CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

022581Orig1s000

PROPRIETARY NAME REVIEW(S)

Department of Health and Human Services

Public Health Service

Food and Drug Administration

Center for Drug Evaluation and Research

Office of Surveillance and Epidemiology

Date	April 14, 2011
Application Type/Number:	NDA 022581
Through:	Irene Z. Chan, PharmD, BCPS, Team Leader Carol Holquist, RPh, Director Division of Medication Error Prevention and Analysis (DMEPA)
From:	John Casalino, PharmD, Safety Evaluator Division of Medication Error Prevention and Analysis (DMEPA)
Subject:	Proprietary Name Review
Drug Name:	Phoslyra (Calcium Acetate) Oral Solution 667 mg/5 mL
Applicant:	Fresenius Medical Care North America
OSE RCM #:	2011-1214

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

1 INTRODUCTION

This re-assessment of the proprietary name, Phoslyra, responds to the anticipated approval of NDA 022581 within 90 days from the date of this review. The Division of Medication Error Prevention and Analysis (DMEPA) found the proposed proprietary name, Phoslyra, acceptable in OSE Review 2009-2010, dated May 10, 2010.

2 METHODS AND RESULTS

For the proposed proprietary name, DMEPA staff search a standard set of databases and information sources (see Section 4) to identify names with orthographic and/or phonetic similarity to the proposed name that have been approved since the completion of the previous OSE proprietary name review. We use the same search criteria outlined in OSE Review #2009-2010, for the proposed proprietary name, Phoslyra. Since none of the proposed characteristics were altered, we did not evaluate previous names of concern. Our searches of the databases did not yield any new names thought to look or sound similar to Phoslyra and represent a potential source of drug name confusion.

Additionally, DMEPA searches the USAN stem list to determine if the name contains any USAN stems as of the last USAN updates. DMEPA did not identify any United States Adopted Names (USAN) stems in the proposed proprietary name, Phoslyra, as of April 12, 2011.

3 CONCLUSIONS AND RECOMMENDATIONS

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

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

If you have further questions or need clarifications, please contact Nina Ton, OSE Senior Regulatory Project Manager, at 301-796-1648.

4 REFERENCES

1. Holmes L. OSE Review #2009-2010: Proprietary Name Review for Phoslyra. May 10, 2010.

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

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

4. ***USAN Stems (http://www.ama-assn.org/ama/pub/category/4782.html)***

USAN Stems List contains all the recognized USAN stems.

5. ***Division of Medication Error Prevention and Analysis proprietary name 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.

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

/s/

JOHN B CASALINO
04/14/2011

IRENE Z CHAN
04/14/2011

CAROL A HOLQUIST
04/14/2011

Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
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Date:	May 10, 2010
To:	Norman Stockbridge, MD, PhD, Director Division of Cardiovascular and Renal Products (DCRP)
Through:	Kristina A. Toliver, PharmD, Team Leader Denise P. Toyer, PharmD, Deputy Director Carol A. Holquist, RPh, Director Division of Medication Error Prevention and Analysis (DMEPA)
From:	Loretta Holmes, BSN, PharmD, Safety Evaluator Division of Medication Error Prevention and Analysis (DMEPA)
Subject:	Proprietary Name Review
Drug Name:	Phoslyra (Calcium Acetate) Oral Solution 667 mg/5 mL
Application Type/Number:	NDA 022581
Applicant:	Fresenius Medical Care North America
OSE RCM #:	2009-2010

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CONTENTS

EXECUTIVE SUMMARY

This review summarizes DMEPA's evaluation of the proposed proprietary name, Phoslyra, for Calcium Acetate Oral Solution. Our evaluation of the proposed proprietary name, Phoslyra, 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, Phoslyra, conditionally 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.

1 BACKGROUND

1.1 INTRODUCTION

This review responds to a request from Fresenius Medical Care North America on October 9, 2009, for an assessment of the proposed proprietary name, Phoslyra, regarding potential name confusion with other proprietary or established drug names in the usual practice settings. Additionally, the Applicant submitted an independent name assessment completed by (b) (4)

Comments on the container labels, carton and insert labeling are forthcoming under separate cover in OSE Review 2009-2012 (Label and Labeling Review).

1.2 REGULATORY HISTORY

The proposed proprietary name, Phoslyra, represents a dual proprietary name. The Applicant currently markets Phoslo (Calcium Acetate) Capsules. Calcium Acetate 667 mg tablets was approved on December 10, 1990, (NDA 019976) under the proprietary name, Phoslo, and is indicated for the control of hyperphosphatemia in end stage renal failure. The capsule formulation (NDA 021160) was approved on April 2, 2001. The tablets were subsequently discontinued in 2006.

1.3 PRODUCT INFORMATION

Phoslyra is the proposed proprietary name for Calcium Acetate Oral solution. Phoslyra is a phosphate binder indicated for the control of hyperphosphatemia in patients with end stage renal disease. The recommended initial dose for the adult dialysis patient is 10 mL (1334 mg) with each meal. The dosage may be increased gradually to lower serum phosphorus levels to the target range of 3.5 mg/dL to 5.5 mg/dL as long as hypercalcemia does not develop. Most patients require 15 mL (2001 mg) to 20 mL (2668 mg) with each meal.

Phoslyra will be available in a 667 mg/5 mL strength and supplied in (b) (4) 473 mL (trade) bottles. Phoslyra will be packaged with a marked dosing cup. The product should be stored at 25˚C (77˚F).

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, Phoslyra.

2.1 SEARCH CRITERIA

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

To identify drug names that may look similar to Phoslyra, the DMEPA staff also considers the orthographic appearance of the name on lined and unlined orders. Specific attributes taken into consideration include the length of the name (eight letters), upstrokes (one, lower case 'l'), downstrokes (one, lower case 'y'), cross strokes (none), and dotted letters (none). Additionally, several letters in Phoslyra, may be vulnerable to ambiguity when scripted, including the capital letter 'P' which may appear as capital letters 'F', 'R' or 'T; lower case 'h' may look like lower case 'k', 'n', 'r', or upper case 'L'; lower case 'o' may look like lower case 'a', 'c', or 'u'; lower case letter 's' may appear as lower case 'g', 'n', or 'r'; lower case 'l' may appear as lower case 'e', undotted 'i' or uncrossed 't'; lower case 'y' may appear as lower case 'g', 'q', 'v', or 'x'; lower case 'r' may appear as lower case 'n', 's', or 'v'; and lower case 'a' may appear as lower case 'ce', 'ci', 'o', or 'u'. As a result, the DMEPA staff also considers these alternate appearances when identifying drug names that may look similar to Phoslyra.

When searching to identify potential names that may sound similar to Phoslyra, the DMEPA staff search for names with similar number of syllables (three), stresses (PHOS-lyr-a, phos-LYR-a, or phos-lyr-A), and placement of vowel and consonant sounds. Additionally, the DMEPA staff considers that pronunciation of parts of the name can vary such as 'Phos-' may sound like 'Fos-' and '-lyra' may sound like '-lira', '-lera' or '-leera'. The Applicant provided their intended pronunciation of the proprietary name ("fos leer' a") in the proposed name submission and, therefore, it was taken into consideration. However, names are often mispronounced and/or spoken with regional accents and dialects, so other potential pronunciations of the name are considered.

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.

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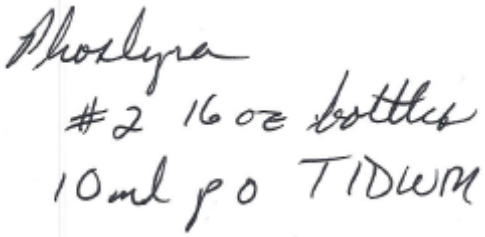
[1] Institute for Safe Medication Practices. Confused Drug name List (1996-2006). Available at http://www.ismp.org/Tools/confuseddrugnames.pdf

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

Figure 1. Phoslyra Prescription Study (conducted on October 30, 2009)

HANDWRITTEN REQUISITION MEDICATION ORDER	VERBAL PRESCRIPTION
Inpatient Medication Order: 	"Phoslyra 2 teaspoonfuls by mouth three times per day with meals. Dispense # 2, 16 ounce bottles"
Outpatient Prescription: 	

2.3 AERS SELECTION OF MEDICATION ERROR CASES

Since Phoslo is a currently marketed product in the U.S., and Phoslyra will represent a dual proprietary name, DMEPA conducted a search of the FDA Adverse Event Reporting System (AERS) for medication errors associated with the use of Phoslo to determine if any identified medication errors may impact the use or labeling of Phoslyra. DMEPA conducted two separate AERS searches using the High Level Group Terms "Medication Errors" and "Product Quality Issues" and the proprietary name "Phoslo" in one search and the active ingredient name "Calcium Acetate" in the other. The searches were conducted on December 22, 2009 and January 7, 2009. Those cases that did not describe a medication error were excluded from further analysis.

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

3 RESULTS

3.1 DATABASE AND INFORMATION SOURCES

The DMEPA searches yielded a total of nine names as having some similarity to the name Phoslyra.

Six of the names were thought to look like Phoslyra. These include Phospha 250, Rhinoflex, Phos-Flur, Physiosol, Placidyl, and Phosphotec. Two of the names were thought to sound like Phoslyra. These include Fosrenol and Phyxxlice. The remaining name, Phoslo, was thought to look and sound similar to Phoslyra.

Additionally, DMEPA staff did not identify any United States Adopted Names (USAN) stems in the proposed proprietary name as of April 2, 2010.

3.2 CDER 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 and/or phonetic similarity to Phoslyra.

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 22 practitioners responded. None of the responses overlapped with any existing or proposed drug names. Fourteen of the practitioners interpreted the name correctly as "Phoslyra" with correct interpretation occurring in both the inpatient written studies (n=8) and the outpatient written studies (n=6). The remainder of the practitioners misinterpreted the drug name. In the verbal studies, all responses were misspelled phonetic variations of the proposed name, Phoslyra. See Appendix C for the complete listing of interpretations from the verbal and written prescription studies.

3.4 AERS SELECTION OF MEDICATION ERROR CASES

We retrieved a total of five cases (n=5) from AERS. None of the cases were found to be relevant to this proprietary name review. These cases describe the following. One case involved calcium acetate capsules found in a patient's stool, while in another case, Phoslo was prescribed for the wrong indication. The third case involved a product complaint where the reporter complained generic calcium acetate was difficult to swallow and caused vomiting. The remaining two cases involved dispensing errors (the incorrect dose was specified on a Phoslo prescription bottle label in one case and in the other case the patient requested refills for Verapamil SR and Phoslo but upon receipt the patient noted both bottles contained Phoslo). See Appendix B.

3.5 EXTERNAL NAME STUDY

The proposed name risk assessment submitted by the Applicant and conducted by (b) (4) (b) (4) concluded that the proposed name did not pose a risk for confusion. (b) (4) identified and evaluated a total of 33 drug names for their potential confusion with the proposed proprietary name Phoslyra.

Three of the 33 names (Phos-Flur, Fosrenol, and Phoslo) were identified by DMEPA.

The 30 names not identified by DMEPA were added to the list and evaluated in our risk assessment of this name.

3.6 SAFETY EVALUATOR RISK ASSESSMENT

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

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

3.7.1 Initial Phase of the Review

DCRP did not respond to the October 30, 2009 e-mail sent by OSE during the initial phase of the name review in which we inquired about any comments and or concerns they may have about the proposed name. Thus, we considered the lack of comment as no concern.

3.7.2 Midpoint of the Review

DMEPA notified DCRP via e-mail that we had no objections to the proposed proprietary name, Phoslyra, on January 4, 2010. Per e-mail correspondence from DCRP on January 8, 2010, they stated "there are no objections to the proprietary name Phoslyra".

3.7.3 April 6, 2010 Meeting with Division

DMEPA discussed the issue of dual proprietary names for the Applicant's Calcium Acetate products with DCRP in a labeling meeting on April 6, 2010. At that time, the DCRP communicated their preference that dual proprietary names be used for the Applicant's Calcium Acetate products because the oral solution contains the inactive ingredient maltitol, an ingredient that may cause diarrhea, and if administered with other products containing this ingredient, the effect may be more pronounced. Phoslo does not contain this ingredient and thus it may be misleading to market both products under the name Phoslo. Additionally, if both products are marketed under one name, patients may not be aware of this difference between the products. Furthermore, DCRP indicated concomitant administration of the products was not a safety concern since it is not uncommon for patients with end stage renal disease to require more than one product to lower serum phosphate levels.

4 DISCUSSION

Phoslyra is the proposed proprietary name for Calcium Acetate Oral Solution. 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. Since this Applicant, Fresenius Medical Care, is also the NDA holder for PhosLo (Calcium Acetate Capsules), NDA 021160, DMEPA also evaluated the Applicant's proposal to use two different proposed names for the active ingredient, Calcium Acetate. Therefore, Phoslyra will represent a dual proprietary name since the Applicant plans to continue to market PhosLo when Phoslyra is approved.

Phoslo and Phoslyra have identical product characteristics [active ingredient, indication of use, strength (667 mg vs. 667 mg/5mL), dosing, frequency of administration, and route of administration)] except for the dosage form. Phoslo is marketed as a capsule whereas Phoslyra will be marketed as an oral solution. We evaluated the risks of using two different proprietary names for Fresenius Medical Care's Calcium Acetate products. We note that the Applicant did not provide a rationale for this decision.

4.1 CALCIUM ACETATE PRODUCT LINE EXTENSION

In evaluating the potential risks of the Applicant's decision to market their Calcium Acetate products under two different proprietary names, DMEPA evaluates the potential risk of medication errors when using a single proprietary name versus a dual proprietary name for these products. Our evaluation

determined that the use of two proprietary names introduces the additional risk of concomitant administration which can occur if a patient is prescribed both Phoslo and Phoslyra by two different prescribers. We discussed the potential for concomitant administration of Phoslo and Phoslyra with DCRP to determine if this risk introduces a safety concern. DCRP indicated that concomitant administration of these two products would not introduce a safety concern, since it is not uncommon for patients with end stage renal disease to require more than one product to lower their serum phosphate levels.

DCRP also indicated that they favored the use of two different proprietary names for Fresenius Medical Care's Calcium Acetate products because the Calcium Acetate Oral Solution formulation contains an inactive ingredient, maltitol. Maltitol causes diarrhea in some patients. Additionally, when the oral solution formulation containing maltitol is administered with other products containing maltitol the diarrhea adverse effect may be more pronounced. Thus, DCRP is concerned that use of a single proprietary name, Phoslo, may be misleading because the oral solution contains maltitol whereas the tablets do not. DCRP's concern is that patients may not be aware of the difference in formulation between the two products if a single proprietary name is used. Since DCRP believes there is a safety concern if one proprietary name is used for both of Fresenius Medical Care's Calcium Acetate products, DMEPA finds the use of the dual proprietary name Phoslyra acceptable for the Applicant's Calcium Acetate Oral Solution product.

4.2 PHOSLYRA ASSESSMENT OF RISK OUTSIDE THE CALCIUM ACETATE PRODUCT LINE

4.2.1 Promotional Assessment

DDMAC did not find the name, Phoslyra, promotional. The Division of Cardiovascular and Renal Products and the Division of Medication Error Prevention and Analysis concurred with this assessment.

4.2.2 Safety Assessment

DMEPA identified and evaluated 39 names for their potential similarity to the proposed name, Phoslyra. DMEPA did not identify any other source of confusion with the proposed name. Thirty-one of the 39 names were not evaluated further because they lacked orthographic and/or phonetic similarity to Phoslyra (see Appendix D).

Failure mode and effects analysis (FMEA) was then applied to determine if the proposed name could potentially be confused with the remaining eight names and lead to medication errors. This analysis determined that the look-alike and sound-alike name similarity between Phoslyra was unlikely to result in medication errors due to orthographic and/or phonetic similarities with any of the eight products for the reasons presented in Appendices E through G. This finding was consistent with and supported by an independent risk assessment of the proprietary name submitted by the Applicant.

5 CONCLUSIONS AND RECOMMENDATIONS

The Proprietary Name Risk Assessment findings indicate that the proposed name, Phoslyra, is not promotional nor is it vulnerable to name confusion that could lead to medication errors. Additionally, we find the use of dual proprietary names (Phoslyra and Phoslo) for the Applicant's Calcium Acetate products acceptable from a safety perspective. Thus, the Division of Medication Error Prevention and Analysis (DMEPA) has no objection to the proprietary name, Phoslyra, for this product at this time.

However, if any of the proposed product characteristics as stated in this review are altered prior to approval of the product, 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. If the approval of this application is delayed beyond 90 days

from the signature date of this review, the proposed name must be re-evaluated. If you have further questions or need clarifications, please contact Nina Ton, OSE Project Manager, at 301-796- 1648.

5.1 COMMENTS TO THE APPLICANT

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

6 REFERENCES

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

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

2. Phonetic and Orthographic Computer Analysis (POCA)

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

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

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

4. AMF Decision Support System [DSS]

DSS is a government database used to track individual submissions and assignments in 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, Rudolph's 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. [3]

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

The Safety Evaluator assigned to the Proprietary Name Risk Assessment is responsible for considering the collective findings, and provides an overall risk assessment of the proposed proprietary name. DMEPA bases

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

the overall risk assessment on the findings of a Failure Mode and Effects Analysis (FMEA) of the proprietary name, and focuses on the avoidance of medication errors.

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

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

Typical product characteristics considered when identifying drug names that could potentially be confused with the proposed proprietary name include, but are not limited to; established name of the proposed product, proposed indication of use, dosage form, route of administration, strength, unit of measure, dosage units, recommended dose, typical quantity or volume, frequency of administration, product packaging, storage conditions, patient population, and prescriber population. Because drug name confusion can occur at any point in the medication use process, DMEPA staff considers the potential for confusion throughout the entire U.S. medication use process, including drug procurement, prescribing and ordering, dispensing, administration, and monitoring the impact of the medication.[5] DMEPA provides the product characteristics considered for this review in section one.

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

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

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

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

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

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

1. Database and Information Sources

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

proprietary name. The individual findings of multiple safety evaluators are pooled and presented to the CDER Expert Panel.

2. CDER Expert Panel Discussion

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

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

3. FDA Prescription Analysis Studies

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

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

4. Comments from the OND review Division or Generic drugs

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

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

5. Safety Evaluator Risk Assessment of the Proposed Proprietary Name

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

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

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

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

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

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

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

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

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

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

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: **AERS Search Results (ISR Numbers)**

AERS Search Results	
ISR Numbers	6386863-1
	6373660-6
	3882135-5
	4112194-6
	4333877-9

Appendix C: **FDA Prescription Study Responses**

Inpatient Medication Order	**Outpatient Medication Order**	**Voice Prescription**
Phoseyra	Phoslyra	Fosera
Phoslyra	Phoslyra	Fosfera
Phoslyra	Phoslyra	fosleera
Phoslyra	Phoslyra	Foslera
Phoslyra	Phoslyra	Foslira
Phoslyra	Phoslyra	Fosvera
Phoslyra		Phoslera
Phoslyra		
Phoslyra		

Appendix D: **Names Lacking Orthographic and/or Phonetic Similarity.**

Name	**Similarity to Phoslyra**
Rhinoflex	Look
Physiosol	Look
Placidyl	Look
Phosphotec	Look
Fosrenol	Sound

Name	Similarity to Phoslyra
Phyxxlice	Sound
Flurate	(b) (4)
Foleve	
Folitab 500	
Foltrate	
Fostex	
Hepsera	
Humira	
Hylira	
Lyrica	Look and Sound (b) (4)
Phospholine Iodide	(b) (4)
Photofrin	
Polycitra	
Polycitra-K	
Poly-Iron	
Poly-Pred	
Polytar	
Polytrim	
Prosacea	
Proscar	
Provera	
Solaraze	
Solia	
Suphera	

Name	Similarity to Phoslyra
Theolair	(b) (4)
Tussall-ER	

Appendix E: Products with no numerical overlap in dose and/or route of administration

Product name with potential for confusion	Similarity to Phoslyra	Strength	Usual Dose
Phoslyra	**N/A**	**667 mg/5 mL**	**10 mL to 20 mL (2 tsp. to 4 tsp. or 1334 mg to 2668 mg) with each meal**
Phos-Flur (Sodium Fluoride) Gel	Look	1.1%	Apply a thin ribbon to teeth with a toothbrush for 1 minute then expectorate/rinse mouth
Fludara (Fludarabine Phosphate) for Injection	(b) (4)	50 mg per vial	25 mg/m^2 via intravenous infusion once daily for five days every 28 days

Appendix F: Products with numerical overlap or similarity in strength, dose or achievable dose with multiple differentiating product characteristics

Product name with potential for confusion	Similarity to Phoslyra	Strength	Usual Signa (if applicable)	Differentiating Product Characteristics (Phoslyra vs. Product)
Phoslyra	**N/A**	**667 mg/5mL**	**10 mL to 20 mL (2 tsp. to 4 tsp. or 1334 mg to 2668 mg) with each meal**	
phisoHex (Hexachlorophene) Emulsion	(b) (4)	3%	Wet hands with water and apply approximately 5 mL into the palm, work up lather with water and apply to area to be cleansed	The ending letters of the names look different ("lyra" vs. "hex"). *Route of administration*: Oral vs. topical *Frequency of administration*: With each meal vs. variable. *Context of use*: phisoHex is a topical skin cleanser that is likely to be used in a surgical type setting whereas Phoslyra would not be used in that setting. Additionally, a prescription for Phoslyra would likely specify that it should be taken with meals whereas phisoHex would not have these instructions. A dose of 5 mL may overlap between the two products, however, the dose of phisoHex would probably not be written since it is a skin cleanser.
Posture [Calcium Phosphate (Tribasic)] Tablets OTC Product	(b) (4)	600 mg	2 tablets orally once daily	The upstroke letter "h" and downstroke letter "y" in Phoslyra helps to differentiate the names. *Frequency of administration*: With meals vs. once daily *Status*: Prescription vs. OTC *Dosage form*: Oral solution vs. tablets

Product name with potential for confusion	**Similarity to Phoslyra**	**Strength**	**Usual Signa (if applicable)**	**Differentiating Product Characteristics (Phoslyra vs. Product)**
Phoslyra	**N/A**	**667 mg/5mL**	**10 mL to 20 mL (2 tsp. to 4 tsp. or 1334 mg to 2668 mg) with each meal**	
Phospha 250 Neutral (Potassium Acid Phosphate and Sodium Acid Phosphate) Tablets	Look	852 mg Dibasic Sodium Phosphate, 155 mg Monobasic Potassium Phosphate, and 130 mg Monobasic Sodium Phosphate Monohydrate	1 to 2 tablets orally four times per day	The ending letters of the names look different ("lyra" vs. "pha"). Additionally, Phospha 250 Neutral is a compound name (i.e., also contains "250" and "Neutral" in the name) which when scripted will help to differentiate the names. *Dosage form*: Oral solution vs. tablets
Soliris (Eculizumab) Injection	(b) (4)	300 mg/30 mL (10 mg/mL)	600 mg via intravenous infusion every 7 days for 4 weeks, then 900 mg for the 5th dose 7 days later, then 900 mg every 14 days thereafter	The beginning syllables ("Phos-" vs. "So-") do not sound similar. *Route of administration*: Oral vs. intravenous *Frequency of administration*: With meals vs. every 7 days for 5 doses, then every 14 days

Appendix G: Potential confusing names with numerical similarity in strength or dose

Proprietary Name: **Phoslyra**	**Strength:** **667 mg/5 mL**	**Usual Dose:** **10 mL to 20 mL (2 tsp. to 4 tsp. or 1334 mg to 2668 mg) with each meal**
Failure Mode: Name confusion	**Causes (could be multiple)**	**Rationale**
Phoslo (Calcium Acetate) Capsules Gelcaps *Strength*: 667 mg *Dosage*: 2 to 4 capsules orally with each meal	Orthographic similarity: The beginning letters of both names are identical (i.e., Phosl) The products overlap in strength: (667 mg/5 mL vs. 667 mg capsules The potential exists for a numerical overlap in dose (i.e., 2, 3, or 4 teaspoonsful vs. 2, 3, or 4 capsules) The products share overlapping indications of use, dosage, and frequency of administration	Medication errors unlikely to occur due to orthographic differences between the names and different dosage units. *Rationale*: The ending letters of the names look different ("o" vs. "yra"). Additionally, Phoslyra appears longer in length when scripted because it contains 8 letters vs. Phoslo which contains 6 letters. Phoslyra will be available in an oral solution dosage form so a prescription is likely to specify the dosage units in terms of teaspoonsful, tablespoons, or milliliters which may help to differentiate the names.
Pylera (Bismuth Subcitrate Potassium, Metronidazole, and Tetracycline) Capsules *Strength*: 140 mg/125 mg/125 mg *Dosage*: 3 capsules four times per day (after meals and at bedtime)	Orthographic similarity: Both names begin with the letter "P" and the ending letters ("lyra" vs. "lera") look similar. Phonetic similarity: The ending syllables may sound similar ("-lyra" vs. "-lera") The potential exists for a numerical overlap in dose (i.e., 3 teaspoonsful vs. 3 capsules)	Medication errors unlikely to occur due to orthographic differences between the names and different dosage units. *Rationale*: The letters "hos" vs. "y" at the beginning of the names look different. Additionally, the downstroke letter "y" at the ending portion of Phoslyra helps to differentiate the ending portion of the names. Furthermore, Phoslyra appears longer in length when scripted because it contains 8 letters vs. Pylera which contains 6 letters. The beginning syllables in the names sound different ("Phos-" vs. "Py-"). Phoslyra will be available in an oral solution dosage form so a prescription is likely to specify the dosage units in terms of teaspoonsful, tablespoons, or milliliters which may help to differentiate the names

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22581	ORIG-1	FRESENIUS BIOTECH NORTH AMERICA INC	PHOSLYRA(CALCIUM ACETATE)ORAL SOL 667MG/

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

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