

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

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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**

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Application Type/Number: NDA 202123

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Subject: Proprietary Name Review

Drug Name(s): Complera (Emtricitabine, Rilpivirine and Tenofovir Disoproxil) Tablets
200 mg/25 mg/245 mg

Applicant: Gilead Sciences, Inc.

OSE RCM #: 2010-2477

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

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1 INTRODUCTION

This re-assessment of the proprietary name responds to a proprietary name request submitted February 14, 2011. The Division of Medication Error Prevention and Analysis (DMEPA) found the proposed proprietary name, Complera, acceptable in OSE Review #2010-2477 dated February 2, 2011 and OSE Review #2010-58 dated June 10, 2010.

1.2 REGULATORY HISTORY

This application was originally submitted on November 22, 2010 by Gilead Sciences. A refusal to file was issued by the Agency on December 20, 2010 because the application was not sufficiently complete to permit a substantive review. The Applicant resubmitted the application on February 10, 2011.

2 METHODS

For the proposed proprietary name, DMEPA staff searched a standard set of databases and information sources (see section 4) to identify names with orthographic and phonetic similarity to the proposed name that have been approved since the previous OSE proprietary name review. We used the same search criteria that were used in OSE Review #2010-2477 for the proposed proprietary name, Complera. The established name and strength presentation have changed since the original submission. Complera is a single-strength tablet consisting of 200 mg of emtricitabine, 25 mg of rilpivirine and 245 mg of tenofovir disoproxil. Since the proposed product characteristics were altered we did re-evaluate the previous names of concern. Additionally, DMEPA searched the USAN stem list to determine if the name contains any USAN stems as of the last USAN updates.

3 RESULTS AND DISCUSSION

Due to the proposed product characteristics being altered, DMEPA re-evaluated the previous names of concern and found no names likely to result in medication errors with Complera. DMEPA staff also did not identify any United States Adopted Names (USAN) stems in the proposed proprietary name Complera, as of April 20, 2011.

The searches of the databases listed in section 5 identified one additional name thought to look similar to Complera and represent a potential source of drug name confusion, Caprelsa^{***}. However, failure mode and effects analysis (FMEA) determined that the orthographic similarity between Complera and Caprelsa^{***} was unlikely to result in medication errors for the reasons presented in Appendix A.

4 CONCLUSIONS AND RECOMMENDATIONS

The Proprietary Name Risk Assessment indicates that the proposed name, Complera, 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 proprietary name, Complera, for this product at this time. The Applicant will be informed of this finding by letter.

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

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

5 REFERENCES

1. OSE review #2010-2477 Proprietary Name Review of Complera; Toombs, L. Shenee’.
2. OSE review #2010-58 Proprietary Name Review of Complera; Park Judy.
3. **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/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.
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.

Appendix A: Potential confusing names with orthographic and product differences which minimize potential for confusion

Proposed Name: Complera (Emtricitabine/Rilpivirine/ Tenofoviridisoproxil)	Strength: Tablet: 200 mg/25 mg/ 245 mg	Usual Dose: One tablet once daily with food
Failure Mode: Orthographic and Product Characteristic Similarities	Causes (could be multiple)	Effects
<p>Caprelsa^{***} (Vendetanib) Tablet : 100 mg, 300 mg Treatment of patients with unresectable locally advanced or metastatic medullary thyroid cancer. 300 mg once daily with dose reductions to 200 mg per day or 100 mg per day to manage adverse events.</p>	<p>Orthographic similarity stems from sharing the same first letter ('C') and last letter ('a') as well as having the same down stroke ('p') and upstroke ('l') within their names. Shared product characteristics include dosage form (tablet), route of administration (oral), and frequency of administration (daily).</p>	<p>The orthographic differences and differing product characteristics will minimize the likelihood of medication errors in usual practice settings. Rationale: The proposed name, Complera contains a down stroke immediately followed by an up stroke ('-pl-') which differs from the proposed name, Caprelsa^{***} where there are two letters which separates the same letters. This difference may distinguish these names from each other. Differing product characteristics: Strength: (single vs multiple) Since Caprelsa^{***} is available in more than one strength. This information must be provided in order to dispense/administer the medication as intended. Conversely, Complera is a single strength product and physicians will likely omit the strength. This product characteristic difference will minimize confusion between the two products.</p>

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Office of Surveillance and Epidemiology

Date:	February 2, 2011
Application Type/Number:	NDA 202123
Through:	Irene Z. Chan, PharmD, BCPS, Acting Team Leader Carol Holquist, RPh, Director Division of Medication Error Prevention and Analysis (DMEPA)
From:	L. Sheneé Toombs, Pharm.D., Safety Evaluator Division of Medication Error Prevention and Analysis
Subject:	Proprietary Name Review
Drug Name(s):	Complera (Emtricitabine, Rilpivirine Hydrochloride and Tenofovir Disoproxil Fumarate) Tablets 200 mg/27.5 mg/300 mg
Applicant/sponsor:	Gilead Sciences, Inc.
OSE RCM #:	2010-2477

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EXECUTIVE SUMMARY

This review summarizes DMEPA's evaluation of the proposed proprietary name, Complera, for Emtricitabine, Rilpivirine Hydrochloride and Tenofovir Disoproxil Fumate Tablets. Our evaluation did not identify concerns that would render the name unacceptable based on the product characteristics and safety profile known at the time of this review. Thus, DMEPA finds the proposed proprietary name, Complera, acceptable for this product. The proposed proprietary name must be re-reviewed 90 days before the 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 Gilead Sciences, dated November 9, 2010, for an assessment of the proposed proprietary name, Complera, regarding potential name confusion with other proprietary or established drug names in the usual practice settings. The name was also evaluated for promotional concerns.

1.2 PRODUCT INFORMATION

Complera (Emtricitabine, Rilpivirine Hydrochloride and Tenofovir Disoproxil Fumate) is indicated for the treatment of HIV-1 infection. It is available in a fixed combination strength of 200 mg/27.5 mg/300 mg. The recommended dose is 1 tablet orally once daily with food. It will be supplied in bottles containing 30 tablets.

1.3 REGULATORY HISTORY

DMEPA previously reviewed this proposed proprietary name, Complera, under IND 106252 (OSE Review #2010-58 dated June 10, 2010). We found the name conditionally acceptable at that time.

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, and 2.2, identify specific information associated with the methodology for the proposed proprietary name Complera.

2.1 SEARCH CRITERIA

For this review, particular consideration was given to drug names beginning with the letter 'C' 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}

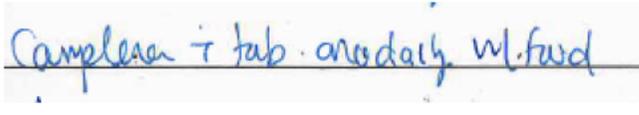
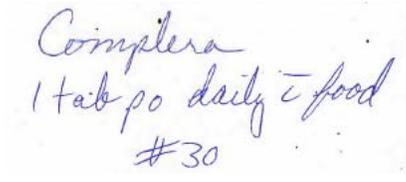
To identify drug names that may look similar to Complera, the DMEPA staff also considers the orthographic appearance of the name on lined and unlined orders. Specific attributes taken into consideration include the length of the name (eight letters), upstrokes (two, capital letter ‘C’ and lower case ‘l’), downstrokes (one, lower case ‘p’), cross-strokes (none) and dotted letters (none). Additionally, several letters in Complera may be vulnerable to ambiguity when scripted (see Appendix B). As a result, the DMEPA staff also considers these alternate appearances when identifying drug names that may look similar to Complera.

When searching to identify potential names that may sound similar to Complera, the DMEPA staff searches for names with similar number of syllables (3), stresses (COM-pler-a or com-PLER-a or com-pler-A), and placement of vowel and consonant sounds. The Applicant’s intended pronunciation (kom pler’ a) was also taken into consideration, as it was included in the Proprietary Name Review Request. However, names are often mispronounced and/or spoken with regional accents and dialects, so other potential pronunciations of the name are considered. Additionally, the DMEPA staff considers that pronunciation of parts of the name can vary (see Appendix B).

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 prescriptions were communicated during the FDA prescription studies.

Figure 1. Complera Rx Study (conducted on December 3, 2010)

HANDWRITTEN REQUISITION MEDICATION ORDER	VERBAL PRESCRIPTION
<p><u>Inpatient Medication Order :</u></p> 	<p>Complera 1 tablet once daily with food</p>
<p><u>Outpatient Prescription:</u></p> 	

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

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

3 RESULTS

The following sections represent the results from DMEPA's database searches, Expert Panel Discussion (EPD), Prescription studies and the Safety Evaluator Risk Assessment. We also sought input from the Division of Antiviral Products (DAVP) regarding the proprietary name.

3.1 DATABASE AND INFORMATION SOURCES

The DMEPA database searches yielded a total of 24 names as having some similarity to the proposed proprietary name, Complera.

Nineteen of the names were thought to look like Complera by the DMEPA Safety Evaluators (Angelica, Campath, Camphor, ^{(b) (4)}, Clorpress, Combigan, Compazine, Compleat, Complere, Complete, Complex B, Compoz, Comtan, Concerta, Copegus, Corlopan, Cuvposa, Lamprene, Zemplar)

One of the names (Camila) was thought to sound like Complera

The four remaining names were thought to look and sound similar to Complera by the DMEPA Safety Evaluators (Campral, Camptosar, Cardura, Compro)

Additionally, DMEPA did not identify any United States Adopted Names (USAN) stems in the proposed proprietary name as of February 1, 2011.

3.2 CDER EXPERT PANEL DISCUSSION

The Expert Panel reviewed the pool of names identified by DMEPA Safety Evaluators (See Section 3.1 above) and did not note any additional names thought to have orthographic or phonetic similarity to Complera.

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 36 practitioners responded to the prescription analysis studies. One of the practitioners from the written outpatient study interpreted the name as a currently marketed product, Complexa. This name was also identified in the prescription studies of OSE review #2010-58. However, Complexa is a cosmetic product; therefore, Complexa was not evaluated further.

Twelve practitioners in the combined written studies and 1 respondent in the verbal study interpreted the name correctly as Complera. The remainder of the respondents (n=22) misinterpreted the drug name, primarily because lower case letter 'o' was misinterpreted as 'a', or lower case letter 'm' was misinterpreted as 'v' or 'n', or lower case letter 'r' was misinterpreted as 'x', or the letter string 'ra' was misinterpreted as 'en' in the written studies. In the verbal studies responses were misspelled phonetic variations of the proposed name, Complera, with the most common variation occurring in the second syllable of the name ('pla' or 'pa' vs 'ple'). See Appendix C for the complete listing of interpretations from the verbal and written prescription studies.

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3.4 SAFETY EVALUATOR RISK ASSESSMENT OF PROPOSED PROPRIETARY NAME

Independent searches by the primary Safety Evaluator resulted in the identification of one additional name (Gamophene) which was thought to look similar to Complera and represent a potential source of drug name confusion.

Thus, a total of 25 names were identified for their similarity to Complera from the combined searches: 1 identified by the primary safety evaluator, and 24 identified in section 3.1 above.

3.5 COMMENTS FROM THE DIVISION OF ANTIVIRAL PRODUCTS (DAVP)

3.5.1 Initial Phase of Review

In response to the OSE December 13, 2010 e-mail, the Division of Antiviral Products (DAVP) had no additional comments regarding the proposed proprietary name at the initial phase of the review.

3.5.2 Midpoint of Review

On December 21, 2010 DMEPA notified the Division of Antiviral Products (DAVP) via e-mail that we had no objections to the proposed proprietary name Complera. Per e-mail correspondence from DAVP on February 2, 2011 they indicated they have no issues with our assessment of the proposed proprietary name, Complera.

4 DISCUSSION

Complera is the proposed proprietary name for Emtricitabine, Rilpivirine Hydrochloride and Tenofovir Disoproxil Fumarate Tablets. 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 their comments accordingly.

4.1 PROMOTIONAL ASSESSMENT

DDMAC had no concerns regarding the proposed name from a promotional perspective, and did not offer any additional comments relating to the proposed name. DMEPA, and DAVP concurred with the findings of DDMAC's promotional assessment of the proposed name.

4.2 SAFETY ASSESSMENT

We identified a total of 25 names as having some similarity to Complera: 24 of which were identified in Database and Information Sources (Section 3.1), and one was identified by the primary Safety Evaluator (Section 3.4). No other aspects of the name were determined to represent a potential source of confusion.

Seventeen of the 25 names were eliminated for the following reasons (see Appendices D, E, F, and G): eight names were previously reviewed in OSE review 2010-58 dated June 10, 2010. Since the product characteristics of Complera have not changed since our previous review, these names were not re-reviewed. Seven of the names lacked convincing orthographic and/or phonetic similarity to the proposed proprietary name, Complera, one name was an herbal product not identified as a drug dispensed pursuant to a prescription, and one name was a discontinued product with no available generics.

Failure Mode and Effects Analysis (FMEA) was then applied to determine if the proposed proprietary name, Complera, could potentially be confused with the remaining eight names and lead to medication errors. This analysis determined that the name similarity between Complera was unlikely to result in medication errors with any of the eight products for the reasons presented in Appendices H through I.

5 CONCLUSIONS AND RECOMMENDATIONS

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

If any of the proposed product characteristics as stated in this review are altered, DMEPA rescinds this finding and the name must be resubmitted for review. The conclusions upon re-review are subject to change.

If you have further questions or need clarifications on this review, please contact the OSE Regulatory Project Manager, Brantley Dorch, at 301-796-0150.

5.1 COMMENTS TO THE APPLICANT

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

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

6 REFERENCES

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

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

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

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. This is a database which was created for the Division of Medication Error Prevention and Analysis, FDA.

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

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

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

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

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

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

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

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

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

Provides a compilation of approved drug products with therapeutic equivalence evaluations.

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

Provides information regarding patent and trademarks.

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

Contains full monographs for the most common drugs in clinical use, plus mini monographs covering investigational, less common, combination, nutraceutical and nutritional products. 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)

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)

Contains full-text information from approximately 30 texts. Includes tables and references. Among the database titles are: Handbook of Adverse Drug Interactions, Rudolphs Pediatrics, Basic Clinical Pharmacology and Dictionary of Medical Acronyms Abbreviations.

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

List contains all the recognized USAN stems.

14. *Red Book Pharmacy's Fundamental Reference*

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

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

A web-based searchable version of the Drug Information Handbook.

16. *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.⁵

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

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

FMEA is a systematic tool for evaluating a process and identifying where and how it might fail.⁶ 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

⁵ National Coordinating Council for Medication Error Reporting and Prevention. <http://www.nccmerp.org/aboutMedErrors.html>. Last accessed 10/11/2007.

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

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.⁷ DMEPA provides the product characteristics considered for this review in section one.

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

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

Type of similarity	Considerations when searching the databases		
	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	<ul style="list-style-type: none"> Names may appear similar in print or electronic media and lead to drug name confusion in printed or electronic communication Names may look similar when scripted and lead to drug name confusion in written communication
	Orthographic similarity	Similar spelling Length of the name Upstrokes Down strokes Cross-strokes Dotted letters Ambiguity introduced by scripting	<ul style="list-style-type: none"> Names may look similar when scripted, and lead to drug name confusion in written communication

⁷ Institute of Medicine. Preventing Medication Errors. The National Academies Press: Washington DC. 2006.

		letters Overlapping product characteristics	
Sound-alike	Phonetic similarity	Identical prefix Identical infix Identical suffix Number of syllables Stresses Placement of vowel sounds Placement of consonant sounds Overlapping product characteristics	<ul style="list-style-type: none"> Names may sound similar when pronounced and lead to drug name confusion in verbal communication

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

1. Database and Information Sources

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

2. CDER Expert Panel Discussion

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

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

3. FDA Prescription Analysis Studies

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

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

4. Comments from the OND review Division or Generic drugs

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

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

5. Safety Evaluator Risk Assessment of the Proposed Proprietary Name

The primary Safety Evaluator applies his/her individual expertise gained from evaluating medication errors reported to FDA, conducts a Failure Mode and Effects Analysis, and provides an overall risk assessment of name confusion. Failure Mode and Effects Analysis (FMEA) is a systematic tool for evaluating a process and identifying where and how it might fail.⁸ 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

⁸ Institute for Healthcare Improvement (IHI). Failure Mode and Effects Analysis. Boston. IHI:2004.

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 has not been marketed, the primary Safety Evaluator anticipates the use of the product in the usual practice settings by considering the clinical and product characteristics listed in Section one. The Safety Evaluator then analyzes the proposed proprietary name in the context of the usual practice setting and works to identify potential failure modes and the effects associated with the failure modes.

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

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

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

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

“Could the confusion of the drug names conceivably result in medication errors in the usual practice setting?”

The answer to this question is a central component of the Safety Evaluator’s overall risk assessment of the proprietary name. If the Safety Evaluator determines through FMEA that the name similarity would not 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:

1. DDMAC finds the proposed proprietary name misleading from a promotional perspective, and the Review Division concurs with DDMAC’s findings. The Federal Food, Drug, and Cosmetic Act provides that labeling or advertising can misbrand a product if misleading representations are made or suggested by statement, word, design, device, or any combination thereof, whether through a PROPRIETARY name or otherwise [21 U.S.C 321(n); See also 21 U.S.C. 352(a) & (n)].
2. 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)].
3. 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.

4. The proposed proprietary name contains an USAN (United States Adopted Names) stem.
5. DMEPA identifies a potential source of medication error within the proposed proprietary name. For example, the proprietary name may be misleading or, inadvertently, introduce ambiguity and confusion that leads to errors. Such errors may not necessarily involve confusion between the proposed drug and another drug product.

If DMEPA objects to a proposed proprietary name on the basis that drug name confusion could lead to medication errors, the primary Safety Evaluator uses the FMEA process to identify strategies to reduce the risk of medication errors. DMEPA is likely to recommend that the Applicant select an alternative proprietary name and submit the alternate name to the Agency for DMEPA to review. However, in rare instances FMEA may identify plausible strategies that could reduce the risk of medication error of the currently proposed name. In that instance, DMEPA may be able to provide the Applicant with recommendations that reduce or eliminate the potential for error and, thereby, would render the proposed name acceptable.

In the event that DMEPA objects to the use of the proposed proprietary name, based upon the potential for confusion with another proposed (but not yet approved) proprietary name, DMEPA will provide a contingency objection based on the date of approval. Whichever product, the Agency approves first has the right to use the proprietary name, while DMEPA will recommend that the second product to reach approval seek an alternative name.

The threshold set for objection to the proposed proprietary name may seem low to the Applicant. However, the safety concerns set forth in criteria a through e are supported either by FDA regulation or by external healthcare authorities, including the Institute of Medicine (IOM), World Health Organization (WHO), Joint Commission on Accreditation of Hospitals (JCOAH), and the Institute for Safe Medication Practices (ISMP). These organizations have examined medication errors resulting from look- or sound-alike drug names and called for regulatory authorities to address the issue prior to approval. Additionally, DMEPA contends that the threshold set for the Proprietary Name Risk Assessment is reasonable because proprietary drug name confusion is a predictable and a preventable source of medication error that, in many instances, the Agency and/or Applicant can identify and rectify prior to approval to avoid patient harm.

Furthermore, post-marketing experience has demonstrated that medication errors resulting from drug name confusion are notoriously difficult to rectify post-approval. Educational and other post-approval efforts are low-leverage strategies that have had limited effectiveness at alleviating medication errors involving drug name confusion. Applicants have undertaken higher-leverage strategies, such as drug name changes, in the past but at great financial cost to the Applicant and at the expense of the public welfare, not to mention the Agency's credibility as the authority responsible for approving the error-prone proprietary name. Moreover, even after Applicants' have changed a product's proprietary name in the post-approval phase, it is difficult to eradicate the original proprietary name from practitioners' vocabulary, and as a result, the Agency has continued to receive reports of drug name confusion long after a name change in some instances. Therefore, DMEPA believes that post-approval efforts at reducing name confusion errors should be reserved for those cases in which the potential for name confusion could not be predicted prior to approval (see Section 4 for limitations of the process).

Appendix B: Letters with possible orthographic or phonetic misinterpretation

Letters in Name, Complera	Scripted may appear as	Spoken may be interpreted as
Capital 'C'	E, O, L, D, A, Z, G	K
lower case 'o'	any vowel	any vowel
lower case 'm'	n, r, w, v	n
lower case 'p'	g, z, y, q, j	b
lower case 'l'	d, e, r, b	-----
lower case 'e'	any vowel	any vowel
lower case 'r'	n, s, e, v	'ra' misinterpreted as 'ah'
lower case 'a'	any vowel	any vowel

Appendix C: FDA Prescription Study Responses (conducted February 1, 2010).

Written Outpatient	Written Inpatient	Verbal Prescription
Complera	Camplera	Complera
Complera	Cavplera	Complara
Complera	Canplera	Complera
Complera	Camplera	Complara
Complera	Camplera	Complara
Complera	Camplera	Complara
Complexa	Camplexa	Compara
Complera	Compleren	Complara
Complera	Camplera	
Complera	Camplera	
Complera	Campleren	
Complera	Camplere	
	Complera	
	Canplera	
	Canplere	
	Camplera	

Appendix D: Names previously reviewed in OSE Review # 2010-58

Name	Similarity to Complera
Camphor	Look
Campral	Look and Sound
Camptosar	Look and Sound (Look)
Compazine	Look
Compleat	Look
Complere	Look
Complete	Look
Compro	Look and Sound (Look)

Appendix E: Names Lacking Orthographic and/or Phonetic Similarity.

Name	Similarity to Complera
Campath	Look
Comtan	Look
Concerta	Look
Copegus	Look
Clorpres	Look
Compoz	Look
Camila	Sound

Appendix F: OTC, herbal product not identified as drug and not dispensed pursuant to a prescription.

Proprietary Name	Similarity to Complera	Reason
Angelica	Look	Herbal root

Appendix G: Discontinued products with no available generics

Proprietary Name	Active Ingredient	Similarity to Complera
Gamophene	Hexachlorophene	Look

Appendix H: Products with multiple differentiating characteristics

Product name with potential for confusion	Similarity to Miproa	Strength/Dosage Form	Usual Dose (if applicable)	Differentiating Product Characteristics and Orthographic Differences
Complera (Emtricitabine/Rilpivirine/Tenofovir disoproxil fumarate)	N/A	Tablet: 200 mg/27.5 mg/ 300 mg	One tablet once daily with food	
Cardura (doxazosin)	Look and Sound	Tablets: 1 mg, 2 mg, 4 mg, 8 mg	1 mg to 16 mg once daily	-Strength (single vs multiple) Orthographic differences: letter strings 'mpl' vs 'rdu' Phonetic differences: First syllable: 'Com' vs 'Car' Second Syllable: 'ple' vs 'du'
(b) (4)				
Combigan (brimonidine/timolol)	Look	Ophthalmic: 0.2%/0.5%	Instill one to two drops in affected eye twice daily	-Dosage form (tablet vs. solution (ophthalmic)) -Route of administration (oral vs. intraocular) -Frequency of administration (once daily vs twice daily) Orthographic differences: -Letter strings 'ple' vs 'big'

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Zemplar (paricalcitol)	Look	Capsules: 1 mcg, 2 mcg, 4 mcg Injectable: 2 mcg (2 mcg/mL) 5 mcg (5 mcg/mL) 10 mcg (5 mcg/mL)	0.04 mcg/kg to 0.1 mcg/kg administered every other day during dialysis If satisfactory response is not observed, the dose may be increased by 2 mcg to 4 mcg at 2 to 4 week intervals.	-Strength (single vs multiple) -Frequency of Administration: every other day; three times per week.
Complex B (Hydroquinone)	Look	Topical Cream: 4% Topical Gel: 4%	Apply to affected area twice daily.	-Dosage form (tablet vs. topical cream/gel) -Route of administration (oral vs. topical) -Frequency of administration (once daily vs twice daily) Orthographic differences: -Addition of the modifier 'B' in Complex B may help differentiate the name pair.
Cuvposa (Glycopyrrolate)	Look	Oral solution: 1 mg /5 mL	0.02 mg/kg three times daily. Titrate dose by 0.02 mg/kg every 5-7 days. Maximum recommended dose is 0.1 mg/kg three times daily not to exceed 1.5 mg to 3 mg per dose based upon weight	-Dosage form (tablet vs. oral solution) -Frequency of administration (once daily vs three times daily) -Patient population (adults vs pediatrics (3 to 16 years)) Orthographic differences: Upstroke 'l' in Complera adds a visual difference
Corlopan (Fenoldopam)	Look	Injectable: 10 mg, 20 mg (10 mg/mL)	0.1 to 1.6 mcg/kg/min continuous infusion. Titrate based on clinical response	-Dosage form (tablet vs injectable) -Route of administration (oral vs intravenous) -Frequency of administration (once daily vs continuous infusion) -Duration of therapy: (maintenance vs 48 hours)

Appendix I: Potential confusing names with orthographic differences which minimize potential for confusion

Proposed Name: Complera (Emtricitabine/Rilpivirine/Tenofoviridisoproxil fumarate)	Strength: Tablet: 200 mg/27.5 mg/ 300 mg	Usual Dose: One tablet once daily with food
Failure Mode: Orthographic and Product Characteristic Similarities	Causes (could be multiple)	Effects
<p>Lamprene (Clofazimine) Capsule : 50 mg Treatment of lepromatous leprosy, including dapsone-resistant lepromatous leprosy and lepromatous leprosy complicated by erythema nodosum leprosum. 100 mg to 200 mg once daily Orphan Drug</p>	<p>Orthographic similarities: -Ability for capital letter 'L' to look similar to capital letter 'C' when scripted. -similar letter string ('-omp- vs '-amp' -similar letter string ('-era' vs '-ene') - same length of letters (8 letters), -Single strength products which increases potential for strength omission on prescription.</p>	<p>The orthographic differences and differing product characteristics will minimize the likelihood of medication errors in usual practice settings. Rationale: Although both names have orthographic and product similarities, orthographic differences including: -placement of the upstroke (lowercase 'l' in the fifth letter position which visually differentiates the two names. Furthermore, although Lamprene is available in a single strength 50 mg tablet, the usual dose is 100 mg. Therefore a physician will have to specify "100 mg" or "two tablets" on the prescription. This will help to differentiate the products if the two names are confused Additionally, Lamprene is an orphan drug with limited use for the leprosy patient population.</p>

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/s/

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