

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

207500Orig1s000 / 207501Orig1s000

PROPRIETARY NAME REVIEW(S)

MEMORANDUM
REVIEW OF PROPRIETARY NAME

Division of Medication Error Prevention and Analysis (DMEPA)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

Date of This Memorandum: March 1, 2015

Requesting Office or Division: Division of Anti-Infective Products (DAIP)

Application Type and Number: NDA 207500
NDA 207501

Product Name and Strength: Cresemba (Isavuconazonium Sulfate) capsules, 186 mg
Cresemba (Isavuconazonium Sulfate) for injection, 372 mg

Submission Date: February 20, 2015

Applicant/Sponsor Name: Astellas Pharmaceuticals

OSE RCM #: 2015-48830
2015-48831

DMEPA Primary Reviewer: Jacqueline Sheppard, PharmD

DMEPA Acting Team Leader: Vicky Borders-Hemphill, PharmD

1 PURPOSE OF MEMO

This memorandum is to re-assess the proposed proprietary name, Cresemba based on revised strengths and dosing. The proposed name, Cresemba, was found acceptable in OSE review # 2013-16658 and 2013-16659 dated April 30, 2014¹ and OSE review #2014-25973 and 2014-25974 dated August 22, 2014.² The established name of the product was

¹ Winiarski A. Proprietary Name Review for Cresemba (INDs 072593 and 119307). Silver Spring (MD): Food and Drug Administration, Center for Drug Evaluation and Research, Office of Surveillance and Epidemiology, Division of Medication Error Prevention and Analysis (US); 2014 Apr 30. 29 p. OSE RCM No.: 2013-16658 and 2013-16659.

² Winiarski A. Proprietary Name Memo for Cresemba (NDAs 207500 and 207501). Silver Spring (MD): Food and Drug Administration, Center for Drug Evaluation and Research, Office of Surveillance and Epidemiology, Division of Medication Error Prevention and Analysis (US); 2014 Aug 2. 3 p. OSE RCM No.: 2014-25973 and 2014-25974.

originally presented as the

(b) (4)

Astellas Pharmaceuticals has revised the strength of the product to reflect the salt, isavuconazonium sulfate as the established name with a revised capsule strength of 186 mg and powder for injection strength as 372 mg.

2 METHODS AND MATERIALS REVIEWED

For reassessment of the proposed proprietary name, we evaluated previous proprietary name reviews dated April 30, 2014 and August 22, 2014 to assess whether the change in strengths would alter our previous conclusion regarding the acceptability of the proposed proprietary name. DMEPA searched the USAN stem list to determine if the name contains any USAN stems as of the last USAN updates. The February 12, 2015 search of USAN stems did not find any USAN stems in the proposed proprietary name. We searched the POCA database (see section 5 for description) to identify names with orthographic and phonetic similarity to the proposed name that have been approved since the most recent assessment of the name. Additionally, since Cresemba is being proposed in strengths that are not a commonly marketed, we searched the Pragmatic® Regulated Product Labeling Listing and Registration System (PR^oPLLR™) database to identify any names with potential orthographic, spelling, and phonetic similarities with Cresemba that were not identified in POCA, and found to have an overlap in strength with Cresemba.

Our POCA search and PRPLLR search did not identify any new names that represent a potential source of drug name confusion. Our evaluation has not altered our previous conclusion regarding the acceptability of the proposed proprietary name. As a result, we maintain that the name is acceptable.

3 CONCLUSIONS

The proposed proprietary name is acceptable.

If you have further questions or need clarifications, please contact Karen Townsend, OSE Project Manager, at 301-796-5413.

4 COMMENTS TO APPLICANT

We have completed the re-evaluation of the proposed proprietary name, Cresemba, and have concluded that this name is acceptable.

5 REFERENCES

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

USAN Stems List contains all the recognized USAN stems.

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

POCA is a system that FDA designed. As part of the name similarity assessment, POCA is used to evaluate proposed names via a phonetic and orthographic algorithm. The proposed proprietary name is converted into its phonemic representation before it runs through the phonetic algorithm. Likewise, an orthographic algorithm exists that operates in a similar fashion. POCA is publicly accessible.

3. ***Pragmatic® Regulated Product Labeling Listing and Registration System (PR^oPLLR)***

Pragmatic® Regulated Product Labeling Listing and Registration System (PR^oPLLR™) accessed February 6, 2015 at <http://elist/prpllr/>.

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

/s/

JACQUELINE E SHEPPARD
03/02/2015

JAMES H SCHLICK on behalf of BRENDA V BORDERS-HEMPHILL
03/02/2015

**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 Memorandum

Date: August 22, 2014

Reviewer: Aleksander Winiarski, PharmD
Division of Medication Error Prevention and Analysis

Acting Team Leader Tingting Gao, PharmD
Division of Medication Error Prevention and Analysis

Drug Name and Strength:  (b) (4)

Application Type/Number: NDA 207500 and NDA 207501

Applicant/Sponsor: Astellas

OSE RCM #: 2014-25973 and 2014-25974

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

1 INTRODUCTION

The proposed proprietary name, Cresemba, was found acceptable in OSE Review# 2013-16658 and 2013-16659, dated April 30, 2014 under IND 072593 and IND 119307. This memorandum is to communicate that DMEPA maintains the proposed proprietary name, Cresemba, is acceptable from both a promotional and safety perspective under NDA 207500 and NDA 207501.

If you have further questions or need clarification, please contact Karen Townsend, OSE project manager, at 301-796-5413.

1.1 COMMENTS TO THE APPLICANT

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

If any of the proposed product characteristics as stated in your July 29, 2014 submission are altered, the name must be resubmitted for review.

2 REFERENCES

1. OSE Review# 2013-16658 and 2013-16659: Proprietary Name Review for Cresemba (Isavuconazonium Sulfate), April 30, 2014.

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

/s/

ALEKSANDER P WINIARSKI
08/22/2014

TINGTING N GAO
08/22/2014

**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: April 30, 2014

Reviewer: Aleksander Winiarski, PharmD
Division of Medication Error Prevention and Analysis

Acting Team Leader: Julie Neshiewat, PharmD, BCPS
Division of Medication Error Prevention and Analysis

Acting Team Leader: Tingting Gao, PharmD, BCPS
Division of Medication Error Prevention and Analysis

Drug Names and Strengths:  (b) (4)

Application Type/Number: IND 072593 and IND 119307

Applicant/Sponsor: Astellas

OSE RCM #: 2013-16658 and 2013-16659

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

CONTENTS

1	INTRODUCTION.....	1
1.1	Regulatory History	1
1.2	Product Information.....	1
2	RESULTS.....	1
2.1	Promotional Assessment	2
2.2	Safety Assessment.....	2
3	CONCLUSIONS	4
3.1	Comments to the Applicant.....	4
4	REFERENCES	5
	APPENDICES.....	8

1 INTRODUCTION

This review evaluates the proposed proprietary name, Cresemba, 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

Cresemba is the proprietary name submitted by the Applicant under INDs: 072593 (powder for injection) and 119307 (capsules). The request for proprietary name review was submitted on December 11, 2013. Cresemba is the third proprietary name submitted under the INDs. Two previous names, (b) (4) were denied based on look-alike similarities and overlapping product characteristics with (b) (4) respectively.

1.2 PRODUCT INFORMATION

The following product information is provided in the December 11, 2013 proprietary name submission.

- Active Ingredient: Isavuconazonium Sulfate
- Indication of Use: (b) (4) and *Aspergillus* infections
- Route of Administration: Oral and Intravenous
- Dosage Form: Capsule and Powder for injection
- Strength (b) (4) mg capsule, (b) (4) mg/vial
- Dose and Frequency:
(b) (4)
- How Supplied:
 - Powder for injection: vial
 - Oral capsules: blister packs (b) (4) quantity unspecified
- Storage:
 - Vial - refrigerated
 - Capsule - room temperature

2 RESULTS

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

2.1 PROMOTIONAL ASSESSMENT

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

2.2 SAFETY ASSESSMENT

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

2.2.1 United States Adopted Names (USAN) Search

There is no USAN stem present in the name.¹

2.2.2 Components of the Proposed Proprietary Name

The Applicant did not provide information pertaining to the derivation or intended meaning of the proposed name. This proprietary name is comprised of a single word that does not contain any components (such as a modifier, route of administration, dosage form, etc.) that are misleading or can contribute to medication error.

2.2.3 FDA Name Simulation Studies

Fifty-seven practitioners participated in DMEPA's prescription studies. The interpretations did not overlap with or appear or sound similar to any currently marketed products or any products in the pipeline.

In the outpatient study, 15 of 19 participants correctly interpreted the name as Cresemba. Of the outpatient participants who misinterpreted the name, they misinterpreted the letter 'm' as 'n', and misinterpreted the letter 'a' as letter strings 'er' and 'ar'.

None of the 20 verbal study participants interpreted the name correctly. Most misinterpretations included the 'C' as 'K' and 'Ch', the 's' as 'z', and vowels 'e' as 'a', 'i', and 'y'.

In the inpatient study, 10 of 18 participants correctly interpreted the name as Cresemba. Most inpatient participants misinterpreted the letter 'e' as the letter 'i' and one participant also misinterpreted the letter 'C' as a 'P'.

All of the identified misinterpretations were considered in the search and evaluation of phonetically and orthographically similar names (See Appendix B).

Appendix C contains the results of the verbal and written prescription studies.

¹ The March 10, 2014 search of the United States Adopted Name (USAN) stems.

2.2.4 Comments from Other Review Disciplines at Initial Review

In response to the OSE, January 6, 2014 e-mail, the Division of Anti-Infective Products (DAIP) did not forward any comments or concerns relating to the proposed name at the initial phase of the proprietary name review.

2.2.5 Failure Mode and Effects Analysis of Similar Names

Appendix B lists possible orthographic and phonetic misinterpretations of the letters appearing in the proposed proprietary name. These variations were used in the search for names similar to Cresemba. Table 1 lists the names with potential orthographic, phonetic, or spelling similarity to the proposed proprietary name, Cresemba, identified by the primary reviewer, the Expert Panel Discussion (EPD), and by the Drug Safety Institute (DSI). Our analysis of the 23 names determined all 23 names will not pose a risk for confusion as described in Appendices D through E.

Table 1: Collective List of Potentially Similar Names (DMEPA, EPD, Other Disciplines, and External Name Study)					
Look Similar					
<i>Name</i>	<i>Source</i>	<i>Name</i>	<i>Source</i>	<i>Name</i>	<i>Source</i>
Celexa	DSI	Pamelor	DSI	(b) (4)	FDA
Clobex	DSI	Soma	DSI	Casodex	FDA
Copegus	DSI	Complera	DSI	Cambia	FDA
Caprelsa	DSI	Viorele	DSI	Orencia	FDA
Versacloz	DSI	Lazanda	DSI	Concerta	FDA
Sound Similar					
<i>Name</i>	<i>Source</i>	<i>Name</i>	<i>Source</i>	<i>Name</i>	<i>Source</i>
Cerezyme	DSI				
Look and Sound Similar					
<i>Name</i>	<i>Source</i>	<i>Name</i>	<i>Source</i>	<i>Name</i>	<i>Source</i>
Crescormon	DSI	Cresylate	DSI	Cymbalta	DSI
Crestor	DSI/FDA	Cryselle	DSI	Treanda	DSI
Kcentra	DSI				

2.2.6 Communication of DMEPA’s Analysis at Midpoint of Review

DMEPA communicated our findings to the Division of Anti-Infective Products (DAIP) via e-mail on April 4, 2014. At that time we also requested additional information or concerns that could inform our review. Per e-mail correspondence from DAIP on April 11, 2014, they stated no additional concerns with the proposed proprietary name, Cresemba.

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

3 CONCLUSIONS

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

If you have further questions or need clarifications, please contact Karen Townsend, OSE project manager, at 301-796-5413.

3.1 COMMENTS TO THE APPLICANT

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

Additionally, the proposed proprietary name must be submitted at the time of NDA submission. If any of the proposed product characteristics as stated in your December 11, 2013 submission are altered, the name must be resubmitted for review.

4 REFERENCES

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

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

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

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

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

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

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

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

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

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

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

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

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

USPTO provides information regarding patent and trademarks.

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

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

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

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

10. *Natural Medicines Comprehensive Databases* (www.naturaldatabase.com)

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

11. *Access Medicine* (www.accessmedicine.com)

Access Medicine® from McGraw-Hill contains full-text information from approximately 60 titles; it includes tables and references. Among the titles are: Harrison's Principles of Internal Medicine, Basic & Clinical Pharmacology, and Goodman and Gilman's The Pharmacologic Basis of Therapeutics.

12. *USAN Stems* (<http://www.ama-assn.org/ama/pub/about-ama/our-people/coalitions-consortiums/united-states-adopted-names-council/naming-guidelines/approved-stems.shtml>)

USAN Stems List contains all the recognized USAN stems.

13. *Red Book* (www.thomsonhc.com/home/dispatch)

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

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

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

15. *Medical Abbreviations* (www.medilexicon.com)

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

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

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

17. Walgreens (www.walgreens.com)

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

18. Rx List (www.rxlist.com)

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

19. Dogpile (www.dogpile.com)

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

20. Natural Standard (<http://www.naturalstandard.com>)

Natural Standard is a resource that aggregates and synthesizes data on complementary and alternative medicine.

APPENDICES

Appendix A

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

The safety assessment is conducted by DMEPA. DMEPA staff search a standard set of databases and information sources to identify names that are similar in pronunciation, spelling, and orthographically similar when scripted to the proposed proprietary name. Additionally, we consider inclusion of USAN stems or other characteristics that when incorporated into a proprietary name may cause or contribute to medication errors (i.e., dosing interval, dosage form/route of administration, medical or product name abbreviations, names that include or suggest the composition of the drug product, etc.). DMEPA defines a medication error as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer.²

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

² 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.³

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).

³ 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		
	<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/Similar shape 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, 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 Office of Prescription Drug Promotion (OPDP). We also consider input from other review disciplines (OND, ONDQA/OBP). The Expert Panel also discusses potential concerns regarding drug marketing and promotion related to the proposed names.

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

3. FDA Prescription Simulation Studies

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

In order to evaluate the potential for misinterpretation of the proposed proprietary name in handwriting and verbal communication of the name, inpatient medication orders and/or outpatient prescriptions are written, each consisting of a combination of marketed and unapproved drug products, including the proposed name. These orders are optically

scanned and one prescription is delivered to a random sample of participating health professionals via e-mail. In addition, a verbal prescription is recorded on voice mail. The voice mail messages are then sent to a random sample of the participating health professionals for their interpretations and review. After receiving either the written or verbal prescription orders, the participants record their interpretations of the orders which are recorded electronically.

4. Comments from Other Review Disciplines

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

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

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

5. Safety Evaluator Risk Assessment of the Proposed Proprietary Name

The primary Safety Evaluator applies his/her individual expertise gained from evaluating medication errors reported to FDA, considers all aspects of the name that may be misleading or confusing, conducts a Failure Mode and Effects Analysis, and provides an overall decision on acceptability dependent on their risk assessment of name confusion. Failure Mode and Effects Analysis (FMEA) is a systematic tool for evaluating a process and identifying where and how it might fail.⁴ 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

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

use of the product in the usual practice settings by considering the clinical and product characteristics listed in Section 1.2 of this review. The Safety Evaluator then analyzes the proposed proprietary name in the context of the usual practice setting and works to identify potential failure modes and the effects associated with the failure modes.

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

“Is the proposed proprietary name convincingly similar to another drug name, which may cause practitioners to become confused at any point in the usual practice setting? And are there any components of the name that may function as a source of error beyond sound/look-alike?”

An affirmative answer indicates a failure mode and represents a potential for the proposed proprietary name to be confused with another proprietary or established drug name because of look- or sound-alike similarity or because of some other component of the name. If the answer to the question is no, the Safety Evaluator is not convinced that the names 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. OPDP finds the proposed proprietary name misleading from a promotional perspective, and the Review Division concurs with OPDP’s findings. The Federal Food, Drug, and Cosmetic Act provides that labeling or advertising can misbrand a product if misleading representations are made or suggested by statement, word, design, device, or any combination thereof, whether through a PROPRIETARY name or otherwise [21 U.S.C 321(n); See also 21 U.S.C. 352(a) & (n)].
- b. DMEPA identifies that the proposed proprietary name is misleading because of similarity in spelling or pronunciation to another proprietary or established name of a different drug or ingredient [CFR 201.10.(C)(5)].

- c. FMEA identifies the potential for confusion between the proposed proprietary name and other proprietary or established drug name(s), and demonstrates that medication errors are likely to result from the drug name confusion under the conditions of usual clinical practice.
- d. The proposed proprietary name contains an USAN (United States Adopted Names) stem.
- e. DMEPA identifies a potential source of medication error within the proposed proprietary name. For example, the proprietary name may be misleading or, inadvertently, introduce ambiguity and confusion that leads to errors. Such errors may not necessarily involve confusion between the proposed drug and another drug product but involve a naming characteristic that when incorporated into a proprietary name, may be confusing, misleading, cause or contribute to medication errors.

If DMEPA objects to a proposed proprietary name on the basis that drug name confusion could lead to medication errors, the primary Safety Evaluator uses the FMEA process to identify strategies to reduce the risk of medication errors. DMEPA generally recommends that the 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 and Letter Strings with Possible Orthographic or Phonetic Misinterpretation

Letters in Name	Scripted May Appear as	Spoken May Be Interpreted as
Upper case C	A, L, G, O, Q, V, P	S, Z, K, Ch, P
Lower case c	a, e, i, l, r, v	s, z, k, ch, p
Lower case r	s, n, e, v	-
Lower case e	a, i, l, p, c, u, q	Any vowel, y
Lower case s	5, g, n, r	X, z
Lower case e	a, i, l, p, c, u, q	Any vowel, y
Lower case m	rn, nn, n, v, w, wi, vi, onc, z	n
Lower case b	l, h, k, t	p, d, v, th
Lower case a	el, o, u, e, i, er	Any vowel
Letter Strings		
cr	W	
re	a	

Appendix C: Prescription Simulation Samples and Results

Figure 1. Cresemba Study (Conducted on December 23, 2013)

Handwritten Requisition Medication Order	Verbal Prescription
<p>Medication Order:</p> <p><i>Cresemba 200mg IV daily</i></p> <hr/> <p>Outpatient Prescription:</p> <p>(b) (4)</p>	<p>Cresemba (b) (4) mg</p> <p>Directions: Take (b) (4) capsules daily</p> <p>Dispense #28</p>

FDA Prescription Simulation Responses (Aggregate 1 Rx Studies Report)

199 People Received Study
57 People Responded

Study Name: Cresemba

Total	19	20	18	57
INTERPRETATION	OUTPATIENT	VOICE	INPATIENT	TOTAL
CHRISYMBA	0	1	0	1
CHRYSIMBA	0	2	0	2
CHRYSIMVA	0	1	0	1
CRESEMBA	15	0	10	25
CRESEMBER	2	0	0	2
CRESENBA	1	0	0	1
CRESIMBA	0	3	0	3
CRISEMBA	0	1	7	8
CRISIMBA	0	5	0	5
CRIZENTHA	0	1	0	1
CRYSIMBA	0	1	0	1
CRYSYMBA	0	1	0	1
CRESEMBAR	1	0	0	1
KRASIMBA	0	1	0	1
KRAZEMBA	0	1	0	1
KRYSIMBA	0	1	0	1
PRESIMBA	0	0	1	1
PRISIMBA	0	1	0	1

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

No.	Proprietary Name	Active Ingredient	Similarity to Cresemba	Failure preventions
1.	Celexa	citalopram	Looks alike	The pair has sufficient orthographic differences
2.	Cerezyme	imiglucerase	Sounds alike	The pair has sufficient phonetic differences
3.	Clobex	clobetasol	Looks alike	The pair has sufficient orthographic differences
4.	Copegus	ribavirin	Looks alike	The pair has sufficient orthographic differences
5.	Crescormon	somatropin	Looks and Sounds alike	The pair has sufficient orthographic and phonetic differences
6.	Caprelsa	vandetanib	Looks alike	The pair has sufficient orthographic differences
7.	Cresylate	meta cresyl acetate	Looks and Sounds alike	The pair has sufficient orthographic and phonetic differences
8.	Cryselle	Norgestrel and ethinyl estradiol	Looks and Sounds alike	The pair has sufficient orthographic and phonetic differences
9.	Cymbalta	Duloxetine	Looks and Sounds alike	The pair has sufficient orthographic and phonetic differences
10.	Soma	Carisoprodol	Looks alike	The pair has sufficient orthographic differences
11.	Complera	emtricitabine, rilpivirine hydrochloride, and tenofovir disoproxil fumarate	Looks alike	The pair has sufficient orthographic differences

12.	(b) (4)	(b) (4)	(b) (4)	The name was evaluated in OSE # (b) (4) and was found acceptable. NDA (b) (4) has an Approvable status, and the product is not currently marketed. Once the issues in the Approvable letter are addressed, a re-review of the name would be needed.
13.	Cambia	diclofenac potassium	Looks alike	The pair has sufficient orthographic differences
14.	Orencia	abatacept	Looks alike	The pair has sufficient orthographic differences

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

Appendix E: Risk of medication errors due to product confusion minimized by dissimilarity of the names and/ or use in clinical practice for the reasons described.

No.	Proposed name: Cresemba Dosage Form(s): Capsule and Powder for injection Strength: (b) (4) Usual Dose: (b) (4)	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion Causes (could be multiple)	Prevention of Failure Mode In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names
1.	Crestor (rosuvastatin calcium) tablets <u>Strength:</u> 5 mg, 10 mg, 20 mg, and 40 mg <u>Dose, Route and Frequency:</u> 5 mg to 40 mg orally once daily	Orthographic similarity Both names start with the same 4 letters Cres-. Phonetic similarity The first 4 letters are the same and make the same sound. Overlapping product characteristics Route (oral), numerical similarity in strength and dose (200 mg and 20 mg), numerical similarity in strength (100 mg and 10 mg), frequency (once daily)	Orthographic differences The letter string -emba in Cresemba appears elongated compared to the letter string -tor in Crestor. Additionally, the upstrokes in both names are in different positions, giving the names different shape. Phonetic differences Cresemba has 3 syllables compared to 2 syllables in Crestor.

No.	Proposed name: Cresemba Dosage Form(s): Capsule and Powder for injection Strength: (b) (4) Usual Dose: (b) (4)	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion Causes (could be multiple)	Prevention of Failure Mode In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names
2.	Versacloz (clozapine) oral suspension Strength: 50 mg per mL Dose, Route and Frequency: 12.5 mg once daily to 900 mg per day in divided doses or 0.25 mL to 18 mL	Orthographic similarity Both names have an upstroke in the same position. When scripted Cres- may look like Vers- and -ba may look like -lo. Overlapping product characteristics Route (oral), dose (200 mg), frequency (once daily or three times daily)	Orthographic differences The infix -em- in Cresemba appears elongated and sufficiently different compared to the infix -ac- in Versacloz.

No.	Proposed name: Cresemba Dosage Form(s): Capsule and Powder for injection Strength: (b) (4) Usual Dose: (b) (4)	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion Causes (could be multiple)	Prevention of Failure Mode In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names
3.	Pamelor (nortriptyline) capsule Strength: 10 mg, 25 mg, 50 mg and 75 mg <u>Dose, Route and Frequency:</u> 25 mg orally three times or four times daily up to 150 mg per day OR 30 mg to 50 mg in divided doses or once daily	Orthographic similarity Both names have an upstroke in similar positions. When scripted Cre- may look like Pa- and -ba may look like -lo. Overlapping product characteristics Route (oral), dose similarity (200 mg vs. 20 mg [e.g. 20 mg twice daily]), strength similarity (100 mg vs. 10 mg), frequency (once daily or three times daily)	Orthographic differences The infix -sem- in Cresemba appears elongated compared to the infix -me- in Pamelor.

No.	Proposed name: Cresemba Dosage Form(s): Capsule and Powder for injection Strength: (b) (4) Usual Dose: (b) (4)	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion Causes (could be multiple)	Prevention of Failure Mode In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names
4.	Treanda (bendamustine) for injection Strength: 25 mg per vial and 100 mg per vial <u>Dose, Route and Frequency:</u> 25 mg/m ² , 50 mg/m ² 100 mg/m ² intravenously on Days 1 and 2 of a 28-day cycle 60 mg/m ² or 90 mg/m ² or 120 mg/m ² intravenously on days 1 and 2 of a 21-day cycle	Orthographic similarity Both names have an upstroke in similar positions . Phonetic similarity Both names have 3 syllables, and the 1 st syllables (tre vs. cre) and 3 rd syllables (da vs. ba) may sound similar. Overlapping product characteristics Route (intravenous), strength (100 mg), dose (Treanda has an achievable dose of 200 mg, resulting in overlap with Cresemba 200 mg)	Orthographic differences The infix -sem- in Cresemba appears elongated compared to the infix -an- in Treanda. Phonetic differences The 2 nd syllables in each name (sem vs. an) sound sufficiently different from each other.

No.	Proposed name: Cresemba Dosage Form(s): Capsule and Powder for injection Strength: (b) (4) Usual Dose: (b) (4)	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion Causes (could be multiple)	Prevention of Failure Mode In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names
5.	Viorele (desogestrel and ethinyl estradiol and ethinyl estradiol) kit <u>Strength:</u> (0.15 mg/0.02 mg tablets, 0.01 mg tablets, and inert tablets) <u>Dose, Route and Frequency:</u> one tablet orally daily	Orthographic similarity Both names have an upstroke in similar positions. When scripted Cre- may look like Vio-. Overlapping product characteristics Route (oral), strength (Viorele tablets are a continuously administered kit and the strength is commonly omitted from prescriptions vs. single strength capsule for Cresemba), frequency (once daily)	Orthographic differences The infix -sem- in Cresemba elongates the name compared to the infix -re- in Viorele. Key differences in product characteristics <u>Dose:</u> There is no overlap in dose: 200 mg or 2 capsules vs. 1 tablet

No.	Proposed name: Cresemba Dosage Form(s): Capsule and Powder for injection Strength: (b) (4) Usual Dose: (b) (4)	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion Causes (could be multiple)	Prevention of Failure Mode In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names
6.	Casodex (bicalutamide) tablet Strength: 50 mg <u>Dose, Route and Frequency:</u> 50 mg once daily orally (no dose adjustments)	Orthographic similarity Both names start with the same letter 'C' and have an upstroke in similar positions. When scripted Crese- may look like Caso-. Overlapping product characteristics Route (oral), single strength tablet vs. single strength capsule, frequency (once daily)	Orthographic differences The infix -sem- in Cresemba appears elongated compared to the infix -so- in Casodex. Key differences in product characteristics <u>Dose:</u> There is no overlap in dose: 200 mg or 2 capsules vs. 1 tablet or 50 mg

No.	Proposed name: Cresemba Dosage Form(s): Capsule and Powder for injection Strength: (b) (4) Usual Dose: (b) (4)	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion Causes (could be multiple)	Prevention of Failure Mode In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names
7.	Concerta (methylphenidate) extended-release tablet Strength: 18 mg, 27 mg, 36 mg and 54 mg Dose, Route and Frequency: 18 mg to 72 mg every morning orally	Orthographic similarity Both names start with the same letter 'C', have the same number of letters (n=8), and have an upstroke in the same position. When scripted -ba may look like -ta. Overlapping product characteristics Route (oral), dose (2 tablets [2x 36 mg = 72 mg dose] vs. 2 capsules), frequency (once daily)	Orthographic differences The infix -sem- in Cresemba appears elongated compared to the infix -cer- in Concerta. Key differences in product characteristics Strength: There is no overlap in strength: 100 mg and 200 mg/vial vs. 18 mg, 27 mg, 36 mg and 54 mg

No.	Proposed name: Cresemba Dosage Form(s): Capsule and Powder for injection Strength: (b) (4) Usual Dose: (b) (4)	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion Causes (could be multiple)	Prevention of Failure Mode In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names
8.	Lazanda (fentanyl citrate) spray Strength: 100 mcg/100 mcL and 400 mcg/100 mcL concentration solution. <u>Dose, Route and Frequency:</u> starting with 100 mcg (1 spray in 1 nostril) then titrated up for breakthrough pain no more often than every 2 hours. Up to 800 mcg per dose. Additional: REMS restricted access, all parties must enroll in program	Orthographic similarity Both names have an upstroke in similar positions. When scripted the Cres- may look like Laz-. Overlapping product characteristics Strength and dose (200 mg and 100 mg vs. 200 mcg and 100 mcg).	Key differences in product characteristics <u>Inpatient Setting</u> <u>Route:</u> Cresemba may be administered orally or intravenously; therefore, one route must be specified to prevent prompting a clarification, especially if the dosage form (e.g. tablet or injection) is omitted. Lazanda is only administered intranasally and the route may be omitted from the order. There is no overlap in route. <u>Outpatient Setting</u> <u>Frequency:</u> Cresemba is administered three times daily for the first two days and administered once daily on subsequent days. Lazanda is administered as needed for breakthrough pain (according to a strict titration schedule). <u>Additional prescription elements:</u> Lazanda will be prescribed for a limited quantity such as #1 (one spray device) with no refills because it's a Schedule 2 Controlled Substance (CII), compared to Cresemba which will likely require dispensing several tablets for the treatment of fungal infections.

No.	Proposed name: Cresemba Dosage Form(s): Capsule and Powder for injection Strength: (b) (4) Usual Dose: (b) (4)	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion Causes (could be multiple)	Prevention of Failure Mode In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names
9.	Kcentra (Prothrombin Complex Concentrate) kit <u>Strength:</u> 500 units per 20 mL and 1000 units per 40 mL vial <u>Dose, Route and Frequency:</u> INR based and weight based dosing: 25 units, 35 units, or 50 units per kg (up to 100 kg) Administered as 0.12 mL/kg/min (3 units/kg/min) up to up to a maximum rate of 8.4 mL/min (210 units/min) via intravenous infusion once	Orthographic similarity Both names have an upstroke in the suffix. Phonetic similarity Both names may be pronounced with 3 syllables, K-cen-tra vs. Cre-sem-ba. The “K” sound in the first syllables sound the same and the second syllables may sound similar Overlapping product characteristics Route (intravenous), dose similarity (200 units per minute vs. 200 mg or 2000 units [e.g 80 kg person at 25 units/kg] vs. 200 mg)	Orthographic differences The prefix Kc- is significantly shorter than the prefix Cres-. Phonetic differences The names share the “K” sound in the first syllables; however, Cresemba also contains a “re” sound in the first syllable which Kcentra does not. Also, the last syllables in both names sound sufficiently different from each other (ba vs. tra).

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

/s/

ALEKSANDER P WINIARSKI
04/30/2014

TINGTING N GAO
05/01/2014

JULIE V NESHIEWAT
05/01/2014