this product. The product is available without a prescription and is packaged in bottles containing 120 tablets.</p> <p>Forfivo XL is dosed as one tablet (450 mg) and is packaged in bottles containing 30 tablets.</p>
<p>Fosrenol (Lanthanum Carbonate) 500 gm, 750 mg, and 1000 mg chewable tablets Usual dose: Chew and swallow one to two tablets (500 mg to 1500 mg) three times daily with meals</p>	<p>Orthographic similarity with Forfivo XL: Both names have a similar length when scripted, begin with the same two letters (Fo-), and end with the same letter 'l.'</p> <p>Both products are oral tablets (chewable vs., extended-release).</p>	<p>Orthographic difference stems from the fact that Forfivo XL includes the letter 'f' in Forfivo XL which provides an upstroke and may provide a down stroke or cross stroke when scripted. In addition, the modifier, XL, includes two letters providing upstrokes at the end of the name.</p> <p>Fosrenol is available in three strength presentations and thus a strength is necessary for a complete prescription or to order this product. In additional, Fosrenol is taken with each meal or three times daily.</p> <p>Forfivo XL has one strength presentation (450 mg) which is not similar to those of Fosrenol and is taken once daily.</p>

Proposed name: Forfivo XL (Bupropion HCL extended-release tablets) Strength: 450 mg tablet Usual dose: One tablet by mouth daily.	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of name confusion	Other failures to consider with this product: <ul style="list-style-type: none"> <i>This product has a single strength presentation. Therefore, the strength may be omitted from a prescription or an order request but still results in sufficient information to dispense or procure the medication.</i> <i>The proprietary name includes the modifier 'XL' and no immediate release "Forfivo" exists. Therefore, the modifier is not necessary and may be omitted from a prescription or an order request but still results in sufficient information to dispense or procure the medication.</i>
	Causes (could be multiple)	Prevention of Failure Mode:
<p>Fusilev (Levoleucovorin Calcium) 50 mg vial (for injection) and 175 mg/17/5 mL and 250 mg/25 mL vials (injection)</p> <p>Usual dose: After methotrexate: 7.5 mg intravenously every 6 hours for ten doses.</p> <p>With 5-fluorouracil: 10 mg/m² or 100 mg/m² intravenously daily for five days.</p>	<p>Orthographic similarity to Forfivo: Both names contain seven letters and have similar length when scripted, begin with the same letter (F) and include a letter near the center of the name that provides an upstroke (l vs. f). The products may be administered daily.</p>	<p>Orthographic difference stems from the fact that Forfivo XL includes the letter 'f' in Forfivo XL which may provide a down stroke when scripted. In addition, the modifier, XL, includes two letters providing upstrokes at the end of the name. Additionally, Forfivo XL includes two letters separating the Capital 'F' from the lower case f and three letters following the lower case 'f,' while Fusilev which includes three letters separating the Capital 'F' from the letter 'l' and two letters following the letter 'l.'</p> <p>Fusilev is an injectable medication used in conjunction with chemotherapy medications. The dose is 7.5 mg or based on mg/m² which is administered intravenously. Finally, Fusilev is available in three strengths which must be specified to procure the medication.</p> <p>Forfivo XL is available as an oral tablet in one strength presentation (450 mg) which is not similar to those of Fusilev.</p>

<p>Proposed name: Forfivo XL (Bupropion HCL extended-release tablets) Strength: 450 mg tablet Usual dose: One tablet by mouth daily.</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of name confusion</p>	<p>Other failures to consider with this product:</p> <ul style="list-style-type: none"> • <i>This product has a single strength presentation. Therefore, the strength may be omitted from a prescription or an order request but still results in sufficient information to dispense or procure the medication.</i> • <i>The proprietary name includes the modifier ‘XL’ and no immediate release “Forfivo” exists. Therefore, the modifier is not necessary and may be omitted from a prescription or an order request but still results in sufficient information to dispense or procure the medication.</i>
	<p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode:</p>
<p>Pentasa (Mesalamine) 250 mg and 500 mg controlled-release capsules Usual dose: Two or four capsules (1000 mg) by mouth four times daily.</p>	<p>Orthographic similarity with Forfivo: Both names contain seven letters and have similar length and shape when scripted, begin with a letter that may appear similar (P vs. F) and include a letter in the center of the name that provides an upstroke and cross stroke (t vs. f).</p> <p>Both products are oral solid dosage forms (capsules vs. tablets).</p> <p>The frequency abbreviations may be confused (qid vs. qd).</p>	<p>Orthographic difference may be provided by the letter ‘f’ in Forfivo which may be scripted with a down stroke. Additionally, the modifier “XL” when scripted provides added length to the name, if included.</p> <p>Pentasa is available in two strength presentations. A strength is necessary for a complete prescription or to order this product. The dose is two or four capsules depending on the strength.</p> <p>Forfivo XL has one strength presentation (450 mg) which is not similar to those of Pentasa. In addition, Forfivo XL is dosed as one tablet.</p>

Proposed name: Forfivo XL (Bupropion HCL extended-release tablets) Strength: 450 mg tablet Usual dose: One tablet by mouth daily.	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of name confusion	Other failures to consider with this product: <ul style="list-style-type: none"> • <i>This product has a single strength presentation. Therefore, the strength may be omitted from a prescription or an order request but still results in sufficient information to dispense or procure the medication.</i> • <i>The proprietary name includes the modifier 'XL' and no immediate release "Forfivo" exists. Therefore, the modifier is not necessary and may be omitted from a prescription or an order request but still results in sufficient information to dispense or procure the medication.</i>
	Causes (could be multiple)	Prevention of Failure Mode:
Pexeva (Paroxetine Mesylate) 10 mg, 20 mg, 30 mg, and 40 mg tablets Usual dose: one to two tablets (10 mg to 60 mg) by mouth daily.	Orthographic similarity to Forfivo: Both names have similar length, begin with a letter that may appear similar when scripted (P vs. F) and include a letter in the center of the name that provides a cross stroke (x vs. f). Both products are oral tablets taken once daily.	Orthographic difference stems from the fact that Forfivo XL includes the letter 'f' in Forfivo XL which may provide an upstroke and down stroke when scripted. Additionally, the modifier "XL" when scripted provides added length to the name, if included. Pexeva is available in four strength presentations. Thus, a strength is necessary for a complete prescription or to order this product. Forfivo XL has one strength presentation (450 mg) which is not similar to those of Pexeva.

Proposed name: Forfivo XL (Bupropion HCL extended-release tablets) Strength: 450 mg tablet Usual dose: One tablet by mouth daily.	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of name confusion	Other failures to consider with this product: <ul style="list-style-type: none"> • <i>This product has a single strength presentation. Therefore, the strength may be omitted from a prescription or an order request but still results in sufficient information to dispense or procure the medication.</i> • <i>The proprietary name includes the modifier 'XL' and no immediate release "Forfivo" exists. Therefore, the modifier is not necessary and may be omitted from a prescription or an order request but still results in sufficient information to dispense or procure the medication.</i>
	Causes (could be multiple)	Prevention of Failure Mode:
<p>Taztia XT (Ditiazem HCl) 120 mg, 180 mg, 240 mg, 300 mg, and 360 mg extended-release capsules Usual dose: One capsule by mouth daily.</p>	<p>Orthographic similarity to Forfivo XL: Both names begin with a letter that may appear similar (T vs. F), include a letter providing an upstroke and cross stroke in the center of the name (t vs. f) and include a similar Modifier (XT vs. XL).</p> <p>Both are oral solid dosage forms (capsules vs. tablets) taken once daily.</p>	<p>Orthographic difference stems from the fact that Forfivo XL includes the letter 'f' in Forfivo XL which may provide a down stroke when scripted. In addition, Taztia XT includes the letter 'z' which may provide a down stroke in a different position in the name.</p> <p>Taztia XT is available in five strength presentations. Thus, a strength is necessary for a complete prescription or to order this product.</p> <p>Forfivo XL has one strength presentation (450 mg) which is not similar to those of Taztia XT.</p>

Proposed name: Forfivo XL (Bupropion HCL extended-release tablets) Strength: 450 mg tablet Usual dose: One tablet by mouth daily.	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of name confusion	Other failures to consider with this product: <ul style="list-style-type: none"> • <i>This product has a single strength presentation. Therefore, the strength may be omitted from a prescription or an order request but still results in sufficient information to dispense or procure the medication.</i> • <i>The proprietary name includes the modifier 'XL' and no immediate release "Forfivo" exists. Therefore, the modifier is not necessary and may be omitted from a prescription or an order request but still results in sufficient information to dispense or procure the medication.</i>
	Causes (could be multiple)	Prevention of Failure Mode:
<p>Toprol XL (Metoprolol tartrate) 25 mg, 50 mg, 100 mg and 200 mg extended-release tablets Usual dose: One tablet (any strength) by mouth daily.</p>	<p>Orthographic similarity with Forfivo XL: Both names begin with letters that appear similar when scripted (T vs. F), have a similar length, and include the same modifier (XL).</p> <p>Both are extended release tablets taken once daily.</p>	<p>Orthographic difference stems from the fact that Forfivo XL includes the letter 'f' in Forfivo XL which may provide an upstroke and cross stroke when scripted. In addition, Toprol XL includes the letter 'l' as the end of the root name which provides an upstroke.</p> <p>Toprol XL is available in four strength presentations. Thus, a strength is necessary for a complete prescription or to order this product.</p> <p>Forfivo XL has one strength presentation (450 mg) which is not similar to those of Toprol XL.</p>

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/s/

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

Date: January 11, 2010

To: Thomas Laughren, M.D., Director
Division of Psychiatry Products

Through: Kristina Arnwine, Pharm.D., Team Leader
Denise Toyer, Pharm.D., Deputy Director
Carol Holquist, R.Ph., Director
Division of Medication Error Prevention and Analysis (DMEPA)

From: Lori Cantin, RPh, Pharm.D., Safety Evaluator
Division of Medication Error Prevention and Analysis (DMEPA)

Subject: Proprietary Name Review

Drug Name(s): Forfivo XL (Bupropion Hydrochloride) Extended-Release Tablets
450 mg

Application Type/Number: NDA 022497

Applicant/Applicant: Cary Pharmaceuticals, Inc.

OSE RCM #: 2009-2072

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

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EXECUTIVE SUMMARY

Forfivo XL is the proposed proprietary name for Bupropion Hydrochloride Extended-release Tablets, 450 mg. This proposed name was evaluated from a safety and promotional perspective based on the product characteristics provided by the Applicant. We sought input from pertinent disciplines involved with the review of this application and considered it accordingly. Our evaluation did not identify concerns that would render the name unacceptable based on the product characteristics and safety profile known at the time of this review. Thus, DMEPA finds the proposed proprietary name, Forfivo XL, acceptable for this product.

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

Additionally, DMEPA notes that DPP is currently evaluating whether or not there is a significant food effect on the pharmacokinetics of Forfivo XL. If it is determined that Forfivo XL has a significant food effect and must be administered on an empty stomach, DMEPA would have concerns regarding the approval of this product from a medication error perspective (see Section 4.3 for discussion).

1 BACKGROUND

1.1 INTRODUCTION

This review is in response to the October 23, 2009, request from the Applicant, Cary Pharmaceuticals, Inc, for an assessment of the proposed proprietary name, Forfivo XL, regarding potential name confusion with other proprietary or established drug names. The Applicant submitted an Independent Name Assessment with the proprietary name review request. Container labels, carton and package insert labeling were also submitted by the Applicant and will be reviewed under separate cover (OSE Review #2009-2112).

1.2 PRODUCT INFORMATION

FORFIVO XL PRODUCT INFORMATION	
Mechanism of Action	Structurally related to the neurotransmitter GABA (gamma-aminobutyric acid) and possesses analgesic and anticonvulsant activity; exact mechanism of action is unknown
Proposed Indication for Use	Treatment of Major Depressive Disorder
Usual Dose	450 mg per day (Forfivo XL 450 mg should only be used in patients who have been receiving 300 mg once daily of another extended-release Bupropion product for at least 2 weeks). Forfivo XL 450 mg extended-release tablet may replace Wellbutrin XL 450 mg/day.
Maximum Daily Dose	450 mg per day
Dosage Form	Extended-Release Tablets

FORFIVO XL PRODUCT INFORMATION	
Product Strengths	450 mg
Route of Administration	Oral
Frequency of Administration	Once daily
Dosing in Specific Populations	Forfivo XL should not be used in patients with impaired hepatic or impaired renal function Contraindicated in patients with a seizure disorder
Storage Requirements	USP Controlled Room Temperature
How Supplied	450 mg x 30-count bottle

1.3 REGULATORY HISTORY

NDA 022497 for Forfivo XL (Bupropion Hydrochloride) is a 505(b)(2) application that was received by the Agency on April 6, 2009. The reference listed drug is Wellbutrin XL. The PDUFA goal date for this NDA is February 6, 2010. A request for a review of the proposed proprietary name, Forfivo XL, was received on October 26, 2009.

2 METHODS AND MATERIALS

Appendix A describes the general methods and materials used by the Division of Medication Error Prevention and Analysis (DMEPA) when conducting a proprietary name risk assessment for all proprietary names. Sections 2.1, 2.2 and 2.3 identify specific information associated with the methodology for the proposed proprietary name, Forfivo XL.

2.1 SEARCH CRITERIA

For this review, particular consideration was given to drug names beginning with the letter ‘F’ when searching to identify potentially similar drug names, as 75% of the confused drug names reported by the USP-ISMP Medication Error Reporting Program involve pairs beginning with the same letter.^{1,2}

DMEPA staff evaluates whether the modifier ‘XL’ can be misinterpreted and is appropriate for this product. DMEPA staff considers ‘Forfivo XL’ as a complete name as well as ‘Forfivo’, the root term with omission of the modifying term ‘XL’ because omission of a modifier is cited in literature as a common cause of medication error.³ To identify drug names that may look similar to Forfivo XL, the DMEPA staff also consider the other orthographic appearance of the name on lined and unlined orders.

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

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

³ Lesar TS. Prescribing Errors Involving Medication Dosage Forms. *J Gen Intern Med.* 2002; 17(8): 579-587.

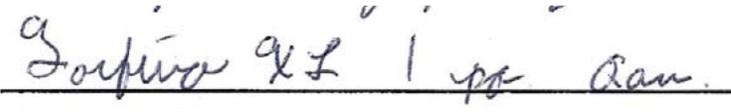
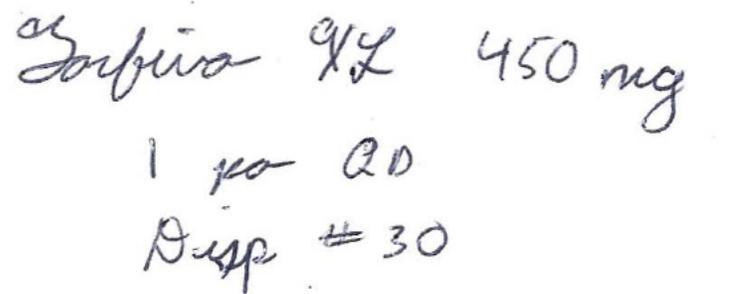
Specific attributes taken into consideration include the length of the name (seven letters for the root name plus two letters for the modifier), upstrokes (two, 'F' and 'f'), down-strokes (one, 'f'), cross-strokes (one, 'f'), and dotted letters (one, 'i'). Additionally, several letters in Forfivo XL may be vulnerable to ambiguity when scripted (see Appendix B). As a result, the DMEPA staff also considers these alternate appearances when identifying drug names that may look similar to Forfivo XL.

When searching to identify potential names that may sound similar to Forfivo XL, the DMEPA staff search for names with similar number of syllables (three), stresses (FOR-fiv-o, For-FIV-o, For-fiv-O), and placement of vowel and consonant sounds. The DMEPA staff also considers that pronunciation of parts of the name can vary, such as "-fiv-o" may sound like "-viv-o". Additionally, several letters in Forfivo XL may be subject to interpretation when spoken (see Appendix B). The Applicant's intended pronunciation of the proprietary name (fore fye' voe) was taken into consideration, as this was provided with the proposed name submission, however DMEPA understands that pronunciation of the product will vary greatly from region to region and be based upon cultural background.

2.2 FDA PRESCRIPTION ANALYSIS STUDIES

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

Figure 1. Forfivo XL Study 1109 (conducted on November 9, 2009)

HANDWRITTEN REQUISITION MEDICATION ORDER	VERBAL PRESCRIPTION
<p><u>Inpatient Medication Order:</u></p> 	<p>Forfivo XL 1 po qam</p>
<p><u>Outpatient Prescription:</u></p> 	

2.3 EXTERNAL PROPRIETARY NAME RISK ASSESSMENT

For this product, the Applicant submitted an external evaluation of the proposed proprietary name. The Division of Medication Error Prevention and Analysis conducts an independent analysis and evaluation of the data provided, and responds to the overall findings of the assessment. When the external proprietary name risk assessment identifies potentially confusing names that were not captured in DMEPA's database

searches or in the Expert Panel Discussion, these names are included in the Safety Evaluator's Risk Assessment and analyzed independently by the Safety Evaluator to determine if the potentially confusing name could lead to medication errors in usual practice settings.

After the Safety Evaluator has determined the overall risk associated with proposed name, the Safety Evaluator compares the findings of their overall risk assessment with the findings of the proprietary name risk assessment submitted by the Applicant. The Safety Evaluator then determines whether the Division's risk assessment concurs or differs with the findings. When the proprietary name risk assessment differs, the Division of Medication Error Prevention and Analysis provides a detailed explanation of these differences.

3 RESULTS

3.1 DATABASE AND INFORMATION SOURCES

The searches yielded a total of twenty-two (22) names as having some similarity to the name Forfivo XL. Nineteen (19) of the names were thought to look like Forfivo XL. These names are: Fortical, Fortavit, Fortovase, Frova, Florvite, (b) (4) Fortamet, Sebivo, Tarceva, Lodine XL, Lodrane XR, Zofran, Fortaz, Forbaxin, Borofair, Feverfew, Sustiva, Porfimer, and Zorbtive.

Three (3) names were thought to look and sound similar to Forfivo XL. These names are: (b) (4) (b) (4), and Forteo.

Additionally, DMEPA staff did not identify any United States Adopted Names (USAN) stems in the proposed proprietary name, as of November 19, 2009.

3.2 EXPERT PANEL DISCUSSION

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

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

3.3 FDA PRESCRIPTION ANALYSIS STUDIES

A total of twenty-two (22) practitioners responded but none of the responses overlapped with any existing or proposed drug names. Only two (2) of the participants interpreted the name correctly as "Forfivo XL." The remainder of the participants misinterpreted the drug name. The letter 'F' was misinterpreted as either G, L, T, or Z by seventeen (17) participants, and six (6) participants omitted the modifier 'XL' in their response. The modifier 'XL' was misinterpreted as 'XO' by the one participant in the Rx voice study. See Appendix C for the complete listing of interpretations from the verbal and written prescription studies.

3.4 COMMENTS FROM THE DIVISION OF PSYCHIATRY PRODUCTS (DPP)

3.4.1 Initial Phase of Review

In response to the OSE November 5, 2009, e-mail, DPP did not forward any comments and/or concerns on the proposed name at the initial phase of the name review.

3.4.2 Potential Food Effect on Forfivo XL

During DPP's December 4, 2009, status meeting, the issue of a potential food effect on the pharmacokinetics of Forfivo XL (Bupropion Hydrochloride) 450 mg was raised. The reference listed

drug, Wellbutrin XL, which is also administered once-daily, may be administered without regard to food. The maximum recommended dose of Bupropion Hydrochloride is 450 mg, due to a significant increase in the risk of seizures at doses higher than 450 mg. The review team expressed concern that administering Forfivo XL 450 mg with food may increase the Cmax for this drug product and lead to an increase risk of seizures. This issue is the subject of ongoing review and is currently being evaluated by the review team.

3.4.3 Midpoint of Review

DMEPA notified the DPP, via e-mail, that we had no objections to the proposed proprietary name, Forfivo XL, on December 24, 2009. Per e-mail correspondence from the Division on December 31, 2009 they indicated they concur with our assessment of the proposed proprietary name, Forfivo XL.

3.5 EXTERNAL NAME STUDY

In the submission dated October 23, 2009, the Applicant provided a proprietary name analysis conducted by Drug Safety Institute (DSI), Inc., which identified nine (9) names as having some similarity to Forfivo XL. These names are: Certiva, Formadon, Fortaz, Forteo, Fortical, Fortovase, Raptiva, Sustiva, and Tarceva. Six (6) of the nine names identified by DSI were also identified by DMEPA staff. The remaining three (3) names will be analyzed in the safety evaluator risk assessment.

DSI's evaluation of the proposed name, Forfivo XL, found that there was minimal, if any, risk of name confusion that could result in medication error. Also, DSI concluded that the use of the modifier 'XL' was appropriate based on the extended-release properties of the proposed product, and the modifier also served to further differentiate the proposed product from the other products identified in their review. Thus, DSI's research favorably supported the use of the name 'Forfivo XL' as a proprietary name for Cary Pharmaceutical's proposed product. The issue of a potential food effect was not evaluated by DSI.

3.6 SAFETY EVALUATOR RISK ASSESSMENT

Independent searches by the primary Safety Evaluator did not identify any additional names which were thought to look or sound similar to Forfivo XL and represent a potential source of drug name confusion.

4 DISCUSSION

DDMAC had no concerns with the proposed name and neither did the Division of Psychiatry Products.

DMEPA's evaluated the appropriateness of the modifier 'XL' and 'Forfivo XL' as a complete name, as well as the root name 'Forfivo'. Additionally, we considered whether the meaning of the modifier 'XL' was consistent with the meaning of the modifier 'XL' for Wellbutrin XL and other extended-release once-daily Bupropion products. We also considered the impact that a food effect would have on the administration of Forfivo XL from a medication error perspective.

4.1 MODIFIER 'XL'

The Applicant proposes the use of the modifier 'XL' to indicate that Forfivo is an extended-release tablet. There is no drug product named 'Forfivo' currently marketed. Thus, the use of a modifier is not necessary to distinguish this product from a currently marketed product that has the same root name. However, the modifier 'XL' helps to identify formulation characteristics for this product that are consistent with other currently marketed extended-release once-daily formulations of Bupropion (e.g., Bupropion Hydrochloride XL, Wellbutrin XL). Therefore, the use of the modifier XL is important as it informs healthcare providers that this new Bupropion product is not an immediate release formulation intended for twice or thrice-daily administration. Additionally, the modifier XL is widely recognized to mean an extended-release tablet that is dosed once daily, so its use for this product is appropriate. We

believe that the risk of medication error due to wrong frequency would be increased if this product were to be marketed without the modifier 'XL'. Thus, we find the use of the modifier 'XL' acceptable for this product.

4.2 FORFIVO XL

DMEPA did not identify aspects of the name that would render it unacceptable other than the identification of names with similar appearances and sound to Forfivo XL. In total, twenty-five (25) names were evaluated for their potential similarity to Forfivo XL. Six (6) names lacked orthographic and/or phonetic similarity to Forfivo XL and were not evaluated further (see Appendix D). Three (3) are proposed proprietary names submitted to the Agency (see Appendix E for detailed information). One (1) was a common name for a natural medicine product, which is not likely to be written on a prescription (see Appendix F). Two (2) were proprietary names for products that have been either discontinued or withdrawn from the US market, and there is no generic equivalent available (see Appendix G).

Failure Mode and Effects Analysis was then applied to determine if the proposed name, Forfivo XL, could potentially be confused with the remaining twelve (12) names and lead to medication errors. This analysis determined that the name similarity between Forfivo XL was unlikely to result in medication errors with any of the 12 products for the reasons presented in Appendix H.

4.3 POTENTIAL SAFETY CONCERNS WITH FORFIVO XL

DMEPA notes that DPP is currently evaluating whether or not there is a significant food effect on the pharmacokinetics of Forfivo XL. If it is determined that Forfivo XL has a significant food effect and must be administered on an empty stomach, DMEPA would have concerns regarding the approval of this product from a medication error perspective. Forfivo XL is to be available only in a 450 mg tablet, which is the maximum recommended daily dose for Bupropion. If a food effect is demonstrated for this product, and it is taken with food, the risk of seizures is significantly increased because this adverse event is dose-related.

DMEPA is concerned that the product labeling with respect to a food effect will not be adequate to ensure communication of this important information to healthcare providers and patients. The molecular entity, Bupropion, was originally approved in 1985. Wellbutrin, Zyban, and Aplenzin, as well as several generic equivalent Bupropion Hydrochloride products have been approved and are currently marketed. Thus, healthcare professionals and patients have over 20 years of experience with Bupropion, and are accustomed to prescribing, dispensing, and administering Bupropion without providing specific instructions regarding food intake. It would be unreasonable to expect that healthcare professionals will be able to reliably know and recall that one product, Forfivo XL, is different from all other currently marketed Bupropion products with respect to food intake, and instruct their patients accordingly. Patients that have taken another Bupropion product irrespective of food intake prior to converting to Forfivo XL may be more likely to administer Forfivo XL in the same manner. Even if properly instructed with regard to food intake, patient compliance can not be ensured. Additionally, confusion between the currently marketed Bupropion products has been the source of medication errors, and the addition of a Bupropion product to the marketplace that is "different" from the others with respect to administration is likely to add to existing confusion.

As the only expected advantage of Forfivo XL is patient convenience (i.e., need to take only 1 tablet per day as opposed to two or three), DMEPA does not believe that the risk would outweigh the benefit for this drug product, as there are several other currently marketed Bupropion products (e.g., Wellbutrin SR, Wellbutrin XL, Zyban, Aplenzin, and generic Bupropion Hydrochloride products) that have not been shown to have a food effect and would be considered safer in this regard.

5 CONCLUSIONS AND RECOMMENDATIONS

The Proprietary Name Risk Assessment findings indicate that the proposed name, Forfivo XL, is not vulnerable to name confusion that could lead to medication errors, nor was the name considered promotional. Thus, the Division of Medication Error Prevention and Analysis (DMEPA) has no objection to the proprietary name, Forfivo XL, for this product at this time.

However, if any of the proposed product characteristics as stated in this review are altered, DMEPA rescinds this Risk Assessment finding and the name must be resubmitted for review. In the event that our Risk Assessment finding is rescinded, the evaluation of the name on resubmission is independent of the previous Risk Assessment, and as such, the conclusions on re-review of the name are subject to change.

In addition, the proposed name must be re-evaluated 90 days before the expected approval date of the NDA, even if the proposed product characteristics as stated in this review are not altered.

If you have further questions or need clarifications, please contact Sandra Griffith, Safety Regulatory Project Manager, at 301-796-2445.

6 COMMENTS TO THE APPLICANT

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

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

7 REFERENCES

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

USPTO provides information regarding patent and trademarks.

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

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

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

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

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

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

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

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

13. USAN Stems (<http://www.ama-assn.org/ama/pub/category/4782.html>)

USAN Stems List contains all the recognized USAN stems.

14. Red Book Pharmacy's Fundamental Reference

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

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

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

16. Medical Abbreviations Book

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

APPENDICES

Appendix A:

FDA's Proprietary Name Risk Assessment considers the potential for confusion between the proposed proprietary name and the proprietary and established names of drug products existing in the marketplace and those pending IND, NDA, BLA, and ANDA products currently under review by the Center. DMEPA defines a medication error as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer.⁴

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

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

FMEA is a systematic tool for evaluating a process and identifying where and how it might fail.⁵ DMEPA uses FMEA to analyze whether the drug names identified with orthographic or phonetic similarity to the proposed proprietary name could cause confusion that subsequently leads to medication errors in the clinical setting. DMEPA uses the clinical expertise of its staff to anticipate the conditions of the clinical setting where the product is likely to be used based on the characteristics of the proposed product.

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

Typical product characteristics considered when identifying drug names that could potentially be confused with the proposed proprietary name include, but are not limited to; established name of the proposed product, proposed indication of use, dosage form, route of administration, strength, unit of measure, dosage units, recommended dose, typical quantity or volume, frequency of administration, product packaging, storage conditions, patient population, and prescriber population. Because drug name confusion can occur at any point in the medication use process, DMEPA staff considers the potential for confusion throughout the entire U.S. medication use process, including drug procurement, prescribing and ordering, dispensing, administration, and monitoring the impact of the medication.⁶ DMEPA provides the product characteristics considered for this review in section one.

The Division of Medication Error Prevention and Analysis considers the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted. DMEPA also compares the spelling of the proposed proprietary name with the proprietary and established name of existing and proposed drug products because similarly spelled names may have greater likelihood to sound similar to one another when spoken or look similar to one another when scripted. DMEPA staff also examines the orthographic appearance of the proposed

⁴ National Coordinating Council for Medication Error Reporting and Prevention. <http://www.nccmerp.org/aboutMedErrors.html>. Last accessed 10/11/2007.

⁵ Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

⁶ Institute of Medicine. Preventing Medication Errors. The National Academies Press: Washington DC. 2006.

name using a number of different handwriting samples. Handwritten communication of drug names has a long-standing association with drug name confusion. Handwriting can cause similarly and even dissimilarly spelled drug name pairs to appear very similar to one another. The similar appearance of drug names when scripted has led to medication errors. The DMEPA staff applies expertise gained from root-cause analysis of such medication errors to identify sources of ambiguity within the name that could be introduced when scripting (e.g., “T” may look like “F,” lower case ‘a’ looks like a lower case ‘u,’ etc). Additionally, other orthographic attributes that determine the overall appearance of the drug name when scripted (see Table 1 below for details). In addition, the DMEPA staff compares the pronunciation of the proposed proprietary name with the pronunciation of other drug names because verbal communication of medication names is common in clinical settings. If provided, DMEPA will consider the 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.

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		
	<i>Potential causes of drug name similarity</i>	<i>Attributes examined to identify similar drug names</i>	<i>Potential Effects</i>
Look-alike	Similar spelling	Identical prefix Identical infix Identical suffix Length of the name Overlapping product characteristics	<ul style="list-style-type: none"> Names may appear similar in print or electronic media and lead to drug name confusion in printed or electronic communication Names may look similar when scripted and lead to drug name confusion in written communication
	Orthographic similarity	Similar spelling Length of the name Upstrokes Down strokes Cross-strokes Dotted letters Ambiguity introduced by scripting letters Overlapping product characteristics	<ul style="list-style-type: none"> 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	<ul style="list-style-type: none"> Names may sound similar when pronounced and lead to drug name confusion in verbal communication

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

1. Database and Information Sources

DMEPA staff conducts searches of the internet, several standard published drug product reference texts, and FDA databases to identify existing and proposed drug names that may sound-alike or look-alike to the proposed proprietary name using the criteria outlined in Section 2.1. Section 6 provides a standard description of the databases used in the searches. To complement the process, the DMEPA staff use a computerized method of identifying phonetic and orthographic similarity between medication names. The program, Phonetic and Orthographic Computer Analysis (POCA), uses complex algorithms to select a list of names from a database that have some similarity (phonetic, orthographic, or both) to the trademark being evaluated. Lastly, the DMEPA staff review the USAN stem list to determine if any USAN stems are present within the proprietary name. The individual findings of multiple safety evaluators are pooled and presented to the CDER Expert Panel.

2. CDER Expert Panel Discussion

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

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

3. FDA Prescription Analysis Studies

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

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

4. Comments from the OND review Division or Generic drugs

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

The OND or OGD Regulatory Division is contacted a second time following our analysis of the proposed proprietary name. At this point, DMEPA conveys their decision to accept or reject the name. The OND or OGD Regulatory Division is requested to concur/not concur with DMEPA's final decision.

5. Safety Evaluator Risk Assessment of the Proposed Proprietary Name

The primary Safety Evaluator applies his/her individual expertise gained from evaluating medication errors reported to FDA, conducts a Failure Mode and Effects Analysis, and provides an overall risk assessment of name confusion. Failure Mode and Effects Analysis (FMEA) is a systematic tool for evaluating a process and identifying where and how it might fail.⁷ When applying FMEA to assess the risk of a proposed proprietary name, DMEPA seeks to evaluate the potential for a proposed proprietary name to be confused with another drug name because of name confusion and, thereby, cause errors to occur in the medication use system. FMEA capitalizes on the predictable and preventable nature of medication errors associated with drug name confusion. FMEA allows the Agency to identify the potential for medication errors due to orthographically or phonetically similar drug names prior to approval, where actions to overcome these issues are easier and more effective than remedies available in the post-approval phase.

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

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

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

An affirmative answer indicates a failure mode and represents a potential for the proposed proprietary name to be confused with another proprietary or established drug name because of look- or sound-alike similarity. If the answer to the question is no, the Safety Evaluator is not convinced that the names possess 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

⁷ Institute for Healthcare Improvement (IHI). Failure Mode and Effects Analysis. Boston. IHI:2004.

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.

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

- a. DDMAC finds the proposed proprietary name misleading from a promotional perspective, and the Review Division concurs with DDMAC's findings. The Federal Food, Drug, and Cosmetic Act provides that labeling or advertising can misbrand a product if misleading representations are made or suggested by statement, word, design, device, or any combination thereof, whether through a PROPRIETARY name or otherwise [21 U.S.C 321(n); See also 21 U.S.C. 352(a) & (n)].
- b. DMEPA identifies that the proposed proprietary name is misleading because of similarity in spelling or pronunciation to another proprietary or established name of a different drug or ingredient [CFR 201.10.(C)(5)].
- c. FMEA identifies the potential for confusion between the proposed proprietary name and other proprietary or established drug name(s), and demonstrates that medication errors are likely to result from the drug name confusion under the conditions of usual clinical practice.
- d. The proposed proprietary name contains an USAN (United States Adopted Names) stem.
- e. DMEPA identifies a potential source of medication error within the proposed proprietary name. For example, the proprietary name may be misleading or, inadvertently, introduce ambiguity and confusion that leads to errors. Such errors may not necessarily involve confusion between the proposed drug and another drug product.

If DMEPA objects to a proposed proprietary name on the basis that drug name confusion could lead to medication errors, the primary Safety Evaluator uses the FMEA process to identify strategies to reduce the risk of medication errors. DMEPA is likely to recommend that the Applicant select an alternative proprietary name and submit the alternate name to the Agency for DMEPA to review. However, in rare instances FMEA may identify plausible strategies that could reduce the risk of medication error of the currently proposed name. 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. However, the safety concerns set forth in criteria a through e are supported either by FDA regulation or by external healthcare authorities, including the Institute of Medicine (IOM), World Health Organization (WHO), Joint Commission on Accreditation of Hospitals (JCOAH), and the Institute for Safe Medication Practices (ISMP). These organizations have examined medication errors resulting from look- or sound-alike drug names and called for regulatory authorities to address the issue prior to approval. Additionally, DMEPA contends that the threshold set for the Proprietary Name Risk Assessment is reasonable because proprietary drug name confusion is a predictable and a preventable source of medication error that, in many instances, the Agency and/or 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. (See Section 4 for limitations of the process).

Appendix B: Letters with possible orthographic or phonetic misinterpretation

Letters in Name:	Scripted may appear as	Spoken may be interpreted as
Forfivo XL		
Upper case 'F'	'G', 'L', 'T', 'Z', or 'S'	"Pf", "Ph", or "V"
Lower case 'o'	'a', 'e', or 'u'	Any vowel
Lower case 'r'	'i', 'n', 's', or 'v'	
Lower case 'f'	'b', 't', or 'x'	"v"
Lower case 'i'	'a', 'i', or 'o'	"e"
Lower case 'v'	'r', 'n', 'u'	"b" or "f"
Lower case 'o'	'a', 'e', or 'u'	"a"
Modifier 'XL'		'XO'

Appendix C: FDA Prescription Study Responses.

Inpatient Medication Order	Outpatient Medication Order	Voice Prescription
Torpiva	Zorfivo XL	Forfivo XO
Zorfivo XL	Farfiva	
Torfina XL	Gorfiva XL	
Lorfivo XL	Zorfivo	
Gorfiva	Zarfiva XL	
Torfiva	Gorfivo XL	
Forfivo XL	Farvira XL	
Torfivo XL		
Gorfivo		
Forfivo XL		
Zorfivo XL		
Torfivo XL		
Gorifvo XL		
Gorfiva XL		

Appendix D: Names Lacking Orthographic and/or Phonetic Similarity to Forfivo XL

Name	Similarity to Forfivo XL
Borofair	Look
Florvite	Look
Fortamet	Look
Frova	Look
Lodrane XR	Look
Forbaxin	Look

Appendix E: Proposed Names within the Agency

Name	Similarity to Forfivo XL	Comments
(b) (4)		

Appendix F: Natural Medicine Product not Likely to be Written on a Prescription

Proprietary Name	Similarity to Forfivo XL	Comments
Feverfew Common name for Tanacetum parthenium	Look	Used for fever, headaches, prevention of migraines, and menstrual irregularities Numerous commercially available preparations containing feverfew

Appendix G: Proprietary name of product or device that is withdrawn/discontinued/no longer marketed, and no generic equivalent is available

Proprietary Name	Similarity to Forfivo XL	Comments
<p>Fortovase (Saquinavir) 200 mg oral soft-gel NDA 020828</p>	<p>Look</p>	<p>Discontinued per Orange Book; no generic equivalent</p> <p>Discontinued in 2006 due to decreased demand for the drug product</p> <p>Invirase (Saquinavir mesylate) is available in 200 mg and 500 mg strengths.</p> <p>If an Rx for Forfivo was misinterpreted as Fortovase, Fortovase could not be dispensed, as it is not available. Invirase (the mesylate salt of Saquinavir) is not bioequivalent, thus, Invirase can not be substituted for Fortovase without a physician's order</p>
<p>Raptiva (Efalizumab) 125 mg vial Powder for Injection</p>	<p>Look</p>	<p>Withdrawn from US market (April 8, 2009) due to increased risk of progressive multifocal leukoencephalopathy (PML)</p> <p>Off market per Clinical Pharmacology Online</p>

Appendix H: Products with orthographic, phonetic and/or multiple differentiating product characteristics minimize the risk for medication errors

Product name with potential for confusion	Similarity to Forfivo XL	Strength	Usual Signa (if applicable)	Differentiating Product Characteristics
<p>Forfivo XL (Bupropion Hydrochloride) Extended-release Tablet</p>		450 mg	450 mg orally once daily	
<p>Lodine XL* (Etodolac) Extended-release tablet</p> <p>*Lodine XL is a discontinued product per the Orange Book, however, there are generic equivalents available</p>	Look	400 mg 500 mg 600 mg	400 mg to 1000 mg orally once daily	<p>Orthographic differences in the names, in conjunction with differences in product characteristics, minimize the likelihood of medication error in the usual practice setting.</p> <p>Orthographic:</p> <p>Forfivo XL contains a downstroke and cross-stroke ('f') and Lodine XL has no cross-strokes or downstrokes</p> <p>Usual dosage: (450 mg vs. 400 mg to 1000 mg). Dose of 450 mg is not achievable with the available strengths of Lodine XL, and the usual doses of Lodine XL can not be achieved with Forfivo XL</p> <p>Although the dose in terms of the number of tablets may overlap with Lodine XL (e.g., 1 tablet), the presence of the product strength for Lodine XL tablets will help distinguish it from Forfivo</p>

Appendix H: Products with orthographic, phonetic and/or multiple differentiating product characteristics minimize the risk for medication errors

Product name with potential for confusion	Similarity to Forfivo XL	Strength	Usual Signa (if applicable)	Differentiating Product Characteristics
Forfivo XL (Bupropion Hydrochloride) Extended-release Tablet		450 mg	450 mg orally once daily	
Zorbtive (Somatropin) Powder for Injection	Look	8.8 mg vial	0.1 mg/kg subcutaneously once daily for 4 weeks	<p>Orthographic differences in the names, in conjunction with differences in product characteristics, minimize the likelihood of medication error in the usual practice setting.</p> <p><u>Orthographic:</u></p> <p>Forfivo XL contains a downstroke ('f') when scripted, and Zorbtive has no downstrokes</p> <p>Forfivo XL has one upstroke in the middle of the root name ('f'), while Zorbtive has two consecutive upstrokes ('b' and 't') in the middle of its name</p> <p>Forfivo XL contains a modifier 'XL' which will help to differentiate it from Zorbtive medication error.</p> <p><u>Product Characteristic Differences:</u></p> <p><i>Route of Administration:</i> Oral vs. subcutaneous</p> <p><i>Usual dosage:</i> "450 mg" or " 1 tab" vs. weight-based dosing of 0.1 mg/kg (e.g. 3.8 mg for a 38 kg patient)</p> <p>Although dose similarity can occur between weight-based doses of Zorbtive such as Zorbtive 4.5 mg and Forfivo XL 450 mg, the presence of a decimal point and lack of a trailing zero after a dose of 4.5 mg would help to differentiate these two doses and minimize the risk of medication error, in addition to orthographic and phonetic differences and the difference in route of administration.</p>

Appendix H: Products with orthographic, phonetic and/or multiple differentiating product characteristics minimize the risk for medication errors

Product name with potential for confusion	Similarity to Forfivo XL	Strength	Usual Signa (if applicable)	Differentiating Product Characteristics
Forfivo XL (Bupropion Hydrochloride) Extended-release Tablet		450 mg	450 mg orally once daily	
Fortaz (Ceftazidime Pentahydrate)	Look	Vials, Powder for Injection: 500 mg, 1 g, g and 6 g Premixed Solution for Injection: 1 g/50 mL 2 g/50	Adults: 1 g to 2 g intravenously or intramuscularly every 8 hours Children/Infants*: 30 to 50 mg/kg intravenously every 8 to 12 hours Neonates*: (< 7 days old, > 2 kg): 100 to 150 mg/kg intravenously, divided every 8 to 12 hours *A dose of 450 mg is achievable with Fortaz and overlaps with 450 mg of Forfivo	Orthographic differences in the names, in conjunction with differences in product characteristics, minimize the likelihood of medication error in the usual practice setting. Orthographic: Forfivo XL contains a modifier 'XL' which will help to differentiate it from Fortaz Fortaz has one potential downstroke ('z') at the end of the name vs. Forfivo which does not end in a downstroke Forfivo has a downstroke in the middle of the name vs. Fortaz which does not have a downstroke in the middle of the name Route of Administration: oral vs. intravenous or intramuscular Frequency: Once daily vs. every 8 to 12 hours
Fortical (calcitonin-salmon) Nasal Spray 3.7 mL bottle	Look	200 international units per actuation 3.7 mL bottle	200 international units (1 spray) in one nostril once daily	Orthographic differences in the names, in conjunction with differences in product characteristics, minimize the likelihood of medication error in the usual practice setting. Orthographic: Forfivo XL has one downstroke ('f') and Fortical has zero downstrokes Forfivo has two upstrokes ('F', 'f') and Fortical has three upstrokes ('F', 't', and 'l') Fortical ends in an upstroke, Forfivo XL does not Forfivo XL contains a modifier 'XL' which will help to differentiate it from Fortical Route of Administration: Oral vs. Intranasal Dosage form: Tablet vs. Nasal Spray

Appendix H: Products with orthographic, phonetic and/or multiple differentiating product characteristics minimize the risk for medication errors

Product name with potential for confusion	Similarity to Forfivo XL	Strength	Usual Signa (if applicable)	Differentiating Product Characteristics
Forfivo XL (Bupropion Hydrochloride) Extended-release Tablet		450 mg	450 mg orally once daily	
Fortavit (Multivitamin with minerals) Liquid OTC	Look	Multi-ingredient single-strength product	Dosage and administration information not found	Orthographic differences in the names, in conjunction with differences in product characteristics, minimize the likelihood of medication error in the usual practice setting. <u>Orthographic:</u> Forfivo XL has one downstroke ('f') and Fortavit has zero downstrokes Forfivo XL contains a modifier 'XL' which will help to differentiate it from Fortavit Forfivo has two upstrokes ('F', 'f') and Fortavit has three upstrokes ('F', 't', and 'l') Fortavit ends in an upstroke, Forfivo does not <u>Dosage Units:</u> Tablet vs. Teaspoon(s)ful (tsp) or milliliters (mL) Drug not found in NDC directory or Red Book 2008 or 2009 edition; no other equivalent product listed in Facts and Comparisons 4.0

Appendix H: Products with orthographic, phonetic and/or multiple differentiating product characteristics minimize the risk for medication errors

Product name with potential for confusion	Similarity to Forfivo XL	Strength	Usual Signa (if applicable)	Differentiating Product Characteristics
Forfivo XL (Bupropion Hydrochloride) Extended-release Tablet		450 mg	450 mg orally once daily	
Forteo (Teriparatide) Injection Supplied in 2.4 mL and 3 mL multi-dose prefilled delivery device	Look/ Sound	Pens deliver a dose of 20 mcg	20 mcg subcutaneously once daily	Orthographic and phonetic differences in the names, in conjunction with differences in product characteristics, minimize the likelihood of medication error in the usual practice setting. <u>Phonetic:</u> The infix and suffix “-fi-vo” does not sound like the infix and suffix “-te-o” Forfivo XL contains a modifier ‘XL’ which will help to differentiate it from Forteo <u>Orthographic:</u> Forfivo XL has one downstroke (‘f’) and Forteo has zero downstrokes Forfivo XL contains a modifier ‘XL’ which will help to differentiate it from Forteo ‘Forfivo’ appears longer than ‘Forteo’ when scripted <u>Dose:</u> “1 tablet”, “One” or 450 mg vs. “20 mcg” <u>Route of Administration:</u> Oral vs. Subcutaneous <u>Dosage Form:</u> Oral tablet vs. Multi-dose prefilled pen device

Appendix H: Products with orthographic, phonetic and/or multiple differentiating product characteristics minimize the risk for medication errors

Product name with potential for confusion	Similarity to Forfivo XL	Strength	Usual Signa (if applicable)	Differentiating Product Characteristics
Forfivo XL (Bupropion Hydrochloride) Extended-release Tablet		450 mg	450 mg orally once daily	
Certiva (Diphtheria Toxoid Adsorbed, Pertussis Vaccine Acellular Adsorbed, Tetanus Toxoid Adsorbed) Suspension for Injection 7.5 mL vial	Look/Sound	Triple-ingredient vaccine containing 15 units, 40 mcg and 5 units per 0.5 mL	0.5 mL	Orthographic and phonetic differences in the names, in conjunction with differences in product characteristics, minimize the likelihood of medication error in the usual practice setting. Phonetic: The prefix “For-” does not sound like the prefix “Cer-” Forfivo XL contains a modifier ‘XL’ which will help to differentiate it from Certiva Orthographic: Forfivo XL has one downstroke (‘f’) when scripted vs. Certiva which has zero downstrokes Forfivo XL contains a modifier ‘XL’ which will help to differentiate it from Certiva ‘F’ does not look like ‘C’ when scripted Dose: “1 tablet”, “One” or 450 mg vs. “0.5 mL” Frequency: Once daily vs. Single dose Route of Administration: Oral vs. Intramuscular Dosage Form: Oral tablet vs. Suspension for Injection <i>Note: Product off-market per Clinical Pharmacology Online; not listed in Red Book or in NDC directory</i>

Appendix H: Products with orthographic, phonetic and/or multiple differentiating product characteristics minimize the risk for medication errors

Product name with potential for confusion	Similarity to Forfivo XL	Strength	Usual Signa (if applicable)	Differentiating Product Characteristics
Forfivo XL (Bupropion Hydrochloride) Extended-release Tablet		450 mg	450 mg orally once daily	
Formadon (formaldehyde) 10% Topical Solution 60 mL and 120 mL	Look	10%	Apply to affected area(s) once daily	<p>Orthographic differences in the names, in conjunction with differences in product characteristics, minimize the likelihood of medication error in the usual practice setting.</p> <p>Orthographic:</p> <p>Forfivo XL has one downstroke ('f') and Formadon has zero downstrokes</p> <p>Forfivo XL has one cross-stroke ('f'), Formadon has zero cross-strokes</p> <p>Forfivo XL contains a modifier 'XL' which will help to differentiate it from Formadon</p> <p>Dose: "1 tablet", "One" or 450 mg vs. "Sufficient amount"</p> <p>Route of Administration: Oral vs. Topical</p> <p>Dosage Form: Oral tablet vs. Topical Solution</p>
Porfimer (Porfimer Sodium) Powder for Injection	Look	75 mg vial	2 mg/kg intravenously over 3 to 5 minutes followed 40 to 50 hours later by laser illumination; up to 3 courses may be given (each separated by a minimum of 30 days)	<p>Orthographic differences in the names, in conjunction with differences in product characteristics, minimize the likelihood of medication error in the usual practice setting.</p> <p>Orthographic:</p> <p>Forfivo XL contains a modifier 'XL' which will help to differentiate it from Porfimer</p> <p>The suffix '-vo' does not look like the suffix '-mer' when scripted</p> <p>Dose: "1 tablet", "One" or 450 mg vs. 2 mg/kg (dose would only overlap with Forfivo XL 450 mg in a 225 kg patient)</p> <p>Route of Administration: Oral vs. Intravenous</p> <p>Dosage Form: Oral tablet vs. Powder for Injection</p> <p>Frequency: Once daily vs. one dose, may be repeated for a total of 3 doses (separated by at least 30 days)</p>

Appendix H: Products with orthographic, phonetic and/or multiple differentiating product characteristics minimize the risk for medication errors

Product name with potential for confusion	Similarity to Forfivo XL	Strength	Usual Signa (if applicable)	Differentiating Product Characteristics
Forfivo XL (Bupropion Hydrochloride) Extended-release Tablet		450 mg	450 mg orally once daily	

(b) (4)

Appendix H: Products with orthographic, phonetic and/or multiple differentiating product characteristics minimize the risk for medication errors

Product name with potential for confusion	Similarity to Forfivo XL	Strength	Usual Signa (if applicable)	Differentiating Product Characteristics
Forfivo XL (Bupropion Hydrochloride) Extended-release Tablet		450 mg	450 mg orally once daily	
Zofran (Ondansetron)	Look	Injection: 32 mg/50 mL D5W, 2 mg/mL (2 mL single-dose vial and 20 mL multidose vial) Solution: 4 mg/5 mL Tablets: 4 mg and 8 mg Orally Disintegrating Tablets: 4 mg and 8 mg	<p>Parenteral dose (intravenously, intramuscularly)</p> <p>Adults:</p> <p>Dose range: 0.15 mg/kg, 32 mg, 4 mg, 8 mg</p> <p>Frequency: Single dose 15 minutes to 30 minutes prior to chemotherapy, then repeated 4 hours and 8 hours after the first dose, over 15 minutes for 1 dose 30 minutes prior to chemotherapy, 1 to 2 hours prior to radiotherapy, immediately preoperatively</p> <p>Pediatrics (1 month to 12 years old)</p> <p>Dose: 0.1 to 0.3 mg/kg, 4 mg</p> <p>Frequency: Single dose over 15 minutes, 30 minutes prior to chemotherapy, then repeat in 4 hours and 8 hours; Single dose preoperatively or for nausea/vomiting.</p> <p>Oral dosage</p> <p>Adults and children ≥ 12 years</p> <p>Dose: 4 mg, 8 mg, 16 mg, 24 mg</p> <p>Frequency: three times per day, twice daily, single dose, once daily, single dose followed by two subsequent doses four hours and eight hours after the initial dose</p> <p>Pediatrics</p> <p>Dose: 4 mg, 3.2 mg, 1.6 mg</p> <p>Frequency: every 8 hours; 1 dose 15 to 30 minutes prior to chemotherapy, then 1 dose 4 hours and 8 hours after the initial dose</p>	<p>Orthographic differences in the names, in conjunction with differences in product characteristics, minimize the likelihood of medication error in the usual practice setting.</p> <p>Orthographic:</p> <p>Forfivo XL contains a modifier ‘XL’ which will help to differentiate it from Zofran</p> <p>‘-ivo’ does not look like ‘-ran’ when scripted</p> <p>Strength: 450 mg vs. 4 mg, 8 mg, 2 mg/mL, 32 mg/50 mL, and 4 mg/5 mL</p> <p>Dose: “1 tablet”, “One” or 450 mg vs. 1.6 mg, 3.2 mg, 4 mg, 8 mg, 16 mg, 24 mg, 32 mg and 0.1 to 0.3 mg/kg weight-based doses.</p> <p>Although dose similarity can occur between weight-based doses such as Zofran 4.5 mg vs. Forfivo XL 450 mg, this would likely be an infrequent occurrence, and lack of a trailing zero after a dose of 4.5 mg would help to differentiate these two doses and minimize the risk of medication error. Also, Zofran is available in multiple dosage forms, therefore, at a minimum, the dosage form and/or route of administration would be included in the Rx</p> <p>The dose in terms of numbers of tablets or teaspoonsful may overlap (e.g., “1” tablet or “1” teaspoonful), however, the presence of the product characteristics such as strength (tablets), units, frequency/duration of use, or dosage form on the prescription for Zofran will help to distinguish Forfivo XL from Zofran.</p>

Appendix H: Products with orthographic, phonetic and/or multiple differentiating product characteristics minimize the risk for medication errors

Product name with potential for confusion	Similarity to Forfivo XL	Strength	Usual Signa (if applicable)	Differentiating Product Characteristics
Forfivo XL (Bupropion Hydrochloride) Extended-release Tablet		450 mg	450 mg orally once daily	
Sustiva (Efavirenz)	Look	Capsules: 50 mg and 200 mg Tablet: 600 mg	Adults: 600 mg orally once daily Children: 200 mg, 250 mg, 300 mg, 350 mg, 400 mg, or 600 mg orally once daily	Orthographic differences in the names, in conjunction with differences in product characteristics, minimize the likelihood of medication error in the usual practice setting. <u>Orthographic:</u> Forfivo XL contains a modifier 'XL' which will help to differentiate it from Sustiva Forfivo XL contains one downstroke ('f') when scripted vs. Sustiva which has zero downstrokes <u>Dosage:</u> ("1 tablet", "One" or 450 mg vs. 200 mg, 250 mg, 300 mg, 350 mg, 400 mg, or 600 mg). Sustiva is available in three strengths, thus strength and number of tablets/capsules and/or dose would be need to be specified on a prescription. We note that a dose of 450 mg is achievable with the 50 mg and 200 mg strength capsules, however, a prescription would not likely be written for Sustiva 450 mg as it is not a recommended or usual dose for this product. If a prescription were written for Sustiva and was misinterpreted as Forfivo, the usual doses of Sustiva would minimize the risk of medication error, as the prescriber would need to be contacted for dosage clarification. If a prescription was written for Forfivo XL 450 mg or Forfivo XL 1 tablet and was misinterpreted as Sustiva, characteristics such as the modifier and/or the usual dose of Forfivo XL would lead to a call to the prescriber to clarify the name/dose.

Appendix H: Products with orthographic, phonetic and/or multiple differentiating product characteristics minimize the risk for medication errors

Product name with potential for confusion	Similarity to Forfivo XL	Strength	Usual Signa (if applicable)	Differentiating Product Characteristics
Forfivo XL (Bupropion Hydrochloride) Extended-release Tablet		450 mg	450 mg orally once daily	
Tarceva (Erlotinib)	Look	Tablets: 25 mg, 100 mg, and 150 mg	100 mg to 150 mg orally once daily (Dose may need to be increased up to 450 mg when co-administered with strong CYP3A4 inhibitors)	Orthographic differences in the names, in conjunction with differences in product characteristics, minimize the likelihood of medication error in the usual practice setting. <u>Orthographic:</u> Forfivo XL contains 2 upstrokes (F and f) vs. one upstroke (T) in Tarceva. Forfivo XL contains one downstroke ('f') vs. no downstrokes in Tarceva. Forfivo XL contains a modifier 'XL' which will help to differentiate it from Sustiva Tarceva is available in three strengths, thus strength and number of tablets or dose would be specified on an Rx. We note that a dose of 450 mg is achievable with the 150 mg strength tablet, and is recommended when it is required that a patient administer Tarceva concomitantly with a strong CYP3A4 inhibitor such as Rifampicin. However, the use of this dose would be expected to be infrequent, and if an Rx for Tarceva 450 mg was misinterpreted as Forfivo 450 mg, lack of a modifier and no downstroke or upstroke in the 3 rd position would minimize the risk of medication error.

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22497	ORIG-1	CARY PHARMACEUTICA LS INC	BUP-450 (BUPROPION HCL)450MG ER ORAL TAB

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